

PSYCHEDELIC SOCIALITY: PHARMACOLOGICAL AND EXTRAPHARMACOLOGICAL PERSPECTIVES

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and Evgenia Fotiou

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PSYCHEDELIC SOCIALITY: PHARMACOLOGICAL AND EXTRAPHARMACOLOGICAL PERSPECTIVES

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Editorial: Psychedelic sociality: Pharmacological and extrapharmacological perspectives

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Editorial on the Research Topic

Psychedelic sociality: Pharmacological and extrapharmacological perspectives

The heralded psychedelic renaissance is currently at a new level where psychedelics are being accepted by the scientific community and the public. Medicalization and the ongoing introduction of market forces are imposing a trend in which psychedelic treatments are reduced to focus into strictly pharmacological and psychological effects on the self, rather than interactions with broader social context. Such narrowing of how psychedelic treatments are being conceived, used, and researched is a source of concern for those who understand that psychedelics' therapeutic effects as also derived from socially and culturally meaningful elements. Alienation—the sense of isolation from others—and the mental health problems associated with it are on the rise. Consequently, there is not only a need for new therapies but also for a renewed social adhesion and a commitment to a more just and equal society. Psychedelics have a long history of bringing people together, facilitating intense shared experiences, and revitalizing cultures. This social dimension of use of psychedelics—*psychedelic sociality*—should be considered in the current mainstreaming, as therein lies their potential to support change in individual therapy and beyond.

This multidisciplinary Research Topic of *psychedelic sociality* invited scholars to discuss these Research Topic through empirical research, reviews, perspectives, and theoretical papers. Overall, 21 papers were accepted to this Research Topic, covering

different sections of *Frontiers* (Neuropharmacology, Psychopharmacology, Ethnopharmacology, Personality and Social Psychology, and Consciousness Research). We are especially proud of the broad scope of this Research Topic and the diversity of disciplines represented in it. We believe that a beneficial mainstreaming of psychedelics requires going beyond the boundaries of disciplinary orientation. Interdisciplinary integration is necessary for the paradigmatic shift in mental health that many are yearning for: a shift from a narrow biomedical model to an expanded biopsychosocial model that emphasizes the interplay between biological, psychological, sociopolitical and environmental factors in mental health. The centrality of the experience and set and setting in psychedelic research¹ is an invitation to transcend some of the boundaries between the natural sciences and the humanities (see [Langlitz et al.](#)). The biopsychosocial model is especially relevant to psychedelic research because to answer questions regarding how psychedelics work, we must incorporate different levels of inquiry—from receptors to persons to culture.

Psychedelic pharmacological interventions are influenced by contextual factors such as social relations, language, books, theories, symbols, music, and beliefs. Notably, this is a reciprocal relationship, and the psychedelic effects can, in turn, change context, e.g., enhance openness, facilitate the creation of new music, modify social relationships, change personalities, and revitalize cultures. Psychedelic communities, Western and indigenous, each have their own musical and artistic expression, suggesting that the communal use of psychedelics intensifies cultural modes of communication. The context-sensitive role of 5-HT_{2A} receptors in sociality is also noticeable in that they can be anxiogenic when trust is compromised but rewarding within secure contexts, and hence enhancing sociality by encouraging healthy contexts.

These facts amplify the relevancy of the human sciences for psychedelic research, and vice versa, as what makes humans so unusual are two interrelated aspects: our capacity for culture (especially cumulative technological and social knowledge); and our sociality, an unprecedented and unparalleled ability to live in large groups of unrelated people. The human capacity for sociality involved a Darwinian coevolution of culture and genes ([Richerson and Boyd, 2008](#)); our biology evolved to create our capacity for culture and culture shaped our biological evolution. As psychedelics are notoriously context-dependent, one can speculate that their effects on the 5-HT_{2A} receptor function could have played a crucial role in the selection for this unique human capacity. The activation of the 5-HT_{2A} receptor intensifies the influence of social relations, stories,

beliefs, and symbols by incorporating them with our sensory experience, making them more tangible, hence enhancing their meaning and increasing our capacity for sociality. This suggestion is also supported by a number of human fMRI studies from various labs, showing increased functional connectivity between sensory regions (especially visual) and higher level regions ([Roseman et al., 2014](#); [Carhart-Harris et al., 2016](#); [Tagliazucchi et al., 2016](#); [Müller et al., 2018](#); [Preller et al., 2018](#); [Mason et al., 2020](#); [Preller et al., 2020](#)).

In this Research Topic, [Arce and Winkelman](#) theorize that psychedelics enhanced human evolution in the cultural niche as hominins became dependent on shared cultural models for basic survival. The sociality-amplifying effects of psilocybin and its ability to enhance openness and increase novel representations and flexibility in cognitive processes could have created considerable fitness differences among ancestral hominin populations. Individual and eventually population differences in abilities to respond to these effects would have provided genetic variation upon which selection pressures could act in favour of those with the capacities for sociality and cognition stimulated by psilocybin. Their paper provides a summary of the role of 5-HT_{2A} activation and reviews clinical research showing how psychedelics promote sociality through managing psychological stress, improving interpersonal relations, facilitating of collective relations, and enhancing group decision making.

The influence set and setting have on psychedelic experiences provides some of the most convincing arguments for *psychedelic sociality*. The recent book *American Trip* by Ido [Hartogsohn](#) (2020), reviewed here by [Lansky](#), presents an historical analysis that clearly shows how different set and setting factors embodied in research orientations led to different psychedelic experiences and different understandings of psychedelics' action. Some papers in this Research Topic are also examining how social and cultural context affect the psychedelic experience. [Pontual et al.](#) and [Pontual et al.](#) presents results from a large online cross-cultural study used in development of the Setting Questionnaire for the Ayahuasca Experience (SQAE), and showed its relation to the quality of the psychedelic experience. The SQAE has six dimensions (Leadership, Decoration, Infrastructure, Comfort, Instruction, and Social). High ratings on the SQAE were associated with low ratings of challenging experiences and high ratings of mystical experiences in three different ayahuasca practices (Santo Daime, UDV, and neoshamanic).

A similar observation is presented here by [Hartogsohn](#), who researched the migration of Santo Daime ceremonies to online zooms during the COVID-19 pandemic. While online ceremonies created new possible global connections, the lack of immediate and embodied social context was also associated with reduced intensity of the experience. [Murphy et al.](#) present similar results in a seminal controlled clinical trial comparing psilocybin-assisted therapy for depression versus a control group with escitalopram. They found pre-session therapeutic alliance

¹ All pharmacological interventions are dependent on extrapharmacological factors to some extent, exemplified in the placebo response, yet this interaction seems much more pronounced with serotonergic psychedelics.

and rapport predicted the intensity of the acute psychedelic experience (emotional breakthrough and the mystical experience); these in turn were associated with improvements in depressive symptom severity 6 weeks after the experience. The above studies show that social bonding and trust are vital components for effective and safe psychedelic therapy.

It is important to recognize that it is not only the immediate interpersonal context that interacts with psychedelics, but also the cultural context. In this Research Topic, [de Mori](#), using ethnographic data, shows that the attribution of efficacy in diverse psychedelic practices differs based on cultural priors, ideologies or biases. Along similar lines, [Dupuis](#) expands on his previous ethnographic work to show that psychedelic-induced belief transmission is a process that oscillates between adherence and doubt. This oscillation strongly mobilizes the reflexivity and agentivity of the recipient and can paradoxically enhance belief transmission. Furthermore, as the phenomenological content of the experience itself is influenced by cultural priors, it can strengthen the newly acquired belief through “experiential verification.” When stories become visions, they also become more convincing.

Some central qualities of psychedelic experiences exhibit sociality. In some contexts, psychedelics acutely increase relational feelings of connectedness with nature, other humans, or with spirituality ([Forstmann and Sagioglou, 2017](#); [Watts et al., 2017](#); [Yaden et al., 2019](#); [Kettner et al., 2021](#)). Psychedelics can produce an animistic mindset, where the natural world is humanized, personalized and socialized with human traits (sentience, relationality, intentionality, cooperation, intelligence) ([Winkelman, 2013](#)). In this Research Topic, [Michael et al.](#) presents a microphenomenological analysis of DMT experiences. Most experiential reports described an encounter with “sentient beings” that were experienced as “other.” The encounters were rich in different features, such as the entities’ appearances, demeanour, roles, function, and included communication and interaction. The complex interactive social imagery likely reflects psychedelic action on the 5-HT_{2A} receptors; psychedelic entity experiences also reflect activation of innate cognitive modules directly related to unique human capacities for sociality ([Winkelman, 2018](#)).

Diverse findings indicate that psychedelics promote prosocial effects. In this Research Topic, [Holze et al.](#) show in a placebo-controlled trial that LSD acutely increases empathy and plasma oxytocin levels. [Weiss et al.](#) online prospective study found psychedelics increased social connectedness and agreeableness. [Luoma and Lear](#) review evidence that MDMA-assisted therapy can successfully treat Social Anxiety Disorder, reminding us of the empathogenic effects of the serotonergic system in general. [Evens et al.](#) found in an online retrospective study that during the first wave of COVID-19 (April to August 2020), the quality of the psychedelic experience became more prosocial. Their finding reflects some of the zeitgeist of the first

wave, when liminality and global *communitas* were experienced, in which people found a momentary sense of solidarity and liberation from day-to-day social hierarchies and tensions. Another study in this Research Topic suggests that regular psychedelic use is associated with better coping with COVID-19 social confinements ([Révész et al.](#)). However, causality cannot be inferred from this study as other factors were different for psychedelic users, such as more substantial social support during the pandemic. [Newson et al.](#) study here with a preregistered online survey on people who attend raves and “free-parties” found psychedelics and dancing lead to personal transformation and that the acute experience of awe mediated this transformation. In turn, both awe and personal transformation increase bonding to fellow ravers and prosocial behaviour (donation to a rave charity). Similarly, [Murphy et al.](#) psilocybin clinical trial mentioned above found not only that the therapeutic alliance facilitates stronger emotional breakthroughs, but also that emotional breakthroughs enhance the therapeutic alliance in return. Shared intense emotional experiences can promote social bonding, whether one is a patient or a raver.

[Markopoulos et al.](#) presents a compelling summary of 20 clinical and experimental trials since 2008 that show psychedelics’ prosocial and empathogenic effects. Drawing from these findings and LSD trials from the 60s’ that showed that psychedelic-assisted therapy helped children with Autism Spectrum Disorder (ASD), they argue for the potential use of psychedelics in the treatment of ASD. Yet, they note, that some children had adverse reactions which led to increased anxiety and aggression, and even to self-harm. Importantly, in these trials “greater improvements were observed when the therapist was more actively involved with the children; when they were given the possibility to experience meaningful interpersonal psychotherapeutic interactions; and when the settings were free of artificial or experimental restrictions.” Once again, we see that the reaction to the drug is modulated by contextual factors. Consequently, the prosocial effects cannot be attributed to the drug alone but to drug and context interactions.

This point is illustrated in several papers in this Research Topic. [Pace and Devenot](#) critique universal claims that psychedelics—in their pharmacological essence—necessarily improve society, increase environmental concern and promote liberal politics. They present examples of right-wing psychedelia in which conservative ideologies assimilate psychedelic experiences of interconnection but amplify authoritarian worldviews. They suggest that psychedelics are “politically pluripotent” in that the changes they induce are based on the political setting. [Langlitz et al.](#) also raise caution against universal claims about psychedelics’ moral psychopharmacology, which requires an interdisciplinary inquiry to prevent naïve interpretations of results: “While members of the American counterculture used LSD, mescaline, and psilocybin as psychopharmacological tools to

liberate individuals from the ills of their society, Huichol youth ingested peyote buttons to become full members of their own society, and Native American Church worshippers consumed peyote to foster indigenous resistance to North American colonialism. In the 1960s, psychedelics were taken to experience a mystical union that users claimed fostered a sense of universal love, but anthropologists have also described Amazonian societies that used them in rituals to prepare for violent intergroup conflict.”

Roseman and Karkabi—in a sequel paper to Roseman et al. (2021)—made similar critical observations regarding politically pluripotent dynamics while studying ayahuasca groups in which Israeli and Palestinians drink together in rituals organized by Israelis. While the collective experience of “oneness” and interconnectedness can create strong social bonds between Israelis and Palestinians, it does not necessarily produce more equality and justice. The “irony in harmony” is that too much focus on harmony can bypass political tensions, and so stabilize the hegemonic structures in which Israelis subjugate Palestinians. When harmony is the main goal of the status quo, any mention of injustice can be silenced to prevent disharmony. Prosocial effects and increased group cohesion are not inherently just, and can sometimes be in service of hierarchies, unequal social structures, and violence. Yet, the authors also identify unique revelatory events which momentarily rupture the harmony of the ritual by revealing agonizing visions of Palestinian trauma which are not aligned with the hegemonic Israeli narrative. Such events can ignite a liberative procedure in which the subjects attempt to change the social structure. The authors argue that such revelatory events can ignite resistance towards the status-quo and can activate the subject with revolutionary hope, acting towards a more egalitarian structure.

Recognition of cultural and social influences on psychedelics’ mechanisms of action reveals a complexity of mechanisms that raise caution with oversimplified and hyped claims about psychedelics. Studying psychedelics only through the dominant paradigms in psychiatry and psychology ignores many of their functions. While integrating psychedelics into such paradigms is necessary for their mainstream acceptance, this comes with a risk that psychedelics will be assimilated into these paradigms instead of changing them, and consequently restricting psychedelic practices and the science of psychedelics. The simplified mainstream narratives ignore broader knowledge and perspectives about psychedelic use and mechanism of action. The seemingly controversial argument that psychedelics’ therapeutic efficacy is dependent on suggestibility, social context, and cultural priors challenges traditional psychopharmacological views. But for anyone who seeks universal scientific truths about psychedelics, these might be their principal mechanism of action, a non-specific amplification of context, which is strongly related to sociality, especially interpersonal relations and cultural setting.

Novel theoretical orientations that incorporate biopsychosocial notions are therefore required. Lepow et al. presents these here in a testable hypothesis in which psychedelics induce a critical period plasticity that “remove the brakes on adult neuroplasticity, inducing a state similar to that of neurodevelopment.” It is suggested that this enhanced sensitivity to environmental input and increased relearning capacity are then utilized in the therapeutic procedure to create enduring effects.

Future studies need to expand beyond conventional clinical research into process-oriented research, such as examining how mediating variables produce different outcomes, and reporting clinical case studies. The extrapharmacological complexity of psychedelic effects means that evidence-based medicine has its (double-)blind spots, as it provides us with controls to eliminate the very conditions that psychedelics exploit—the interpersonal dynamics and placebo and expectancy effects.

This can miss the underlying mechanism of psychosociotherapeutic processes engaged or released by psychedelics. Therefore, another potential research avenue into *psychedelic sociality* is cultural-controlled trials (Wallace, 1959) which experimentally examine cultural differences in trial outcomes. Such trials can even incorporate biological measures such as oxytocin levels to assess how context influences the most basic sociopharmacological dynamics. Other studies can investigate interpersonal dynamics as introduced in this Research Topic in Wagner on evaluating MDMA couples therapy.

To conduct biopsychosocial psychedelic research, interdisciplinary collaborations are encouraged. Such collaborations are healthy for psychedelic research, but more crucially, they might impact science at large. In the current state of academic affairs, biologists, psychologists and social scientists are studying the same human without clearly communicating their findings to each other. Psychedelic research can serve as a glue that integrates interdisciplinary knowledge on mind, body and culture, and so reveal what is unique about humans.

Author contributions

LR was invited by Frontiers to develop a Research Topic and he invited MW to join the project. MW proposed the Research Topic of “*Psychedelic Sociality*” and they together developed the proposal. KP and EF were subsequently invited to join the project.

Conflict of interest

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Cross-Sectional Associations Between Lifetime Use of Psychedelic Drugs and Psychometric Measures During the COVID-19 Confinement: A Transcultural Study

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Background: One of the main public health strategies adopted at the beginning of the COVID-19 pandemic consisted of implementing strict lockdowns to stop the transmission of the virus. Despite being an effective measure, the confinement and the associated social isolation create a stressful, potentially lengthy situations that has been proven to have several psychological consequences. Given the potential benefits that certain psychedelic drugs have shown for the treatment of psychological disorders, this study aimed to assess the impact of lifetime psychedelic drug use on mental health in relation to the first strict lockdown adopted by various countries (April–July 2020).

Methods: Subjects completed an online survey that inquired about sociodemographic factors, activities, and lifestyle factors during confinement, as well as health and mental health related factors. Subjects were asked about their lifetime use of psychedelic drugs (MDMA, ayahuasca, psilocybin-containing mushrooms, LSD, peyote, San Pedro, Bufo alvarius or 5-MeO-DMT, and others), being classified as regular users (more than once per 6 months), occasional users, or non-users. The survey included psychometric tests used to assess psychological distress, peritraumatic stress, social support, psychopathological symptoms, and personality. Linear regressions were performed with psychedelic drug users as the independent variable and psychometric factors as the outcomes, while correcting for age, gender, language, religion, spirituality, and use of non-psychedelic drugs.

Results: The study included 2,974 English, Portuguese, and Spanish speakers (497 regular users of psychedelic drugs, 606 occasional users, and 1,968 non-users). On average, respondents were 36 years old and 70% were female. Psychedelic drug users, especially regular ones, reported less psychological distress, less peritraumatic stress, and more social support. Regarding personality measures, psychedelic drug

users scored higher on the novelty-seeking and self-transcendence scales, and lower on cooperativeness.

Conclusion: Our findings showed that regular users of psychedelic drugs had less psychological stress and some personality differences when compared to occasional users and non-users. This suggests that either the use of psychedelics might be a protective factor itself or people with certain previous traits are more prone to frequently using psychedelic drugs. Future prospective longitudinal research should investigate the underlying processes observed in this study to develop consistent hypotheses.

Keywords: psychedelic drugs, distress, social support, psychopathology, personality, COVID-19, cross-cultural

INTRODUCTION

The new 2019 coronavirus (SARS-COV-2) is a serious and fatal public health concern that has spread globally following the outbreak of the virus between late December 2019 and early January 2020 (1). On March 11th, 2020, the World Health Organization (WHO) officially declared this to be a worldwide pandemic. At the time of this manuscript's preparation (March 2021), the total number of confirmed cases is about 124,535,520 million worldwide, with almost 2,738,876 deaths linked to this virus (2). As this virus is closely related to previous coronavirus outbreaks, such as the severe acute respiratory syndrome (SARS)-CoV and the Middle East respiratory syndrome (MERS)-CoV, the primary symptoms of COVID-19 contraction are generally related to these other respiratory syndromes, including pneumonia, acute respiratory distress syndrome, fever, cough, fatigue, hemoptysis, acute cardiac injury, hypoxemia, dyspnea, and lymphopenia, but also other more specific symptoms, such as rhinorrhea, sneezing, sore throat, and diarrhea (1). The primary dispersion mechanism is believed to be direct contact or droplets spread by infected individuals coughing or sneezing.

Considering the seriousness of this virus and how quickly it spreads, medical experts have advised governments around the world to implement social distancing policies in their countries in order to hamper the virus's transmission. Nevertheless, in addition to the fear of contracting the disease, quarantine causes its own set of problems, particularly associated with mental health and well-being (3–9). Several stressors, including infection fears, frustration, boredom, inadequate supplies, inadequate information, financial loss, and stigma have been found to be correlated with psychopathological symptoms (4, 5) as well as post-traumatic symptoms (4, 10).

Indeed, in late February 2020, the first nationwide large-scale survey of psychological distress in the general population of China during the COVID-19 epidemic was performed ($N = 52,730$) (11). This survey demonstrated that almost 35% of the population was experiencing psychological distress (such as anxiety and depression), with females more affected than males, and people from 18 to 30 and above 60 years of age were more affected than the rest of the population (11). Other surveys showed similar findings (12–15). Health professionals (e.g., doctors, nurses) seem to be at a greater risk of developing mental health problems

during the COVID-19 pandemic, including depression, anxiety, insomnia, and distress, as they are constantly exposed to contamination sources in hospitals and are afraid of spreading the virus to family and friends (8, 16–21). Remarkably, adopting a positive coping style has been negatively correlated with anxiety and depression (21). Studies conducted outside of Asia and Europe, while transcultural, reported similar results (22, 23).

Parallel with the pandemic, several studies have been published regarding the potential therapeutic effects of psychedelic drugs, such as ayahuasca, psilocybin, and lysergic acid diethylamide (LSD) (24–27), especially for the treatment of mental health issues (25, 28–30). Other studies have shown their potential for the treatment of pain (31, 32) and neurodegenerative disorders (33, 34). These benefits have also been observed in real-world situations through large population surveys, where psychedelic drug users have been shown to have a lower rate of mental health problems (35, 36), reduced psychological distress and suicidality (37), and better outcomes in terms of internationally-validated health indicators (38). Regarding the latter study, a remarkable result concerned the involvement of complex psychological variables previously unassessed in this population, such as coping strategies and personal values (38). Notably, the benefits associated with psychedelic drugs go beyond clinical outcomes, reaching social aspects. For instance, a relationship between psychedelic drug use and pro-environmental behavior has been found (39), as well as with a lower risk of partner violence (40). Considering these results, some authors have suggested that psychedelic drugs can also play a role in terms of helping individuals face the psychological challenges associated with this pandemic (41).

Given the negative impact of the COVID-19 pandemic on mental health (42), the aim of this study was to explore the potential protective effect of lifetime use of psychedelic drugs through psychometric measures. In order to perform a comprehensive analysis, this research was carried out using a multi-language and transcultural approach, analyzing the associations between psychedelic drug use and psychopathology, peritraumatic stress, and personality. We also investigated other lesser-explored sociodemographic data possibly related to the current pandemic and its associated social distancing measures.

MATERIALS AND METHODS

Setting and Participants

An online survey was launched in three languages (Spanish, English, and Portuguese) on April 7th, 2020, when most countries were moving to implement lockdown measures. Through snowball sampling, researchers from various countries, including mainly Spain and Brazil, spread the questionnaires among direct contacts and through social media. The questionnaire was also shared on the websites of the Mental Health Post-graduate Program of the Ribeirão Preto Medical School at the University of São Paulo, in the scientific journal *Archives of Clinical Psychiatry*, and on websites offering information about psychedelics and cannabis (Lasdrogas.info, Cannabis Magazine, social media pages of ICEERS and local community websites). The three versions of the questionnaire remained open for a period of 6 weeks.

The study was approved by the Research Ethics Committee of the Universidad Autónoma de Madrid (Autonomous University of Madrid, Spain). All experimental procedures were performed in accordance with the relevant guidelines and regulations, and all respondents gave informed consent.

Psychometric Outcomes

General Health Questionnaire-12

The GHQ-12 is a 12-item questionnaire widely used to screen for psychological distress in the general population. The validated Spanish (43), English (44), and Portuguese (45) versions were used. The GHQ-12 consists of 12 items scored using 4-point Likert scales. There are various methods of correction. We used the dichotomous score (0-0-1-1), also called the “GHQ score.” As informed by other studies (46), a score of >4 was established as a cut-off point for considering the presence of mental health disturbance. A higher score represents greater psychological distress.

Social Support by the Duke-UNC-11

The Duke-UNC-11 is an 11-item measure of perceived social support. The validated Spanish (47) and English (48) versions were used. The questionnaire was translated to Portuguese by native Portuguese-speaking researchers for the Portuguese version of the questionnaire. The Duke-UNC-11 questionnaire has two dimensions, regarding confidential support (communication with other people) and affective support (expressions of love and affect to/by others). The items are scored using a Likert scale ranging from 1 (“much less than I would like”) to 5 (“as much as I would like”). The total score is calculated as the mean of all of the items. The higher the score, the more social support was perceived.

Peritraumatic Stress Inventory

The PSI is a proposed measure of post-traumatic stress disorder (PTSD); that is, symptoms associated with the exposure to a potentially traumatic experience. The validated English version (49) was used. The questionnaire was translated into Spanish and Portuguese by native Spanish and Portuguese researchers, respectively. The 13 items of the PSI use a 5-point Likert scale response format, ranging from 0 (“not

at all”) to 4 (“extremely true”). The total score is obtained by determining the mean response across all 13 items. Higher scores represent greater exposure to potentially traumatic experiences.

Brief Symptom Inventory

The BSI is a brief form of the SCL-90-R questionnaire regarding psychopathology. It is a self-report symptom inventory designed to assess psychological status. The 53-item English validated version (50) was used. For the Portuguese version, the same 53 BSI items were extracted from the Portuguese validated version of the SCL-90-R (51). For the Spanish version of the questionnaire, a similar 45-item validated short version of the SCL-90-R [SA-45; (52)] was used. The three instruments use a 5-point Likert scale ranging from 0 (“not at all”) to 5 (“extremely”). The scales included are the same as those included in the SCL-90-R: somatization (SOM), obsessive-compulsive (O-C), interpersonal sensitivity (IS), depression (DEP), anxiety (ANX), hostility (HOST), phobic anxiety (PHOB), paranoid ideation (PAR), and psychoticism (PSY). Additionally, the general severity index (GSI) was also extracted, with higher scores indicating more severe symptoms.

Temperament and Character Inventory-67

The TCI-R-67 is a short version of the TCI-R (53) self-report measure of personality. The Spanish (54) validated version was used. The same 67 items were extracted from the original questionnaire (53) and from the validated Portuguese version (55) in order to use them in the English and Portuguese versions of the questionnaire, respectively. The questionnaire uses a 5-point Likert scale ranging from 1 (“strongly disagree”) to 5 (“strongly agree”). The questionnaire includes four temperamental scales: novelty seeking (NS), harm avoidance (HA), reward dependence (RD), and persistence (PE). It also includes three character scales: self-directedness (SD), cooperativeness (CO), and self-transcendence (ST). Additionally, it includes a validity scale of 5 items. Each score represents the degree to which respondents have particular personality traits.

Psychedelic and Non-psychedelic Drug Use

Participants were asked about their use of drugs before and during confinement. We included the use of these psychedelic drugs: MDMA, ayahuasca, psilocybin-containing mushrooms, LSD, peyote, San Pedro, *Bufo alvarius* or 5-MeO-DMT, change, and other psychedelics. We described the consumers of psychedelic drugs and compare them to the never-users. Furthermore, we categorized participants as (a) regular users (more than once per 6 months), (b) occasional users (tried it, but do not use it regularly), and (c) never-users.

We also asked for the settings in which participants were using psychedelic drugs: alone, with friends or a partner, at parties or festivals, at rituals or in a therapeutic setting, or microdosing. We only added MDMA to the list of psychedelic drugs when it is used at rituals or in therapeutic settings. We defined non-psychedelic

drugs as alcohol, tobacco, cannabis, cocaine, amphetamines, and MDMA when consumed in other contexts.

Sociodemographic Data, Religion/Spirituality, and Health Factors

We recorded age, gender (male, female, transgender, or androgynous), the language of the participant (Spanish, English, or Portuguese), and nationality. For each participant, we recorded their partner status (yes/no). We asked for their religion (atheist, agnostic, or religious) and whether they practice their religion. They were asked about whether they felt like a spiritual person or not, and whether they perform any spiritual practices (e.g., prayer, meditation). Each person was asked whether they have any chronic physical or psychological conditions, and housing-related information such as the kind of house they lived in during the confinement or with whom they lived.

Preliminary Factors Related to the Confinement Period

As most participants were still in confinement, we will show preliminary analyses of the following factors. We asked whether persons were diagnosed with COVID-19 or showed any COVID-like symptoms, whether their relatives had COVID-19, and whether anyone around them died from this virus. We asked the number of days they spent in confinement, how well they maintained their confinement, and whether they had a house with an outdoor area. We also asked how many hours per week participants spent outdoors, and whether they followed any anti-contagion advice (e.g., wore gloves, masks). We also asked them to rate their well-being and level of discomfort during confinement on a scale from 1 to 10, with 1 indicating a very low level of well-being and no discomfort at all, while 10 indicated excellent well-being and a very high level of discomfort.

Additionally, subjects were asked about their lifestyle and the activities they had been engaging in during confinement (yes/no), including aerobic exercise; martial arts; music and singing; playing videogames; watching pornography; reading; watching TV, movies, series, or COVID-19 related news; weightlifting or bending; yoga; pilates; and meditation. We also assessed changes in diet since confinement, in terms of whether participants were eating better, the same, or worse. We also asked whether they had less libido or sex during this confinement period.

Regarding societal and economic changes, we determined how participants' vision of the economic system and the predominant values of our society (i.e., consumerism, competitiveness, progress) were altered. We asked whether they were now in favor of changes, against changes, or that they did not change in this respect. We asked them whether they had lost their job as a consequence of the COVID-19 crisis or if their income was reduced. We also asked participants if their past psychedelic substance use impacted their ability to manage their confinement.

Covariates

Age, gender, language, and religion were used as covariates in the linear regression models.

Statistical Analyses

All variables were described as percentages or means and standard deviations. Baseline sample characteristics of regular, occasional, and never-users of psychedelic drugs were compared using chi-square tests for categorical variables and independent sample *t*-tests for continuous variables. We first did this for the sociodemographic factors, religion and spirituality factors, health factors, and drug use. Then we did the same for all COVID-19-related factors. Then, we made an overview in a figure of how psychedelic substances were rated by participants in terms of helping them to manage their period of confinement better. Next, we stratified for the regular and occasional users. As additional analyses, we compared the means for all psychometric outcomes among the Spanish, Portuguese, and English speakers, using analyses of variances (ANOVA).

Subsequently, we performed linear regression analyses to determine associations between consuming psychedelic drugs (yes/no) and the general health score, peritraumatic stress scores, social support, Brief Symptom Inventory scores, and the personality scales. Next, we ran linear regressions with regular and occasional users vs. the never-users of psychedelic drugs as predictors and psychometric factors as outcomes. For each analysis, we adjusted for age, gender, language, religion, and practitioner of religion. All analyses were conducted using SPSS version 24.0 (IBM Corp., Armonk, NY, USA). After Bonferroni-correction (*p*-value of 0.05 divided by 33), we set the significant *p*-value at 0.002, two-tailed.

RESULTS

Sample Characteristics

A total of 2,974 subjects were recruited, with an average age of 36 years, and 29% were male, 70% female, and 1% queer, androgynous, or other genders (**Table 1**). Of all the participants, 54% completed the questionnaires in Spanish, 23% in Portuguese, and 23% in English. In accordance with these numbers, the largest group of subjects responded from Spain ($N = 1,191$), followed by Brazil ($N = 652$), and the United States ($N = 265$). Most of the sample was single (37.6%), followed by "in a relationship" (29.9%), and married (22.8%). The majority of the participants lived in an apartment or flat (51.3%) or a house with a garden (41.4%), in both cases with more than 70 square meters (62.4%). Only 11.6% of the sample lived alone, while 22% shared a house with their partner, and 21.2% lived with their parents. Only 8.5% of the respondents were taking care of people aged between 60 and 90 years, and 2.3% of the sample was living with someone with special needs.

Regarding ethnicity, most respondents to the Portuguese questionnaire were "white" (*branca*, 85.2%), and most respondents to the English and Spanish questionnaires were Caucasian (88.5%). Other ethnicities included *preta*/black (3.8% in Brazil and 0.43% for the other questionnaires) or *indígena*/indigenous (0.5% in Brazil and 2.2% for the other questionnaires). The majority of the sample defined themselves as religious (43.0%), followed by atheists (30%) and agnostics (24.6%). For the Portuguese questionnaire, the majority of respondents were Catholics (38%), followed by agnostics (17%),

TABLE 1 | Sample characteristics of the total sample, and regular vs. occasional vs. never users of psychedelic substances in the past.

	Total (N = 2,974)	Regular users (N = 497)	Occasional users (N = 606)	Never users (N = 1,868)	p^a
Sociodemographics, N (%)					
Age [years, mean (SD)]	36.3 (13.3)	40.0 (11.0)	38.5 (12.0)	34.7 (14.1)	<0.001
Gender					<0.001
Men	852 (28.6)	247 (49.8)	202 (33.7)	403 (21.7)	
Women	2,087 (70.2)	248 (50.0)	392 (65.3)	1,447 (77.8)	
Queer/androgynous/others	18 (0.6)	1 (0.2)	6 (1.0)	11 (0.6)	
Language questionnaire					<0.001
English	673 (22.6)	223 (44.9)	205 (33.8)	243 (13.0)	
Portuguese	689 (23.2)	47 (9.5)	70 (11.6)	572 (30.6)	
Spanish	1,613 (54.2)	227 (45.7)	331 (54.6)	1,053 (56.4)	
Partner status	1,565 (52.6)	268 (54.0)	322 (53.2)	974 (52.2)	0.74
Religion and spirituality, N (%)					
Religion groups					<0.001
Atheist	845 (28.4)	96 (21.8)	185 (33.8)	564 (30.8)	
Agnostic	695 (23.4)	164 (37.3)	194 (35.4)	337 (18.4)	
Religious	1,280 (43.0)	180 (40.9)	169 (30.8)	930 (50.8)	
Practitioner of religion	931 (31.3)	186 (42.7)	176 (33.5)	569 (34.5)	0.003
Spiritual person	1,948 (65.5)	435 (87.5)	451 (74.4)	1,062 (56.9)	<0.001
Spiritual practices	1,686 (56.7)	404 (81.3)	397 (65.5)	885 (47.4)	<0.001
Health factors, N (%)					
Chronic diseases	736 (24.7)	115 (23.1)	150 (24.8)	471 (25.2)	0.63
Mental diseases	670 (22.5)	96 (19.3)	153 (25.2)	421 (22.5)	0.06
Substance use, N (%)					
Non-psychedelic					
Alcohol	1,684 (56.6)	330 (66.4)	403 (66.5)	950 (50.9)	<0.001
Tobacco	681 (22.9)	155 (31.2)	206 (34.0)	320 (17.1)	<0.001
Cannabis	1,212 (40.7)	345 (69.4)	438 (72.5)	429 (23.0)	<0.001
Cocaine	331 (11.1)	119 (23.9)	174 (28.7)	38 (2.0)	<0.001
Amphetamines	266 (8.9)	113 (22.7)	132 (21.8)	21 (1.1)	<0.001
Psychedelic					
MDMA, ecstasy, molly ^b	701 (23.6)	303 (61.0)	325 (53.6)	73 (3.9)	<0.001
Ayahuasca	609 (20.5)	357 (71.8)	252 (41.6)	0	<0.001
Magic mushroom	841 (28.3)	418 (84.1)	423 (69.8)	0	<0.001
LSD	737 (24.8)	354 (71.2)	383 (63.2)	0	<0.001
Other psychedelics	487 (16.4)	296 (59.6)	191 (31.5)	0	<0.001
Context of use of psychedelic substances					<0.001
Not using anything	1,899 (63.8)	6 (1.8)	25 (5.6)	1,868 (100)	
Alone	65 (2.2)	42 (12.9)	23 (5.2)	0	
With friends or partner	293 (9.8)	91 (28.0)	202 (45.5)	0	
At parties or festivals	60 (2.0)	8 (2.5)	52 (11.7)	0	
Rituals/therapeutic	315 (10.6)	174 (53.5)	141 (31.8)	0	
Microdosing	5 (0.2)	4 (1.2)	1 (0.2)	0	

^aChi square tests for categorical variables and independent sample T-test for continuous variable; ^bIs only determined as a psychedelic drug when used for rituals or therapeutic settings. Significant (Bonferroni-corrected) $p < 0.002$ are represented bold.

atheists (13.9%), *Espírita*/Spiritism (12.3%), and afro-Brazilian (3.5%). Among the total sample, only 35.6% were active religious practitioners, while 65.5% considered themselves spiritual.

A notable percentage of the total sample reported having a physical diseases (28.3%) or mental disorder (31.1%). The most

commonly reported physical disorder was asthma (4.7%), and the most commonly reported psychological disorders were anxiety (12.3%), depression (10.4%), and PTSD (1.6%).

There were 1,103 participants (37%) who had used psychedelic drugs, and these included 606 occasional users (20%) and 497

regular users (17%). We considered a regular user to be anyone who reported having used psychedelic drugs more than once per 6 months. **Table 1** shows differences in sample characteristics between the never, occasional, and regular users of psychedelic drugs. Regular users were slightly older, more often men, more often English speakers, more often agnostic or religious, practiced religion more often, and they more often considered themselves spiritual or performed spiritual practices. Regular users of psychedelic drugs used more non-psychedelic drugs than the occasional or never users. Also, regular users more often used psychedelic drugs alone or in rituals or therapeutic contexts, while the occasional users used them with friends or at parties and festivals.

Preliminary Factors Related to COVID-19 Confinement Period

All confinement-related factors are shown in **Table 2**, both for the entire sample and in terms of comparisons between regular, occasional, and never users of psychedelic drugs. The majority of the sample (90.4%) did not experience COVID-19-related symptoms, while 9.3% experienced symptoms and were not tested, and 0.3% had symptoms with a positive result after testing. Among those who tested positive, 5.1% required health care. Moreover, 17.3% of subjects had a relative who had COVID-19, and 4.7% reported the death of a relative due to COVID-19. Users spent more time outdoors and had more access to an outdoor space. Although the regular users followed fewer of the anti-contagion tips, they reported higher levels of well-being and lower discomfort during the confinement period as compared to the never users of psychedelic drugs. While some activities were performed more often by regular users (e.g., music, singing and yoga, pilates, and meditation), others were performed more often by the never users (e.g., aerobic exercise; watching COVID-related news, TV, movies, and series; and playing videogames). Furthermore, regular users reported having better diets during the confinement period, and a higher libido and more sex. Regular users were also more often in favor of change regarding the economic system or the predominant values of our society, and suffered more from working less and having a decreased income. A high percentage of the sample (80.4%) declared having some personal space in which to relax. Similarly, 61.9% of subjects had a specific space inside the house in which to work. Remarkably, 17% of respondents lost their jobs due to the pandemic, while 47.4% experienced a reduction in their income.

Similarly, the self-rated well-being of participants (on a scale ranging from 1 to 10) decreased significantly, as they rated their well-being before the lockdown with a mean of 7.3, while the current rating was 5.8. The rating of their house environment decreased as well, but to a much lesser degree (7.6 vs. 7.2). Regarding confinement measures, most of the sample went outside only to buy food or medicines (52.5%), or they were completely locked down (13.5%). Indeed, 90% of the sample was in confinement for at least 20 days. Accordingly, 61% of the sample noted that they did not normally go out, leaving home only out of necessity. Further, 43.8% of the subjects

reported eating healthier since the beginning of confinement measures, while nearly half of the sample (48.7%) noted a reduction in their libido. Most of the subjects rated the quality or reliability of the information about COVID-19 received from either politicians or the media as mostly poor (4 and 4.4, respectively).

Regarding drug use during confinement, 51.3% of subjects used alcohol, 23.1% cannabis, 21.6% tobacco, 4.9% psilocybin-containing mushrooms, 3.3% LSD, 2.4% ayahuasca, 2.1% ecstasy, and 1.5% cocaine, among other drugs. Notably, there were more subjects who reported using fewer drugs than usual during confinement (18.7%) than those who reported using more than usual (13.4%). The most remarkable increase was in the case of alcohol, with 3.9% of the sample drinking more during confinement, followed by cannabis (2.3% of the sample). Only 0.9% of subjects reduced their alcohol use.

Psychometric Measures Among English, Spanish, and Portuguese Speakers

Most of the countries were under strict lockdowns when the questionnaire was launched, with the remarkable exception of Brazil. This information is relevant when considering differences across countries and/or cultures. Indeed, respondents to the Portuguese questionnaire showed a higher mean score in the GHQ-12 questionnaire, which reflects greater psychological distress (**Table 3**). In the case of Spanish speakers, they showed significantly higher scores for peritraumatic stress than the English speakers ($p = 0.001$), but not than the Portuguese. Spanish speakers also showed significantly higher scores on the psychopathology scales for somatization and depression. The score for perceived social support provided by the Duke-UNC-11 questionnaire was almost the same across the three questionnaires.

Associations Between Use of Psychedelic Drugs and Psychometric Measures

Among the users of psychedelic drugs, 49% reported that their past drug use had a large positive impact on how they managed to cope with the confinement period, while 16% reported that it had a small positive impact, and 35% did not notice a difference (**Figure 1**). Among the regular users of psychedelic drugs, 73% saw a large positive impact, while only 31% of occasional users reported a large positive impact.

Lifetime use of psychedelic drugs was associated with less psychological distress (**Table 4**). Lastly, having used psychedelic drugs was associated with higher scores for the novelty seeking and self-transcendence scales in the TCI-R-67 test, but lower scores for cooperativeness. When we examined the frequency of psychedelic drug consumption, regular users had lower psychological distress and peritraumatic stress scores and more social support, while occasional users only showed lower peritraumatic stress (**Table 4**). Among the personality traits, both occasional and regular users had higher scores for self-transcendence, while only regular users reported more novelty seeking and less cooperativeness.

TABLE 2 | Preliminary factors related to COVID-19 and the confinement period in the total sample, and in regular vs. occasional vs. never users of psychedelic substances in the past.

N (%)	Total (N = 2,974)	Regular users (N = 496)	Occasional users (N = 606)	Never users (N = 1,865)	p
Diagnosed with COVID-19					0.06
No	2,686 (90.3)	433 (87.1)	545 (89.9)	1,708 (91.4)	
No test, but clear symptoms	275 (9.2)	62 (12.5)	58 (9.6)	155 (8.3)	
Yes, tested positive	10 (0.3)	2 (0.4)	3 (0.5)	5 (0.3)	
Relatives with COVID-19	514 (17.3)	95 (19.2)	108 (17.8)	311 (16.7)	0.40
Deaths for COVID-19	140 (4.7)	25 (5.1)	21 (3.5)	94 (5.0)	0.27
Confinement, N (%)					
Days in confinement [mean (SD)]	29.2 (12.5)	30.7 (12.6)	30.9 (13.1)	28.2 (12.1)	<0.001
Maintaining confinement					<0.001
I go out every day (with dog)	227 (7.6)	78 (15.8)	60 (10.0)	88 (4.7)	
I go out 4–6 days/week	136 (4.6)	36 (7.3)	30 (5.0)	70 (3.8)	
Up to 3 days/week	654 (22.0)	152 (30.9)	162 (26.9)	340 (18.2)	
Only for necessities or not at all	1,943 (65.3)	227 (46.0)	350 (58.1)	1,366 (73.5)	
House with outdoor area	1,274 (42.8)	243 (48.9)	265 (43.9)	766 (41.1)	0.01
Hours/week outdoors [median (IQR)]	2.0 (4)	4.0 (8)	3.0 (6)	2.0 (3)	<0.001
Following anti-contagion tips	2,685 (90.3)	420 (84.5)	533 (88.0)	1,731 (92.7)	<0.001
Well-being [1–10, mean (SD)]	5.8 (2.1)	6.6 (2.1)	5.9 (2.1)	5.6 (2.1)	<0.001
Level of discomfort [1–10, mean (SD)]	5.6 (2.5)	4.6 (2.4)	5.4 (2.4)	5.9 (2.5)	<0.001
Lifestyle during confinement, N (%)					
Aerobic exercise	1,674 (56.3)	273 (54.9)	325 (53.6)	1,075 (57.5)	0.19
COVID-19 related news	2,531 (85.1)	379 (76.3)	504 (83.2)	1,648 (88.2)	<0.001
Martial arts	136 (4.6)	28 (5.6)	42 (6.9)	65 (3.5)	0.001
Music and singing	1,026 (34.5)	258 (51.9)	244 (40.3)	524 (28.1)	<0.001
Playing videogames	1,005 (33.8)	107 (21.5)	174 (28.7)	723 (38.7)	<0.001
Pornography	739 (24.8)	149 (30.0)	179 (29.5)	410 (21.9)	<0.001
Reading	2,436 (81.9)	430 (86.5)	529 (87.3)	1,477 (79.1)	<0.001
TV, movies or series	2,702 (90.8)	420 (84.5)	552 (91.1)	1,729 (92.6)	<0.001
Weight lifting or bending	1,115 (37.5)	179 (36.0)	220 (36.3)	715 (38.3)	0.52
Yoga, pilates or meditation	1,684 (56.6)	404 (81.3)	452 (74.6)	827 (44.3)	<0.001
Change in diet					<0.001
Better	1,303 (43.8)	259 (52.1)	287 (47.4)	756 (40.5)	
Same	1,166 (39.2)	187 (37.6)	227 (37.5)	752 (40.3)	
Worse	503 (16.9)	51 (10.3)	92 (15.2)	360 (19.3)	
Less libido or sex	1,448 (48.7)	218 (43.9)	280 (46.2)	950 (50.9)	0.01
Societal and economic changes, N (%)					
Change in values of society					<0.001
Yes, in favor of change	841 (28.3)	195 (39.2)	188 (31.0)	458 (24.5)	
Yes, against change	948 (31.9)	128 (25.8)	201 (33.2)	619 (33.2)	
No changes	1,180 (39.7)	174 (35.0)	217 (35.8)	789 (42.3)	
Working less					<0.001
No	2,313 (77.7)	333 (67.4)	438 (73.2)	1,541 (82.9)	
Yes (or reduced hours)	595 (20.0)	154 (31.2)	149 (24.9)	292 (15.7)	
Retired	44 (1.5)	7 (1.4)	11 (1.8)	26 (1.4)	
Income decreased	1,404 (47.2)	266 (53.6)	314 (52.2)	824 (44.3)	<0.001

Significant (Bonferroni-corrected) $p < 0.002$ are represented bold.

DISCUSSION

For this study, a large sample was recruited from different countries and cultures and comprehensively assessed in terms

of sociodemographic, activity, and lifestyle factors during the confinement, health-related factors, lifetime psychedelic drug use, and psychometric questionnaires. Most of the subjects recruited were in the unique situation of being confined at home

TABLE 3 | Comparing means of psychometric measures among Spanish, Portuguese, and English speakers.

	Portuguese [mean (SD)] <i>N</i> = 689	English [mean (SD)] <i>N</i> = 672	Spanish [mean (SD)] <i>N</i> = 1,610–1,613	<i>p</i> -value
Stress and social support				
Psychological distress	3.56 (3.60)	3.13 (3.33)	2.66 (3.35)	<0.001
Peritraumatic stress	1.52 (0.75)	1.46 (0.78)	1.57 (0.77)	0.01
Social support	41.29 (9.69)	40.82 (9.59)	41.71 (9.15)	0.11
Brief symptom inventory scores				
Somatization	0.64 (0.75)	0.62 (0.70)	1.21 (1.10)	<0.001
Obsessive-compulsive	1.45 (0.93)	1.37 (0.96)	1.30 (0.98)	0.002
Interpersonal sensitivity	1.16 (0.98)	1.13 (0.99)	1.02 (0.97)	0.002
Depression	1.37 (0.97)	1.31 (1.00)	1.56 (1.08)	<0.001
Anxiety	1.30 (0.93)	1.03 (0.90)	1.34 (1.02)	<0.001
Hostility	0.95 (0.81)	0.84 (0.81)	0.71 (1.03)	<0.001
Phobic anxiety	1.07 (1.07)	1.15 (0.99)	0.85 (1.20)	<0.001
Paranoid ideation	0.88 (0.81)	0.81 (0.78)	0.90 (1.01)	0.12
Psychoticism	0.84 (0.78)	0.79 (0.76)	0.46 (0.75)	<0.001
General severity index	0.95 (0.72)	1.15 (0.86)	1.13 (0.80)	<0.001
Personality scales				
Novelty seeking	23.11 (2.54)	22.65 (3.48)	23.25 (3.91)	0.001
Harm avoidance	23.64 (2.86)	23.70 (3.57)	20.39 (4.37)	<0.001
Reward dependence	21.36 (2.78)	21.02 (3.38)	23.09 (3.37)	<0.001
Persistence	26.15 (3.22)	26.03 (3.10)	27.74 (6.13)	<0.001
Excitability	18.38 (2.42)	18.75 (2.40)	17.49 (2.85)	<0.001
Self-directedness	24.07 (3.98)	23.38 (3.77)	17.94 (6.06)	<0.001
Cooperativeness	23.48 (3.09)	22.10 (4.04)	20.45 (3.45)	<0.001
Self-transcendence	24.91 (3.22)	25.12 (3.40)	22.14 (9.24)	<0.001

Significant (Bonferroni-corrected) $p < 0.002$ are represented bold.

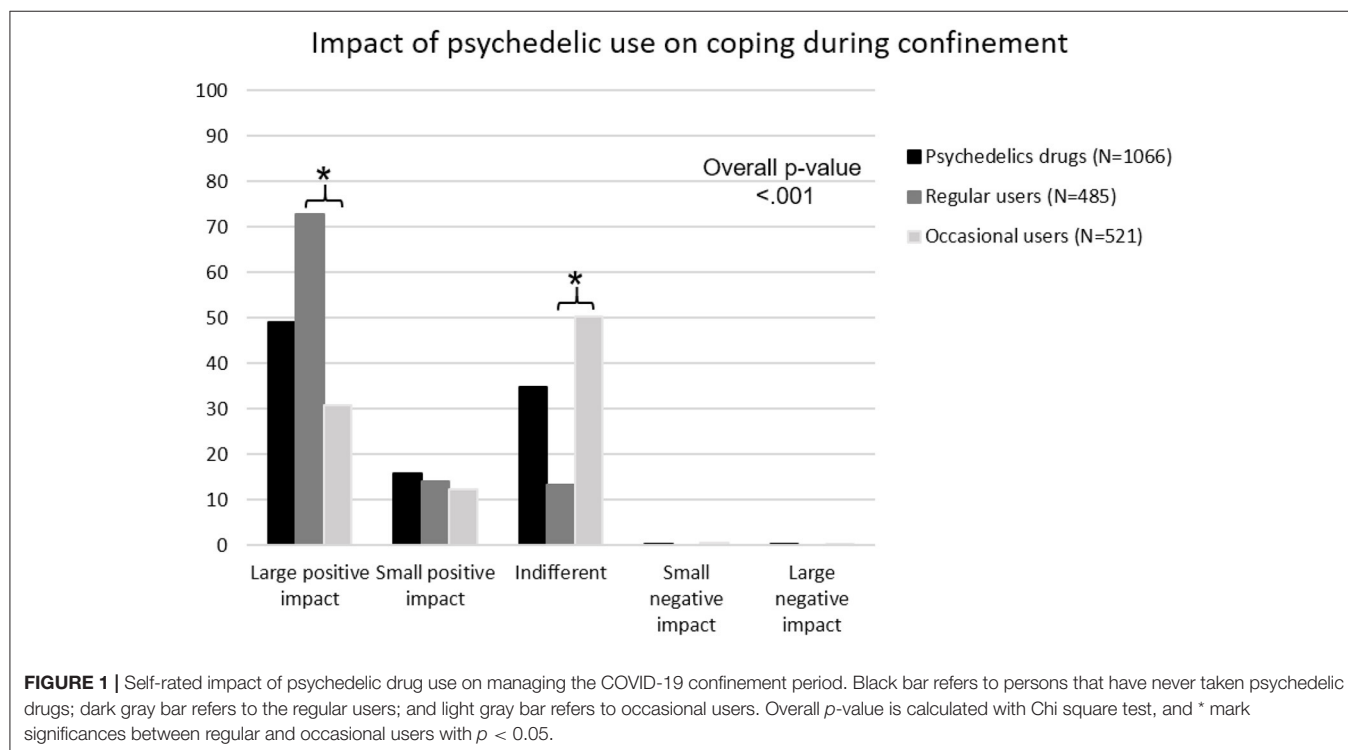


TABLE 4 | Baseline associations between lifetime psychedelic drug users vs. non-users and more specifically, regular vs. occasional vs. never users of psychedelic drugs in the past and psychometric measures.

	Psychedelic vs. never		Occasional vs. never		Regular vs. never	
	B (SE)	p	B (SE)	p	B (SE)	p
Stress and social support (N = 2,467–2,468)						
Psychological distress (GHQ)	−0.52 (0.18)	0.004	−0.32 (0.21)	0.12	−0.79 (0.23)	<0.001
Peritraumatic stress	−0.17 (0.04)	<0.001	−0.16 (0.05)	0.001	−0.18 (0.05)	<0.001
Social support (Duke 11)	1.53 (0.51)	0.003	1.03 (0.57)	0.07	2.19 (0.63)	<0.001
Brief symptom inventory scores (N = 2,468)						
Somatization	0.01 (0.05)	0.81	0.03 (0.06)	0.56	−0.02 (0.06)	0.80
Obsessive-compulsive	−0.05 (0.05)	0.30	−0.05 (0.06)	0.42	−0.06 (0.06)	0.33
Interpersonal sensitivity	0.01 (0.05)	0.88	0.01 (0.06)	0.81	−0.00 (0.07)	0.99
Depression	−0.08 (0.06)	0.15	−0.06 (0.06)	0.36	−0.11 (0.07)	0.12
Anxiety	−0.05 (0.05)	0.38	0.00 (0.06)	0.99	−0.11 (0.07)	0.10
Hostility	−0.06 (0.05)	0.28	−0.03 (0.06)	0.62	−0.09 (0.06)	0.15
Phobic anxiety	−0.14 (0.06)	0.03	−0.10 (0.07)	0.16	−0.19 (0.08)	0.02
Paranoid ideation	−0.02 (0.05)	0.69	0.04 (0.06)	0.54	−0.10 (0.06)	0.13
Psychoticism	−0.05 (0.04)	0.28	−0.03 (0.05)	0.58	−0.07 (0.05)	0.16
General severity index	−0.01 (0.04)	0.86	−0.02 (0.05)	0.63	0.01 (0.05)	0.79
Personality scales (N = 2,467)						
Novelty seeking	0.75 (0.18)	<0.001	0.62 (0.21)	0.003	0.93 (0.23)	<0.001
Harm avoidance	−0.10 (0.21)	0.62	−0.14 (0.24)	0.55	−0.05 (0.26)	0.84
Reward dependence	0.08 (0.18)	0.64	0.07 (0.20)	0.72	0.10 (0.22)	0.65
Persistence	−0.18 (0.27)	0.49	−0.37 (0.30)	0.22	0.07 (0.33)	0.83
Excitability	0.12 (0.14)	0.39	0.14 (0.16)	0.37	0.09 (0.18)	0.61
Self-directedness	−0.22 (0.28)	0.44	−0.10 (0.32)	0.75	−0.37 (0.35)	0.28
Cooperativeness	−0.63 (0.19)	0.001	−0.29 (0.21)	0.17	−1.09 (0.23)	<0.001
Self-transcendence	2.26 (0.36)	<0.001	1.89 (0.41)	<0.001	2.75 (0.44)	<0.001

All linear regressions were corrected for age, gender, languages, religion, practitioner of religion, alcohol, tobacco, cannabis, cocaine and amphetamine use. Significant (Bonferroni-corrected) $p < 0.002$ are represented in bold.

due to COVID-19, a very unusual scenario in recent history. We were interested in assessing the potential psychological consequences of such an uncommon social scenario and, more specifically, the possible role that lifetime use of psychedelic drugs might play in dealing with those consequences, given the recently reported clinical and community benefits associated with psychedelic drugs (41). We found that lifetime use of psychedelic drugs, especially when used regularly (defined as at least once per 6 months), was associated with less psychological distress, less peritraumatic stress, and more social support. Regarding personality measures, psychedelic drug users scored higher on the novelty seeking and self-transcendence scales, and lower on cooperativeness.

Regular psychedelic drug users scored better on several psychometric measures. There are various potential explanations for our finding. For instance, this could be related to the better mental health measures that have been found among psychedelic drug users (35–37). Moreover, other survey studies informed about an increasing trend in the use of psychedelic drugs, particularly for self-treatment of mental health conditions (56). The intensity of the so-called mystical-type experience induced by these substances has also been associated with a higher change in well-being (57). It should be noted that psychedelic drug

users (both regular and occasional) had various confinement-related differences. For example, they were confined more days than never-users, but the difference, while statistically significant, might not be relevant (a mean of 30.7 and 30.9 days in the case of users, and 28.2 in never-users). A more clearly relevant difference regards time spent outdoors and access to outdoor spaces, where psychedelic drug users had more access. This is in accordance with the enhancement observed in relating to nature after using psychedelic drugs (39, 58, 59). Psychedelic drug users also showed more interest in having healthy habits, such as maintaining a better diet during confinement. This was also found in a previous study with long-term ayahuasca ceremony participants (38), suggesting that beyond the plant/drug itself, other factors might contribute to the generally better health found among this population. Psychedelic drug users also showed higher levels of well-being and lower discomfort levels during confinement, in contrast with the never users. This finding might be linked to the reality that 49% of users self-rated their past psychedelic drug use as having a positive impact on their management of lockdown, while 16% considered it to have a small positive impact. Interestingly, the percentage of people who noted a strong positive impact in **Figure 1** is larger among regular users (73%) and reaches only the

31% among occasional users. This may suggest that regular users believe that psychedelic drugs offer greater benefits, or that those supposed benefits are observed only after sustained use. Another potential explanation is that the sample may be biased, being only those who have a strong positive impact the ones who use psychedelic drugs regularly. Moreover, the more psychedelic drugs participants used, the more likely they were to be religious practitioners or define themselves as spiritual and/or performing spiritual practices. These tendencies are highly related to the self-transcendence personality trait (60), which was also measured by the TCI-R-67 test and, accordingly, showed higher scores among psychedelic drug users (both regular and occasional). Regarding religious/spiritual tendencies, previous studies (61, 62) in which personality traits were measured by the TCI/TCI-R-67 questionnaires, involving both long-term ayahuasca ceremony participants and non-users controls, found significant differences for the self-transcendence scale and no differences for the cooperativeness scale. Bouso et al. (61) study was performed with Brazilian ritual ayahuasca users living in urban and jungle areas, whereas the sample for Bouso et al. (62) consisted of Spanish people living in urban areas. The lower score for cooperativeness obtained from psychedelic drug users in our study could be related to differential effects between ayahuasca and psychedelic drugs in general, as well as being affected by participants belonging to formal religious groups, in the case of the samples used by Bouso et al. (61, 62). Interestingly, in another study with Spanish ayahuasca-naïve subjects (28), the score for self-transcendence increased through the follow-ups until 6 months after ayahuasca intake, whereas the score for cooperativeness did not. Although this was not statistically significant, it suggests that having an intense psychedelic experience for the first time can potentiate this trait, and thus the higher scores observed among long-term users can be partially regarded as a consequence of their habits and not due only to previous personality patterns. It should be noted that Bouso et al. (62) found associations between greater self-transcendence scores and increased cortical thinning of the posterior cingulate cortex in the ayahuasca group. The provision of a potential neural basis for this character dimension, and the fact that subjects could experience increased self-transcendence after starting to use psychedelic drugs, supports the hypothesis that this trait is especially notable among long-term psychedelic drug users.

Other factors that explain the better scores obtained by psychedelic drug users might include the physical activity of regular users in our sample. Indeed, psychedelic drug users reported playing music, singing, and doing yoga, pilates, or meditation during confinement, while non-users spent more time watching COVID-related news or TV in general. Some research has warned about inappropriate media exposure during the current pandemic (63), so this may have affected the non-users included in our sample. Additionally, regular users also reported having improved their dietary habits during the lockdown, and having a higher libido and more sex than non-users. However, as a counterpart, they suffered more from working less and having a reduced income. The reasons why the regular use of psychedelic drugs might be protective during

a period of confinement can only be speculative. First, they are 5-HT_{2A} agonists and have interesting anti-inflammatory, plasticity-promoting, and neuroprotective properties that could be associated with mood enhancement (34, 64–66). Also, the feelings of awe produced by the psychedelic experience (67) and the enhancement of certain traits or psychological processes, such as decentering (68), can be especially beneficial during a prolonged lockdown. It seems that long-term psychedelic users tend to show these traits (38, 61, 62). This evidence can partially explain some of the differences observed in this study between users and non-users, but further studies should reveal the specific mechanisms at work.

Regular users of psychedelic drugs also reported having used more non-psychedelic drugs in the past. Although drug use is generally associated with poorer outcomes in terms of psychological and physical health, in this case, as we will discuss below, regular psychedelic users scored better on several measures. Notably, we also observed that regular users were more likely using psychedelic drugs alone, in rituals/ceremonies, and in therapeutic contexts, while occasional users used them with friends or at parties and festivals. From a harm reduction perspective, it has been observed that ritualistic and therapeutic contexts are generally safer (69–71). Thus, it might be suggested that regular users tend to choose healthier approaches to drug use, whether psychedelic or not, and, as a consequence, they are less likely to experience negative outcomes.

Our sample was gender-biased (70% women), and was composed of mostly Spanish speakers (54%), mostly from Spain but also from various South American countries. Thus, the results should be interpreted in light of these characteristics. Additionally, it should be noted that the sample was confined for only 20–30 days at the time when they responded to the questionnaire. The lockdown was quite strict in most cases, and these measures lasted much longer than 30 days, so longitudinal studies should discuss the impact of prolonged lockdown in order to appropriately assess the consequences for both physical and psychological health. While most of the sample was under strict lockdown measures, the exception of Brazil is remarkable. Some state and municipal Brazilian governments had implemented certain social distancing measures, whereas the central government opposed such measures (72). In this context, we should ask about the degree of distress that the absence of sensible public health policies can cause, and if such distress is similar to or even greater than the stress caused by the strict lockdowns found in most of countries. Indeed, the GHQ-12 score was significantly higher among the respondents to the Portuguese questionnaire, a finding that supports other data recently published (73). Moreover, according to our results, the feeling of untrustworthiness with regards to politicians and the media was generalized among the entire sample. The reasons underlying this issue are beyond the scope of this manuscript, but due to our social responsibility as scientists we cannot dismiss the opportunity to encourage social scientists, philosophers, and policymakers to analyze and confront this unfortunate social phenomenon.

The most remarkable difference between different versions of the questionnaire and psychopathology measures was observed

in the case of Spanish speakers, who scored significantly higher than the other speakers on the somatization and depression scales. This is in line with a recent study (74) that analyzed several variables related to the mental health impacts of the COVID-19 crisis, in which it can be observed that the percentage of the population using benzodiazepines doubled during the lockdown (5.8% of the Spanish population was prescribed benzodiazepines as a consequence of the crisis). The high scores that were observed for some scales (depression and obsessive-compulsiveness) were consistently higher across all countries. Thus, this might suggest similar sources of distress across cultures that could be related to the well-known stressors associated with a global pandemic (e.g., social isolation, disease, and poverty, among others). Unemployment and poverty could be related to enhanced distress (75, 76). The fact that 17% of our sample recently lost their job and that almost half of the total sample reported reductions in income is worrying, since this suggests potential vulnerabilities in terms of health, while also suggesting enormous costs in terms of the global economy. Nearly half of the sample reported a reduction in their libido as well. This has been observed in various studies with contrasting results. While the same percentage of the sample analyzed by Arafat et al. (77) reported that the pandemic affected their sexual life, no alterations were observed in terms of the psychometric measures. Similarly contradictory findings were reported by Yuksel and Ozgor (78), where they found that sexual desire and frequency of intercourse significantly increased during the pandemic, whereas quality of sexual life decreased. This is a complex matter, and future studies should explore the effects of the pandemic on it in depth.

Non-psychedelic drug use during confinement mainly involved alcohol, cannabis, and tobacco. Remarkably, more people reported a general reduction in drug use (18.7%) than reported increased use (13.4%) during lockdown. Specifically, 3.9 and 2.3% of participants increased their use of alcohol and cannabis, respectively, whereas only 0.9% of participants reported a decrease in their alcohol use. These results are in line with findings reported by the Global Drug Survey (GDS) using a sample of 55,000 people recruited in May-June 2020, which also showed a general increase in alcohol and cannabis use, while a smaller part of the sample reduced their use. The use of other drugs decreased dramatically (79). The increase in alcohol use was also reported in US population by the APA (9). However, a Spanish study (80) found that the risky consumption of alcohol actually decreased during the confinement period. Some studies have warned about the clinical risks that cannabis users may face, since they could be more exposed to contagion and have specific vulnerabilities in terms of respiratory issues (81). However, other studies have suggested that some compounds of cannabis might be beneficial for the treatment of some COVID-19 symptoms (82–86). Moreover, other studies reported that cannabis use had positive effects in terms of helping individuals to cope with stressful situations, effects that could partially explain its benefits with regards to chronic disorders (87). These factors should also be considered in the conducting of a risk-benefit assessment. Another online survey (88) that recruited a sample with a similar size as the present study ($n = 3,632$) did not find an increase in

cannabis use during lockdown, but the increase in alcohol use was consistent with this study's findings.

This study has some limitations that should be discussed. First, despite the large sample size, the proportion of Spanish speakers was higher than the proportion of English and Portuguese speakers, so the results might not be equally representative for all of these populations. Additionally, regular users of psychedelic drugs were not matched with non-users for some characteristics (e.g., age, gender, and religion). It should be noted that the impact of confinement is difficult to measure, as it includes several aspects that have been only marginally addressed in the recent history of psychology and psychiatry. Thus, the real impact of the pandemic might not be fully reflected in the measures used. Despite our intention to examine the pandemic using a transcultural approach, the psychometric scores obtained should be compared to the normative data for each country to ensure their appropriate interpretation. This is highly challenging since our sample included a large number of nationalities, so we encourage caution when comparing scores between different nationalities without considering intrinsic cultural differences. Lastly, apart from the main interest of this manuscript (i.e., the influence of psychedelic drug use on stress associated with the pandemic), we tried to address some preliminary factors involved in general health and well-being, ranging from self-ratings of discomfort, housing, or family issues, to activities performed during the lockdown. Nevertheless, we are aware of the complexity of the variables we are studying, so we must clarify that other unassessed variables could have influenced the results obtained. Furthermore, when classifying our sample in regular/occasional/never users we should not forget that maybe our results reflect more the characteristics of the people who use psychedelic drugs frequently or not rather than the effects of psychedelic drugs. It should be noted that in the analyses performed in this manuscript it was not taken into consideration whether subjects were living alone or not during the confinement period. Nevertheless, this study has several strengths, such as its large sample size, its precise timing during the first lockdown and related confinement, and the inclusion of persons from various cultures.

CONCLUSION

The global pandemic caused by SARS-COV-2 has had a notable impact on several countries across the globe. The consequences go far beyond the virus itself, given the necessary measures for controlling the spread of the virus, which generally consist of limiting social contact. Our sample showed some clear and remarkable signs of psychological distress, and several variables have been analyzed. We found that psychedelic drug use, mostly when used regularly, was associated with better outcomes in terms of general health and regarding stress measures. However, given the observational nature of the design of this study, other factors than psychedelic drug use (e.g., previous personality traits, local lockdown measures, or differences in sociodemographic factors) could be involved in this outcome. This suggests that the use of psychedelic drugs might be a protective factor itself, or

people with better psychometric characteristics are more prone to frequently using psychedelic drugs. Therefore, future studies should investigate the different roles that psychedelic drugs can play in this pandemic or in a future pandemic outbreak.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Comité ético de la investigación (Universidad Autónoma de Madrid). The patients/participants provided their written informed consent to participate in this study.

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AUTHOR CONTRIBUTIONS

JB conceived the study. JB, GO, MA-C, RdS, and JH designed the study. GO developed the online survey. GO, GR, and JR performed the data collection. DR performed the statistical analyses. GO, GR, JR, and DR wrote the first draft of the manuscript. All authors contributed to the final version of the manuscript.

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The Setting Questionnaire for the Ayahuasca Experience: Questionnaire Development and Internal Structure

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The growing interest in research on psychedelic consumption in naturalistic contexts and their possible medical and therapeutic benefits requires assessment of the relationships between the substance and the individual who consumes it (set) and its context of use (setting). This study provides a novel measurement scale for the setting of Ayahuasca consumption, the Setting Questionnaire for the Ayahuasca Experience (SQAE), and examines its psychometric properties. Construction of the scale began with a literature review, followed by interviews on 19 Ayahuasca users from different backgrounds and different consumption experience, and an online survey for quantitative data collection ($n = 2,994$). Exploratory Graph Analysis (EGA) was used to investigate the questionnaire's dimensional structure with ($n = 1,497$, half of the sample), and multidimensional item response theory (MIRT) was used to compare the fit of the theoretical dimensions with the EGA proposed dimensions ($n = 1,497$, independent other half). EGA identified six dimensions, which corresponded partially to the theorized model (Leadership, Decoration, Infrastructure, Comfort, Instruction, and Social). The MIRT comparison found that the proposed theoretical model fit significantly better than the EGA model, providing support for the former ($\chi^2/df = 1,967$; CFI = 0,972; TLI = 0,969; RMSEA = 0,059; WRMR = 1,087). Our findings present evidence of validity of this instrument, justifying its use for future research on the influence of the setting during the ayahuasca experience. Its findings may provide a basis for expanding the settings investigated in the use of psychedelics in general.

Keywords: ayahuasca, setting, instrument, psychedelics, psychometrics

INTRODUCTION

Studies with psychedelics have been steadily growing in the last two decades, with research centers in different countries investigating their effects and possible use as therapeutic tools in clinical environments (Johnson et al., 2019; Lawrence et al., 2021). There is also a growing interest in understanding how healing, self-empowerment, self-knowledge, and related processes occur with

the consumption of psychedelics in naturalistic contexts (Labate, 2004; Winkelman, 2005; Luna, 2011; Gomes, 2013; Maia et al., 2020).

Beyond the pharmacological effects of the drug itself, other variables must be taken into account in addressing the total effect of this group of substances, the so-called set and setting (Hartogsohn, 2016; Haijen et al., 2018). Briefly defined, set involves variables related to the subject who is ingesting the substance—such as their personal characteristics and traits like personality and life history—and setting refers to the culture, place and situation where the consumption occurs, including decoration and objects displayed, together with what other people are present, the interpersonal relationships established among the participants, what activities are being performed and the metaphysical beliefs shared among the group (Leary and Alpert, 1962; Zinberg, 1984; MacRae, 2001; Hartogsohn, 2016). The broader beliefs regarding psychedelics are particularly relevant with the beverage ayahuasca because of its characteristic setting features that arise from its ritual origins in indigenous ritual practices from the Amazon basin and South American religious syncretism (Labate, 2004; Luna, 2011).

Ayahuasca consumption settings have different forms that stem from different traditions, cultures and their adaptations. Within each tradition, there may be different arrangements adapted for different goals. A curing ritual, for example, may be organized differently from a celebration ritual by the same group (Gomes, 2013). Nevertheless, a typical ayahuasca general setting is always composed of a spiritual leader (vegetalista, mestre, curandero, shaman, “master,” or “godfather”) who, together with their helpers, supervises the consumption of the beverage by the participants and conducts the spiritual ritual in an appropriately decorated environment (Labate, 2004). These participants, in turn, also compose the setting, typically as group rituals. Accommodations for people to sit, lay or stay on, such as chairs, cushions, hammocks or grass may also vary, but are generally present and reported as influential (Pontual et al., in revision). Singing, chanting, dancing, smoke blowing and communicating with spirits are commonly found during ayahuasca rituals, and its presentation is part of an Amerindian cosmology and its beliefs about the presence and roles undertaken by spirits, plant spirits, and ayahuasca animals (Labate, 2004).

In spite of the importance of the quality of acute psychedelic experience in determining the long-term outcomes from psychedelic experiences (Johnson et al., 2017; Roseman et al., 2018), there seems to be a lack of measurement tools available to evaluate and measure the setting and its respective impact on the experiences of ayahuasca consumers and their outcomes (Pontual et al., in revision). This statement may be broadened to the study of the setting in the field of psychedelics in general, which, although highly reliant on psychometric instruments as a way of conducting its studies (Bouso et al., 2016), seems to be lacking appropriate and modern psychometric tools to evaluate the impact of settings. Perkins et al. (2021) addressed the relationship between ayahuasca traditional settings and possible therapeutic outcomes. For this, a statistical correlation was calculated between responses on standard psychological and health questionnaires among participants of different ayahuasca

denominations. Kettner et al. (2021) developed and investigated the psychometric properties of a short instrument—eight items—to assess what the authors have called Intersubjective Experience During Psychedelic Group Sessions, evaluating how participants of ayahuasca rituals related to each other during sessions and established social bonds among themselves. However, as the ayahuasca consumption setting is complex and involves other domains in addition to these, the development of more instruments is necessary.

The objective of the present study was to develop and validate a new multidimensional questionnaire with strong psychometric properties, appropriate for different ayahuasca intake contexts, that could assess the perception of the setting and be easily validated in other languages.

METHODS

Design

An interview was first conducted with 19 ayahuasca drinkers and group leaders from different backgrounds—Santo Daime (five participants), União do Vegetal (UDV) (four participants), Shipibo tradition (two participants), Neo-Shamanic (three participants), and mixed traditions (five participants). It was opted to invite participants from different backgrounds in order to expand the perception possibilities of the ayahuasca settings, with a variety of rituals and rules. These respondents also varied in the number of experiences—from less than five experiences (three participants) to more than 500 experiences (four participants). These participants were interviewed about the setting of their consumption and how they thought these setting features related to the nature of their personal experience. Based on these interviews and on the literature on setting (Zinberg, 1984; MacRae, 2001; Labate, 2004; Hartogsohn, 2016), thematic analysis (Braun and Clarke, 2013), and scale development guidelines (Pasquali, 1998; DeVellis, 2016) were used to elaborate 33 short items (see **Supplementary Material 1**) in six general dimensions: Leadership, with six items about the people conducting the ceremony; Infrastructure, with seven items about the facility; Instruction, with five items about information and guidance; Social, with seven items about the other participants; Comfort, with four items about the body position; and Decoration, with four items about the place's ornamentation. To these, 15 additional descriptive questions were added about music played, activities performed, and presence of natural elements. All items were elaborated as statements that avoided idiosyncratic and culturally-specific expressions and idiomatic language that can cause problems with cross-cultural translation, helping to assure that the items would allow easy translation and cross-cultural adaptation (Hambleton et al., 2004; Vijver and Matsumoto, 2011). Items were submitted to a committee formed by five ayahuasca researchers in the field, native Portuguese speakers, —one PhD in anthropology, one PhD in biology and three PhD candidates in psychology—who judged their content and pertinence to the six general dimensions using an agreement table where items were positioned as rows and their proposed subscale as column. Items were kept in the questionnaire if they achieved a kappa score superior to 0.8.

An individual video conference was then held with a sample of four ayahuasca drinkers from the lower educational level of the target demographic. These respondents were presented with the questionnaire, asked to read each item once, report if its content was simple to understand, and explain their interpretation of it to the researcher. Items that didn't achieve a perfect score on all participants were flagged to have their wording re-formulated.

Items included in the questionnaire were set up online, in Portuguese, using LimeSurvey version 1.01, on the University of Campinas server, in Brazil. The content order was randomized for each respondent, who were asked to score them on a Likert scale based on their last ayahuasca consumption: 1 - Strongly Disagree; 2 - Partially Disagree; 3 - Neither Agree nor Disagree; 4 - Partially Agree; and 5 - Strongly Agree. Invitations to participate were sent to members of ayahuasca churches, healing groups, online discussion communities and posted on social media.

Together with the setting questionnaire, there were descriptive questions and questions on demographics and on ayahuasca consumption habits and affiliations. Also added was a question about previous participation in the study to avoid repeated data. Exclusion criteria were not completing all fields/having missing data, completion of the questionnaires in <5 min—which was considered to be insufficient time—or having provided the same answer for all items—which was interpreted as invalid data. A total of 2,994 responses were considered valid and used for analysis, a sufficient number for accurate MIRT parameter estimates (Jiang et al., 2016).

Procedures of Exploratory Graph Analysis

The responses were randomly split in two halves, for Exploratory Graph Analysis—EGA—and multidimensional item response theory—MIRT. EGA is a recently developed method from network psychometrics, that has produced comparable or better accuracy in identifying dimensions than other more common methods (e.g., principal component analysis, factor analysis, and parallel analysis; Golino and Epskamp, 2017; Golino et al., 2020). EGA consists of identification of communities of items, interpreted as possible dimensions, when they are represented in a “regularized partial correlation network” using a walktrap algorithm that computes distances *via* random walks (Pons and Latapy, 2005). The items are presented in a network made of nodes representing variables (questionnaire items) and edges representing how they are connected. The representations of these connections use penalized inverse covariances between variables to remove spuriousness. Doing so, only relevant inverse covariances remain, visually organizing items and clustering them according to their affinity to each other in a more precise way.

Correlations between items were first estimated by calculating a correlation matrix of all the variables and its inverse variance-covariance. The inverse covariance, together with a model that utilizes penalized maximum likelihood estimation to regularize it, is used to avoid overfitting. Least absolute shrinkage and selection operator (LASSO) was used as a method for regularization of the partial correlation network edges, a procedure in which a penalty [the lambda parameter (λ)] is imposed on the coefficients, an effect sufficient for some of

the values to be zeroed and thus absent from the model. This absence indicated conditional independence and facilitated interpretability of the model as the communities of items tend to cluster in such a way that resemble a dimension, but without the need of loading into a latent variable as it would happen in an exploratory factor analysis. Because of the reduced number of correlations, as the regularized network becomes sparser than the non-regularized network, the clustering of items on the network becomes more self-evident (Golino and Epskamp, 2017).

The degree of regularization is determined by the variation of the Extended Bayesian Information Criterion (EBIC) (Epskamp et al., 2018). The parameter adjusted through EBIC, the gamma hyperparameter (γ), determines the final number of edges that are retained in the network. This is useful to avoid overfitting of the model. The final design of the partial item correlation network is determined by a pairwise Markov random field model, more specifically the Gaussian Graphical Model (GGM). This model generates an undirected network based on the assumption that edges indicate a full conditional association between the two given nodes after conditioning on all other nodes in the network. The Fruchterman-Reingold algorithm is used to iteratively compute the optimal placement of nodes, resulting with the most central nodes placed centralized, least central nodes in the periphery. For the EGA calculations, the R software version 4.0.2 was used (R Core Team, 2020) together with the packages lavaan, semPlot, psych, ega, igraph, qgraph were applied (Csardi and Nepusz, 2006; Epskamp et al., 2012; Rosseel, 2012; Epskamp, 2015; Golino and Epskamp, 2017; Revelle, 2017).

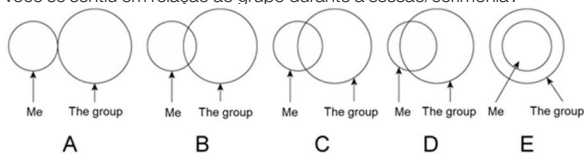
Procedures of Multidimensional Item Response Theory Analysis

The second half of the sample was used for a confirmatory cross-validation of the original proposed theoretical factors and the solution using the communities of items found in the EGA. A multidimensional item response theory approach was used for this analysis, namely Samejima graded response model, with parameter estimation performed by the weighted least squares means and variances adjusted (WLSMV). This approach is similar to a confirmatory factor analysis, but instead of assuming one linear regression for each item loaded on a latent variable, it estimates one function for each Likert-scale category of each item. This approach was chosen instead of a classic confirmatory factor analysis because of the multivariate non-normality of the data, suggesting that the observed variables should be treated as categorical-ordinal, something enabled by item response theory, instead of the linear approach used in classical confirmatory factor analysis (Samejima, 1997; Osteen, 2010).

The degrees to which the observed data followed the theoretical model, as well as the model suggested by the item communities found in the EGA, were evaluated by several goodness-of-fit indices: chi-square divided by degrees of freedom (χ^2/df), Comparative Fit Index (CFI), Tucker-Lewis Index (TLI), Weighted Root Mean Square Residual (WRMR), and Root Mean Square Error of Approximation (RMSEA). The model was considered to have a good fit with values of $\chi^2/\text{df} < 5$ (Ullman and Bentler, 2003), CFI higher than 0.95, TLI higher than 0.95

TABLE 1 | Item statistics.

Item	Responses mean	sd	Item-rest correlation	Multidimensional IRT analysis	
				a parameter*	r ²
L1 Confiei todas minhas preocupações ao grupo de apoio do ritual.	4.174	1.229	0.307	0.887	0.874
L2 Me senti desamparado e tendo que cuidar de mim [~]	1.313	0.787	0.473	0.884	0.871
L3 Quem teve necessidade foi prontamente atendido.	4.797	0.603	0.443	0.884	0.872
L4 A liderança do ritual me transmitiu segurança.	4.825	0.566	0.557	0.882	0.871
L5 Os organizadores se mostraram inexperientes [~]	1.286	0.874	0.327	0.887	0.873
L6 Tive dúvidas quanto à capacidade dos organizadores em lidar com possíveis intercorrências [~]	1.485	1.059	0.546	0.882	0.868
D0 O lugar tinha características em comum com outros ambientes que frequentei no dia-a-dia. [#]	3.005	1.443	0.160	0.890	0.880
D1 Para o meu gosto, a decoração estava adequada.	4.600	0.889	0.407	0.885	0.872
D2 Eu mudaria algum objeto ou imagem da decoração [~]	1.616	1.109	0.390	0.886	0.872
D3 Certos componentes do ritual não estavam de acordo com a minha espiritualidade pessoal [~]	1.632	1.119	0.477	0.884	0.870
C1 Minha posição física foi confortável durante o ritual.	4.426	0.968	0.442	0.885	0.871
C2 Gostaria de ter ficado em outra posição durante o ritual [~]	1.885	1.254	0.456	0.885	0.870
C3 O lugar em que eu estava sentado/deitado me incomodava [~]	1.576	1.056	0.510	0.884	0.869
C4 Senti falta de um apoio para a coluna, cabeça ou braços [~]	1.870	1.309	0.452	0.885	0.871
I0 A cerimônia foi realizada em um espaço suficientemente aberto. [#]	4.439	1.072	0.251	0.888	0.875
I1 Me senti confinado [~]	1.330	0.908	0.403	0.885	0.872
I2 Me preocupei com a circulação do ar naquele local [~]	1.464	1.062	0.342	0.887	0.873
I3 Achei o banheiro inadequado [~]	1.551	1.103	0.378	0.886	0.872
I4 Havia locais acessíveis para fazer minhas necessidades.	4.809	0.592	0.356	0.886	0.873
I5 Me preocupei com a falta de saídas de emergências ou algo relacionado à segurança [~]	1.269	0.813	0.426	0.885	0.871
I6 Havia um local adequado para vomitar.	4.691	0.787	0.330	0.887	0.873
G0 Aconteceram eventos que me pegaram de surpresa [~] . [#]	2.352	1.513	0.306	0.887	0.876
G1 O ritual ocorreu conforme o esperado.	4.621	0.774	0.405	0.885	0.872
G2 Do começo ao fim, o ritual pareceu sob controle.	4.692	0.755	0.384	0.886	0.872
G3 Fui previamente instruído quanto a todo o ritual.	4.733	0.736	0.418	0.885	0.872
G4 Houve momentos em que senti falta de instruções [~]	1.407	0.960	0.504	0.883	0.870
S0 Os outros participantes se assemelham aos meus amigos. [#]	3.891	1.161	0.338	0.887	0.873
S00 Olhar para as outras pessoas me incomodava [~] . [#]	1.777	1.144	0.325	0.887	0.874
S1 Os outros participantes pareciam estar bem.	4.346	0.909	0.418	0.885	0.871
S2 Tenho características em comum com aquele grupo de pessoas.	4.398	0.841	0.459	0.884	0.871
S3 Me considerei diferente dos outros participantes [~]	1.861	1.159	0.443	0.885	0.871
S4 Me senti entre iguais naquele grupo.	4.531	0.839	0.529	0.883	0.870
S5 Qual das imagens melhor representa como você se sentiu em relação ao grupo durante a sessão/cerimônia?	4.294	1.106	0.553	0.882	0.868



[~]Reverse-scaled item.

[#]Removed item.

*All estimates were significant with a *p*-value < 0.001.

TABLE 2 | Demographic characteristics of the total sample.

		<i>n</i> = 2,994	Percent
Gender	Male	1,248	48.8
	Female	1,286	50.2
	Other / Prefer not to answer	25	1.0
	Missing ^a	435	14.5
Age	18–23 years old	395	13.2
	24–30 years old	665	22.2
	31–40 years old	934	31.2
	41–60 years old	880	29.4
	+60 years old	120	4.0
Highest level of education	Basic Education	60	2.0
	Middle Education / High School	497	16.6
	Major / Professional	2,437	81.4
Number of ayahuasca experiences	One	126	4.2
	Less than five	210	7.0
	Between 5 and 20	452	15.1
	Between 20 and 100	673	22.5
Ritual denomination	More than 100	1,533	51.2
	Barquinha	13	0.4
	Neo-Shamanic	594	19.8
	Traditional Indigenous	63	2.1
	Santo Daime	604	20.2
	União do Vegetal	1,605	53.6
	Other	74	2.5
	Don't know	41	1.4

^aThe first online version didn't have a question about gender.

(Hu and Bentler, 1999), WRMR lower than 1.5 (Hu and Bentler, 1999), and RMSEA lower than 0.05 (Browne and Cudeck, 1992).

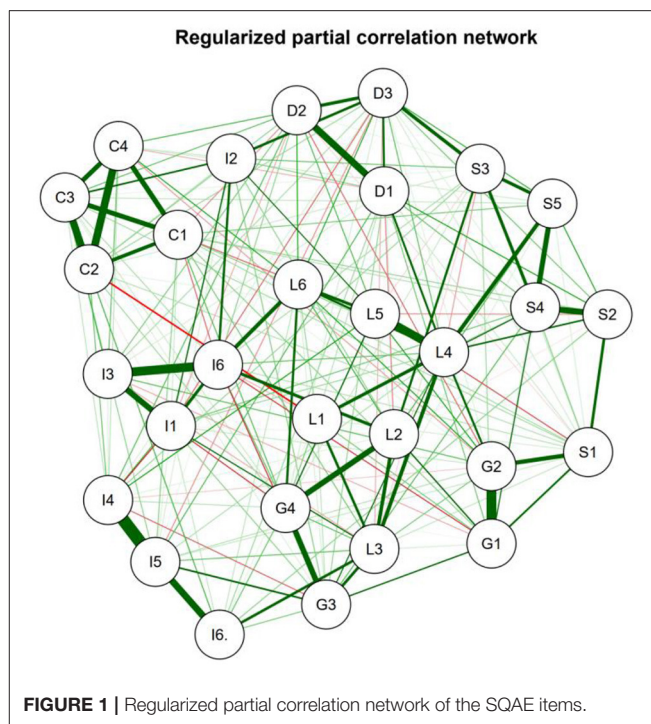
The quality of each item was evaluated in terms of discrimination, R-squared and residual variances. These indicators were not used as threshold to determine item exclusions, but any items presenting a low discrimination, a low R-squared coefficient and a high residual variance were scrutinized for its appropriateness and content validity.

Reliability

Cronbach's alpha coefficients were calculated for the full questionnaire and its six subscales. Coefficients above 0.7 were considered acceptable (Streiner et al., 2015). In addition to the alpha, Gutmann and McDonalds coefficients, we have also calculated individual reliability estimates based on the individual estimates for the standard error of measurement from the Samejima graded response model.

Ethics

The study was approved by the Research Ethics Committee of the University of São Paulo and an Informed Consent Form was presented to all participants (Authorization number 64130517.8.0000.5407).



RESULTS

During the development phase, two items from the 33 elaborated—items number 02 and 28—, didn't achieve a satisfactory agreement between all members of the committee formed by five researchers on the field, achieving a kappa score of <0.8 and were flagged to be removed from the questionnaire. Among the semantic judges formed from ayahuasca drinkers of the lower educational demographic, only one item was not fully comprehensible to a respondent after first reading and was reworded—item number 12. All items are listed in **Table 1**, including removed items.

For the investigation of evidence of validity of the questionnaire, data from 3,472 participants was collected. After application of the exclusion criteria, a total of 2,994 responses were considered valid and used for analysis. **Table 2** reports their demographics. Gender and age groups were well-distributed among the sample, with the largest group being 31–40 years old ($n = 934$). The majority of the participants had completed a major or a professional education degree (81.4%). And it is observed that regarding the number of experiences, the most frequent responses (51.2%) were grouped in the highest classification, more than 100 experiences with ayahuasca. Participants who had their last experience in a União do Vegetal ritual were the largest group of respondents (53.6%).

SQAE Dimensions

EGA was conducted to explore the factor structure underlying the SQAE with half of the valid responses ($n = 1,497$). The result of the EGA analyses revealed six communities of items, which were, in overall terms, compatible with the six-factor theoretical

model (**Figure 1**). The constructs according to the proposed theoretical model are: Social (S1 to S5), Leadership (L1 to L6), Decoration (D1 to D3), Comfort (C1 to C4), Infrastructure (I1 to I6), and Instruction (G1 to G5) (**Figure 2**). **Figure 1** depicts a regularized partial correlation network between items—nodes—and their regularized partial correlations—edges. The thickness of the edge is the degree of correlation, with positive correlations depicted as green, and negative as red. A strong correlation also brings their respective items closer. It is possible to observe the proximity of the items from the same proposed theoretical construct. The Leadership dimension took on a centralized position, having more interconnection with other dimensions, especially with Instruction; in contrast, Comfort assumed a marginal position, with less correlation with other dimensions. Infrastructure item I2 wasn't positioned well and was removed after it also presented a poor adjustment on the MIRT.

Figure 2 shows the original proposed theoretical model and the model proposed by the walktrap algorithm. Nodes of the same color indicate common dimensionality, with the color of the edges representing positive (green) or negative (red)

correlation, and their thickness representing their strength. The number of dimensions proposed to be kept by it is befitting with the proposed theoretical model, but it varies on the sixth dimension, sectioning the Infrastructure dimension in two and grouping together Leadership with Instruction. It also disagrees on some items, specially centralized items (**Figure 2**).

Taking the walktrap at face value for a model, both models would present fit indices in multidimensional item response theory analysis used for confirmatory purposes ($n = 1,497$) that suggest good fit, but with the theoretical model presenting superior results in all indices (**Table 3**), with $\chi^2/\text{df} = 2.387$; CFI = 0.963; TLI = 0.958; SRMR = 0.052; RMSEA [HI95%] = 0.030; Diff. test = 367.466 (15).

The internal consistency of the SQAE and its subscales are described in **Table 4**. The SQAE presented acceptable reliability coefficients, with the Social, Comfort and Leader individual subscales also presenting acceptable internal consistency indices, and Infrastructure, Decoration and Instruction presenting scores below the 0.7 threshold.

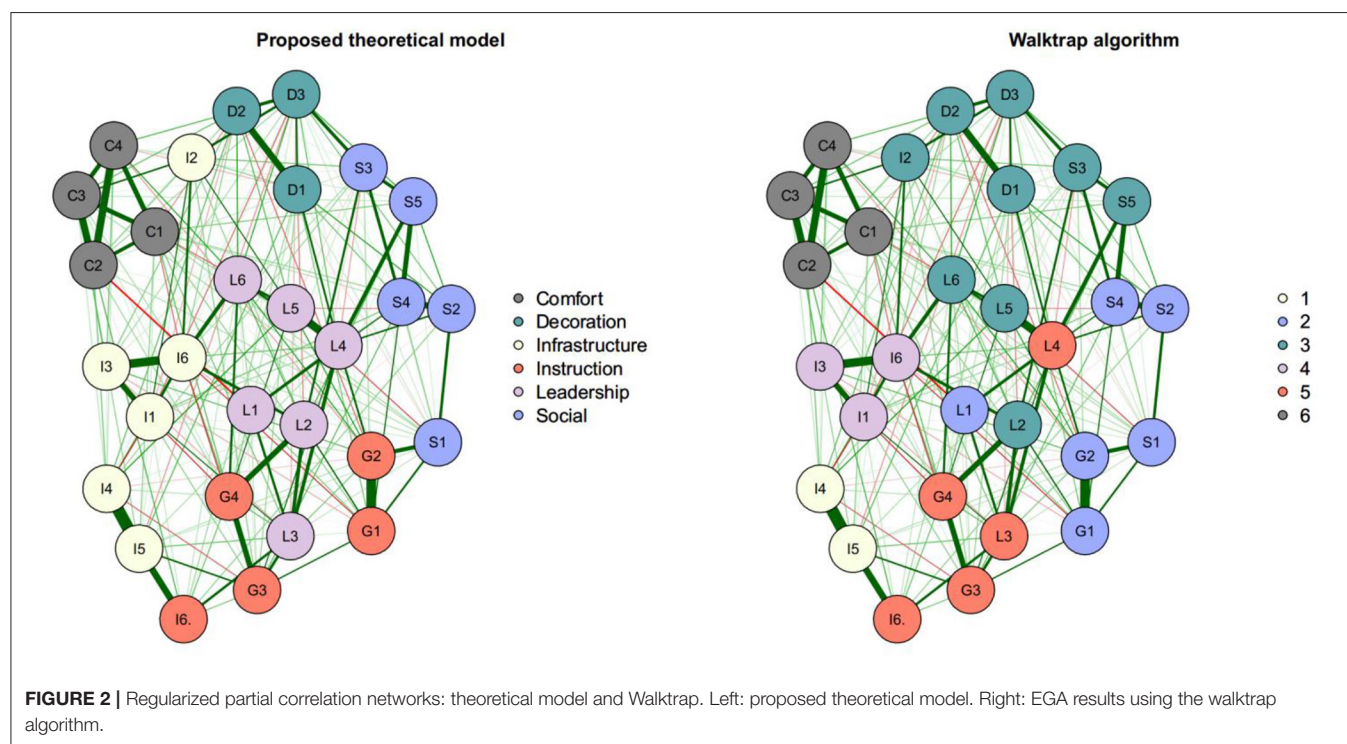


TABLE 3 | Goodness-of-fit indices for the item response theory analyses according to the tested models.

	Fit indices					
	χ^2/df	CFI	TLI	SRMR	RMSEA	Diff. test
Unidimensional	4.897	0.890	0.881	0.071	0.051	-
Multidimensional, as suggested by EGA	3.398	0.935	0.927	0.060	0.040	496.503(16)*
Multidimensional, according to theoretical framework	2.387	0.963	0.958	0.052	0.030	367.466(15)*

*Chi-square difference testing with unidimensional model was significant with $p < 0.001$.

Table 5 presents a correlation matrix between the subscales of the SQAE. With exception of Instruction and Leadership, that correlates highly—0.941—, statistically suggesting a possible common dimensionality, almost all correlations presented a good coefficient, between 0.623 and 0.840.

Figure 3 depicts individual reliability estimates for each individual participant in the study according to the proposed theoretical dimensions. Individual responses that tended to weight frequently on multiple items' extreme (1 - Strongly Disagree on reversed items or 5 - Strongly Agree on direct items) showed decreased reliability in comparison to more moderated responses.

DISCUSSION

This study has demonstrated the processes used for the development of the Setting Questionnaire for the Ayahuasca Experience (SQAE) as a tool to help researchers to investigate the setting component of ritualistic ayahuasca consumption, and the properties of the data collected on a large Brazilian sample. The study proceeded further to obtain evidence of validity for the SQAE based on its internal structure using exploratory graph analysis and multidimensional item response theory analysis. The semantic, expert and statistical analyses revealed that most items developed for the SQAE performed as expected, in alignment to the theoretical framework used for the SQAE construction. The study also demonstrated an acceptable of reliability for the overall instrument and for two of its subscales—Social and Comfort—using internal consistency coefficients calculated for the sample. However, conditional reliability curves calculated using the individual standard errors of measurement from the multidimensional item response theory analysis demonstrated that diversity tends to decrease in those candidates with a higher level of overall endorsement in the items of all subscales, homogenizing the responses and decreasing the reliability of the subscales with this data.

Significantly, both gender and age differences were well-represented, since the perceptions of setting may be different between genders or age groups. Participants from the highest education groups were over-represented, likely because the data collection was online. The total sample included people with

many experiences as well as those little and medium experiences, guaranteeing a view of the setting from a range of experiences.

In comparison with other protocols used for factor extraction (e.g., Principal Component Analyses, Kaiser Rule, and Varimax rotation), EGA and MIRT can be considered modern and rigorous statistical analysis, and to achieve these results with a large database can be considered a positive evidence of validity. Some items and subscales indeed presented better psychometric indicators than others, but all items included were justified by theoretical thresholds or theoretical arguments. It is also possible to infer from the items' means (**Table 1**) that the sentences are postulated in a format that facilitates responses too close to extremes (1 - Strongly Disagree or 5 - Strongly Agree), leading to a reduced individual reliability (Image 3) and consequently lowering subscales reliability (**Table 4**). This frequency of extreme responses is not uncommon in studies that report responses' means with instruments in the field (Bouso et al., 2016) and could be scrutinized and improved in future versions of the questionnaire, wording items on low reliability subscales in a way that promote more heterogeneous levels of endorsement.

To start a psychometric investigation of a broad theme such as the setting is a complex venture, and many decisions had to be made. During the interviews, some influential aspects of the setting were brought to light by different participants with distinct points of views. For some participants, for example, leaders have responsibility to assure participants are fully informed a priori about what to expect of the ritual and how to behave in different situations, but for others good leadership has more to do with a spiritual and energetic issue rather than formalities, which should be regarded as different topic. These two subscales, Leadership and Instruction, were the closest in correlation among all six scales, something that can clearly be seen with the EGA and in the correlation matrix between the subscales. Another hard decision that had to be made was the exclusion of the items D0—"the place had characteristics in common with other environments that I frequent in everyday life" and S0—"the other participants are similar to my friends"—from the subscales Decoration and Social, respectively. Although these items were introduced based on interview reports, they were removed because they strongly correlated with each other, creating an undesirable new dimension "Familiarity," that was

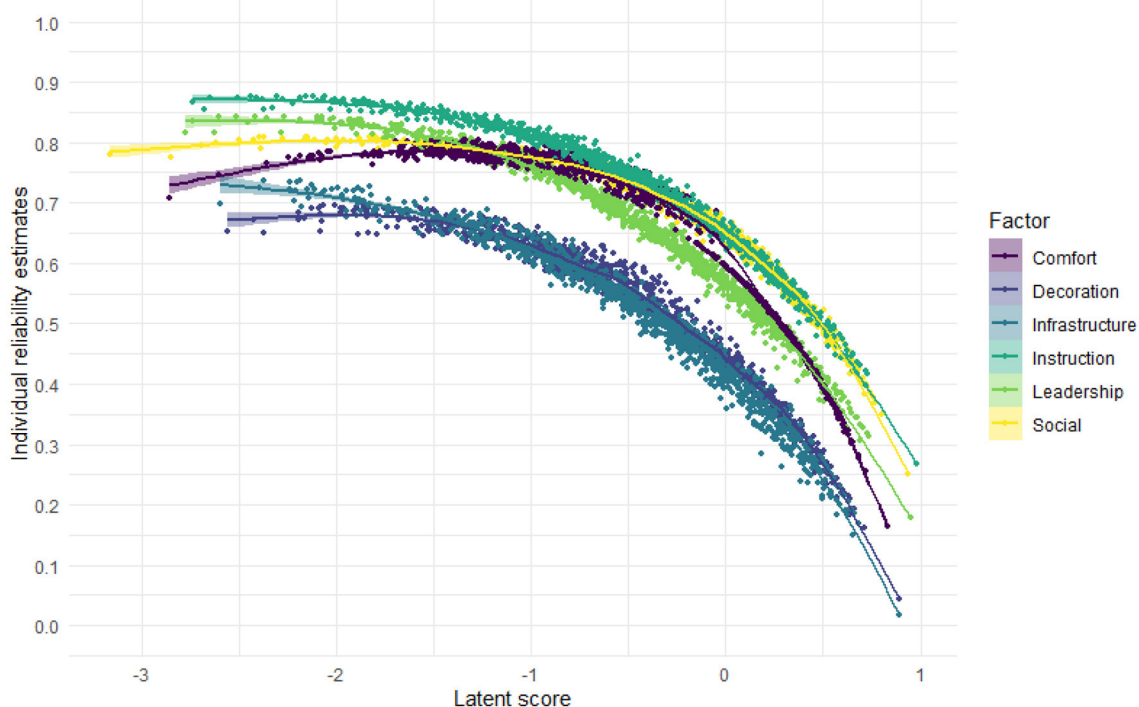
TABLE 4 | Scale reliability statistics.

	Mean	Sd	McDonald's ω	Cronbach's α	Guttman's λ_6	Greatest lower bound	Average interitem correlation
SQAE	3.097	1.620	0.862	0.860	0.875	0.905	0.192
Social	3.620	1.260	0.712	0.704	0.674	0.745	0.334
Leadership	2.971	1.878	0.622	0.613	0.619	0.648	0.240
Infrastructure	2.465	1.776	0.542	0.536	0.515	0.585	0.169
Decoration	2.562	1.755	0.552	0.547	0.450	0.552	0.289
Instruction	3.879	1.723	0.559	0.559	0.502	0.598	0.246
Comfort	2.364	1.457	0.761	0.752	0.703	0.771	0.439

TABLE 5 | Correlation matrix of the subscales.

	Leadership	Decoration	Comfort	Infrastructure	Instruction	Social
Leadership						
Decoration	0.766					
Comfort	0.623	0.630				
Infrastructure	0.840	0.799	0.637			
Instruction	0.941	0.800	0.649	0.830		
Social	0.827	0.766	0.628	0.645	0.874	

*All estimates were significant with a two-tailed p -value < 0.001.

**FIGURE 3 |** Individual reliability estimates according to the theoretical dimensions from the multidimensional item response theory analysis of the SQAQ.

opted out for not being contemplated by the initial reviewed literature and the theory adopted.

Although dealing with a new endeavor and not having other similar instruments to compare, we believe that the SQAQ can be well-paired with other instruments that have been recently developed to be used in psychedelic studies, such as the Emotional Breakthrough Inventory (EBI) (Roseman et al., 2019), Challenging Experience Questionnaire (CEQ) (Barrett et al., 2016), recent versions of the Mystical Experience Questionnaire (MEQ) (Barrett et al., 2015; Schenberg et al., 2017), and 5d-ASC (Studerus et al., 2010). If the broadly accepted assumptions of the effects of set and setting are accurate, a positive measurement of the setting should positively correlate with a less challenging experience, and promote more mystical experience and higher levels on Emotional Breakthroughs. If the scores on these instruments are intercorrelated, it shouldn't be interpreted as redundant information: on the contrary, it should be considered as valuable predictive information for the psychedelic experience

and a guide on where to manipulate to improve the chances to achieve the desirable outcome with the psychedelic use. Right now, the combined EBI, MEQ, and CEQ model was able to predict close to 20% of the variance in well-being changes after a psychedelic experience (Roseman et al., 2019), and we believe that the investigation of the setting with the SQAQ can be the next step to improve this number.

We also believe that bringing modern and avant-garde techniques—such as EGA, network analysis and IRT—to psychedelic psychometrics can have a positive impact, making these assessments more comparable with other areas of the field that are also using modern techniques and high standard techniques. In principle, one interesting direction for future research would be the use of cognitive diagnostic modeling to further investigate the internal structure of the SQAQ, given the apparent within-item multidimensionality of some of the items.

The elaboration and investigation of the validity of the SQAQ is the beginning of a long journey that will need use,

improvements and future adaptations to extend its capacity to measure the various dimensions of setting and predicting their influence on the psychedelic experience. For this, more data and broad-use are needed. This was the premise of this work, so both in the elaboration of the items and in the statistical analysis, many precautions were taken to assure each step, testing their validity and reliability, to provide foundations that can accommodate changes and future improvements.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Research Ethics Committee of the University

of São Paulo. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

AP, CC-W, and LT devised the project and designed the study. AP and CC developed the theory and performed the computations. JR verified the analytical methods. AP took the lead in writing the manuscript. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpsyg.2021.679016/full#supplementary-material>

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Role of the 5-HT_{2A} Receptor in Acute Effects of LSD on Empathy and Circulating Oxytocin

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The psychedelic lysergic acid diethylamide (LSD) has experienced a revival in research, including clinical trials that evaluate LSD-assisted psychotherapy. LSD induces perceptual alterations and influences emotion processing in ways that may support psychotherapy. Here, we investigated the effects of LSD on emotional empathy and mediating role of the serotonin 5-hydroxytryptamine-2A (5-HT_{2A}) receptor by administering 25, 50, 100, and 200 µg LSD alone and 200 µg LSD combined with pretreatment with the 5-HT_{2A} receptor antagonist ketanserin (40 mg) using a placebo-controlled, double-blind, random-order, crossover design in 16 healthy subjects. The Multifaceted Empathy Test (MET) was used to assess the effects of LSD on emotional empathy. Plasma oxytocin levels were also measured. LSD dose-dependently increased implicit and explicit emotional empathy, with the highest 200 µg LSD dose having a significant effect compared with placebo. The 200 µg dose of LSD also moderately increased plasma oxytocin levels compared with placebo. Ketanserin reduced the LSD-induced elevations of oxytocin but not the LSD-induced increases in emotional empathy. These findings confirm that LSD enhances empathy, and this effect may be partially independent of its primary action on 5-HT_{2A} receptors to induce subjective psychedelic effects. In contrast, LSD-induced oxytocin release may depend on 5-HT_{2A} receptor stimulation, which is consistent with the psychedelic effect of LSD. Further studies are needed to investigate whether LSD may also enhance empathy and potentially produce therapeutic effects in patients who have deficits in empathy and impairments in social functioning.

Keywords: LSD, empathy, oxytocin, emotion processing, ketanserin, 5-HT_{2A} receptor, psychedelic

INTRODUCTION

The prototypical psychedelic lysergic acid diethylamide (LSD) is experiencing a revival in psychiatric research. Possible medical benefits of the substance are currently investigated in Phase 2 trials in patients with anxiety (clinicaltrials.gov no. NCT03153579; (Gasser et al., 2014), depression (clinicaltrials.gov no. NCT03866252), and cluster headache (clinicaltrials.gov no. NCT03781128; (Gasser et al., 2014; Carhart-Harris et al., 2015; Dolder et al., 2015; Schmid et al., 2015; Carhart-Harris et al., 2016a; Strajhar et al., 2016; Holze et al., 2020; Holze et al., 2021). The mechanism by which LSD produce potential therapeutic effects in different disorders is not well understood. The

primary target for LSD to produce its acute psychedelic effects in humans appears to be the serotonin 5-hydroxytryptamine-2A (5-HT_{2A}) receptor because the typical acute subjective effects of LSD can be nearly completely blocked by pretreatment with the 5-HT_{2A} receptor antagonist ketanserin (Preller et al., 2017; Holze et al., 2021). Ketanserin alone possesses no psychoactive properties but may result in dry mouth, nasal congestion, tiredness, and reduced blood pressure (Persson et al., 1991). However, LSD also binds with high affinity to 5-HT_{1A} and dopamine receptors (Rickli et al., 2016). Many downstream mechanisms have been proposed to be involved in the potential therapeutic effects of psychedelics, including LSD, such as an increase in neuroplasticity, reflected by increases in brain-derived neurotrophic factor (Ly et al., 2018; Hutten et al., 2020), alterations of brain network connectivity (Carhart-Harris et al., 2016b; Mueller et al., 2018; Mueller et al., 2017b), socioemotional effects (Schmid et al., 2015), and related changes in emotion processing (Dolder et al., 2016; Mueller et al., 2017a). LSD has been shown to produce empathogenic and prosocial effects (Dolder et al., 2016; Schmid et al., 2015). Specifically, LSD acutely increased feelings of subjective well-being, happiness, closeness to others, openness, and trust (Dolder et al., 2016; Schmid et al., 2015), impaired the recognition of sad and fearful faces in the Face Emotion Recognition Task, enhanced emotional empathy in the Multifaceted Empathy Test (MET), and increased prosocial behavior in the Social Value Orientation Test. Such empathogenic and prosocial effects were otherwise typically reported for the prototypical empathogen 3,4-methylenedioxymethamphetamine (MDMA; (Hysek et al., 2014; Bershad et al., 2016; Dolder et al., 2018), which mainly releases serotonin and oxytocin (Dumont et al., 2009; Hysek et al., 2012; Hysek et al., 2014; Francis et al., 2016) and is also investigated in substance-assisted psychotherapy. The findings indicate that LSD and MDMA may have overlapping socioemotional effect properties. Oxytocin is thought to play a critical role in emotion processing. Intranasal oxytocin administration increased emotional empathy, trust, and positive communication and enhanced emotion recognition (Kosfeld et al., 2005; Di Simplicio et al., 2009; Ditzen et al., 2009; Hurlmann et al., 2010). Interestingly, LSD also increased plasma oxytocin levels, although only at a high dose (Schmid et al., 2015; Holze et al., 2020) and to a lesser extent than MDMA (Holze et al., 2020). The effects of different low to high doses of LSD on empathy have not yet been investigated. Unclear is whether the empathy-enhancing and oxytocin-releasing effects of LSD are mediated by 5-HT_{2A} receptors.

Therefore, the present study investigated the effects of LSD (0, 25, 50, 100, and 200 µg) on the MET. Additionally, the 5-HT_{2A} receptor antagonist ketanserin or placebo was administered prior to the highest 200 µg LSD dose to examine whether the effects of LSD on emotional empathy and circulating plasma oxytocin levels are mediated by 5-HT_{2A} receptors. The subjective and autonomic effects of LSD and pharmacokinetics of LSD that were investigated in the present study were reported elsewhere (Holze et al., 2021). However, subjective effects (“any drug effect”) and plasma LSD concentrations are reported herein as peak responses

and at 6 h after LSD administration when the MET was performed.

MATERIALS AND METHODS

Study Design

The study used a double-blind, placebo-controlled, crossover design with six experimental test sessions to investigate the responses to (i) placebo, (ii) 25 µg LSD, (iii) 50 µg LSD, (iv) 100 µg LSD, (v) 200 µg LSD, and (vi) 200 µg LSD 1 h after ketanserin administration (40 mg) as reported in detail elsewhere (Holze et al., 2021). Block randomization was used to counterbalance the different dosing conditions. The washout periods between sessions were at least 10 days. The study was conducted in accordance with the Declaration of Helsinki and International Conference on Harmonization Guidelines in Good Clinical Practice and approved by the Ethics Committee of Northwest Switzerland (EKNZ) and Swiss Federal Office for Public Health. All of the subjects provided written consent before participating in the study, and they were paid for their participation. The study was registered at ClinicalTrials.gov (NCT03321136). Other effects of LSD that were assessed in this study were reported previously (Holze et al., 2021).

Participants

Sixteen healthy subjects (eight men and eight women; mean age ± SD: 29 ± 6.4 years; range: 25–52 years) were recruited by word of mouth or an advertisement that was posted on the web market platform of the University of Basel. Mean body weight was 69 kg. Exclusion criteria were age <25 years or >65 years, pregnancy (urine pregnancy test at screening and before each test session), personal or family (first-degree relative) history of major psychiatric disorders (assessed by the Semi-structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Axis I disorders by a trained psychiatrist), the use of medications that may interfere with the study medications (e.g., antidepressants, antipsychotics, and sedatives), chronic or acute physical illness (e.g., abnormal physical exam, electrocardiogram, or hematological and chemical blood analyses), tobacco smoking (> 10 cigarettes/day), lifetime prevalence of illicit drug use > 10 times (except for Δ⁹-tetrahydrocannabinol), illicit drug use within the last 2 months, and illicit drug use during the study period (determined by urine drug tests). The participants were asked to consume no more than 10 standard alcoholic drinks/week and have no more than one drink on the day before the test sessions. Additionally, the participants were not allowed to drink xanthine-containing liquids after midnight on the study day. The drug use history of the participants was reported elsewhere (Holze et al., 2021). Drug of abuse tests that were performed for each subject once during screening and once during the study were negative.

Study Procedures

The study included a screening visit, six 25-h test sessions (each separated by at least 10 days), and an end-of-study visit. The sessions were conducted in a calm standard hospital room

equipped with a standard hospital bed for the participant and a desk and a chair for the investigator. The room had an adjoining balcony, which participants were allowed to access after peak effects had subsided. Only one research subject and one investigator were present during each test session. Participants were allowed to bring their own music and to bring occupation for the time after effects had subsided or for placebo days (e.g. book, laptop, games etc.). Blindfolds were provided upon request. The test sessions began at 7:45 AM. A urine sample was taken to verify abstinence from drugs of abuse, and a urine pregnancy test was performed in women. The subjects then underwent baseline measurements. Ketanserin (40 mg) or placebo was administered at 8:00 AM. LSD or placebo was administered at 9:00 AM. Standardized lunches and dinners were served at 1:30 PM and 6:00 PM, respectively. The subjects were never alone during the first 16 h after drug administration, and the investigator was in a room next to the subject for up to 24 h. The subjects were sent home the next day at 9:15 AM.

Study Drug

LSD base (> 99% purity; Lipomed AG, Arlesheim, Switzerland) was administered as an oral solution that was produced according to good manufacturing practice in units that contained 100 or 25 µg LSD in 1 ml of 96% ethanol (Holze et al., 2019; Holze et al., 2021). Ketanserin was obtained as the marketed drug Ketensin (20 mg, Janssen-Cilag, Leiden, Netherlands) and encapsulated with opaque capsules to ensure blinding. Placebo consisted of identical opaque capsules that were filled with mannitol. A double-dummy method was used. The subjects received two capsules and two solutions in each session: (i) two placebo capsules and placebo/placebo solutions, (ii) two placebo capsules and 25 µg LSD/placebo solutions, (iii) two placebo capsules and 25 µg LSD/25 µg LSD solutions, (iv) two placebo capsules and 100 µg LSD/placebo solutions, (v) two placebo capsules and 100 µg LSD/100 µg LSD solutions, and (vi) two ketanserin capsules and 100 µg LSD/100 µg LSD solutions.

Measures

Multifaceted Empathy Test. The MET is a reliable and valid task that assesses cognitive and emotional aspects of empathy (Dziobek et al., 2008). The MET has been shown to be sensitive to the effects of oxytocin (Hurlemann et al., 2010), MDMA (Hysek et al., 2014; Kuypers et al., 2014; Schmid et al., 2014), psilocybin (Preller et al., 2015), and LSD (Dolder et al., 2016). The computer-assisted test consisted of 40 photographs that showed people in emotionally charged situations. To measure emotional empathy, the subjects were asked to rate how much they were feeling for an individual in each scene (i.e., explicit emotional empathy) and how much they were aroused by each scene (i.e., implicit emotional empathy) on a 1–9 point scale. The latter rating provides an inherent additional assessment of emotional empathy, which is considered to reduce the likelihood of socially desirable answers. To assess cognitive empathy, the participants were required to infer the mental state of the subject in each scene and indicate the correct mental state from a list of four responses. Cognitive empathy was defined as the percentage of correct responses relative to total responses. The three aspects of empathy were each tested with 20 stimuli with

positive valence and 20 stimuli with negative valence, resulting in a total of 120 trials. The MET was performed 6 h after LSD administration.

Subjective mood. The visual analog scale (VAS) for “any drug effect” was assessed repeatedly over 24 h. The VAS was presented as a 100-mm horizontal line ($0 \pm 100\%$), marked from “not at all” on the left to “extremely” on the right. The questionnaire was also administered 6 h after drug administration, immediately before the MET was performed.

Oxytocin concentrations. Oxytocin concentrations in blood plasma were measured using an oxytocin enzyme-linked immunosorbent assay kit (ENZO Life Sciences, Ann Arbor, MI, United States) according to the manufacturer’s protocol (Holt-Lunstad et al., 2008). Plasma was diluted in a 2:1 ratio in 1.5% TFA-H₂O and centrifuged at $17,100 \times g$ for 15 min at 4°C. The supernatant was collected and then loaded onto an Oasis PRiME HLB 96-well plate with 30 mg sorbent (Waters, Milford, MA, United States) and washed with 0.1% TFA-H₂O. The sample was then eluted with 95% acetonitrile + 5% of a 0.1% TFA-H₂O solution. The elute was collected and dried in an Eppendorf centrifugal vacuum concentrator (model no. 5301, Eppendorf AG, Hamburg, Germany). For the measurements, the residue was reconstituted in assay buffer. The reconstituted samples, standards, and controls were plated on a goat anti-rabbit immunoglobulin G microtiter plate and incubated with oxytocin conjugate at 4°C overnight. The plate was then washed, and the substrate was added. The reaction was stopped after 1 h, and the plate was read at 405 nm. Oxytocin concentrations were determined from a standard curve that was calculated from a four-parameter logistics curve fit. Blood samples for oxytocin concentration determination were taken 1, 3, and 8 h after LSD or placebo administration.

LSD concentrations. Blood samples for the analysis of plasma LSD levels were collected repeatedly in lithium heparin tubes. Plasma concentrations of LSD were determined by ultra-high-performance liquid chromatography tandem mass spectrometry with a lower limit of quantification of 5 pg/ml as reported elsewhere (Holze et al., 2019; Holze et al., 2021).

Statistical Analyses

Dose-response effects of LSD (25, 50, 100, and 200 µg) on emotional empathy measures were assessed using repeated-measures analysis of variance (ANOVA), with drug as the within-subjects factor, followed by the Tukey *post hoc* test based on significant main effects. Separate ANOVAs were applied to assess the effect of ketanserin on the LSD response, with drug (LSD alone, LSD + ketanserin, and placebo) as the within-subjects factor, followed by the Tukey *post hoc* test based on significant main effects. The data were analyzed using Statistica 12 software (StatSoft, Tulsa, OK, United States). The criterion for significance was $p < 0.05$.

RESULTS

Empathy

The effects of LSD on explicit and implicit emotional empathy are shown in **Figure 1**. There were significant main effects of LSD on

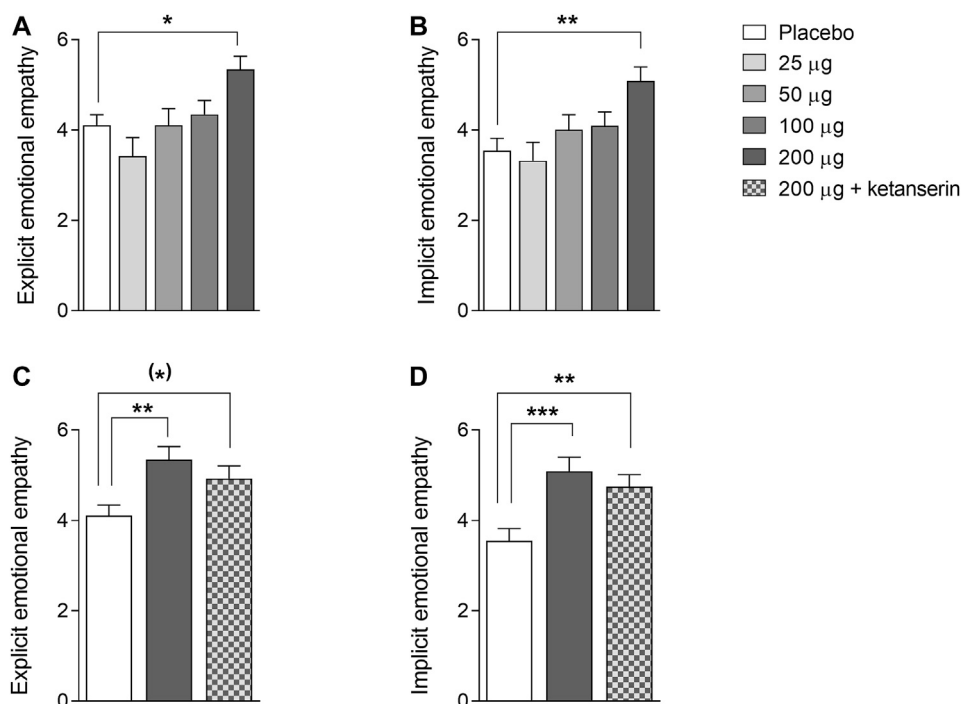


FIGURE 1 | Acute effects of LSD on emotional empathy on the Multifaceted Empathy Test. LSD dose-dependently increased explicit (A) and implicit (B) emotional empathy compared with placebo, with the 200 µg LSD dose producing significant effects. The increases in explicit (C) and implicit (D) empathy that were induced by the 200 µg LSD dose were only slightly reduced by ketanserin pretreatment compared with placebo pretreatment and remained elevated compared with placebo. The data are expressed as the mean ± SEM in 16 subjects (^a $p < 0.1$, ^{*} $p < 0.05$, ^{**} $p < 0.01$, ^{***} $p < 0.01$).

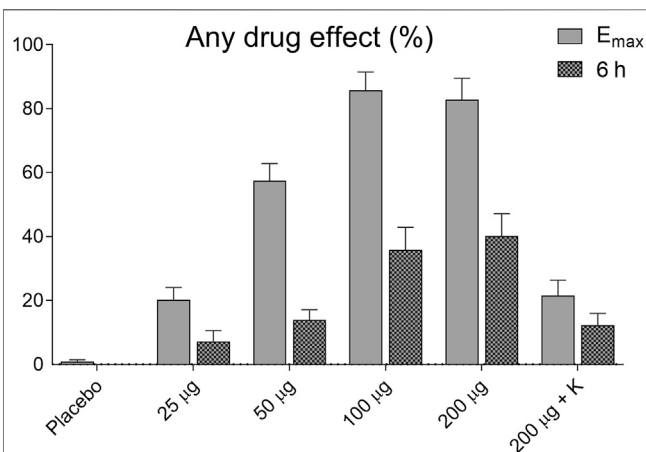


FIGURE 2 | Acute subjective effects of LSD. LSD dose-dependently induced subjective effects, measured as “any drug effects,” on the VAS. The data show the subjective effects as maximal response and at 6 h after drug administration when the empathy test was performed. The data are expressed as the mean ± SEM in 16 subjects.

explicit and implicit emotional empathy ratings ($F_{4,44} = 4.64$, $p < 0.01$, and $F_{4,44} = 4.82$, $p < 0.01$, respectively), indicating that LSD dose-dependently and significantly increased both aspects of emotional empathy. Only the highest 200 µg dose of LSD significantly affected explicit ($p < 0.05$) and implicit ($p < 0.01$)

empathy scores compared with placebo. LSD did not alter cognitive empathy (data not shown).

We then examined the effect of pretreatment with ketanserin on the LSD-induced increase in empathy. There were significant main effects of drug on explicit and implicit emotional empathy ratings ($F_{2,28} = 4.53$, $p < 0.05$, and $F_{2,28} = 8.56$, $p < 0.01$, respectively). The *post hoc* tests showed that both LSD and LSD + ketanserin increased explicit ($p < 0.05$ and $p = 0.09$, respectively) and implicit ($p < 0.001$ and $p < 0.01$, respectively) empathy compared with placebo. Ketanserin did not significantly reduce the LSD-induced increase in empathy (Figure 1).

Subjective Drug Effects

The subjective effects of LSD on “any drug effect,” assessed by the VAS, are shown in Figure 2. LSD dose-dependently produced subjective effects that reached half-maximal levels 6 h after LSD administration when the MET was administered.

Oxytocin Concentrations

There were significant main effects on oxytocin release 1 and 3 h after drug intake ($F_{2,28} = 7.00$, $p < 0.01$, and $F_{2,28} = 4.21$, $p < 0.05$, respectively). The *post hoc* tests showed that only LSD alone increased oxytocin levels 1 and 3 h after drug intake ($p < 0.01$ and $p = 0.06$, respectively) compared with placebo and at 1 and 3 h after drug intake ($p < 0.01$ and $p < 0.05$, respectively) compared with the LSD + ketanserin (Figure 3). Thus, ketanserin effectively prevented the LSD-induced increase in circulating oxytocin.

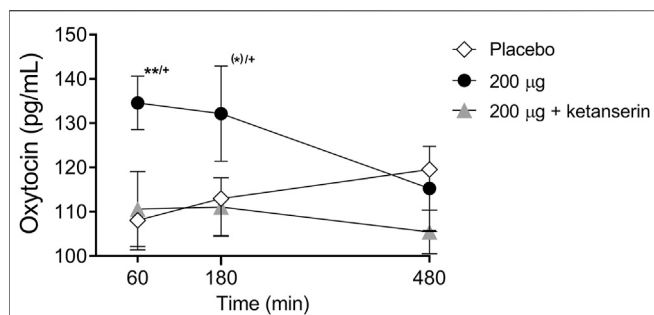


FIGURE 3 | Effects of LSD on circulating oxytocin. LSD alone significantly increased plasma oxytocin concentrations 60 min after administration compared with placebo. LSD did not increase oxytocin levels after ketanserin pretreatment compared with placebo pretreatment. The data are expressed as the mean $\pm$ SEM in 16 subjects (*) $p < 0.1$, ** $p < 0.01$, compared with placebo; + $p < 0.05$, compared with LSD + ketanserin.

Plasma Drug Levels

Plasma LSD concentrations were 2.2 ± 1.0 ng/ml (mean $\pm$ SD) 6 h after administration of the 200 μ g dose and 2.5 ± 0.9 ng/ml 6 h after the administration of 200 μ g LSD + ketanserin, which was at the time when the empathy task began. For comparison, $E_{\max}$ concentrations after 200 μ g LSD and 200 μ g LSD + ketanserin were 3.9 ± 0.8 and 4.4 ± 0.8 ng/ml, respectively. The full pharmacokinetic data on LSD from this study were published previously in detail (Holze et al., 2021).

DISCUSSION

LSD enhanced explicit and implicit emotional empathy and increased plasma oxytocin concentrations at a dose of 200 μ g. The results confirmed previous findings (Schmid et al., 2015; Dolder et al., 2016). Consistent with past study findings, both explicit and implicit emotional empathy were enhanced by LSD and only by the highest 200 μ g dose and not by doses of 100 μ g or lower (Dolder et al., 2016). Similarly, the psychedelic psilocybin and empathogen MDMA have been shown to increase emotional empathy on the MET (Hysek et al., 2014; Kuypers et al., 2014; Preller et al., 2015), indicating that all of these psychoactive substances that are currently being investigated to assist psychotherapy similarly influence emotion processing. Additionally, the present study investigated the mediating role of 5-HT_{2A} receptor stimulation on psychedelic-induced alterations of emotional empathy. Ketanserin has been previously shown to very effectively diminish all acute subjective responses to LSD (Preller et al., 2017; Holze et al., 2021), while not influencing plasma LSD concentrations (Holze et al., 2021). In the present study, ketanserin only weakly attenuated the LSD-induced increases in explicit and implicit empathy, and ratings remained elevated compared with placebo. This finding indicates that the empathogenic effects of LSD may not critically depend on 5-HT_{2A} receptor activation, unlike its subjective psychedelic effects, but could potentially be mediated by other receptors, including serotonin 5-HT₁ receptors. A previous study that tested the 5-HT_{1A} agonist buspirone

demonstrated the involvement of 5-HT_{1A} receptors in emotion processing (Bernasconi et al., 2015). LSD shows strong binding to 5-HT_{1A} receptors (Rickli et al., 2016), and this receptor is not blocked by ketanserin and could thus play a role in the LSD-induced enhancement of emotional empathy. Oxytocin has been shown to contribute to emotional processes, including empathy (Kosfeld et al., 2005; Di Simplicio et al., 2009; Ditzen et al., 2009; Hurlmann et al., 2010). Therefore, we also tested whether LSD increases circulating levels of oxytocin and whether this effect depends on 5-HT_{2A} receptor activation. LSD increased plasma oxytocin concentrations at the 200 μ g dose (not measured for lower doses), consistent with a previous study (Schmid et al., 2015). In contrast, a lower dose of 100 μ g LSD did not increase plasma oxytocin levels in another study (Holze et al., 2020). Furthermore, the LSD-induced increase in oxytocin in the present and previous studies by a high dose (Schmid et al., 2015) was only 1.25 to 3-fold higher compared with placebo, whereas MDMA increased plasma oxytocin levels 3 to 11-fold compared with placebo (Dolder et al., 2018; Holze et al., 2020). Thus, LSD may less effectively induce the release of oxytocin compared with MDMA. With regard to the mechanism of action, preclinical data indicate that MDMA induces its marked effects on oxytocin release via serotonin release and consecutive 5-HT₁ receptor stimulation (Thompson et al., 2007; Hunt et al., 2011). In contrast, in the present study, ketanserin prevented the moderate LSD-induced increase in plasma oxytocin, indicating that the effects of LSD on the oxytocin system involve 5-HT_{2A} receptors, which is consistent with most other effects of LSD (Kraehenmann et al., 2017a; Kraehenmann et al., 2017b; Preller et al., 2017; Barrett et al., 2018; Preller et al., 2018; Holze et al., 2021). Thus, the mechanisms that result in oxytocin release may be distinct for MDMA and LSD and need further investigation. For example, the effects of LSD on oxytocin may be more indirect. LSD acutely induces marked alterations of perception and also moderately increases anxiety at 200 μ g (Holze et al., 2021) while additionally elevating autonomic stimulation and plasma markers of serotonergic activity and stress, including circulating prolactin (Schmid et al., 2015) and glucocorticoids (Strajhar et al., 2016). Oxytocin may moderately increase in response to LSD-induced psychological stress. For example, oxytocin has been considered an anti-stress hormone (Rae et al., 2021). Thus, the oxytocin response might be triggered by subjective LSD-induced effects rather than by a direct pharmacological effect of LSD. Supporting this possibility, oxytocin levels did not increase when the subjective mind-altering effects of LSD were blocked with ketanserin. Instead, oxytocin levels only increased when subjective effects were also highly elevated. Taken together, the present findings indicate that LSD-induced empathogenic effects are neither mediated *via* oxytocin release nor via direct 5-HT_{2A} receptor activation and that the involvement of other factors and receptors in emotion processing is likely.

The present study has several strengths. The study used a pharmaceutically well-defined investigational drug product (Holze et al., 2019; Holze et al., 2021) and a highly valid double-blind, multi-dose, random-order design that included both inactive and “active” placebo in the form of low-dose LSD. Additionally, we assessed emotional empathy not only

for a single dose but also for a range of doses and included an evaluation of the mediating role of a key target receptor of LSD within the same study and participants.

The present study also has limitations. We only included a small sample size of 16 participants. However, because we used a within-subjects design, we included data from 96 study sessions. Oxytocin was only measured for the highest 200 µg dose of LSD because the 100 µg dose showed no effect in previous studies. Because of the strong acute effects of LSD on cognitive performance and concentration (Schmid et al., 2015; Holze et al., 2020; Holze et al., 2021), the MET could not meaningfully be performed during the peak response to LSD. Instead, it was conducted 6 h after LSD administration when plasma LSD concentrations and subjective effects declined to approximately half-maximal levels. One possibility or likelihood was that the lower dose of LSD of 100 µg similarly enhanced empathy during the peak response at 3 h as the 200 µg at 6 h after LSD administration, but this was not tested. Thus, we cannot exclude the possibility that lower doses of LSD also significantly increase empathy. Furthermore, the present study included healthy subjects in a highly controlled laboratory setting, and the effects of LSD may be different in situations of uncontrolled recreational use or in therapeutic settings in patients (de Wit et al., 2021a; Schmid et al., 2021).

In conclusion, the present findings indicate that LSD enhances empathy, which is likely also beneficial for therapeutic application in patients. Psychedelics and MDMA have been shown to potentially trigger therapeutic processes and marked changes in personal attitudes and well-being after single-dose administration and with often lasting effects even in healthy subjects (Griffiths et al., 2008; Schmid and Liechti, 2018; de Wit et al., 2021b). These sometimes long-lasting effects are at least partially associated with alterations of mind and mystical-type experiences (Griffiths et al., 2008; Schmid and Liechti, 2018) and may also be linked to the acute experience of feeling strong emotional concern for others (i.e., emotional empathy) and a connection with other people (de Wit et al., 2021b). Remaining to be investigated is whether LSD also enhances empathy in patients with deficits in empathy and impairments in social functioning

and whether such effects contribute to potential therapeutic effects of LSD.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethikkommission Nordwest- und Zentralschweiz (EKNZ). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

FH, IA, NV, and AE analyzed the data. FH, IA, and ML wrote the manuscript. ML conceived the study and obtained funding.

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Book Review: American Trip: Set, Setting, and the Psychedelic Experience in the Twentieth Century

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Keywords: consciousness, LSD, psilocybin, STS, context

A Book Review on

American Trip: Set, Setting, and the Psychedelic Experience in the Twentieth Century

Ido Hartogsohn (Cambridge, MA: MIT Press), 2020, 432 pages, ISBN: 9780262539142

SUMMARY

American Trip (Figure 1) is an erudite and readable social history of psychedelics in North America with special attention to *Set and Setting* as it shaped not only individual psychedelic experiences during the Sixties, but also the psychedelic experience of the society at large and its impact upon psychiatry, fashion, art, music, and the digital revolution. Hartogsohn elaborates how in the 1960's, America itself went on an epic acid trip.

In considering the book's chapters, the reader should remember that the social context for each chapter represents a different cultural and societal set and setting with its own specific effects on the LSD experiences of individuals taking LSD within that specific context. In this book review, "LSD" is used both for the specific compound, lysergic acid diethylamide, and to other psychedelic congeners (e.g., psilocybin, dimethyltryptamine) that act pharmacologically at serotonin receptors, especially 5-HT_{2A}R, to mitigate serotonergic suppression of catecholaminergic (i.e., noradrenergic and dopaminergic) ergotropic arousal (Lansky, 1975), leading to rapture, ecstasy, introspection, synesthesia, hallucinations, telepathy, extracorporeal visitations, totem animals, past lives, death, birth, increased creativity, awareness, intensity, and "suchness" of the physical and spiritual worlds (Winkelman, 2021). The 10 chapters are:

1. The Experimental Psychosis Movement presents the *psychotomimetic*, prevailing paradigmatic model (Kuhn, 1962), that LSD effects mimicked those of natural psychoses, and so were a putative means for better understanding, and pharmacologically treating, psychoses. The movement was called Experimental Psychiatry.
2. LSD, the CIA, and the Military reveals the extent of the US Military's interest in LSD as a possible psychochemical weapon, and of the CIA's for intelligence gathering, all within the context of the Cold War and existential nuclear threats.
3. From Psychotomimetics to Psychedelics illustrates the shift from the psychotomimetic model of disease-mimicking, to the psychedelic model of healing from the psychedelic reset, especially under optimized set and setting of empathic therapists, comfortable physical space, and conducive music.

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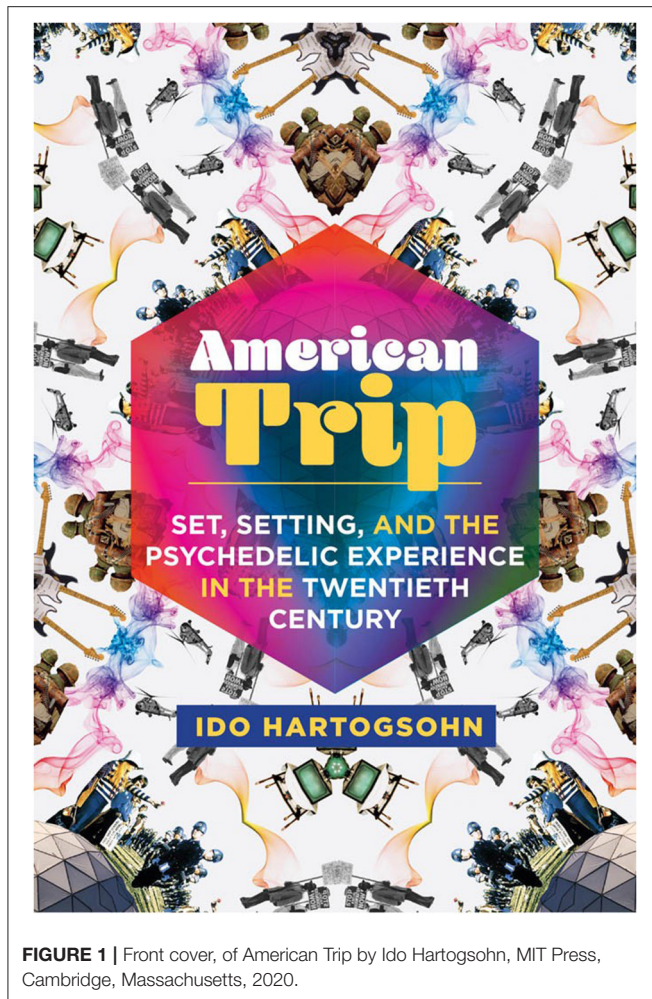


FIGURE 1 | Front cover, of *American Trip* by Ido Hartogsohn, MIT Press, Cambridge, Massachusetts, 2020.

4. Experiments in Set and Setting follows Watts' maxim, "there is no drug reaction, but always setting-plus drug," and that set may be optimized by pre-session rituals including meditation, introspection, fasting, and continence. In a classic study psychedelic inebriation was provided to divinity students in a chapel and was highly successful in producing mystical experience, while administration to prisoners in prison to reduce recidivism, was less effective, possibly due to the less benevolent setting.
5. *Psychedelics, Creativity, and Culture* explores LSD as a tool to enhance creativity in art and music, originally inspired by psychotomimetic research, it later came to mirror the spirit of creativity and boldness of the time, the can-do attitude, and the rise of space exploration, a metaphor for psychonauts.
6. *Psychedelics Go to Silicon Valley* describes the use of LSD to aid technical problem solving, and inspire design of personal computers and their software, with particular attention to the interface between computers, cybernetics, and psychedelic feedback loops.
7. *The Psychedelic Controversy* highlights the schism between cultural elements intent on demonizing LSD as a dangerous

and subversive drug, and LSD adherents touting its catalytic guidance toward peace, love, harmony, and understanding.

8. *American Trip* pits the idea of *pharmacologicalism*, that drugs have inherent effects irrespective of set and setting, against the psychedelically inspired view that set and setting define drug experience of the drug's inherent properties.
9. LSD and the 1960s emphasizes the liberalisms of the period: sexual freedom, individuality, rebelliousness, and anti-psychiatry, coincident with material abundance and societal positive and adventurous spirit to the moon and beyond, and why these conditions supported the emergence of American psychedelic experimentation.
10. *The Future of Set and Setting* drives home the centrality of set and setting for defining drug effects. Much of the harm associated with drugs, especially LSD, was secondary to the societal settings at the time, and by easing restrictions, improving education, and bolstering public image of LSD, harm reduction can be more surely enhanced than by punishing users.

ASSESSMENT

Overall, Hartogsohn successfully contained the paradox between pharmacologicalism on the one hand, and set and setting on the other as competing concepts within pharmacology for understanding drug effects. Pharmacological effects will always be important, but Hartogsohn's easy and informative style has done much good to bridge the gap between pharmacologicalism and the equally important extrapharmacological factors of set and setting, which are inclusive of societal as well as individual influences. *American Trip* is written from a sociological perspective, or that of the broader Science, Technology, and Society (STS), and will naturally appeal to social scientists or persons engaged with psychedelics, but the book is nonetheless also valuable for clinicians. Natural scientists pursuing deeper understanding of set and setting upon drug effects and experience will forgive Hartogsohn's occasional errors. For example, he called Ph.D. pharmacologist Roland Fischer a "psychotomimetic psychiatrist," confused a strain of *Cannabis indica* with low THC and high CBD with a synthetic cannabinoid, and called quasi-psychedelic MDMA a "semi-psychedelic." Nevertheless, as the mind provides cultural, personal, and transpersonal overlay to all degrees of physiological arousal (Fischer, 1971), so it is the set and setting, not the drug, that characterizes the individuality of drug experience. Hartogsohn's book is a seminal contribution to his discipline and the larger issue of extrapharmacological factors shaping drug effects.

IMPLICATIONS

American Trip is relevant both on the societal and individual levels. Cultural context, laws, and mindset impact individual LSD experiences as do personal mindset and the physical setting of the inebriation. Pharmacologists informed by these findings will teach drug effects with latitude, varying according to the set and setting of the patient approaching, during, and following

the session. Clinicians will ready their patients for LSD sessions through pre-session guidance, and the treatment room for the patient by attending to the patient's personal and transpersonal sensibilities. Therapeutic music should be selected according to the patient's input, musical sophistication, and cultural context. Set and setting will affect both the patient's reportage and the physical examination, and should be duly noted for each clinical encounter, prior to, during, following, and even excluding psychedelic interventions.

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Moral Psychopharmacology Needs Moral Inquiry: The Case of Psychedelics

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The revival of psychedelic research coincided and more recently conjoined with psychopharmacological research on how drugs affect moral judgments and behaviors. This article makes the case for a moral psychopharmacology of psychedelics that examines whether psychedelics serve as non-specific amplifiers that enable subjects to (re-)connect with their values, or whether they promote specific moral-political orientations such as liberal and anti-authoritarian views, as recent psychopharmacological studies suggest. This question gains urgency from the fact that the return of psychedelics from counterculture and underground laboratories to mainstream science and society has been accompanied by a diversification of their users and uses. We propose bringing the pharmacological and neuroscientific literature into a conversation with historical and anthropological scholarship documenting the full spectrum of moral and political views associated with the uses of psychedelics. This paper sheds new light on the cultural plasticity of drug action and has implications for the design of psychedelic pharmacopsychotherapies. It also raises the question of whether other classes of psychoactive drugs have an equally rich moral and political life.

Keywords: psychedelics, hallucinogens, morality and values, extrapharmacological variables, anthropology, ethnography, history, psychotherapy

INTRODUCTION: A NEW FIELD OF RESEARCH

Since the 2000s, neuropsychopharmacologists have grown interested in the neurochemical foundations of moral behaviors. Experimental paradigms from social psychology and behavioral economics have been used to study the effects of drugs, for example how antidepressants such as citalopram enhanced harm aversion and affected people's inclination to retaliate against unfairness (1), how oxytocin affected one's readiness to trust others (2) and motivated both in-group favoritism and out-group derogation (3), how regular users of stimulants showed less prosocial behavior (4), or how MDMA and LSD increased emotional empathy and altruism (5). Analogous to moral psychology, a field that emerged at about the same time, this rapidly growing body of research gave birth to a new subfield that could aptly be called "moral psychopharmacology."

THE CONTEXT DEPENDENCE OF PSYCHEDELICS VARIES THEIR MORAL EFFECTS

In the case of psychedelics, research on their moral effects is of particular importance. Politically, psychedelic drug use is likely to increase and take place in a variety of non-medical contexts as a number of jurisdictions introduce decriminalizing legislation concerning psychedelics. In May 2021, for example, Psilonautica and Drug Science, two UK-based organizations, revealed findings from a study showing that a majority of the British public support the medical use of psychedelics for trauma-based injuries and end-of-life anxiety. American cities like Denver, Oakland and Santa Cruz went further and decriminalized psilocybin, and in 2020 the state of Oregon decriminalized psilocybin and approved it for medical use. The legal prohibition on psychedelics is beginning to change, but its regulatory future remains context specific. Scientifically, the moral psychopharmacology of psychedelics is especially interesting because their effects have long been shown to depend crucially on extra-pharmacological factors. Since the 2010s, what is colloquially called “set and setting,” the subject’s mindset and their social and physical environment, has attracted renewed interest in the revival of psychedelic research. Carhart-Harris et al. (6) argued that the drugs’ 5HT_{2a} receptor agonism renders the psychedelic experience exceptionally sensitive to context, both internal and external. While common psychophysiological effects on serotonin-mediated neurobehavioral circuits may shape some of the cross-cultural similarities in patterns of psychedelic use and experiences, their cultural desirability is mostly shaped by political factors (7). What distinguishes research in this vein from research on the placebo effect is that, in the case of psychedelics, the effects of extra-pharmacological factors appear to be pharmacologically mediated and amplified. It is part of psychedelic drug action to blur the line between the pharmacological and the nonpharmacological, between drug action and social context.

This context-dependence is also of clinical importance as psychedelic-assisted therapy of depression and other psychiatric conditions combines pharmacotherapy with psychotherapy, actively mobilizing extra-pharmacological factors to improve treatment outcomes (even though ongoing randomized controlled trials do not explicitly focus on the psychotherapeutic contribution). The subjective experience shaped by set and setting might not just be epiphenomenal but causally related to the drugs’ therapeutic effects (8). Although interactions with other people crucially affect how patients experience the effects of psychedelics, in medical research, it is often a mere afterthought that drug treatments of psychiatric patients have significant implications for their social relationships (9). Outside of a clinical setting, these contextual features will be even more difficult to assess, predict, or control.

This relationship to cultural context opens up a dimension of moral psychopharmacology directly relevant to clinical work, which cannot be guided only by considerations of the normal and the pathological that usually inform medical

interventions. Thereby, the question of how drugs affect human relationships and what makes a *good* relationship comes into the purview of psychiatric drug treatment. In the clinical context, moral psychopharmacology moves from the limited ecological validity of behavioral economic games and moral dilemma experiments to issues that are highly relevant to the moral fabric of everyday life (even if the intricacies of romantic relationships or family life have not figured prominently in moral philosophy). In this respect, the moral psychopharmacology of *all* drugs that affect social behavior appears significant. Notably, recent studies highlight how psychedelics and empathogens modulate conscious decision-making and behavioral orientations in various psycho-socio-environmental domains (5, 10, 11). The pronounced context-dependence of psychedelics and their application in the context of different psychotherapeutic approaches or non-clinical uses gives particular urgency to the question of how they affect people’s moral judgment and behavior. After all, the moral effects might not be one-dimensional, simply increasing or decreasing regard for others as concerns about moral “enhancement” and “degradation” imply [(12, 13), p. 233–35, 261–63]. Instead, the moral effects of psychedelics appear to differ depending on the context of their use and the mind-set of the user.

The successful mainstreaming of psychedelics through medical research has introduced these substances to populations beyond the so-called psychedelic research community. The growing diversity of users and uses broadens the range of extra-pharmacological factors that shape the drugs’ moral effects. Historical and ethnographic research can complement contemporary neuropsychopharmacology studies with studies of cultural contexts that examine other sets and settings in relation to drug uses and effects. While members of the American counterculture used LSD, mescaline, and psilocybin as psychopharmacological tools to liberate individuals from the ills of their society, Huichol youth ingested peyote buttons to become full members of their own society (14, 15), and Native American Church worshippers consumed peyote to foster indigenous resistance to North American colonialism (16, 17). In the 1960s, psychedelics were taken to experience a mystical union that users claimed fostered a sense of universal love, but anthropologists have also described Amazonian societies that used them in rituals to prepare for violent intergroup conflict (18–20). At present, psychedelic therapists and progressive intellectuals suggest that psychedelic experiences could help to work through the cultural trauma of racist discrimination (21, 22), and one study found that intense psychedelic experiences predicted liberal political views, openness, and nature relatedness, while negatively predicting authoritarian political views [(23); but see (24)]. At the same time, a budding traditionalist scene finds inspiration in the right-wing writer and psychonaut Ernst Jünger and, according to media reports, psychedelics might also play a role in the political radicalization of far-right groups in the United States (25–27). A moral psychopharmacology of psychedelics needs to explain how pharmacological and extrapharmacological factors interact to produce such seemingly contradictory varieties of psychedelic experience.

TAKING PSYCHEDELIC RESEARCH BEYOND THE TWO-CULTURE DIVIDE

A well-established but potentially misleading account of the moral and political versatility of psychedelics draws from an older naturalist ontology that suggests that there is one nature and many cultures that interpret it differently. It has inspired a neat division of labor between the disciplines: neuropsychopharmacologists study the effects of drugs on the brain, cultural anthropologists and historians study how different groups of humans make sense of them at different points in time. In recent decades, however, both the ontological and the epistemological divide between the two cultures of the natural sciences on the one hand and the humanities and interpretive social sciences on the other hand have been called into question from very different angles. Culture is no longer the exclusive domain of the humanities and human sciences but has become an object of research in cultural neuroscience and cultural primatology (28, 29). The same is true for related ontological categories such as the mind, which used to organize the disciplinary divide between *Geistes-* and *Naturwissenschaften* in the German-speaking world but is now the subject matter of evolutionary and brain research. This new naturalism has inspired research programs in the social sciences that have sought to break down the barrier between the natural and the human by presenting the scientific objects of the natural sciences as constructed by humans (30–32). While these challenges to the dichotomies of nature/culture, nature/human, or mind/matter might not be equally compelling across all areas of study, they are germane to a class of psychoactive drugs whose effects depend on their users' personalities, expectations, and cultural beliefs as well as the social setting in which they are ingested. Studying the moral effects of psychedelics raises epistemological challenges that extend across the divide between the natural sciences and the humanities (33).

More recently, extra-pharmacological factors have attracted attention in psychedelic research, which again stimulates interdisciplinary debates and transdisciplinary collaborations (34, 35). The experiential diversity of psychedelic states calls for novel approaches combining phenomenological methods and empirical research to better understand the structure and dynamics of altered states of consciousness that go beyond their conceptualization as “brain states”. Social anthropologist David Dupuis, clinical psychologist Rosalind Watts, and neuroscientist Christopher Timmermann propose moving beyond research that correlates first-person reports and third-person measurements of brain activity and attend to the second-person dimension of what they call “psychedelic apprenticeship” (36). Their focus on the social mediation of psychedelic-induced experiences can account for why psychedelics have turned out to be a “double-edged sword” that can either benefit or harm their users—or even do both at the same time. Psychedelics have been shown to increase suggestibility while concealing this influence of others by endowing visions with a noetic quality, a deep sense of having obtained unmediated knowledge that requires no external validation or evidence (37–39). This more variable set of outcomes opens up the possibility of harnessing

psychedelic apprenticeships to different therapeutic goals and ethical projects. Subjects undergoing drug-induced mystical experiences might even be steered toward religious conversion and New Age spiritualities—a prospect that has raised concern among psychedelic psychotherapists who seek to secularize the field and worry about the abuse of power on the part of guides and therapists (40, 41).

The context sensitivity of psychedelics entails that randomized placebo-controlled trials are insufficient for appreciating the full range of their possible effects, nor do they capture the diverse ways in which consumers may encounter psychedelics in medical and non-medical settings alike. If the pharmacological activity of a drug changes the relationship between a living thing and its environment in ways that depend on the living thing's mindset and the particular quality of the environment, then the environment would be inscribed in the observed pharmacological effect—even if the placebo effects were subtracted from the effects of the verum. In the 1950s, anthropologist Anthony Wallace had already noted that Euro-American subjects who had received mescaline in the laboratory reported very different psychotropic effects than Native Americans who had eaten peyote buttons in religious ceremonies. At a time when placebo-controlled trials only just emerged as the gold standard of pharmacological research, Wallace proposed to complement them by culture-controlled trials that tested the same drug at the same dosage under different social and cultural circumstances [(13), p. 116–26, 185–92; (42)]. Reanimating this largely forgotten approach today would provide moral psychopharmacology with an opportunity to import experimental paradigms from social, moral, and political psychology.

“UPSTREAM” DESIGN OF NEW USES OF PSYCHEDELICS

The ethical plasticity of psychedelic-induced experiences poses a formidable bioethical problem. Usually, bioethics offers a moral evaluation of the social consequences of new biotechnologies or pharmaceuticals. For example, debates over antidepressants or so-called cognitive enhancers assumed that the drugs have certain effects established by clinical observation and psychopharmacological experiment, while bioethicists evaluated the social consequences of these effects downstream from pharmacology and proposed how to regulate the drugs' applications. A growing body of bioethical literature on psychedelics evaluates the use of psychedelics to neurochemically enhance the sense of meaning in psychedelic-assisted psychotherapy and their use to develop virtues, suppress vices, and enhance moral behavior (43, 44). What distinguishes the notion of psychedelic moral enhancement, as advocated by some authors, from traditional notions is that it recognizes that amplifying particular aspects of prosociality produces trade-offs and adverse effects. For example, MDMA boosts prosocial behavior toward members of one's in-group but not toward the outgroup, which can result in a redistribution of limited resources (45). However, if psychedelics reduced their users'

sense of self-importance, they might free up resources in favor of both neighbors and strangers, increasing other-regard solely at a cost to egocentric motivations (46, 47).

This model of bioethics presupposes conceptions of what counts as moral and measures technologies against them. It is based on a separation of technology and morality, means and ends. However, psychedelics present a case where the means transform the ends. Although a recent trial by Carhart-Harris et al. comparing psilocybin and escitalopram in long-standing, moderate-to-severe major depressive disorder did not show significant difference in antidepressant effects, it produced secondary effects on qualitative dimensions of psychosocial functioning that transformed patients' attitudes toward themselves, others, and the world (48). Notably, patients from other trials undergoing conventional treatment for depression reported that medications and short-term talk therapies tended to reinforce their sense of disconnection and avoidance, whereas psychedelic treatment encouraged connection and acceptance or a sense of "reconnecting" with past values that had faded over the years (49–51). Of course, these experiential reports leave open whether people actually reconnect with their own values, what role their heightened suggestibility plays in this process, and whether the pharmacological modulation of affective relations to the world and to others privileges certain moral and maybe even political transformations over others. Do different psychedelic compounds produce different moral effects and ethical orientations? How do psychedelics compare with other classes of psychotropic drugs? Whatever the mechanism, variability, and scope of such pharmacological transvaluation of values, it led psychiatrist William Smith and medical ethicist Dominic Sisti to call for an enhanced consent process acknowledging that patients might experience significant shifts in their ethical outlook and worldview, which they cannot fully foresee from the perspective of their pre-therapeutic self (52). The challenge is to invent new research practices that observe and reflect on the combining of neurochemistry and morality in the laboratories and clinics where this amalgamation is happening.

Another challenge involves observing how psychedelics are used beyond the laboratory and the clinic, turning psychopharmacology into a field science by adopting practices from ethnopharmacology, ecology, and other areas of field biology. For instance, battery-powered EEG equipment already allows one to study in naturalistic settings how ayahuasca, an Amazonian jungle environment, guidance by experienced ayahuasceros, and other variables concur in their effect on brain waves, and placebo-controlled field experiments seek to tease apart the impact of pharmacological and extra-pharmacological factors in such an ayahuasca ceremony (53, 54). Other field sciences such as cultural primatology that use recent advances in statistics to explain how complex interactions between large numbers of ecological factors shape animal behavior might provide further methodological inspiration for how to study the interplay between pharmacological and extrapharmacological factors [e.g., (29, 55), p.180–90; (56)].

Finally, the challenge is to study historical uses of psychedelics as natural experiments that shed light on the context dependence

of the psychedelic experience. From a regulatory perspective, it will still largely depend on randomized placebo-controlled trials, whether psychedelics will have a wide or a restricted role as prescription medicines. The goal is not to replace but to complement those trials, as a wide range of contextual variables are likely to determine the therapeutic benefits of psychedelics. An upstream approach to the morally transformative effects of psychedelics places psychopharmacologists, psychiatrists, social researchers, and humanities scholars side by side to study, assess, and redesign psychedelic experiences in their social, cultural, and historical contexts (57, 58). Ideally, laboratories and clinical trial sites would embed anthropological, sociological, and philosophical observers instead of keeping them cordoned off in their respective university departments. Ethnographic descriptions and comparisons of the uses of psychedelic drugs at different sites, including non-medical sites, could be fed back into the fashioning of new uses. First-hand familiarity with research and therapeutic practices as well as everyday personal contact enable members of different disciplines to inform each other's thinking and devise approaches that make good use of the context dependence of psychedelics in light of ongoing discussions of what constitutes a *good* use.

CONCLUSION: EXTENDING RESEARCH AND DEVELOPMENT INTO THE EXTRA-PHARMACOLOGICAL REALM

If moral psychopharmacology took it upon itself to develop forms of psychedelic apprenticeship for the currently sprawling medical and non-medical applications of psychedelics, it would extend pharmaceutical research and development into the extra-pharmacological realm. Such a design process needs to be informed by best practices in clinical psychology and cognate fields, but, intellectually, it cannot hide behind professional prescriptions because what counts as good and bad is precisely what is at stake here. It is an open philosophical question that has to be answered in a recursive process of psychopharmacological experimentation, clinical and ethnographic observation, historical research, and ethical reflection. The evaluation of new uses of different drugs in the laboratory, the clinic, and in the wild should not be confined to the armchair, removed from these spaces and the experiences they engender. That is why research and development of psychedelics in context also requires research and development of knowledge cultures that bridge the gap between neuropsychopharmacology, social research, and the humanities. It is an empirical question whether such a blending of moral psychopharmacology with moral inquiry would remain confined to psychedelics because of their peculiar pharmacological properties, or whether it could become a model for working with other classes of psychotropic substances as well.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

NL, DR, MS, and ED contributed to conception and design of the manuscript. NL wrote the first

draft of the manuscript. DR, MS, and ED wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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On Revelations and Revolutions: Drinking Ayahuasca Among Palestinians Under Israeli Occupation

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The ritualistic use of ayahuasca can induce a feeling of unity and harmony among group members. However, such depoliticized feelings can come in the service of a destructive political *status quo* in which Palestinians are marginalized. Through 31 in-depth interviews of Israelis and Palestinians who drink ayahuasca together, and through participatory observations, such rituals were examined. In this setting marginalization was structurally rooted by the group's inability to recognize Palestinian national identity or admit the ongoing Israeli injustice toward Palestinians. Although the groups avoided politics, they still find their way into these rituals. This happened through occasional ayahuasca-induced revelatory events, in which individuals were confronted with a pressing truth related to the oppressive relations between Jewish Israelis and Palestinians. Three case studies of such revelatory events are described in this paper. Affected by emotions of pain, anger, and guilt, these participants developed resistance toward the hegemonic Israeli ritual structure. This was followed by an urge to deliver an emancipatory message to the rest of the group, usually through a song. Moreover, affected subjects developed a long-lasting fidelity to the *truth* attained at these events. In time, this fidelity led to the expansion of ayahuasca practices to other Palestinians and the politicization of the practice. The article draws on Badiou's theory in *Being and Event* (1988) to analyze the relations between the Israeli ritual structure, the Palestinian revelatory event, and the emancipatory fidelity that followed. Badiou's theory elucidates the egalitarian revolutionary potential, which is part of the sociopsychopharmacology of psychedelics.

Keywords: ritual, psychedelics, Badiou's *Being and Event*, Israeli-Palestinian conflict, New Age, activism, DMT, prophecy

INTRODUCTION

During an ayahuasca ritual on the Jewish holiday of Yom Kippur (Day of Atonement), Ruqaiya had a painful historical revelation. She saw cycles of war, blood flowing onto the land, and mothers who sacrifice their children.¹ As a Palestinian citizen of Israel who had denied her national affiliation in the past, she finally recognized the longstanding injustice of the Israeli occupation of her people.

¹ All interlocutors' names are anonymized, and identifying information has been slightly modified to maintain privacy.

Embodying the agony of the land, she expressed her anger in a song, which interfered with the harmony of the ritual. Singing *al-Fatiha* (the opening verses of the Quran) with great vigor, she attempted to deliver an emancipatory message as a Muslim to the Jewish Israeli participants attending the ritual: fasting on Yom Kippur is not enough, since a political reparation is necessary for their atonement. While some of the Jewish Israeli participants rejected her message, the political intensity of the moment was unavoidable. Ruqaiya's particular feelings that evening about Palestinian subjugation were associated with a universal truth of liberation and equality for all. Her loyalty to this revelatory event changed her life and gave her a new sense of mission. She became a facilitator of ayahuasca rituals that incorporate Palestinian cultural elements and political awareness into the practice.

Ruqaiya's delivery of her vision was unusual in the context of organized Israeli ayahuasca rituals in which Palestinians participated. Kept strictly "apolitical," the gatherings, directed by the Israeli organizers, carefully maintained a discourse of denationalized unity. "Mysticism unifies, while politics divide," was a statement occasionally heard while conducting fieldwork in such mixed groups. However, politics were unavoidable, even in such "protected" settings. While participants often experienced visions related to the political violence in Palestine/Israel, some were so deeply affected by what they felt that they were compelled to speak truth to the group. Based on interviews with individuals who went through such life-changing events, this inquiry was initiated to problematize the discourse about peace in these rituals and examine how psychedelics may provoke the formation of politicized subjectivities.

Ayahuasca is a psychedelic Amazonian brew whose main pharmacologically functional components are two plant-derived ingredients: dimethyltryptamine (DMT), a classic tryptamine psychedelic, and a mix of monoamine oxidase inhibitors (MAOIs) that prevent the breakdown of DMT when consumed orally (Rivier and Lindgren, 1972). The effect of psychedelics is known to be context dependent (Carhart-Harris et al., 2017; Hartogsohn, 2017, 2020), and psychedelics are known to produce a myriad of intense experiences (Dobkin de Rios, 1973; Shanon, 2002); they therefore are referred to as "non-specific amplifiers" (Grof, 1975/2016). The cultural influence on the visionary experience (La Barre, 1938/1975; Wallace, 1959; Langdon, 1979) has recently been termed the "socialization of hallucinations" (Dupuis, 2021). It is suggested that the goals of the practice—for example, the ways in which healing is achieved—can influence the content of the psychedelic experience. For instance, within a Christian Amazonian rehabilitation program, ayahuasca healing of "possessed" patients is mediated through the experience of exorcism (Dupuis, 2018). In comparison, within Western clinical trials, psychedelic healing is mediated by the *mystical union* (MacLean et al., 2012; Roseman et al., 2017). In both cases, elements of the context and the intentions behind the practice increase the possibility that the desired experience will take place.

The mystical union is an experience in which one feels interconnectedness with others and the universe (Pahnke and Richards, 1966; Shanon, 2002; MacLean et al., 2012). A fusion of the self with a larger whole, the mystical union represents peace, harmony, oneness, and acceptance. In the context of

peacebuilding, such representations can at times strengthen relations between participants but may also conceal, and even deny, the violence that one group inflicts on another. According to research in intergroup contact, those in power seek harmony, friendship, and "connecting as humans," while those with less power seek liberation and decolonization (Abu-Nimer et al., 2007; Saguy et al., 2009; Maoz, 2011). Indeed, for Palestinians, who suffer from Israeli settler colonization, occupation, and subjugation, "peace" does not necessarily equal harmony. Rather, in their contact with Israelis, they seek justice, equality, and recognition (Leshem and Halperin, 2020).

While psychedelic experiences are often expressed in terms of unity and harmony, history suggests that there is a revolutionary potential in psychedelic molecules that can promote resistance to hegemony and disruption of the *status quo* (La Barre, 1938/1975; Lee and Shlain, 1985; Taussig, 1987; Musalem Nazar, 2016; Hartogsohn, 2020). The association with resistance stems from the fact that not only are psychedelics used by countercultures and colonized people but they also stimulate radical revelatory events. Indeed, after Ruqaiya had her political revelation, she attempted to disrupt the oneness of the ritual by exposing the truth about how Palestinian suffering is caused by Israelis. Since prophetic revelations have a long history of igniting political movements (Mooney, 1896/1991; Wallace, 1956; Taves, 2016), we contend that the potential of revelation-to-revolution is part of the sociopsychopharmacological repertoire of these substances.

In this sense the revelatory experience stands in a dialectical phenomenological tension with the mystical union, as they serve opposing political processes. Unlike the abstract mystical union, the prophetic revelation comes with a concrete ethical-political message. While the archetypal mystic aims to dissociate from worldly matters and transcend good and evil, it is the archetypal prophet who cries out against atrocities and injustice (Thorner, 1965). The former usually maintains the harmony and stability of the *status quo*, whereas the latter seeks to destabilize and dispute the order of things so as to achieve a greater good (Heiler, 1919; Thorner, 1965; Scholem, 1971/2011; Williams, 1983; Idel, 2000).

Drawing on Alan Badiou's theory of events (Badiou, 2007, 2019), we analyze how participants act upon revelatory experiences during, and after, ayahuasca rituals. In his work Badiou argues that every structured situation can be understood as a *status quo*. There will, however, always be ways to engage with experiences that are part of the situation but that are excluded from the structure. Badiou defines such unusual ontological experiences as "events" that may create a rupture in the structure when recognized. Subjects, who go through this moment of recognition, face a "universal truth" beyond the structure, to which they maintain fidelity. According to Badiou, such subjects develop "fidelity" to a mission related to that truth, which they soon seek to fulfill. In this mission, they aim to include what was previously excluded from the structure. Therefore, Badiou's events are not only revelatory but also revolutionary, as they inherently oppose any *status quo* and aim to force radical change.

In this paper, we propose that the structure of the observed ayahuasca rituals mirrors the sociopolitical structures of the Israeli state and society, which exclude Palestinians, their history, and their collective rights. We argue that the New Age emphasis

on mystical union, harmony, and personal transformation in these rituals secures Israeli hegemony over Palestinians by suppressing conflict. Furthermore, we maintain that changes to the *status quo* of the ritual can occasionally occur through the resulting process of fidelity, in which the subject who had the political revelation develops a sense of mission to challenge, and potentially alter, the structure of the rituals according to the newly perceived universal truth. In this sense, such revelatory events are part of the phenomenological repertoire of psychedelics that can make them counterhegemonic by inciting resistance to the *status quo* through the subjective sense of fidelity to the event. While such psychedelically-induced fidelity has an egalitarian trajectory, it can be suppressed by agents who maintain the structure in the name of unity and harmony. Finally, as we demonstrate below, these revelatory events may lead to the expansion and diversification of psychedelic practices.

In what follows, we begin with an elaboration on Badiou's "event," and continue with a background discussion on the distinction between the psychedelic experiences of mystical union and revelation. We then offer a contextualization of the observed ayahuasca rituals in Israel, in which we suggest that they are structured around a depoliticized New Age culture that avoids acknowledgment of the injustice inflicted upon the Palestinian collective by Israelis, especially that which comes about through the denationalization of Palestinian citizens of Israel. Following this, we present three cases in which participants had agonizing political visions related to the excluded Palestinian existence. Attending to interventions in the rituals' structure, we discuss the tensions that exist between the subject's fidelity to the event and conformation to the existing structure. We conclude by suggesting that such events are part of the sociopsychopharmacology of psychedelics and that their analysis in relation to the structure can reveal different political dynamics that are part of psychedelic cultures and the psychedelic movement.

BADIOU'S EVENT: REVELATION, FIDELITY, AND UNIVERSALITY

In *Being and Event* (2007), the cornerstone of his work, Badiou uses set theory to propose a politicized philosophy that describes the process of revolutionary events. Importantly, while such an event is a moment of recognition and revelation of a truth, its aftermath is the active procedure that leads to change. For change to take place, the event must unfold through an individual or a collective, and fidelity to the realized universal truth must follow.

For Badiou, reality is infinite, multiple, and inconsistent, without any inherent unity. Any "situation" consists of a set of elements grouped together, giving it structure. A situation can be made of anything, regardless of its modality. It can be objects, people, language, circumstances, dreams, art, concepts, and so on. The inclusion of different elements in the structured situation is an "operation" which organizes the situation into sets of elements. This operation is termed "count-as-one," suggesting that the structure is the appearance of unity which is imposed on

the situation. Some elements of the situation are included in the structure, while others are excluded—relegated to the "void."

Usually, we experience the world only through structured situations, and the void, according to Badiou, can be thought of as the "unconscious of the situation" (2007, 66). The *status quo*, which consists of such things as ideology, language, discourse, and social norms, prevents the revelation of the excluded elements. These governing principles of the status-quo (termed also the "state-of-the-situation," or the "metastructure") secure the situation and keeps it from being disrupted by what exists in the void. Yet, a truth from the void can occasionally break through. Such truth exceeds the knowledge and language of the situation, and is inherently related to the void—to what is not included in the structured situation. An event is a moment that reveals what the *status quo* tries to conceal—the momentarily irruption of truth. "Event sites," located at "the edge of the void" are where the rupture of the structure—through the event—might occur (2007, 175), and where a truth might enter. The event that momentarily amplifies the site will eventually require a restructuring in order to include the new truth. In such a restructuring, parts of the structure and parts from the void become connected to the event, and this process of establishing new connections occurs through "truth procedures." Such procedures are revolutionary processes, as they oppose the *status quo* in an attempt to restructure the situation, and they may occur in love, art, science, or politics (2007, 335).

In the context of psychedelics, Saldanha (2007b) argues that Albert Hofmann's discovery of LSD in 1943 can be considered a Badiouan event. In a moment of strong rupture in the understanding of the sociochemical structure of that time, the discovery of LSD resulted in a few truth procedures that transformed Western society. These procedures were attempts to include an altered state of consciousness in a structure that excluded them. The mind-liberation movement of the 1960s had a counterhegemonic universal trajectory, and the truth procedures opposed the *status quo* of that time, which was epitomized by the conformity and uniformity of the 1950s. However, we use Badiou's theory differently. We suggest that the sociopsychopharmacological action of psychedelics can increase the possibility of events occurring. In other words, it is not just truth procedures which stem from Hofmann's 1943 event, in attempt of including the excluded psychedelic experience, but also truth procedures which follow specific revelatory events that are recognized in specific situations under the influence of psychedelics.

Truth procedures materialize through the *subject*, who now attempts to change the situation and its structure. The subject is the "bearer" of the truth procedure and is "taken up" in fidelity to the event (2007, 406). The event prompts the subject to question the *status quo* and the knowledge instilled in the structured situation. The subject, in fidelity, is characterized by a sense of mission, confidence, and loyalty to the universal truth of the event, which leads to resistance to hegemonic structures. In this sense, one does not contemplate truth; rather, one acts, as a subject, on it. Acting in fidelity to the event, the subject does not reject the whole situation, but attempts to restructure it by connecting all of the elements that are related to the

event. According to Badiou, such subjects develop an emotional attachment to their new mission. A political subject is filled with enthusiasm for a new maxim of equality, whereas an artistic subject is filled with pleasure regarding a new perceptual intensity; a loving subject experiences happiness because of a new existential intensity; and a scientific subject is filled with the joy of new enlightenment (Badiou, 2019, 76).

While truth procedures are related to a particular situation, Badiou argues that they also reveal something universal. This claim is in opposition to his postmodern and post-structuralist contemporaries. While similar to them, he embraces the emphasis on plurality and multiplicity, he also discusses the possibility of universal truths. Such conceptual and philosophical disagreements about universalism can be considered perennial (Balibar, 2020). One of the main lines of argument against universalistic discourse is that while it insists on total inclusion, it violently silences voices that claim particular marginalized identities (Taylor, 1997). In this sense, universality will always be situational and defined by a particular hegemony. Saldanha's (2007a) description of the exclusively white trance music scene in Goa, India, is a relevant psychedelic case of this conundrum. In his work Saldanha shows how unity is achieved by preserving racial and cultural boundaries. It prevents Indians, as Others, from participating and interfering in the ecstatic oneness on the dance floor. If unity, as similarity, is prioritized over universality, then only an exclusive illusion of universality will take place.

To aspire to broader universalism, the unity of the structure must be challenged. Indeed, for Badiou, universalism is the guiding star of the truth procedure. It points the way to what is not represented by the excluding *status quo*. Badiou's universality is always dependent on the situational particularities that it has to overcome. Therefore the subject's fidelity to the event depends on the exclusivity of the structure, so that the subject is somewhat divided between the event and the structure (Robbins, 2010). The truth procedure is either concluded, once the existing structure is reformed, or reversed, once the structure successfully contains the event without changing.

AYAHUASCA AND REVELATORY EVENTS

No one can claim with certainty when and where ayahuasca practices originated, yet it is known that most of its diffusion across the Amazon Basin occurred during the last 300 years. This was influenced by Christian missions (Gow, 1994), the rubber boom of a century ago (Brabec de Mori, 2011), and the recent expansion of shamanic tourism (Winkelman, 2005; Fotiou, 2010), neoshamanic practices (Scuro and Rodd, 2015), and the Brazilian syncretic ayahuasca churches (Labate and MacRae, 2016). Therefore, many of the characteristics of what is known today as "traditional" Amazonian shamanism were actually developed in response to colonial atrocities (Taussig, 1987) and interaction with the West (Langdon, 2013). Therefore, some of the indigenous and mestizo practices of ayahuasca are political

(Taussig, 1987)². These include strengthening tribal coalitions and relations to the land, as well as resistance to white colonizers (Langdon, 2016; Musalem Nazar, 2016).³ For example, the Siona communities have used ayahuasca as a strategy for ethnic revitalization and re-indigenization of mestizo people; ayahuasca has helped draw those who had been urbanized and acculturated back into the tribe. It also helped in building alliances with academics, political activists, and artists. Such political use of ayahuasca eventually guaranteed their ethnic survival (Langdon, 2016). In Western countercultures, psychedelics have also been historically related to antihegemonic revolutionary tendencies (Lee and Shlain, 1985). Such tendencies occurred as a result of fidelity to the LSD event, in an attempt to popularize psychedelics (Saldanha, 2007b) and/or—as we suggest here—through critical insights and revelations reached while under the influence of psychedelics (La Barre, 1938/1975; Winkelman, 2010; Luna, 2011; Labate and Cavnar, 2014; Strassman, 2014; Davis et al., 2020, 2021). Regardless of the way in which they were induced, similar revelations are known to come with the enthusiasm to deliver the message to others, which at times developed into social movements (Mooney, 1896/1991; Wallace, 1956; Lanternari, 1963; Whitehouse, 2004; Taves, 2016).

In the context of psychedelics, two notable revelatory events had a wide impact. The first is the ayahuasca-induced revelation of the "Queen of the Forest" (the Virgin Mary) to Raimundo Irineu Serra, a Black rubber tapper, who later became the founding father of the Santo Daime church (Moreira and MacRae, 2011; Orgad, 2012; Labate and MacRae, 2016). This moment marks an expansion of the practice from indigenous people in the Amazon Basin to a syncretic inclusive practice that eventually had a global impact. The second revelatory event is that of Alan Ginsberg, guided by Timothy Leary.⁴ During a *Psilocybe* session, Ginsberg had a messianic revelation of world peace, during which he tried to call world leaders on the phone while running naked through the apartment—like Archimedes in his eureka moment. In fidelity to this vision, Leary and Ginsberg decided to promote "psychedelics to the people," beyond academic, clinical, military, and governmental circles (Leary, 1968/1995; Connors, 2010; Hartogsohn, 2020).⁵

There are important ethical considerations related to psychedelic-induced revelations and how one should follow them, as their content may be imposed on participants by facilitators (Timmermann et al., 2020). Therefore a "gentle touch" is required when dealing with such sensitive states of mind. Nevertheless, not every psychedelic insight is an *event* in the Badiouan sense. We claim that some psychedelic revelatory events are unique, as they expose something that is ignored by

²Taussig (1987) argues that ayahuasca visions of the historical collective trauma of indigenous people fueled its revolutionary potential in the Amazon.

³Similar patterns were observed with peyote in Central and North America (Mooney, 1896/1991; La Barre, 1938/1975).

⁴Leary was informed by Ginsberg and William Burroughs as to how the Amazonian curandero (a healer who uses plant medicines) facilitates yagé rituals. Leary then played this ritualistic role.

⁵While breaking off from institutional exclusivism and Huxley's elitism, this schism occurred in parallel in multiple places—e.g., Ken Kesey and the Merry Pranksters' West Coast psychedelia (Wolfe, 1968/2008; Saldanha, 2007b).

the facilitators or the culture in which the experience takes place. Such events can be recognized by some distinctive characteristics. They begin with a degree of separation, at times agonizing, from an exclusively structured “unity” of the group. Revealing what is excluded from the structure, these revelations are by definition counterhegemonic, since they incite resistance to the group’s *status quo*. Soon after, the receiving subject is aligned in fidelity to the event and embarks on an emancipatory mission, in which s/he seeks to spread the attained universal truth. Finally, these revelations may create a split in the structure, to achieve a more inclusive unity.

PALESTINIAN IDENTITY IN THE ISRAELI AYAHUASCA RITUAL STRUCTURE

Ayahuasca rituals spread to Israel two decades ago through the Brazilian Santo Daime church and neoshamanic practices. Palestinians, especially citizens of Israel, joined these rituals around 10 years ago. This came along with the rise in consumption of psychedelic substances, especially in the Palestinian rave scene (Karkabi, 2021). However, their access to ayahuasca practices has been mediated through Jewish Israeli circles. While many Israelis travel to South America on post-military-service journeys (Noy and Cohen, 2005), during which they become acquainted with globalized ayahuasca networks, Palestinians have been more restricted in their international movement. This is so owing mainly to their relatively lower socioeconomic status and travel restrictions imposed on Palestinians from the West Bank and Gaza. Palestinians who joined the Israeli rituals were a small minority, as well as less experienced. Therefore, they often had to rely for support on Jewish Israeli group organizers, facilitators, musicians, helpers, and participants. In addition, some of the sites where the rituals took place were at homes and on land confiscated from Palestinians by the Israeli state and redistributed to Jewish Israelis. As the mother tongue of Jewish Israeli participants, Hebrew was the main language spoken during these rituals, yet for Palestinians it was a second language, after Arabic, or a third, after English.

Palestinians, especially novice participants, were clearly outsiders at these gatherings. They had less subcultural capital, which relied heavily on Israeli New Age spiritual jargon and social norms. More important, they were alienated from the influence of Jewish religious and Israeli national elements. In some groups such influences included a kiddush (religious Jewish blessing) before drinking the “medicine” or an *icaró* (Peruvian shamanic song) based on Hebrew lyrics of the Israeli national anthem, with some New Age adaptations.⁶ Furthermore, well-known Israeli songs, such as “A Walk to Caesarea,” also known as “Eli, Eli” (My God, my God), and “Mi ha’ish” (Who is the man) suggested universal and humanistic messages, but were associated for Israelis with national memorial days, such as Yom ha-Zikaron (Memorial Day for the Fallen Soldiers) and

Holocaust Day. Among Israeli Jews, these songs are endowed with national and spiritual solidarity, unity, belonging, and a sense of homecoming. This “homecoming” of Israeli Jews also implies the displacement of Palestinians.

However, since the Israeli New Age culture holds an allegedly apolitical ideology (Simchai, 2009), most Israeli participants in the observed rituals positioned themselves “beyond left and right.” Claiming that “peace starts from within,” they welcomed Palestinians, based on humanistic ideology. Under this ideology, the ongoing history of colonial oppression is denied, so that the conflict is considered an “illusion,” and “the political game” should be avoided so as not to raise divisions. While downplaying sociopolitical hierarchies, inequalities, and power relations, some of these groups proudly celebrated the different cultural (Jewish and Arab) and religious (Jewish, Christian, and Muslim) background of each participant. They argued that listening to the music of other cultures “opens the heart” so that “peace is felt in the air.”

The denial of national identity of the Palestinian minority in Israel is not exclusive to the context of the Israeli ayahuasca rituals, as it matches wider political tendencies among the majority of Jewish Israelis and reflects many state policies. Defeated and dispossessed of their lands, the Palestinians who remained in Israel after the Nakba (catastrophe) in 1948 faced military rule until 1966 and eventually were granted Israeli citizenship (Robinson, 2013). Since then, however, they have been subject to Israeli policies that have denationalized, racialized, and fragmented them into religious subminorities. Thus, they became known as “Israeli Arabs” or Muslim, Christian, and Druze minorities (Kanaaneh, 2008). As non-Jews, however, they were not fully part of the Israeli nationality and hence could not become equal citizens in Israel, as long as Israel remains defined as the nation-state of the Jewish people. Although this limited assimilation of the “Israeli Arabs” retained Palestinian national identification among some, it led others to adopt an integrative politics of civil equality, in the hope of individual acceptance into Israeli society (Ghanim, 2020). While national exclusion and racism toward Palestinians has only increased in the last decade, backed by a series of undemocratic laws issued in the Knesset (Adalah, 2017), economic liberalization in Israel increased employment opportunities to a growing middle class of Palestinian citizens (Sa’ar, 2016).

It is within this context that we understand the appeal that Israeli ayahuasca rituals have for middle-class Palestinian citizens of Israel. Along with moments of intercultural and interfaith unity, the rituals promised New Age universalist spirituality, based on the allure of a collective experience of “oneness” and “identity dissolution” (Roseman et al., 2021). For example, Sawsan, a Palestinian citizen of Israel, described what drew her to these rituals: “We are all together, no Jewish, Arab, Christian, Muslim. Everything fades. All that nonsense is laid low and all that is left is acceptance and love.” With the same attitude, many other participants, Israelis and Palestinians, asserted that ayahuasca strips away identities and that everyone can connect “on the level of the soul,” as “human to human.” However, relating to difference, Sawsan explained that each language and culture has its own “frequency” and that the union of all frequencies

⁶Rewording songs is a common practice in Israeli New Age culture, see Simchai (2009).

is “the white light.” Here, diversity comes to express oneness, a feeling of connection and harmony. A sense of tribal connection and love develops among group members, but it does not guarantee equality or recognition, mainly because the looming political tension is kept strictly silent.

As research on the New Age culture in Israel suggests, the problem is that “blindness toward ethno-national identity reinforces identification with a self-evident hegemonic perception, thereby leading to the exclusion of peripheral groups such as indigenous populations” (Simchai and Keshet, 2016). While it is easy to unify Jews and Arabs as offspring of the same ancestral patriarch who worship the same God, it is much harder to unify Israelis and Palestinians by their attachment to the same land. Therefore, diversity is included in the ritual as long as it is apolitical and non-conflictual. Similarly to some dialog groups between Palestinians and Israelis that do not involve the use of psychedelics (Maoz et al., 2002; Abu-Nimer et al., 2007; Maoz, 2011), these rituals avoided dealing with the violent atrocities that Israelis have inflicted upon Palestinians. The displacement, dispossession, and colonization of Palestinians, both past and present, was silenced and ignored. The “irony in harmony” is that such pseudo-equality can create false perceptions that eventually inhibit actions that might lead to actual equality (Saguy et al., 2009; Hasan-Aslih et al., 2019). The focus on harmony in the observed groups led to the preservation of ethnonational power relations in these rituals, just as they are in the wider social and political structure in Palestine/Israel. Driven by a settler-colonial exclusivist ideology, which is justified by theological righteousness, most Jewish Israelis are reluctant to give up privileges and share equal civic and political rights with Palestinians (Wolfe, 2016). Thus, the experience of “oneness” challenges neither the Israeli political structure nor the Israeli structure of ayahuasca rituals; rather, it stabilizes it at a *status quo* in which Israelis dominate Palestinians.

In Badiou’s terms, Palestinian identity is kept “on the edge of the void” (2007, 176) to preserve harmony. It is a potential event site that is not connected to other parts of the structure. In this sense, Palestinian language, music, and religions can be part of the ritual structure as long as they are not explicitly considered Palestinian. For example, Arabic music can be part of the structure through New Age multicultural universalism. Similarly, Muslim prayers can be included through perennialism, which argues that the mystical union is at the core of all religions (Huxley, 1945). Yet, what is completely excluded from the structure is the recognition of Palestinian identity as the locus of the ongoing Israeli history of injustice. It is this history that makes the event site unstable, occasionally allowing the experience of radical revelatory events.

In the following sections, we detail three cases in which revelatory events were related to the collective trauma of the Palestinian people. Induced by the consumption of ayahuasca, these were moments in these rituals in which the stabilizing oneness was ruptured. We demonstrate how the affected subjects were first separated from the group and then driven by agony and anger that ignited their truth procedures. Taken up in fidelity to the visionary event, they each attempted to intervene in the rituals’ structure by delivering an emancipatory message,

in the form of a song, to the rest of the group. While their message came as a demand to recognize the injustice that Jewish Israelis have been causing Palestinians, it also aimed to achieve inclusionary universalism, in the rituals and beyond. Although at times these subjects were somewhat successful in changing the rituals’ structure, they often had to act outside of it to establish a more accepting ritualistic structure for Palestinians.

MATERIALS AND METHODS

The three case studies presented in this manuscript are part of a larger research project that examines relations between Palestinians and Israelis in the field of ayahuasca rituals. For detailed methodology section see Roseman et al. (2021) and its supplementary section. In short, most of the data for this project was gathered in 2018–2019 through 31 in-depth interviews: 13 with Palestinians (five women, and eight men; nine have Israeli citizenship and four live under occupation in the West Bank) and 18 with Jewish Israelis (eight women, nine men, and one non-binary person), all between 28 and 59 years old, who participated to various extents in these mixed rituals. Interviewees belonged to five different ayahuasca groups, mostly facilitate by Israeli Jews. Facilitators and musicians lead the ritual with music, yet most rituals had participatory elements as well. There were moments in which the group sang together, and by the second half of the ritual participants were able to share their own music or prayers. Rituals included around 20 participants in average. The first author had an initial connection to some interviewees, which then introduced him to others through a snowball manner. However, the interviewees sample was a *purposeful*, so that we attempted to choose diverse informants in order to achieve reliable and generalizable data (Mason, 1996).

In-depth semi-structured interviews were conducted in Hebrew, Arabic, and English⁷. Each interview lasted from one to two and a half hours. All interviews were recorded and transcribed. The microphenomenological interview technique was used whenever an interviewee reported important experiences and events from the rituals that had political implications (Petitmengin, 2006). This technique was crucial for “zooming-in” on small details of the revelatory events presented in this paper. Author 1 also conducted participatory observations in five rituals of different such groups for complementary ethnographic data collection. Furthermore, follow-up interviews were conducted 1 year, and 2 years, after the first interview for the three interviewees described in the case studies.

The analysis was based on the grounded theory approach (Glaser et al., 1968). This approach emphasizes hypothesis-free bottom-up generation of concepts and themes. In line with this approach, several stages of analysis were undertaken (Berg, 1988/2004; Strauss and Corbin, 1990; Shkedi, 2003, 2019). The first phase included a thematic analysis of the interviews, which revealed thematic categories. Through a process of reading and re-reading the interviews, the number of categories was reduced

⁷Interviews in Hebrew were conducted by the first author, in Arabic by Antwan Saca, and in English by Natalie Ginsberg.

by combining similar categories and focusing on those that emerged as most relevant. These categories were scrutinized again for centrality (repeated appearances across interviews and observations), for the connections between them, and for their relevance to the study and the questions it addresses. The software Narralyzer was used to organize and codify the interviews (Shkedi and Shkedi, 2005). Narralyzer is a simple software for organizing and structuring qualitative data, and no automatic analysis was conducted.

In a previous paper from the same dataset, fifteen conflict-related revelations were identified (Roseman et al., 2021). Out of which five were defined as political revelatory events based on the theoretical framework of the current paper. The three revelatory events that are presented here were chosen based on having a detailed description of both the event itself and the developments that followed it. The description of the case studies is mainly based on the three interviewees, yet some information is used from other interviewees who attended the rituals in which the revelatory events took place. The ethnographic analysis of the context section above is based on all of the gathered data.

REGAINING A SELF-DENIED SELF

Identifying as an “Israeli Arab,” Khalil grew up in the Galilee and went to a Jewish Israeli school, where he was denationalized and assimilated to become very critical toward Palestinians. Looking back, he says that he “was a person who denied his own Arabness.” A supporter of right-wing Israeli politics, in his youth, he even wanted to serve in the Israeli army. Dispossessed of his national history and identity, Khalil reached ayahuasca rituals when he was in his 50s. He wanted to heal a personal trauma inflicted upon him by a childhood friend and heard that ayahuasca can help people purge their trauma. As the healing had already taken place in his first session, he became a regular member of one of the Israeli groups that organized ayahuasca rituals.

After several sessions with that group, Khalil was invited to a ritual in a private house located in a Jewish Israeli town. As was evident from the architecture, the house had formerly been owned by a Palestinian family who, like many other Palestinians, had been displaced during the Nakba. The current Jewish owners enjoyed hosting many rituals in the large and accommodating house. Guided by the Jewish Israeli shaman that Friday evening, this ritual was somewhat different, as it had a major Jewish influence involving the welcoming of Shabbat. Jewish participants were all dressed in white and were singing Jewish religious songs. Khalil came in jeans and a colorful shirt, like the other three Palestinian participants in the ritual, and was asked by the organizers to change his clothes. This contrast of colors intensified the distinction between the Palestinian minority and Jewish majority of participants, which is probably what summoned Khalil's confrontation with his self-denied Arabness from “the void.”

While the group was singing the traditional Shabbat song “Shalom Aleichem” (Peace be on you, in Hebrew), Khalil decided to go out to the porch. Separated from the group, he sat under

a vine tree that reminded him of his grandfather's house. An intense light started flashing. Sitting outside alone, fear took over him. Khalil felt as if he was losing his mind and would never return to his usual self. He imagined himself becoming a “junkie in the streets,” and was wondering “what will I tell my wife and how will I look my children in the eye.” His fear intensified his sense of alienation and separation from the world, believing “that no power can release me from where I found myself.” Such separation is a necessary step for an Badiouan intervention to take place (Badiou, 2007, 201, 209). While lifting his head to the sky to pray for God's help, Khalil had a vision of an old Palestinian couple in traditional Arab clothing, sitting in front of him on the same balcony and drinking coffee. They were the previous Palestinian owners of the house where the ritual was taking place. The woman told him: “I know you went to an Israeli school—you hate everything to do with Arabs, and you have anger. But the story is different. You heard only one side, but you haven't heard our side. You are in our house now and we are not here. We were evicted.”

Khalil deeply identified with the old couple's pain. The revelation confronted him with collective Palestinian traumatic memories of the ongoing effects of the Nakba, which he had previously avoided. Angry at himself, Khalil felt deceived by the Jewish Israeli narrative. Loyal to his vision, he returned to the ritual with the aim of disrupting it. In anger he sang an old Arabic Andalusian song, “Lamma bada yatathanna” (When it began to unfold), in order to declare that this was “in fact a Palestinian house... whether we like it or not.” The psychedelic event led to his recognition of the injustice that Israelis perpetrate against Palestinians, after which, in Badiou's terms, he felt compelled to intervene in the “structure” of the ritual and modify it. Singing in Arabic was a political act for Khalil, but the reaction of those responsible for maintaining the structure of the ritual was swift. When Khalil raised his voice, the shaman invited him to sit next to him and played the joyful song “Bint al-shalabiya” (The pretty girl) by Fayrouz, a famous female Arab singer from Lebanon. Khalil recounts the excitement: “I am mad about her [Fayrouz]. Suddenly, the shaman starts singing in Arabic. We were thirty people and everybody got up to dance and hug.... I was shocked; hugging and dancing, Jews and Arabs! It was wonderful, wonderful.... That's where the journey started.”

Khalil's fidelity to his vision, as we understand it, was expressed through an angry musical interruption. However, this was not enough to change the structure of the ritual that evening. Although it seems that the Jewish-oriented ritual suddenly became Arab, as people cheerfully danced to Fayrouz's song, it became clear to us that the shaman successfully diverted attention from the national political grounds expressed in Khalil's anger to culturally safe grounds. The shaman prevented Khalil's truth from disrupting the harmony of the ritual with Palestinian memories of displacement from the Nakba.

However, Khalil considered his bringing himself to sing in Arabic at the Israeli ritual an outstanding achievement, a pivotal moment when his “journey began.” “Born again” in this event, he felt his brain was “clean to receive the truth.” Attuned to the universal truth that he had attained at the event, Khalil tattooed his chest with a sentence in praise of the land, taken from a

poem by Mahmoud Darwish, the Palestinian national poet. This helped him reassemble elements of his Palestinian identity, as he confessed: “I used to be very radical right wing in my opinions.... [But] I have made peace with the Arab in me, with being a Palestinian Arab.”

Khalil remained loyal to the event after the ritual was over. Uncomfortable with joining Israeli rituals in which he was part of a minority, his fidelity was directed toward the expansion of ayahuasca to Palestinians. He began organizing rituals for Palestinians only, to which he introduced Arab musical instruments, such as the oud and qanun. As a result he became a key figure in the diffusion of ayahuasca to Palestinians living in Israel. Still, he continues to hold a strong universalistic worldview, arguing that what he learned from his event is not specific to Palestinians. This conundrum can be reconciled through Badiou’s conceptualization of universalism, in which existing structures are restructured to include the excluded particulars. Khalil’s mission to expand ayahuasca to Palestinians led to an empowering and intimate circle, in which they are not dependent on Israeli mediation. Although open to Jewish Israelis, Palestinian ayahuasca rituals offer an alternative structure in which they can reclaim the Arabic language and culture as part of their Palestinian heritage, and not as a denationalized discourse of multiculturalism and interfaith dialog. Such an alternative structure of ayahuasca rituals, as we demonstrate in the following section, also allows Palestinians to produce a safe space with a new cultural vocabulary, where they can share the pain and anger that they experience as a result of the Israeli settler colonial structure.

DIVERSIFICATION AND POLITICIZATION

Working at a regular nine-to-five job in finance, Ruqaiya kept away from politics. Although growing up in an Arab family in a village in the north of Israel, she felt an outsider in her Palestinian culture. She married young, in an arranged marriage to an older man, but fell in love outside the marriage. This led to traumatic and violent events. Divorced with two children, Ruqaiya first participated in ayahuasca rituals when she was in her 40s, or as she explains: “Ayahuasca reached me. She searched for me.” During that period, Ruqaiya was at a low point in her life. She was “a person who saw everything in black, with no point in life.” Ayahuasca, her “teacher,” showed her that her trauma was “a gift.” It taught her about “the depth of life,” and that she was able to “adapt to any place and any situation.” Ruqaiya soon became a therapist, “a wounded healer,” as she describes it, focusing on treating trauma.

Four years into her participation in Israeli ayahuasca rituals, she had her major life-changing revelation. As recounted at the opening of this article, it was on the Jewish holiday of Yom Kippur (Day of Atonement). She joined her regular group, her “tribe,” yet was the only Palestinian in the ritual that night. During the ritual someone sang a song about Maria. She felt as if “Maria entered” her, and she soon began vomiting. She then received many insights about Amal, her elder daughter. Similarly to Khalil, Amal attended a Jewish Israeli school. Coming of age at the time of the event, she was considering joining the Israeli

army. Although a Muslim, Amal also fasted on Yom Kippur that day, at the house of her Jewish friend. Strongly assimilated into Jewish Israeli society; her Palestinian identity was, to use Badiou’s phrasing, on “the edge of the void.” In her vision, Ruqaiya saw Amal with some darkness closing in on her, “disappearing into an abyss.” She had to reach out to Amal and pull her out of that darkness and away from her confusion. At that point, as Ruqaiya recounted, “something closed and I was higher. *Al-Fatiha* [the opening verses of the Quran] came out, and another strong frequency was opened.” This vision separated her from the rest of the group and allowed the intervention to take place.

While singing *al-Fatiha* to the rest of the group, Ruqaiya had a strong revelation in which she saw Palestinian and Israeli mothers sacrifice their own children to war, while “*Pachamama*” (Mother Earth, in Quechua; a term popularized in neoshamanic practices) absorbed the bloodshed. Ruqaiya experienced the pain of the land.⁸ The historical vision continued from past traumas into an apocalyptic warning from a potentially disastrous future. As she explained, the vision of mothers who sacrifice their children was related also to her daughter’s intention to join the Israeli army.

Ruqaiya’s singing and vision were simultaneous. She was singing out of agony about the vision, as she recalled: “The voice came from the center. I cannot say it was in the voice of God, though it was the voice of a messenger.” When she sang, she “released a frequency of anger,” and it felt as if she were telling the other participants to “listen and awaken. There is a battle here between light and dark. The dark is growing stronger than the light, so understand where we are now.” When asked about the meaning of *al-Fatiha*, Ruqaiya chose a universalistic interpretation. She said that it is about not getting lost: “All those who go by certain laws, which are illusory and fake, separate from the human itself, from humanity, from what we are. We are human.” After *al-Fatiha*, she sang, in Hebrew, a song that was popular among the group members, but she added a verse in Arabic.⁹

While she was singing, there was an intense feeling in the room, and many participants were vomiting. In relation to the group, Ruqaiya said: “I felt each one, each and every one [in the group]. Where they were with their fear, doubt, and ego. The [protecting] net that each person places himself in. The defense of the illusion.” Her singing was a pivotal moment in the ritual for other group members, but only few understood the message, as she explained: “Many friends deny it [the message]. They don’t want to deal with it.... So who is doing reparation [on Yom Kippur]? No one. They [Jewish Israelis] are just fasting.” Ruqaiya’s fidelity to her vision was counterhegemonic. As a result, she delivered anger in her song, which we believe was related to a political truth that was concealed by the structure of the ritual. Ruqaiya’s critical insight regarding her own ayahuasca “tribe” was that it replicates the power dynamics that exist in larger reality. However, as in the case of Khalil, her attempts to intervene resulted in denial by the representatives of the ritual’s structure.

⁸Three other Palestinian women who were interviewed had a similar revelation, in which the earth absorbed the blood of war. For an ecofeminist perspective on the conflict, see Eisler (1987/1998) and Roseman et al. (2021).

⁹The song was “*Kanfei ruah*” (Spirit wings), whose lyrics were written by Rabbi Abraham Isaac Kook, one of the fathers of religious Zionism.

While the prophetic interventions of Palestinians channel political anger during rituals, we noticed that New Age spirituality often comes to support the Israeli structure of political denial. For example, Nir, an Israeli shaman, suggested that if political revelations take place during the ritual, they are part of the “shadow work” that one needs to go through. In his instructions, Nir meant that once the political “shadow” becomes conscious, a person will be less guided by it. In this sense, a political revelation is personal, meant only to reveal restrictive identities and traumas to oneself, and through this awareness one can work toward liberating oneself from such restrictions. This argument could be used to reverse Palestinian revelatory truths, as it suggests that their expression of anger was needed for their cathartic personal healing, but not as a message to the group. This reversal is supported by New Age ideology in which “the self” is at the center of transformation.

Nevertheless, the revelation that Ruqaiya had during this ritual developed into a sense of mission and meaning in her life. However, we observed that the intensity of her fidelity to the event was reduced, in comparison to the initial intervention, and remained mostly related to the setting of the ayahuasca practice. She explained: “I feel I am an ambassador of the Arabs in that I started to say, ‘Yes! We are here. We have a voice and opinion. We have life. We are allowed to live. Not only if the Jews allow it.’” Ruqaiya took her destiny in her own hands and began singing to liberate the Arabic language from the oppression of the Israeli state and patriarchy. According to her, it is “the woman who brings revolution and change.” This realization came in fidelity to her vision, yet her self-inquiry is still in process: “How to do this? I am checking, receiving answers, in order to extricate the woman who is the educator of all ages and the one who brings children into the world.” Ruqaiya’s transformation was reflected in Amal, her daughter, who eventually decided not to join the Israeli army, conceivably owing to the event. Considering her singing an empowering political act, Ruqaiya encouraged other Palestinian women to join her rituals and “find their voice.” Similarly to Khalil’s fidelity, she sought to expand and diversify the ayahuasca rituals, to make them more egalitarian and inclusive for Palestinians.

Her politicization did not, however, happen at once. Worried that people would not understand her, it seems that she was divided between fidelity to the event and belonging to the structure. As time passed, and as she remained in fidelity to her vision, the structure around her changed, and she was able to admit to herself that her revelation was political. Throughout her process of political self-exploration, she met like-minded people who could understand her mission. Furthermore, two Jewish Israelis who participated in the Yom Kippur ritual received the message of her song and became musical companions in the rituals that she facilitated.¹⁰ Gathering a small group of people around her, Ruqaiya has not only kept her fidelity alive but has been seeking further connections to form a larger social movement. In this sense, she has been trying to establish a politicized collective that she hopes will have a larger impact.

¹⁰One of them also convinced his daughter not to join the Israeli army, owing to Ruqaiya’s intervention.

On a few occasions since her event, Ruqaiya has attempted to deliver explicit political messages during rituals. For example, during a magic mushroom ritual, which Ruqaiya co-facilitated with a small group of spiritual activists, Adi, a Jewish Israeli woman, announced to the group that she has just decided not to move to Portugal. Addressing both Israelis and Palestinians, she declared: “This is my home and these are my people.” Soon after, in a moment of inspiration, Ruqaiya sat in the center of the circle and spoke in archaic Hebrew, which resembled a biblical text. Accusing the “children of Israel” of losing their way, she stated that “those who were liberated by Moses in the past, have now become Pharaoh [to the Palestinians].” Such direct verbal phrasing of the duality of the oppressor/oppressed is a radical break from the previous structure, which sanctified oneness. As part of the inquiry into her truth, we believe that Ruqaiya has been replicating her event and her initial intervention in other contexts. In doing so, she reconnects with the excluded Palestinian identity, by using other parts of which are in either the Israeli structure (Arabic language and music, Islamic religion) or the void (right to the land, historical injustice). Hence, according to Badiou, she became a “subject” through which the restructuring occurs. She admits though that this is not a simple task and that the integration of her event is challenging as it requires replacing the “old language” with a “new language” that fits the event. Such tension is inherent to the truth procedure, as the restructuring cannot be dependent only on the language of the previous structure.

Ruqaiya’s politicized prophetic deliverance in rituals suggests that she is seeking the reformation of New Age culture so as to make it more politically engaged. While borrowing and decontextualizing different religious practices is central to New Age spirituality, Ruqaiya reconstructs ayahuasca rituals in Palestine/Israel in a political frame. As she puts it, she seeks to “wake up” those who “prefer not to see.” Her belief that “all is one” is now aligned with a mission, as her call for action is mobilized to achieve equality at large, beyond the Israeli ritual structure.

THE DIVIDED SUBJECT

While the event site is related to the Israeli subjugation of Palestinians, Jewish Israelis can also experience revelatory events that lead to political awakening. Today in his 30s, Amos grew up in a middle-class Jewish Israeli family with a left-wing orientation. Never politically involved himself, he ended up joining the Israeli army as a soldier in an elite unit. He decided to join a combat unit not for patriotic reasons, but “to be a man.” During his service, Amos went through a few traumatic events in the West Bank, in which his life was under threat and his comrades were severely injured. After his army service, he felt “very tense” when he heard Arabic spoken near him. After some of his classmates from high school died in combat in the Second Lebanon War (2006), he decided to leave the country to travel. Like many other Israelis, he went on a long journey to India and elsewhere to overcome the harsh memories of military service. Amos had his first experiences with psychedelic drugs as a

backpacker-musician. Regularly returning to Israel for occasional jobs, he then became part of the ayahuasca milieu there.

Looking back to his first encounters with Palestinians at Israeli rituals, he confesses that he was initially judgmental toward their appearance. Not conforming with the Israeli hippy dress code, they were, according to him, too neatly dressed and showed off their high socioeconomic status. As he recounts half jokingly: “I remember a [Palestinian] guy who came to a ceremony in leather shoes, jeans, cell phone, BMW keys, pack of cigarettes, and even when he changed clothes, everyone else was in hippy clothes.”

His life-changing revelatory event took place in a session in which he came across Palestinians from the West Bank for the first time in such a setting. As the Palestinian participants began to cry during the ritual, Amos’s vision was triggered:

Suddenly, the ayahuasca showed me them [the Palestinian group] as a separate unit within us [the Israelis in the ritual]. Another one [Palestinian] began to cry. It took me automatically to the madness of the pain of a whole people.... I felt connected to that pain. I caused the pain of their people. I began to break. I couldn’t stand to hear them crying. She [ayahuasca] began showing me so much. I can’t describe it visually, just this crazy pain, and hate, and crying for the evil they experienced. It built up and up, until there was a cut.

The collective cry of the excluded group of Palestinians separated Amos from the room into his own vision, whereby he had a very detailed flashback of his army service. He saw himself making a casual house arrest of Palestinians, “one of dozens, maybe hundreds,” as he confessed. He saw himself with his unit breaking into the house, interrogating the Palestinian family, and then leading a man into a military jeep. Soon Amos had a “cut” in the revelation and he re-experienced the same incident again. This time, however, he experienced the moment from the side of the family, feeling their pain, panic, and heartbreak. Observing himself from the other side, he described himself as looking like “Robocop,” or “like someone from a film about Nazis.” When the revelation ended and Amos returned to the ritual, he felt intense anger and guilt. “That was the point in my life where I most hated myself,” he later admitted.

After recognizing the pain that Palestinians go through, Amos became devastated during the ritual. He began singing with much confidence, even though until then he had been embarrassed to sing by himself in rituals. Delivering the message through song broke the barriers of his shyness. Amos was taken up in fidelity. He requested from the facilitators permission to sing relatively early in the ritual. Thus, he intervened in its regular structure. Amos remembers that he did not sing beautifully, but that there was something authentic and honest in the moment. Amos considers the song to be a direct continuation of the revelation. He mentioned that it felt like the “room was electrified,” and “the world vibrated with me.” He felt as if he embodied the role of a “preacher” delivering a crucial message of truth to the group. “I felt it [the song] was strong, stronger than me, and it came from a black void in the ritual,” Amos’s words interestingly resonate here with Badiou’s terminology.

The song that Amos sang was “Mekomi kadosh” (My place is sacred), a Hebrew song influenced by Native American peyote-ritual music. The lyrics had a universal message for him, stating

that everyone’s connection to the land is sacred and everyone’s voice should be heard. Amos, however, gave it also a localized political meaning, in which he expressed his relationship with Palestinians and their mutual connection to the land. Up to that point most of the songs in this specific group were in Spanish, English, and Portuguese, since the facilitator was European. Singing in Hebrew, Amos felt that the song was “stronger than me.” Although participants are usually encouraged to stay in their place during the ritual, two of the Palestinian participants came and lay down next to him. According to Amos, this was when “my journey of healing my relations with them [the Palestinians] began.” The song ended with a long silence, which allowed people to reflect.

Rashid, who went to lie down next to Amos while he was singing, also found the courage to sing later in the same ritual. It was the first time that a Palestinian sang in Arabic in this particular group. As with Khalil and Ruqaiya, the introduction of both Hebrew and Arabic to the singing indicates that the fidelity to truth led to the expansion of the ayahuasca ritualistic practice to include local identities, as well as to greater universality. Eventually, Amos befriended the Palestinian group in the ritual. He left the reserve army and began to learn Arabic. He also developed great interest in Palestinian culture and history. However, in addition to his connection to Palestinians, Amos argues that this specific ritual made him less judgmental and more compassionate toward all humans. This inductive reasoning suggests that through a particular recognition, something universal was revealed to Amos.

Another indicator of an essential restructuring of rituals toward universality is related to the connection to the land, a theme that appears in all three of the events and fidelities described in this article. In her vision Ruqaiya identified with the pain of the land; Khalil’s new tattoo expresses his belonging to the land; and the lyrics of Amos’s song were about everyone’s sacred place on the land. Reestablishing the connection of Palestinians to the land is a crucial diversion from the Israeli structure, toward both a particular acknowledgment and a more inclusive universalism. Such universal aspirations require resistance to the Israeli settler-colonial project that supports the Zionist narrative calling for the “redemption of the land” from the Palestinians who “occupy” it (Suleiman, 2002).

Although Amos was initially in full fidelity to the event, like any other subject he later became divided between his fidelity to the event and his belonging to the structure. As with any Badiouan event, the forces of the structure are always at work to reverse the event’s truth. In Amos’s case, such a reversal is exemplified by his later reinterpretation of the event based on the previous structure. In the first interview with him, he interpreted the song “Mekomi kadosh” as an expression of Palestinian and Israeli connection to the land. This interpretation is loyal to the event, as it recognizes the Palestinians’ right to the land, which is something that the structure denies. However, in a second interview with him, that took place a year later, Amos gave the lyrics another interpretation associated with self-acceptance. He explained: “There is this thing from the North American Dakota tribe about being a man. OK, so you cried, apologized, and you

are also *evil*... now it is time to move forward. What does it mean? Exactly like in the song, your place is your place and you cannot even control it. You are part of a story and your part is sacred.” We argue that this new interpretation is a diversion from the truth attained during the event, and does not challenge the structure, as it frames the song in a holistic interpretation that accepts good and evil as “sacred.” Thus, the later interpretation waves off Amos’s feelings of guilt and desire for reparation. In this sense, it is also compatible with Ruqaiya’s critique of Jewish Israelis who prefer “not to see.”

Aligned with this interpretation, Amos also said that he learned from “the medicine” that friendship with Palestinians is valuable for him, as “*peace* occurs human to human,” so that he need not “worry about the macro.” While he indeed overcame some of his stigmatization and fears of Palestinians, it seems he maintained an apolitical position that is centered on harmony and friendship, without actively taking responsibility for and acting against the structure of injustice against Palestinians that he is part of. For example, he was upset every time one of his Palestinian friends from the rituals critiqued the “Zionist occupier” on social media. He felt that such outspoken criticism was not aligned with their friendship with him. Instead, such Palestinian expressions of anger seemed to him a contradiction of the harmony and unity that they experienced together in the ritual.

We must ask then, what happened to Amos’s fidelity to his event. Why was he diverted from his initial conviction in a politicized universal truth to a more comfortable position that does not challenge the Israeli structure? It is important to note here that Amos has been a helper and musician in the Israeli rituals. Hence, he is a central representative of the structure, unlike Ruqaiya and Khalil, who were marginal to the structure at the moment of their event. In this sense, we argue that the structure was stronger than the event for Amos, so that his fidelity was eventually reversed. Moreover, while Khalil’s and Ruqaiya’s fidelity was ignited by anger, Amos’s fidelity as a Jewish Israeli was ignited by guilt. As such, guilt carries a strong psychological burden, especially when not directed toward reparation. Six years after the revelatory event, Amos went to an MDMA-assisted therapy session and revisited the haunting memory that appeared to him at the event.¹¹ A few weeks after the MDMA session, he said that it had helped him to overcome the memories and to continue with his life.

CONCLUSION

In this article we argue that Badiou’s theory is relevant to understanding the sociopsychopharmacology of psychedelics and their political implications. Through the three cases presented above, we have demonstrated how ayahuasca can induce political revelatory events that raise matters related to the oppression of Palestinians and are suppressed by the Israeli ritual structure. These events lead the receiving subjects to develop fidelity to

attained truths about the particular context of Palestine/Israel. Although particular, these truths have a universal realization, as they aim toward inclusion and recognition of elements that fall outside the hegemonic structure. The revelatory procedure does not stop at this, as the fidelity to an event’s truth compels the receiving subject to develop and then act upon a sense of mission and confidence to oppose and possibly change both the ritual’s structure and the larger sociopolitical structure. The sociopsychopharmacology of the substances leads the subjects to gather others around the egalitarian revolutionary truth procedure to support the restructuring, by changing the existing rituals or establishing alternative rituals, albeit more inclusive and universal. Through this sense of mission, the subject, in fidelity to the event, supports the diversification of the ayahuasca practice to represent the event site in the structure. However, persistence and commitment to the event’s truth are required for success, since agents of the structure constantly attempt to reverse this truth and place it back in its initial framework. We believe that such a reversal happened in one of our observations, in which Amos was too involved in the structure and was unable to emotionally sustain active fidelity to his event’s truth.

The contrast between the harmonious unity of the Israeli structure and the injustice that Israelis have caused Palestinians amplifies the event site that lies on the border between the structure and the excluded “void” and eventually makes the rupture possible. Therefore, unity and revelatory events are not necessarily independent phenomena, but are in relation to each other. This suggestion can clarify why mystical practices are considered unitive and/or liberative (Ferrer, 2002). Religious rituals with high emotional intensity can lead to a strong identity fusion among group members, but they cannot easily maintain doctrinal orthodoxy, as this mode of religiosity is experiential. Personal revelations will eventually lead to a schism within any doctrine (Whitehouse, 2004; Whitehouse et al., 2014).

The revelatory rupture with the exclusive structure leads to revolutionary motions that diversify the psychedelic practice. In other words, the movement of psychedelic practices outward in a universal manner is also dependent on counterhegemonic revolutionary motion inward toward the structure of the practice itself. Leary’s charismatic fidelity was not just to the 1943 LSD-event, but also to the fact that Ginsberg’s event and intervention liberated psychedelic practices from institutional exclusivism and Huxley’s elitism. Leary was Huxley’s protégé and a professor at Harvard, and hence was deeply embedded in the exclusive structure of psychedelic practices of his time. Ginsberg came from the “void,” ruptured that exclusivity, and ignited a universal motion by arguing that mystical mind states should be accessible to all (Conners, 2010). In a similar sense, Ruqaiya and Khalil diffused the ayahuasca practice not just because they wanted to spread altered states of healing to Palestinians, but also because counterhegemonic fidelity intervened in Israeli exclusivism. Ruqaiya and Khalil drew connections between the Palestinian event site and Arabic music and language, which are already part of the structure but not connected to Palestinian national identity. Ruqaiya has also succeeded in realizing the “frequency of anger” from her initial intervention by introducing critical political engagement into New Age spirituality.

¹¹MDMA is an empathogenic drug that is used for the treatment of post-traumatic stress disorder (PTSD) in clinical trials (Mithoefer et al., 2019).

Truth events are crucial for the emergence of counterhegemonic egalitarian sentiments in psychedelic practices. However, persistence and commitment to the event's truth are required to achieve change, since agents of the structure constantly attempt to reverse the fidelity to this truth and place it back into its original framework. When fidelity is reversed, the revolutionary charisma is routinized. In service of the structure, New Age ideology can reverse political truths by fetishizing harmony, unity, and the self, so as to deflate collective political action. The affected subject is then torn between fidelity to the event and belonging to the structure. Amos experienced just such a reversal of fidelity. He was too involved in the structure and could not emotionally sustain the sense of active responsibility to his event's truth. However, the attained truth does not fade away so easily, as the subject cannot forget the radical event experience. Unable to act upon their truth, such individuals might consider dropping out of the structure instead of trying to change it.¹² Given the strength of Israeli ritual structure and sociopolitical structure, it is not surprising that many of our interlocutors, constantly consider migration abroad, to a friendly community in "nature," frequently in Portugal, with the hope of building a new structure that is rid of political tensions.

At other times, the dynamics between structure and event can subvert the enthusiasm of the rupture in service of the structure itself. Fidelity seems to be common across many psychedelic practices, yet it can become pseudofidelity if the structure successfully claims it. Such pseudofidelity can be clearly recognized by its revolutionary tendencies, but a lack of universal aspirations. It looks like fidelity, but it aspires to restrictive unity. The influence of "conspiratoriality" (Ward and Voas, 2011)—defined as the overlap of conspiracy theories and new age spirituality—on psychedelic practices is an example of how counterhegemonic tendencies can be easily manipulated.

Though we have discussed only political events in this article, Badiou's event also relates to love, science, and art. Attending to these other analytical possibilities may offer new insights into psychedelic experiences. Badiou suggests, that "the militant of a truth is not only the political militant working for the emancipation of humanity in its entirety. He or she is also the artist-creator, the scientist who opens up a new theoretical field, or the lover whose world is enchanted" (2007, xiii). To analyze

¹² See "The Houseboat Summit" for a conversation between Leary, Ginsberg, Watts, and Snyder about political activism vs. dropping out (Watts et al., 1967).

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such events, it is important to examine the revelatory moment in relation to both the structure in which it occurs and the fidelity that ensues.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because the data contains personal information that cannot be easily anonymized. Requests to access the datasets should be directed to LR, leor.roseman13@imperial.ac.uk.

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The studies involving human participants were reviewed and approved by Joint Research Compliance Office at Imperial College London and the Imperial College Research Ethics Committee (ICREC reference 18IC4346). The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

LR designed the study, collected and analyzed the data, and wrote the manuscript. NK supervised the analysis and wrote the manuscript. Both authors contributed to the article and approved the submitted version.

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Critical Period Plasticity as a Framework for Psychedelic-Assisted Psychotherapy

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As psychedelic compounds gain traction in psychiatry, there is a need to consider the active mechanism to explain the effect observed in randomized clinical trials. Traditionally, biological psychiatry has asked how compounds affect the causal pathways of illness to reduce symptoms and therefore focus on analysis of the pharmacologic properties. In psychedelic-assisted psychotherapy (PAP), there is debate about whether ingestion of the psychedelic alone is thought to be responsible for the clinical outcome. A question arises how the medication and psychotherapeutic intervention together might lead to neurobiological changes that underlie recovery from illness such as post-traumatic stress disorder (PTSD). This paper offers a framework for investigating the neurobiological basis of PAP by extrapolating from models used to explain how a pharmacologic intervention might create an optimal brain state during which environmental input has enduring effects. Specifically, there are developmental “critical” periods (CP) with exquisite sensitivity to environmental input; the biological characteristics are largely unknown. We discuss a hypothesis that psychedelics may remove the brakes on adult neuroplasticity, inducing a state similar to that of neurodevelopment. In the visual system, progress has been made both in identifying the biological conditions which distinguishes the CP and in manipulating the active ingredients with the idea that we might pharmacologically reopen a critical period in adulthood. We highlight ocular dominance plasticity (ODP) in the visual system as a model for characterizing CP in limbic systems relevant to psychiatry. A CP framework may help to integrate the neuroscientific inquiry with the influence of the environment both in development and in PAP.

Keywords: critical period plasticity, neuroplasticity, visual system, psychedelics, biological psychiatry, psychotherapy

INTRODUCTION

The psychedelic treatment paradigm is one in which, following a comprehensive preparation process, a psychedelic medicine is administered for one or up to several sessions. The psychedelic produces an altered state of consciousness which is thought to facilitate self-exploration and insight. These insights are then examined in integration sessions in the absence of the

medicine (Doblin et al., 2019). This treatment approach is different from the prevailing model of psychopharmacology in which a medication is used to bring about symptom reduction by providing corrective neurochemical effects on faulty pathways implicated in psychiatric disorders (DePierro et al., 2019). There remains debate about the centrality of the psychotherapy and the acute subjective experience in the psychedelic treatment (Heifets and Malenka, 2019; Olson, 2021; Yaden and Griffiths, 2021). Moreover, it has been suggested that the therapeutic properties of the psychedelic may not require the altered state of consciousness, but is rather based on the pharmacologic profile of the compound (Olson, 2021). Consideration of the extra-pharmacologic factors challenges the classic translational approach of biological psychiatry based in psychopharmacology that targets and reverses causal pathways of disease (DePierro et al., 2019).

Indeed, a prevailing model born from translational research is that chronic stress causes pathological atrophy of cortical neurons in the prefrontal cortex which can be reversed by rapid-acting antidepressant compounds such as ketamine, thus abolishing the patient's psychiatric symptoms (Duman et al., 2016; Moda-Sava et al., 2019). Some argue that psychedelics can be fit into this model since they are thought to engage familiar neuroplasticity targets such as the serotonin 5-hydroxytryptamine-2A receptor (5-HT_{2A}R), the glutamatergic α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) pathway, and brain-derived neurotrophic factor (BDNF)/tropomyosin receptor kinase B (TrkB) signaling in cortical regions (Kadriu et al., 2021). The neuroplastic effect is seen by induced *structural changes*: dendrites in cell culture (Ly et al., 2018); *functional changes*: increased mean firing rate of layer 5 pyramidal neurons in the prefrontal cortex (Vollenweider and Preller, 2020); and *epigenetic changes*: neuroplasticity-related genes (Martin and Nichols, 2018). Novel therapeutics that target these known pathways with increasing specificity and potency yet lack accompanying psychoactive/experiential effects are in the drug development pipeline (Cameron et al., 2021).

However, a different perspective from clinical researchers working with psychedelics has emphasized the centrality of a deep psychological or spiritual exploration that is induced by the compound when given in the appropriate context (Greer and Tolbert, 1986; Belser et al., 2017; Bogenschutz and Forcehimes, 2017; Sessa, 2017; Wagner et al., 2017; Feduccia and Mithoefer, 2018; Garcia-Romeu and Richards, 2018; Nielson and Guss, 2018; Brecksema et al., 2020; Reiff et al., 2020; Sloshower et al., 2020; Mithoefer, n.d.). The common recreational use of psychedelics, yet lack of spontaneous psychiatric illness remission, and even potential psychological harm, in users calls attention to the importance of extra-pharmacologic factors. Yet because of what data is currently available and currently possible to obtain, the two sides remain valid opposing theoretical viewpoints.

To integrate these seemingly disparate mechanisms of action—biological and psychological—one does not have to look far to find a wealth of literature that purports that neuroplasticity can provide a biological model of how the response to the environment manifests in neurobiological change. Highly cited articles such as Castrén (2005); Branchi (2011), and Karpova et al.

(2011) have proposed variations of the “undirected susceptibility to change model” (Branchi, 2011) that the mechanism of antidepressants may be to enhance the malleability of relevant brain circuits to environmental influence. Therefore, the range of clinical outcomes that results from manipulating neural plasticity may greatly depend on the environmental context in which they are taken. Nonetheless, a decade later, induction of synaptic neuroplasticity is still viewed as a proxy or biomarker for positive clinical effect (Moda-Sava et al., 2019; Cameron et al., 2021). To make progress in understanding the neurobiology of psychedelic assisted psychotherapy (PAP), we suggest investigating the interaction of the psychopharmacology and its context. This requires adopting a new theoretical approach to design studies to help explain mechanism.

Now we turn to consider a developmental framework that advancement in psychiatric treatment may result from the discovery of interventions that “release the brakes that retard” adult neuroplasticity (McEwen, 2012) to induce the heightened sensitivity to the environment observed during specific periods of development. “Neuroplasticity” is a heterogeneous phenomenon that has become an imprecise term. This review addresses a specific type of *in vivo* neuroplasticity in living animals: critical period plasticity (CPP), as seen in ocular dominance plasticity (ODP) in the visual system.

A critical period is a window in which environmental input is necessary for the appropriate development of the relevant brain circuit. During a critical period, the brain has a heightened plasticity in which experiences have robust effects on establishing stable neurocircuitry. During this developmental period, the brain's malleability creates both a vulnerability to environmental insults or deprivations as well as a remarkable ability to quickly and robustly acquire skills. After the closure of critical periods, neuronal changes are still possible, but more restricted. Recent studies using the ODP model indicate that the nature and the underlying mechanisms of this juvenile form of robust plasticity—CPP—are distinct from adult types of neuroplasticity (Hensch, 2005; Morishita and Hensch, 2008). While various studies have correlated critical periods to synaptic plasticity mechanisms (Feldman, 2000), other cellular processes have been increasingly implicated in causally regulating CPP (Nabel and Morishita, 2013). The set of mechanisms involved in the opening, maintenance, and closing of CPP in primary sensory modalities—and in ODP specifically—have been elucidated, thus its candidacy to serve as a model system.

This paper highlights advancements in visual science as a model system for elucidating the molecular and circuit machinery responsible for the opening and closing these sensitive periods of development. The previous literature on CPP and other psychotropic medications is briefly reviewed. Finally, a case is made for investigating PAP through the lens of CPP. Perhaps these biological underpinnings of CPP can help understand how encounters with salient environmental stimuli during a sensitive period of development or a psychedelic experience durably alter functional neurocircuitry.

Of note, the definition of a psychedelic in clinical psychiatry, in the community, and in neuroscience remains imprecise. For example, while ketamine shares pharmacologic properties

with psychedelics, it also has distinctions (Kadriu et al., 2021). While the psychedelic-like nature of ketamine continues to be explored (Mathai et al., 2020), it has not been packaged together with psychotherapy for FDA approval as have 3,4-Methylenedioxymethamphetamine (MDMA) and psilocybin and therefore was not included here as a psychedelic.

SENSITIVE PERIODS OF PSYCHOLOGICAL DEVELOPMENT

During development, sensitive periods occur in which the brain is particularly sensitive to environmental input (Knudsen, 2004). If an adverse experience or deprivation occurs during a psychological stage of development, it has the power to affect lifelong psychological functioning whereas experiencing the same events as an adult may not have as robust an impact (Lupien et al., 2009; Pratchett and Yehuda, 2011). In developmental psychology, critical (or “sensitive”) periods have been characterized by rodent studies (Curley and Champagne, 2016), and naturalistic human deprivation studies such as institutional rearing (Bick and Nelson, 2016; Nelson et al., 2019). Such research informs the basis of early-intervention programs such as for Autism (Landa and Kalb, 2012).

Development of the emotional brain likely consists of many different overlapping sensitive periods of higher-order functioning such as attachment, emotion regulation, and social cognition (Piekarski et al., 2017). Adversity differentially affects the developing brain during critical periods (Nelson and Gabard-Durnam, 2020). Targeted enrichment in developmental domains are most effective during well-characterized temporal windows of opportunity (Marín, 2016). Yet the neurobiological mechanisms surrounding the opening and closing of these critical periods have not been well elucidated. Accordingly, there is a need for a model system in which the brain is disproportionately affected by the environment during discrete developmental periods.

CRITICAL PERIOD PLASTICITY IN THE VISUAL SYSTEM

CPP has been well formulated in the visual system across species (Wiesel, 1982; Hensch and Quinlan, 2018). ODP in the primary visual cortex (V1)—necessary for the development of binocular vision—is the most extensively studied form of CPP. Ocular dominance is reflected in the representation of the left versus right eye inputs into striate ocular dominance columns in V1. Similar to social and emotional development, a lack of expected environmental input to the relevant system during childhood either by insult or deprivation results in lasting deficits (Wiesel, 1982; Hensch and Quinlan, 2018). If one eye is deprived of normal input (e.g., from cataracts, or experimental monocular deprivation) during the well-defined critical period, the deprived eye will have poor visual acuity due to a shift of neuronal spiking response in V1 in favor of the open eye; amblyopia (“lazy eye”) will result (Wiesel, 1982; Hensch and Quinlan, 2018). If the strong eye is patched, amblyopia can be reversed and vision restored,

but only if during the critical period in late childhood. Similarly, deprivation outside the critical period does not cause amblyopia (Wiesel, 1982; Hensch and Quinlan, 2018). The temporal window of CPP corresponds with a period of rapid physical growth when the distance between the two eyes increases and thus the visual receptive fields are constantly changing. The mechanism of both the opening and closing of the visual critical period has largely been elucidated, thus its utility as a model system.

By identifying the molecular brakes that typically halt visual CPP, pharmacologic intervention has made it possible to remove the brakes, thus re-opening visual CPP (Morishita and Hensch, 2008; Bavelier et al., 2010). Under these conditions, if the proper environmental stimulus is provided, near-blindness from amblyopia can be reversed in rodent models. But this intervention was not found by the traditional translational approach whereby solely modulating druggable targets in amblyopia’s pathophysiology reverses the illness without being in concert with proper experience. Instead, a pharmacologic intervention creates the molecular conditions in V1 whereby the brakes of CPP are released, and a specific environmental input (that was lacking or polluted during a time when it was necessary) can exert abiding effects (Vetencourt et al., 2008; Sale et al., 2014).

The translatability of molecular targets involved in visual CPP to psychological conditions has already begun to be explored. For example, the excitatory/inhibitory balance of interneurons that shifts during critical periods may also be relevant in limbic circuits (Kuhlman et al., 2013; Murthy et al., 2019). Key features of ODP including perineuronal nets, myelin-related nogo receptor signaling, and Lynx family proteins—key features in ocular dominance CPP—have signs of translatability including their involvement in fear-memory in the hippocampus, amygdala, and prefrontal cortex (Nabel and Morishita, 2013).

CRITICAL PERIODS AND PSYCHOTROPIC MEDICATIONS

The relevance of visual CPP to psychiatry has been a topic revisited by many (Bavelier et al., 2010; Hensch and Bilimoria, 2012; McEwen, 2012; Castreñ, 2013; Nabel and Morishita, 2013). Certain psychotropic medications, before the recent interest in psychedelics, have been highlighted for their unexpected induction of juvenile-like neuroplasticity in the visual system. The growing body of literature is briefly reviewed in this section.

Chronic fluoxetine treatment was shown to reinstate ODP in the adult amblyopic rat (Vetencourt et al., 2008). While a functional intervention for amblyopia is typically only corrective in childhood but not in adulthood, in this experiment, reinstatement of juvenile-like plasticity allowed for complete recovery of vision when paired with the functional intervention (Vetencourt et al., 2008). The induction of plasticity was a result of serotonin-induced reduction in intracortical GABAergic inhibition and increased BDNF expression leading to a shift the intracortical inhibitory-excitatory balance (Vetencourt et al., 2008). Furthermore, the study of ketamine, which similarly reopens a critical period for ODP, has cast light on the reopening process as an neuregulin-1-dependent restoration

of excitatory input onto parvalbumin cells, thus enhancing cortical inhibition (Grieco et al., 2020). Ketamine's rapid effect on ODP has also been shown to be mediated through TrkB signaling (Casarotto et al., 2021). Using ketamine as a tool has helped to better characterize the molecular components involved in the opening and closing of ODP critical periods.

The generalizability of critical periods in the visual system to that of affective circuits is of great relevance should this framework hold promise for the development and adoption of neuropsychiatric therapeutics (Spolidoro et al., 2008; Nabel and Morishita, 2013; Sale et al., 2014). The fear extinction paradigm has been targeted for investigation because of its quantifiable outcome and translatability from animal models. Typically, an enduring loss of a conditioned fear memory is only possible during a juvenile critical period, but not in adult mice. Indeed, selective serotonin reuptake inhibitors (SSRIs) (Karpova et al., 2011) and ketamine (Ju et al., 2017) both lead to enduring loss of a conditioned fear memory when paired with a fear extinction paradigm. Furthermore, fluoxetine's structural and functional effect on the basolateral amygdala was evidence that the reopening of a CP in the fear circuit mirrors that of ODP (Karpova et al., 2011). These are early signs that certain psychotropics may reopen select affective critical periods such as fear, and that the mechanism of reopening in these circuits may be similar to that of reopening critical periods of ODP. At the same time, evidence calls into questions that ketamine's antidepressant effects are plasticity-dependent (Moda-Sava et al., 2019; Abdallah et al., 2020).

As introduced above, SSRIs and ketamine have both been evaluated in the framework of ODP whereby the medication makes a circuit malleable for experiential input, both necessary for an enduring change. However, novel treatments in psychopharmacology have not been conceived, designed, or implemented as an aid to environmental input until the recent development of PAP. The concept of ODP is missing from the psychedelic literature and discourse though its relevance is promising.

PSYCHEDELICS AND CRITICAL PERIOD PLASTICITY

In a CPP framework, the therapeutic mechanism of psychedelics would be understood as the pharmacological properties of psychedelics putting the brain in a CP "open state," while the psychotherapeutic aspect might retrieve appropriate engrams, such as traumatic memories (Inserra, 2018) for modification—now in a context of safety. Furthermore, the specific type and intensity of psychological support framing the experience has been correlated with clinical and efficacy outcomes (Griffiths et al., 2018).

As discussed above, the developmental influence on fear extinction shares features with ODP (Nabel and Morishita, 2013) and fear-extinction has been discussed as a potential component of the psychotherapeutic process in MDMA-assisted

psychotherapy (Feduccia and Mithoefer, 2018). That psychedelics may reopen a psychosocial CPP has been corroborated in a rodent study of MDMA (Nardou et al., 2019). A social critical period was defined in mice behaviorally as an age-dependent peak in social reward learning. Biologically, this period of development was characterized by a change in the magnitude of oxytocin-dependent long-term depression (LTD) of glutamatergic inputs to medium spiny neurons in the nucleus accumbens. Intraperitoneal administration of MDMA reopened the behavioral critical period by binding to the serotonin transporter (SERT) and triggering a cascade leading to a metaplastic upregulation of oxytocin receptors (OXTR) and reopening of the social CPP and LTD at excitatory synapses (Nardou et al., 2019). So far, there is no known connection between the visual system CPP and this social learning CPP, so further investigation is required to know how molecular machinery of CPP may vary in different neural circuits.

Notably, MDMA's reinstating CPP only occurred in a social context and not in isolated animals (Nardou et al., 2019), providing more data to suggest that biological intervention can be context-dependent (Hartogsohn, 2016, 2017; Haijen et al., 2018).

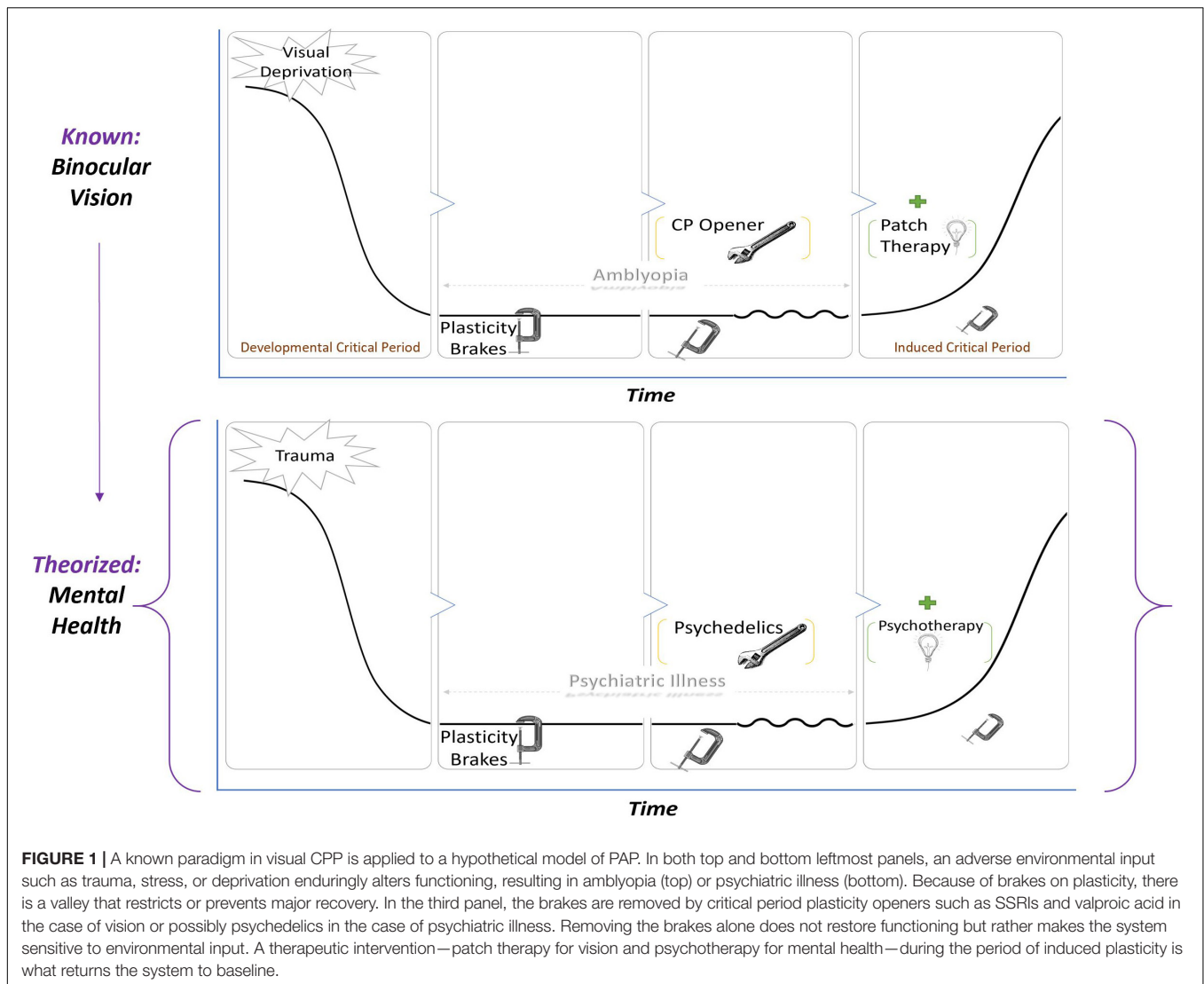
The 5-HT_{2A}R often defines psychedelics as a class of medications and may also provide a nascent avenue for linking psychedelics and CPP. The synaptic plasticity associated with both the "serotonergic" psychedelics such as psilocybin as well as with MDMA has been found to be dependent on 5-HT_{2A}R signaling (Ly et al., 2018; Olson, 2018; Vollenweider and Preller, 2020) and recently 5-HT_{2A}R been thought to be involved in key developmental periods (Carhart-Harris and Nutt, 2017). Although, there is now competing evidence that psychedelic-induced plasticity may have a mechanism independent of 5-HT_{2A}R (Hesselgrave et al., 2021).

More studies are required to fully assess the contribution of CPP re-opening to the mechanism of PAP, particularly in humans. An empirical question remains regarding whether MDMA and other psychedelics reopen ocular dominance CPP as ketamine does (Grieco et al., 2020) and what the implications would be for both visual science and psychiatry. An avenue for future research might be translatable assays that can detect re-opening of CP in humans.

DISCUSSION

The definition of CPP should be reiterated as a state in which neural networks are exquisitely sensitive to environmental inputs. Ocular dominance CPP may provide a theoretical framework (see **Figure 1**) for biological investigation of the synergistic effects of the psychopharmacologic and psychological properties of psychedelic-assisted-psychotherapy on clinical outcomes.

Many types and components of neuroplasticity (e.g., properties of a synapse, morphological plasticity, electrophysiological and biochemical changes, meta-plastic changes) are likely involved in psychedelics, but carefully characterizing and distinguishing the processes may have



clinical implications. Not all neuroplasticity is therapeutic—for example, the morphological plasticity of cocaine is thought to be implicated in its abuse potential (Li et al., 2004; Ferrario et al., 2005; Russo et al., 2010; Marie et al., 2012), however (unlike MDMA), cocaine does not reopen a critical period for social reward learning (Nardou et al., 2019) in mice, illustrating just one instance where the distinctions between these “neuroplastic” processes may be therapeutically significant.

Building on a body of literature that calls attention to ocular dominance CPP as a potentially helpful framework for psychiatry, we posit its relevance to fine-tuning investigation of plasticity in psychedelic research. Moreover, ODP reflects physiological plasticity characterized in living organisms in contrast to other types of plasticity characterized *in vitro* or *ex vivo*. Therefore, CPP may orient future work to a different level of observation missing from psychedelic research. For example, the excitatory/inhibitory balance of interneurons, perineuronal nets, myelin-related nogo receptor signaling, and

Lynx family proteins might be informative upstream biomarkers (Morishita and Hensch, 2008).

It is also possible that the mechanisms of ODP are not the most applicable to psychedelics. While the ODP critical period has been the most well-characterized, other critical periods—such as imprinting behavior in chicks (Jaynes, 1957), birdsong learning (Woolley and Rubel, 2002), rodent barrel cortex (Erzurumlu and Gaspar, 2012), post-stroke motor learning (Zeiler et al., 2013), cognitive flexibility (Gopnik et al., 2017), social/cognitive/affective domains in adolescence (Piekariski et al., 2017; Dahl et al., 2018), etc.—have been studied and likely do not share a single universal set of mechanisms. It seems unlikely that psychedelics might be a sort of master-key to reopen all types of critical periods even beyond the limbic system, but perhaps they might be a tool for better characterizing neuropsychiatric critical periods, as was begun with the critical period for social learning (Nardou et al., 2019). Furthermore, biomarkers associated with psychedelic-induced plasticity may

shed light on the developmental biology of critical periods in limbic circuits (Castrén, 2013). However, a current lack of translational assays to measure changes in CPP-specific biomarkers limits the discussion to speculation. While some translational biomarkers of neuroplasticity have been developed (e.g., visually evoked potentials), they capture downstream observed changes in plasticity not specific to CPP (Normann et al., 2007).

If induction of CPP is a hypothesized mechanism for psychedelics, translational research studies will need to be re-evaluated to consider that what's observed *in vitro* is only a part of the biological mechanism that explains the clinical effect. Equating neuroplastic-induction with clinical outcome misses an opportunity to rigorously investigate the many extra-pharmacologic factors that influence a patient's clinical and biological outcome. Rather than stopping at trying to explain how a drug works, considering context may help our field with trying to explain what halts and what enables the brain to adapt to its environment. With psychedelics as a probe and the translational research paradigms of visual science to draw upon, perhaps biological psychiatry is better poised to understand and manipulate critical periods of plasticity in psychological development. Just as McEwen called himself a "molecular sociologist,"

psychedelics may provide an opportunity to integrate neuroscientific inquiry with the psychosocial context in which a person heals.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

LL: preliminary concept guided and shaped by senior author, RY. HM: contribution of his expertise in the visual system and CPP. LL and RY: manuscript writing with edits by HM. HM: figure conceptualization, executed by LL and edited by RY. All authors contributed to the article and approved the submitted version.

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‘I Get High With a Little Help From My Friends’ - How Raves Can Invoke Identity Fusion and Lasting Co-operation via Transformative Experiences

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Psychoactive drugs have been central to many human group rituals throughout modern human evolution. Despite such experiences often being inherently social, bonding and associated prosocial behaviors have rarely been empirically tested as an outcome. Here we investigate a novel measure of the mechanisms that generate altered states of consciousness during group rituals, the 4Ds: **d**ance, **d**rums, **s**leep **d**eprivation, and **d**rugs. We conducted a retrospective online survey examining experiences at a highly ritualized cultural phenomenon where drug use is relatively uninhibited- raves and illegal free parties. Engaging in the 4Ds at raves or free parties was associated with personal transformation for those who experienced the event as awe-inspiring, especially for people with open personalities ($n = 481$). Without awe, or a ritual context, indulging in the 4Ds was associated with a lack of personal growth, or *anomie*. A complex SEM revealed that personal transformation following awe-inspiring raves was associated with bonding to other ravers and prosocial behavior toward this group at a cost to self in a simple economic game. Bonding to humanity was not associated with these events. The findings suggest that employing the 4Ds in a ritualized environment - particularly dancing and drug use – can help build meaningful social bonds with associated positive behavioral outcomes.

Keywords: psychedelics, identity fusion, rave, awe experiences, transformative experiences, social bonding, 4Ds, dance

INTRODUCTION

Humans have come together for exalted, communal experiences for more than 100,000 years (Ember and Carolus, 2017). These occasions – both ancient and current - often involve repetitive drums, dance, sleep deprivation and, often, psychedelic substances. Their cumulative effect on the group results in a sense of coming together, termed ‘*collective effervescence*’ (Durkheim, 1915) or

'*communitas*' (Turner, 1969). Indeed, one of the main consequences of such collective gatherings is considered a unification of participants, or social bonding (Block, 2020; Savage et al., 2020). Here we examine a novel measure for the mechanisms driving altered states of consciousness during awe-inspiring group experiences in rave culture, a modern cultural phenomenon that has been likened to entheogenic shamanic practices (Tramacchi, 2000; St John, 2015). This measure brings together the 4Ds: **d**ancing, **d**rums, **s**leep **d**eprivation, and **d**rugs. We address a current gap in the literature around psychedelic drug consumption during culturally organic, awe-inspiring rituals and their relation to transformative experiences, social bonding, and prosocial behavior. We also explore the unique role psychedelic drugs play in this process, compared to other popular recreational drugs that invoke feelings of connectedness, such as MDMA.

One aspect of an awe-inspiring event that might help individuals to experience the group as bigger than its individual parts is *liminality* (Van Gennep, 1960; Turner, 1969). Liminality describes a withdrawal from the culturally normal modes of social action, in which ego may be dissolved and new perspectives gained. This 'betwixt and between' state (Turner, 1969) facilitates *communitas* by homogenizing secular distinctions like rank or status, instead replacing them with intense comradeship and egalitarianism. One particularly potent form of social bonding, *identity fusion*, concerning a visceral oneness to the group (Swann et al., 2009) has been described as a socio-cognitive product of *communitas* both theoretically (Whitehouse and Lanman, 2014) and empirically (Páez et al., 2015; Kettner et al., 2021). Here, in a natural setting, we investigate the precursors to awe-inspiring, liminoid experiences, and their relationships with social bonding and prosocial behavior.

Ritual liminality can be induced by several identifiable human behaviors, including what we term 'the 4D's', which are: (1) **d**ancing (Lewis-Williams, 1992); (2) intense rhythmic **d**rums (Savage et al., 2020); (3) sleep **d**eprivation (Dahl, 2013); and (4) **d**rugs, especially psychedelics (Hood, 2014). This suite of behaviors is powerful enough to alter our state of consciousness and in so doing take a group far away from its conventional realms of normality (or the profane), and into the surreal and sacred. Importantly, this liminal state gives group members an opportunity to transcend the boundaries between self and group. Psychedelic drugs have long played a role in ritual and shamanic ceremonies; indeed, human serotonergic receptors are unusually receptive to psychedelic binding compared to other primates (Pregenzer et al., 1997), which has been used as evidence for the role of psychedelics in human evolution (Winkelman, 2017). Nonetheless, it remains unclear just how important psychedelics are in relation to the other elements of the 4Ds, especially in relation to intergroup dynamics and pro-social behaviors within the group.

Here, we first introduce the 4Ds in the research context of rave culture, before discussing the role psychedelics play in ego dissolution and feelings of awe (Millière, 2017; Nour and Carhart-Harris, 2017; van Mulukom et al., 2020). Next, we explain how sharing a transformative experience with other group members

can lead to an intense form of group bonding, i.e., identity fusion (Newson et al., 2016; Buhrmester et al., 2018), and how this may be related to awe-inspiring experiences during raves.

Altered States of Consciousness and the 4Ds

The 4Ds are a novel approach to capture the mechanisms for altered states of consciousness in natural settings, which we investigate here for the first time. The 4Ds include four main ritual features: **d**ance, **d**rums, **s**leep **d**eprivation, and **d**rug consumption. Each element of the 4Ds alone can have a powerful effect on individual and collective consciousness and behavior, but when used together the effects have the potential to be culturally seismic. The 4Ds occur in varying formats cross-culturally but are broadly long-standing in modern human evolution. For instance, while rave culture may use electronic music and chemically synthesized psychedelic drugs to reach a desired altered state of consciousness (St John, 2004), indigenous Amazonian cultures use rhythmic singing and drumming with ayahuasca (Metzner, 2014).

First, dancing has been described as religious by its very nature (Gauthier, 2004) and it is dance which constitutes the architecture of a rave. Dance fills the void of formal structure - no tables, no chairs - just a space constructed by raving bodies, formed simultaneously by free agents and a merged, united mass. Csikszentmihalyi (1975:43) listed dance as a form of play that is intrinsically simulating because it enacts a holistic total body involvement. He termed this 'flow'. Dance as flow merges the dancer with the act resulting in loss of identity and a fusion with the wider world, an experience that can be identified in the popular expression 'I lost myself in the music'. These sentiments are doubtlessly found cross-culturally, from the dancing of Egyptian Sufis (St John, 2004) to the medicinal trance-dance of the !Kung (Lewis-Williams, 1992). Indeed, dance is ubiquitous across human societies, perhaps partly because the synchronous element of dance produces endorphins, which are central to human bonding merge (Tarr et al., 2014; Fink et al., 2021).

Second, and intricately connected to dancing, are 'drums' or intense, repetitive beats, which have long been associated with altered states of consciousness (Winkelman, 1986). The psycho-spiritual benefits of drumming are said to include physical and spiritual healing (Aldridge and Fachner, 2006). Significant decreases in cortisol, a key stress hormone, have been found after just 15 minutes of listening to drumming in a controlled experiment (Gingras et al., 2014). The Dobe Ju|'hoansi (a tribe in modern day Botswana and Namibia) achieve altered states of consciousness through rhythmic beats, all night dancing and flickering lights - techniques which are also used at raves (Hutson, 2000:39; Lee, 1967). Although the DJ has been likened to a shaman (Gerard, 2004), the free party scene has an emphasis on dancers rather than DJ, a feature cited as revolutionary for its move away from 400 years of bourgeoisie-led music (Gauthier, 2004). In Durkheimian terms, this small, temporary, and self-organizing society can self-worship using a stack of speakers for its totem.

Third, sleep deprivation alters brain activation (Gujar et al., 2010) and is linked to disassociation (Selvi et al., 2015). Despite the hegemonic Northern-European/American preference for a single block of uninterrupted nocturnal sleep, the effects of sleep deprivation are not universally perceived as wholly negative. For instance, the ‘vision quests’ associated with delirium induced by sleep-deprivation are actively sought out in some cultures, such as some Native American communities (Dahl, 2013), and many others that practice shamanism (Winkelman, 1990). Raves and free parties primarily feature in the night-time economy, though they may continue for several days, so sleep deprivation tends to be a prerequisite for participation. Drugs may further disturb sleep patterns. For instance, ayahuasca, although commonly consumed nocturnally, alters sleep patterns even when clinically administered in the daytime (Barbanoj et al., 2008). The fourth and final D, drugs are perhaps the most obvious candidate for altering states of consciousness for their potentially rapid and intense changes to perception and behavior (Tart, 1969; Tramacchi, 2000; Preller et al., 2019).

Psychedelics and Ego Dissolution

While the positive long term therapeutic effects of psychedelics have been relatively well attended to since the resurgence of clinical psychedelic research (Rougemont-Bücking et al., 2019), their role in intergroup dynamics is less understood. Psychedelics, serotonergic hallucinogens, induce an altered state of consciousness commonly framed as powerful modifications to perception and mood lasting several minutes to 24 hours, or even more, depending on what is consumed, how much, and the method of ingestion. CSPs (classically serotonergic psychedelics) are generally safe and, unlike many other recreationally used drugs, are not associated with addiction (Nichols, 2016). Psychedelics include naturally occurring substrates, such as psilocybin, ayahuasca, peyote, and mescaline and chemically made drugs including LSD ((5R,8R)-(+)-lysergic acid-*N,N*-diethylamide) or synthetic DMT. In all cases, these psychedelics work on serotonin 5-HT_{2A} (5-hydroxytryptamine 2A) receptors (Nichols, 2016).

Psychedelic experiences are often characterized by a reduced sense of the self (Yaden et al., 2017), or even more extreme, ego dissolution, whereby the boundaries of the ego are temporarily disrupted (Millière, 2017). “Drug-induced ego dissolution”, where the boundary between self and world becomes blurred, has been proposed as a strong candidate for the potentially life-changing or spiritual experiences that psychedelics are reported to induce (Millière, 2017; Nour and Carhart-Harris, 2017). During certain types of ego dissolution, the self can be felt to be integrated into a greater whole, and an increased feeling of unity with one’s surroundings is experienced (Nour et al., 2016).

However, recent research has demonstrated that psychedelic experiences involving strong feelings of awe, but not necessarily ego dissolution, are associated with increased levels of feeling bonded with humanity and nature up to five years after the event (van Mulukom et al., 2020). Awe promotes the ‘small self’ and plays a significant role in prosocial behaviors (Piff et al., 2015). As such, psychedelic-inspired awe may play a key role in psychedelic therapies (Hendricks, 2018).

Importantly, van Mulukom et al. (2020) found that the effect of awe on bonding to humanity and nature was driven by feelings of connectedness (as a subcomponent of awe) during the psychedelic experience, rather than by feelings of self-diminishment or perceived vastness. The study did not measure feeling bonded with psychedelic-taking co-participants however, which begs the question of the more immediate bonds psychedelic drugs can induce.

Another drug regularly taken during raves, MDMA (3,4-Methylenedioxy methamphetamine), can also have dissociative and/or depersonalizing effects. Often classed as an ‘empathogen’, rather than a psychedelic, it is more popular though less associated with ‘mystical’ experiences (Lyvers and Meester, 2012). The altered state of consciousness associated with MDMA does not appear to be associated with the 5-HT_{2A} receptor (Puxty et al., 2017). Instead, increased heart rate associated with a moderate dose of MDMA in clinical settings has been associated with disassociation. Psychedelics consumed at mass festivals have been associated with transformative experiences more than MDMA (Forstmann et al., 2020).

Of the ‘big five’ personality traits (neuroticism, extroversion, openness, agreeableness, and conscientiousness), openness has a special relationship to psychedelics (Nichols, 2016). Previous research has demonstrated a positive association between the openness personality trait and total number of psychedelic experiences, specifically in that psychedelic use is believed to modulate personality (Erritzoe et al., 2019). Furthermore, openness has been associated with serotonergic neurotransmission but not frontal serotonin-2A-receptor binding, i.e., psychedelic rather than MDMA use is particularly related to the openness trait (Erritzoe et al., 2019). Research using double-blind trials suggests that psychedelics lead to lasting augmented trait openness - particularly mystical experiences have been linked to significant increases in otherwise stable trait openness a year later (MacClean et al., 2011). While psychedelics may increase openness to experience, openness may also influence the extent to which a psychedelic experience is perceived as more or less awe-inspiring (Yaden et al., 2019) and, consequently, how personally transformative that experience is. Here, we examine how trait openness relates to psychedelic ritual experiences (i.e., the 4Ds in the context of raves or free parties) and awe.

Transformative Experiences and Social Bonding

Previous research suggests that experiencing highly emotional, momentous events together creates a particularly strong and visceral type of group bonding called *identity fusion* (Swann et al., 2009, 2012). This fusion of personal and group identities is often compared to another, weaker form of group bonding termed *identification* (Whitehouse and Lanman, 2014). In relation to Durkheim’s *collective effervescence*, identity fusion has been likened to organic solidarity – an evolutionary old form of group alignment that kept small groups tightly bound for hunting big game or defending one another in tribal warfare (Whitehouse et al., 2017). Identification, in contrast, anonymizes larger,

agricultural groups for the purpose of swiftly recognizing group members who would otherwise be strangers if it were not for displays of their group membership (i.e., mechanical solidarity). The pictorial fusion scale, used in this study to operationalize group bonding, gives respondents the opportunity for complete immersion in their group (Swann et al., 2009), thus extending the popular Inclusion of Self in Other scale (Aron et al., 1992).

Three main causal pathways to fusion have been posited in recent years: shared experiences, shared biology, and shared ideology (Gómez et al., 2020). Regarding shared experiences, which we investigate here, identity fusion is argued to be a psychological mechanism evolved to hold groups together when individuals undergo intense and personally transformative experiences together (Whitehouse et al., 2017). Examples of emotionally intense, shared events that induce fusion include fighting on the frontline (Whitehouse and Lanman, 2014), experiencing a traumatic childbirth (Tasuji et al., 2020), and even watching one's football team endure a harrowing defeat (Newson et al., 2016; Newson et al., 2021). What is common to these events is that they contain powerful, emotional experiences that are felt to be personally transformative (Newson et al., 2016), and which are perceived to be similarly transformative for fellow participants (Buhrmester et al., 2018; Whitehouse, 2018).

In the psychedelics literature, personally transformative experiences have also been termed 'quantum change' or 'self-transcendent experiences' (Forstmann et al., 2020). Of these, epistemically transformative experiences are so intensely profound that they cause a shift in our values, attitudes, and sense of self in lasting and usually meaningful ways. Such experiences are equivalent to the personally transformative events described in the fusion literature, in that they are powerful enough to effectively re-write one's sense of self to incorporate the group with which one experiences the said event. By a process of reflection (Jong et al., 2015) and a false consensus bias, whereby we believe others to have perceived the event in the same way as us (Ross et al., 1977), individuals who have a personally transformative experience may irrevocably fuse with the group (Whitehouse, 2018).

Indeed, Forstmann et al. (2020) found that transformative experiences and social connectedness both increased after recent use of psychedelics at a series of field studies at mass multi-day gatherings. Furthermore, social connectedness (measured using the inclusion of self in other or IOS scale) following psychedelic use increased via transformativeness. Reports of feeling more connected to humanity among users of psychedelics (Carhart-Harris et al., 2018; van Mulukom et al., 2020) may represent the projection of relational ties on to a larger social group, which is one of the premises of fusion theory (Swann et al., 2012). Recent research has connected identity fusion to the *communitas* felt by participants at arranged ceremonial psychedelic retreats, but the relationship between the actual drugs consumed and fusion was not analyzed (Kettner et al., 2021).

Illegal Raves and Free Parties

Transcending to the sacred plane via awe-inspiring or liminal group experiences has been common in religious rituals

for millennia (Dunbar, 2013), but this mechanism is also exploited by the secular, for instance at large music gatherings (Turner, 1969) or raves (Gauthier, 2004). Of these collective rituals, rave is a relatively recent, but seemingly enduring, subcultural phenomenon. The exhaustive all-night (or weekend-long) dancing, engulfing repetitive bass beats, and, often heavy psychedelic drug use coupled with little sleep, construct a potent liminoid space with the potential to generate intense feelings of awe and social bonds, establishing a collective effervescence unparalleled for many young initiates (Gauthier, 2004; St John, 2015).

In the UK, multiple public order and licensing acts have tried to curb illegal raves. Of particular interest to this research are 'free parties'; raves that occur on the periphery of society and aspire to non-commercialization in contrast to the multi-million-dollar industry of the clubbing scene. This long-lasting counterculture evolved from the 'free festival' movement of the 1960s and 1970s (Griffin et al., 2018) and is often associated with subversive politics and drug use. With the emergence of mass raves and the popularization of electronic dance music (EDM) in the late 1980s and 1990s came a cultural split - the mainstream 'rave' and club scene on the one hand, and the 'free party' scene on the other.

In contrast to more mainstream clubs and music festivals, the liminoid spaces free parties and uncommercial raves occupy offer a greater opportunity for decreased self-regulation (Griffin et al., 2018) and, potentially more feelings of awe. They occur without security, or with underground security firms, un-ticketed or alternative payment systems (e.g., trade and exchange), and no licensing or insurance regulations. As the name implies, the individual has an opportunity to be 'free', whatever that may mean to them at that moment in time (Jaimangal-Jones et al., 2010). In contrast, music festivals offer a more bounded place for leisure or downtime. For an extended review of how raves constitute liminoid spaces, please see **Supplementary Material 1**.

Via liminality, rave culture accesses a 'sacred' realm in which ravers may have feelings of awe and experience *communitas*, in an engagement familiar to ritual devotees all over the world. Due to its transgressive nature, rave has been likened to a new religious movement, comparable to world entheogenic rituals (St John, 2004). This renders the rave an ideal context to test the effects of the '4D's' on awe and personal transformation and how, in turn, these effects of rave attendance may lead to social bonding and prosocial behaviors. As yet, partly due to the challenging nature of recruitment with underground subcultures, rave contexts have not been examined in terms of mechanisms that induce altered states of consciousness, nor has the specific role of psychedelic drugs.

We address these questions using an online survey with a natural population where ecological validity for psychedelic consumption is high compared to laboratory or clinical settings. Compared to the current proliferation of Northern-hemisphere targeted ayahuasca or psilocybin retreats that borrow heavily from indigenous cultures and make up much of the naturalistic psychedelic research, rave is an organic cultural practice. Drug taking is not prescriptive or particularly guided at these events, and usage varies between participants, making it a viable

candidate for experiences with a natural control population of non-drug using participants.

Present Study

So far, research into the socially cohesive benefits of psychedelics beyond clinical or laboratory settings has been lacking (Millière et al., 2018). We help to address this issue by conducting a retrospective online survey in a natural setting ($n = 481$) with a hard to access population of self-identified ‘ravers’ who attended legal and illegal raves or ‘free parties’. In this study, through a set of pre-registered hypotheses, we examine the pathway from engaging in behaviors that alter states of consciousness to awe, which in turn are associated with personally transformative experiences, ultimately leading to group bonding and prosocial behavior in rave contexts (see **Table 1**).

First, we investigated whether participants engaged in the 4Ds (dance, drums, sleep deprivation, and drugs) at particularly memorable raves or free parties and whether this in turn was associated with feelings of awe and personal transformation (H1a). We focused on the roles trait openness (H1b) and ego-dissolving drugs (CSPs, psychedelics) played in the process (H1c). We also tested which types of awe experiences had the strongest association with personal transformativeness (H1d).

Next, we investigated how awe-inspiring raves might be associated with greater bonding to other ravers – or even to humanity – when that rave was a personally transformative event (H2a). We also tested whether a sense of having shared the experience with others might influence this process (H2b). Finally, we investigated prosociality using a simple economic game, and its links to both bonding and transformative experiences (H3).

In a series of exploratory analyses, we also explored self-reported past donations to these charitable targets, as well as the association between time elapsed since the memorable rave and charitable giving. As illegal raves occur at the periphery of society and are more likely to be implicated in illegal drug use, we explored differences between legal raves and illegal raves or free parties, including whether the latter generate more awe and, consequently more bonding. Finally, we checked for gender differences in our key variables.

MATERIALS AND METHODS

This study was pre-registered prior to data collection. The pre-registration, and the data and analytic code, are available on OSF.

Participants

Ravers ($n = 552$) were recruited via adverts on specialized Reddit threads, dedicated rave Facebook groups, and via DJs on Instagram, calling for people aged 18 and over who had been to raves or free parties in the last five years. There were 16 participants who failed to complete two awareness checks and were excluded from the dataset. We further excluded 39 participants who reported having attended a rave more than 5 years ago, 3 who reported never having been to a rave, and 28 who completed less than 45% of the survey, leaving $n = 481$ (see **Table 2** for descriptives). Those who completed at least 45% of the survey completed everything required for this particular study. Further questions pertained to rave attendance and wellbeing during lockdown, for a separate paper.

Recruitment and Sample Size

Recruitment was via snowball sampling. A broad range of rave backgrounds were targeted using multiple Reddit subforums and Facebook specialist groups (including techno, psytrance, drum and bass, traveling communities, psychedelics groups, and the clubbing scene). After two weeks we had only attained half of our intended participants, so we created a pre-screening survey on Prolific to recruit a similar demographic. Snowball-sampled participants (38.7%) were incentivized with the chance to win a £100 prize (1 in 100 chance) and Prolific participants (61.3%) were remunerated for their time (£9.50 p/h). Data were collected in February - March 2021 via a Qualtrics survey. The snowball sample scored significantly higher on several central measures, including transformativeness and awe, compared to the Prolific sample, so we also re-ran the main analyses whilst including recruitment as a covariate and found them to be robust against recruitment (see **Supplementary Material 2**).

We conducted a power analysis with the R package *semPower*. Our goal is to obtain an RMSEA value of .06 (Kline, 2011),

TABLE 1 | Overview of pre-registered hypotheses of the current study.

Nr.	Hypothesis
1a	Engaging in behaviors to alter states of consciousness at raves (i.e., the 4Ds) will be associated with awe, which in turn will be associated with personally transformative experiences.
1b	The effect engaging in the 4Ds has on awe is moderated by the openness personality trait: the more open a person is (traitwise), the more these behaviors contribute to awe experienced during the rave.
1c	Of the 4Ds - extended dancing, drums, sleep deprivation, and drugs - drug use will be most associated with awe, and more specifically, psychedelic drugs.
1d	Of the awe experiences, feelings of connectedness and self-diminishment will have the strongest association with personal transformativeness, over perceived vastness, altered time perception, physical sensations, and need for accommodation.
2a	Awe experienced during the rave will be associated with greater bonding to other ravers and humanity, when the rave was a personally transformative event.
2b	The effect of personal transformativeness on bonding to other ravers is moderated by sharedness, or how shared the rave participants consider their experience to be.
3	Personally transformative raves will have prosocial effects (measured in charity donations) when individuals feel most connected to the target group. Ravers will donate to rave-based/humanitarian charities, when they feel connected to other ravers/all of humanity, and will donate less when they report weaker connections to these targets.

TABLE 2 | Descriptive statistics for key variables.

Demographics			
Age		Ethnicity	
Mean (SD)	30.51 (9.27)	Asian	32.10%
Range	18-68	White	28.10%
		Black	22%
		Mixed	9.80%
Gender		Other	6.40%
Women	54.70%	Chose not to say	2.30%
Men	43.20%		
Chose not to say	2.10%		
Rave/free party attendance			
Awe-inspiring event		Lifetime	
Illegal	28.30%	Ever attended illegal	53%
People in attendance*	300 (6-80,000)	Total attended*	10 (1-2000)
Took drugs	44.7%		
Alcohol	54.7%		
MDMA	34.3%		
Cannabis	22.0%		
Cocaine or other stimulants	17.1%		
Psychedelic drugs	14.1%		
LSD	6.9%		
Mushrooms	3.7%		
DMT or others from the 2C-x family	2.9%		
Other hallucinogens	0.6%		
Ketamine	13.9%		
Other drugs (e.g., self-reports of coffee or laughing gas)	2.5%		
Other opioids	0.4%		
Heroin	0.0%		
Social bonding			
Other ravers		Humanity	
Fused (i.e., option E)	15.6%	Fused (i.e., option E)	17.0%
Previously donated to a rave charity		Previously donated to a humanitarian charity	
Never	87.5%	Never	28.7%
Once or twice	7.4%	Once or twice	32.1%
Sometimes	2.5%	Sometimes	22.6%
Quite often	1.1%	Quite often	10.0%
Regularly	1.5%	Regularly	6.6%

*median (range).

with a standard.05 alpha error probability and 1 - beta value of 0.95 (see R script line below) for our largest model (see Exploratory Analyses; $df = 17$; all variables included and one interaction). The power analysis returned indicated that we would need $N = 477$ participants for a RMSEA fit of .06. R code: `semPower.aPriori(effect = 0.06, effect.measure = "RMSEA", alpha = 0.05, beta = 0.05, df = 17)`.

Measures

First, we asked participants to describe a rave or free party that they felt was particularly profound or awe-inspiring. To control for memory effects, we requested that they recall an event from the last five years. They also stated what year the event happened, roughly how many people were there, how many raves or free parties they had been to in total, and

whether they had been to an illegal rave or free party. We used a figure reported in the BBC that the largest rave ever held in the UK comprised 20,000 ravers and used that as a cut off for outliers.

Personal transformativeness was measured using items that draw from work by Newson et al. (2016) and Buhrmester et al. (2018) on a -3 - + 3 Likert scale (SD - SA), including: The event has shaped me as a person; The event has personally transformed me; I am who I am today because of this event.

The 4Ds were designed to assess rave-specific altered states of consciousness. These were measured with two items each on a 1-7 Likert thermometer (SD - SA) and were presented in a random order. Dance: *I danced constantly; I didn't dance at all* (RC). Drums: *At times, the music was so intense it was all I could hear; The music wasn't loud*

at all (RC). Sleep Deprivation: *I have rarely slept so little; I had my normal amount of sleep* (RC). Drugs: *By my standards, I was very high on drugs; I was completely sober* (RC). The 4Ds were further assessed with additional items on a 1-70 thermometer type scale, but these had poor fit, potentially due to the quite different scales they used, so were excluded from the final scale. These items can be found in **Supplementary Material 2**.

Participants reported whether they had taken any drugs during the experience (see **Table 2** for a breakdown). From these answers (e.g., alcohol, cannabis, cocaine, crack, other stimulants, LSD/acid, magic mushrooms, DMT, 2CB or others in this family, other hallucinogens, heroin, other opioids, other), a binary psychedelics variable and a binary MDMA variable were computed.

Awe was measured using the AWE-S scale (Yaden et al., 2019), measured on a -2 to $+2$ scale (SD vs. SA). The scale includes six subscales (self-diminishment, connectedness, time perception, perceived vastness, physical sensation, and need for accommodation). Please see SI for items. We included two moderators: openness and sharedness. Openness was measured using the BFI subscale on a -2 to 2 scale (SD-SA) (John et al., 1991).

How shared the participant felt the experience to be with other individuals was measured using a scale based on Muzzulini et al. (2021) on a 1-7 scale ('not at all' to 'a lot'), including the following three items: *Consider the rave experience you described and rate the extent to which other people at that event: (1) would give the exact same answer as you; (2) share the same feelings about that event as you; (3) share the same memories about that event as you.*

Social bonding was measured using Swann et al. (2009)'s 5-point pictorial identity fusion scale, which was treated continuously for model analyses given a relatively normal distribution. Identity fusion was measured with reference to 'other people who have been to raves/free parties' and 'all of humanity'.

Prosocial behavior was measured using a simple economic game designed to test participants' preference for self, a rave-based ingroup, or an extended ingroup (humanity) by inviting them to split an imaginary £10 as they wished between the three options. First, participants read a few sentences about each charity, which were taken from the websites of the respective charities but presented anonymously to prevent factors such as nationalism unduly influencing the results. The charities were PsyCare UK and Médecins Sans Frontières (MSF). Participants were told that at the end of the study, the researchers would donate £100 to the charity that received the largest amount of imaginary donations, and that if most people chose to keep the money for themselves, then we would not give a donation to charity. We donated £100 to MSF. The order in which the charity texts were presented was randomized. We also asked participants if they had ever given to similar charities in the past.

Demographic information was asked at the end of the survey, including age, gender, and ethnicity (white, Asian, black, mixed, other, prefer not to say).

Statistical Analyses

We computed means for the personal transformativeness, sharedness, AWE-S, and Openness scales. We also computed means for dancing, drumming, drugs, and sleep deprivation, as well as a 4D mean, which is the mean value of the four 4D scales. All variables were standardized before entering them in mediation/structural equation models and regression models. We used the standard $p < 0.05$ threshold for determining if our results were significantly different from those expected if the null hypothesis were correct. For the overall SEM model (see exploratory analysis), we considered $RMSEA \leq 0.08$, combined with $CFI > 0.90$ and $SRMR \leq 0.08$, to be indicative of an acceptable model fit (Kline, 2011). If a subject did not complete parts of a scale that were required to compute a mean or a total, then their responses to that measure were excluded from analysis. Participants were expected to answer all questions due to forced logic in the survey design. All analyses were conducted in R (R Team, 2013), using the lme4 package for linear regressions (Bates et al., 2007), lavaan for mediation modeling (Rosseel, 2012), and ggplot2 for plotting figures (Wickham, 2011). The default estimator of the lavaan package (which is maximum likelihood) was selected in path analyses as we did not have prior hypotheses about alternative estimation methods.

Pre-registered Hypotheses

To test H1a we conducted a mediation model examining the effect of the 4Ds (X) on personal transformativeness (Y) via awe (M). To test H1b, we conducted a moderated mediation model examining the moderated effect of the 4Ds (X) on personal transformativeness (Y) via awe (M), moderated by openness (mod). To test H1c, we conducted a regression model including the 4Ds (IVs) and awe (DV). To test H1d, we conducted a regression model including all awe experiences (IVs) and personal transformativeness (DV). To test H2a, we conducted a mediation model examining the effect of awe (X) on bonding to target groups (Y) via personal transformativeness (M). To test H2b, we conducted a moderated mediation model examining the effect of awe (X) on bonding to target groups (Y) via personal transformativeness (M), which was moderated by perceived sharedness of the experience (mod). To test H3, we conducted a mediation model examining the effect of personal transformativeness (X) on charity donations to a rave or humanitarian charity (Y) via bonding to other ravers/all of humanity (M).

Exploratory Analyses

To explore the effects of classic serotonergic psychedelic drugs (CSP; cf. van Mulukom et al., 2020), we entered psychedelic use as an additional predictor in the regression predicting awe as a result of the 4Ds. In the same regression, we also explored the effect of MDMA and combinations of CSP drugs and MDMA, given the prevalence of this drug at rave parties, and its effect on group bonding.

We also made a pre-registered prediction under exploratory analyses that self-reported past, as well as imagined, donations to the humanitarian and rave charities would be significantly predicted by social bonding. To explore this, we replaced the

imagined donation DVs in the model from H3 with the past donation DVs. Finally, we combined the mediation models from the pre-registered hypotheses together in one model (**Figure 1**). To achieve this, we added three extra direct paths to account for covariance: from 4Ds (X) to Bonding to target group (Y), from 4Ds (X) to Charity donation (Y), and from Awe (X) to Charity donation (Y).

In addition to our pre-registered hypotheses, we explored whether legal raves were quantifiably different from illegal raves or free parties, by comparing the key variables in our main model by event type using a series of Bonferroni-corrected independent t-tests (or Welch tests where equal variance was not assumed) and chi-squared tests. We also compared men and women's responses to key variables using the same approach. A correlation matrix can be found in **Supplementary Material 4**.

RESULTS

Pre-registered Hypothesis Testing

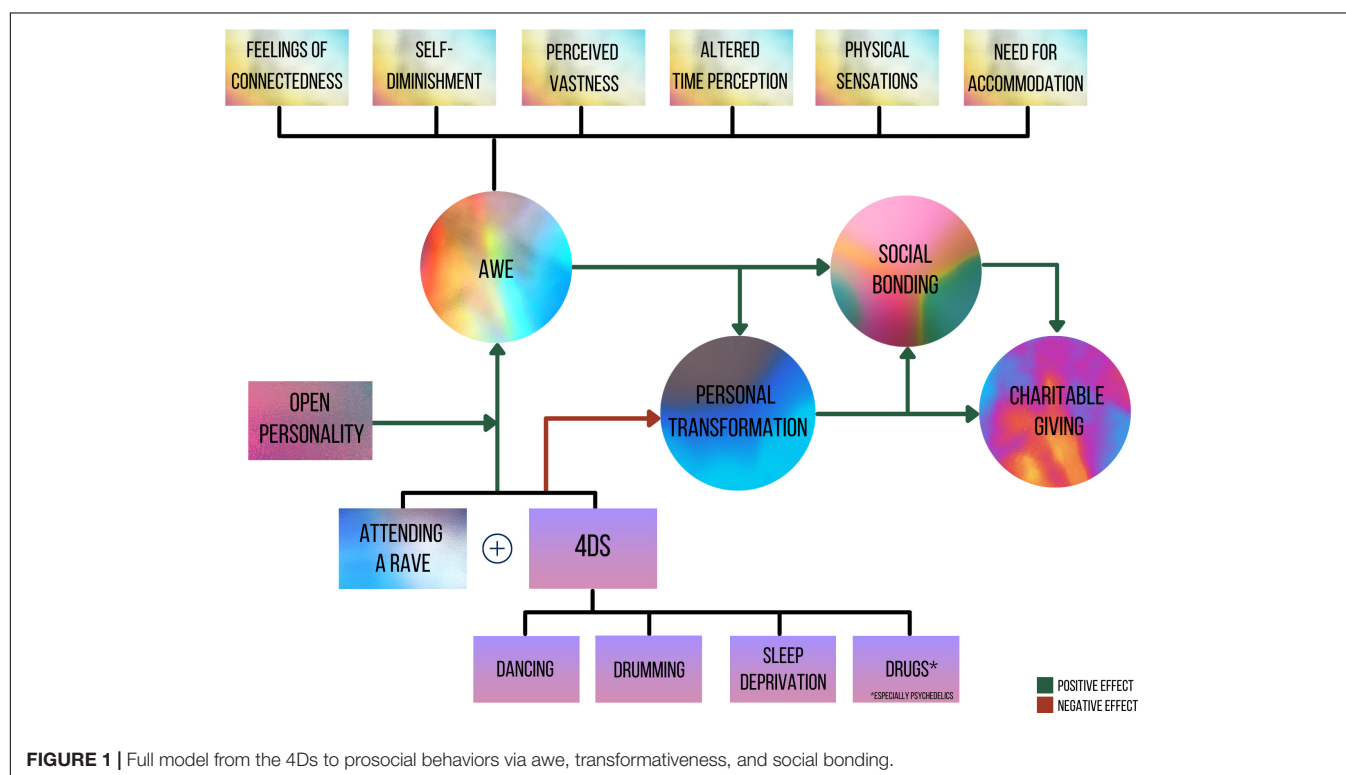
The 4Ds Lead to Personally Transformative Experiences via Awe, Especially for Particularly Open People

We found support for the hypothesis that engaging in behaviors to alter states of consciousness at raves (i.e., having a score for the 4Ds) induces awe, which in turn is associated with personally transformative experiences (H1a), see **Figure 2** for direct effects (see **Supplementary Material 5** for full statistics). The indirect path from the 4Ds to personal transformativeness via awe was significant ($b = 0.17$ [0.12, 0.23], $p < 0.001$), though the total

path was not ($b = 0.03$ [−0.08, 0.12], $p = 0.57$), indicating that the effect of the 4Ds on transformativeness was fully mediated by awe. We also found support for the hypothesis that the more open a person is (traitwise), the more engaging in the 4Ds contributes to awe experienced during the rave (H1b). The indirect path from the 4Ds to personal transformativeness via a moderated awe path was also significant ($b = 0.05$ [0.01, 0.10], $p < 0.001$), though the indirect path without moderation was significantly stronger ($p = 0.001$). When adding recruitment type as a covariate, the indirect path became non-significant ($b = 0.09$ [−0.01, 0.18]), though the mediator was still positively predicted ($b = 0.10$ [0.002, 0.195]).

Next, we investigated the unique roles of each of the 4Ds in relation to awe. While drugs had a strong effect on awe, dance was the largest predictor, followed by sleep deprivation, with no measured effect of more drums, **Table 3**. Given that the direct path from the 4Ds to personal transformativeness was significant, we also explored how the 4Ds were associated with reduced personal transformativeness through a regression including each of the 4Ds as predictors of personal transformativeness (see **Supplementary Material 6** and **Supplementary Table 5**). We found that while dancing ($\beta = 0.17$ [0.08, 0.26], $p < 0.001$) and drug use ($\beta = 0.12$ [0.03, 0.22], $p = 0.009$) predicted increased transformativeness, drums significantly predicted reduced transformativeness ($\beta = -0.20$ [−0.30, −0.11], $p < 0.001$), with no significant direct effect of sleep deprivation ($\beta = -0.05$ [−0.15, 0.05], $p = 0.30$).

We also explored the differential effects of CSP drugs, MDMA, and the combination of MDMA and CSP drugs on awe. Taking different types of drugs had a significant effect



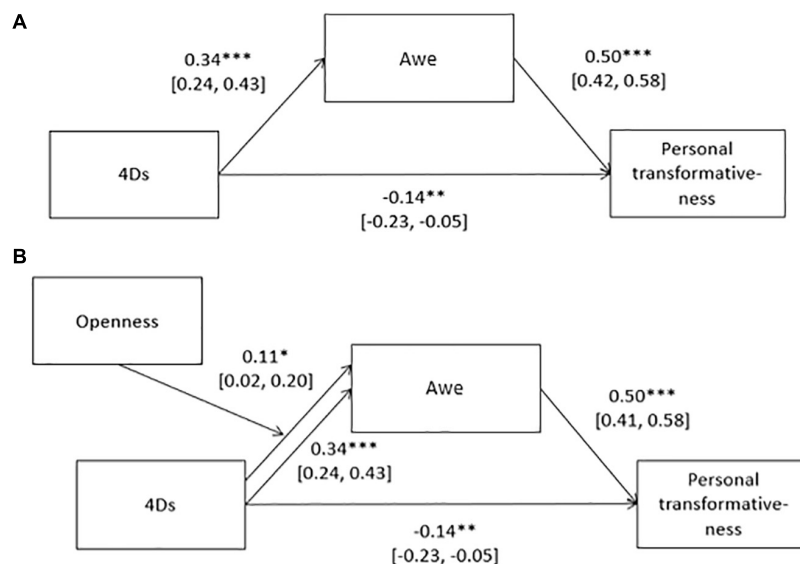


FIGURE 2 | Mediation models testing the effect of the 4Ds on personal transformativeness via awe; **(A)** without moderator of openness **(B)** with moderator. Standardized beta coefficients with 95% CIs. * $p < 0.05$, ** $p < 0.001$, *** $p < 0.001$.

on awe ($F(3, 477) = 11.27$, $p < 0.001$). Bonferroni-corrected *post hoc* comparisons demonstrated that those who took no drugs ($M = -0.05$, $SD = 0.79$) experienced less awe than those who took psychedelic drugs ($M = 0.55$, $SD = 0.52$), MDMA ($M = 0.34$, $SD = 0.62$), or both ($M = 0.30$, $SD = 0.77$). CSP drugs and MDMA both statistically contributed to awe and subsequent transformativeness, however psychedelic drugs had the greatest effect on awe, see **Figure 3** (and **Supplementary Material 6** with the full statistics). For all participants, the 4Ds together had the most significant effect on the awe path ($\beta = 0.28$ [0.20, 0.37], $p < 0.001$). However, the effect of taking (just) psychedelic drugs had the strongest effect on awe, compared to not taking any drugs at all ($\beta = 0.59$ [0.12, 1.07], $p = 0.01$), followed by taking MDMA ($\beta = 0.30$ [0.10, 0.51], $p = 0.004$). The effect of taking both psychedelic drugs and MDMA compared to not taking any drugs was not significant ($\beta = 0.28$ [-0.04, 0.59], $p = 0.09$).

Awe and Personal Transformation

The hypothesis that of the awe sub-scales, feelings of connectedness and self-diminishment would have the strongest

effect on personal transformativeness (H1d) was not supported. Instead, the perception of vastness, feelings of connectedness, and physical symptoms predicted transformativeness over the other awe subscales (**Table 4**). The positive effect of the 4Ds (the mechanisms that precede altered states of consciousness) on transformativeness via awe was driven by dance and drugs (**Table 3** and **Figure 4**, and **Supplementary Material 7**).

Transformative Rave Experiences Lead to Bonding to Ravers, but Not Humanity

We found support for the hypothesis that awe experienced during a rave is associated with greater bonding to ravers when the rave was a personally transformative event (H2a), see **Figure 5** for direct effects (and **Supplementary Material 8** for full statistics of the model). Both the indirect path ($b = 0.11$ [0.07, 0.16], $p < 0.001$), from awe to bonding via personal transformativeness, and total path ($b = 0.37$ [0.29, 0.45], $p < 0.001$) were significant, suggesting a significant role of the direct path from awe to personal transformativeness. However, we did not find support for the hypothesis that the effect of personal transformativeness on bonding to other ravers was moderated by how shared ravers consider their experience to be (**Supplementary Material 8**). In the moderated mediation models, the indirect path *without* sharedness as a moderator ($b = 0.11$ [0.06, 0.16], $p < 0.001$) was significant, whereas the indirect path *with* the moderator ($b < 0.01$ [-0.04, 0.04], $p = 0.84$) was not. The two models were significantly different from each other ($p < 0.001$).

The second path in the model, from awe to bonding to humanity via personal transformativeness, was only partially, negatively supported (see **Figure 5** above for direct effects, and **Supplementary Table 8**). The indirect path from awe to bonding to humanity via personal transformativeness was significant ($b = -0.05$ [-0.10, -0.01], $p = 0.03$), as was the total path ($b = -0.13$ [-0.22, -0.04], $p < 0.001$). In the moderated

TABLE 3 | Model for Hypothesis 1c: Predicting awe with the 4Ds separately.

Variable	β	SE	95% CI	t-value	p-value
Intercept	<-0.01	0.04	[-0.08, 0.08]	< 0.01	> 0.99
Dance	0.21***	0.05	[0.12, 0.30]	4.68	< 0.001
Drums	-0.02	0.05	[-0.11, 0.07]	-0.41	0.68
Deprivation	0.13**	0.05	[0.04, 0.22]	2.80	0.005
Drugs	0.18***	0.04	[0.09, 0.27]	4.04	< 0.001
Statistics	$F(4, 479) = 19.39$, $p < 0.001$				
Fit	$R^2 = 0.139$ *, 95% CI [0.08, 0.19]				

All variables were standardized before they were added to the regression. * $p < 0.05$. ** $p < 0.01$, *** $p < 0.001$.

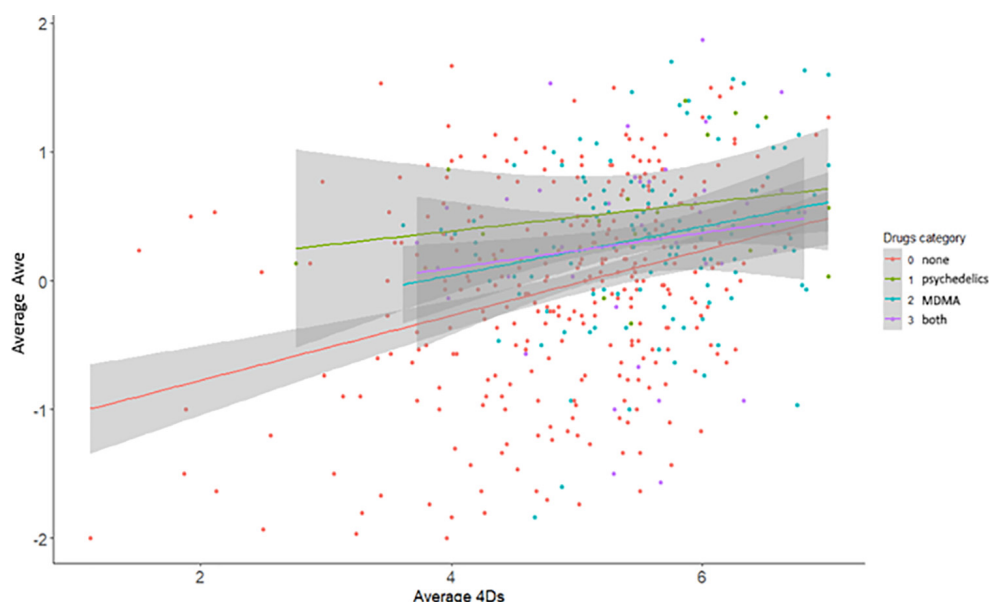


FIGURE 3 | Scatterplots of the effect of the 4Ds on awe, grouped by drugs taken during the rave.

mediation (see **Supplementary Material 8**), the indirect path *without* sharedness as moderator was significant ($b = -0.05$ [$-0.10, <-0.01$], $p = 0.03$), while the indirect path *with* the sharedness moderator was insignificant ($b = 0.02$ [$-0.02, 0.06$], $p = 0.28$), with a significant difference between the two indirect paths ($p = 0.04$). Given the significant direct paths from awe to bonding with ravers and bonding with humanity, we also explored which awe components predicted bonding to ravers and humanity, respectively, see **Supplementary Table 15**. We found that the direct path from awe to bonding with ravers was driven by positive associations with connectedness ($b = 0.31$ [$0.19, 0.41$], $p < 0.001$) and physical sensations ($b = 0.22$ [$0.12, 0.33$], $p < 0.001$), and negative associations with the need for accommodation ($b = -0.24$ [$-0.35, -0.12$], $p < 0.001$). The regression predicting bonding with humanity using the awe subscales was not significant ($F(6,474) = 1.854$, $p = 0.09$).

TABLE 4 | Model for Hypothesis 1d: Predicting transformativeness with the awe subscales.

Variable	β	SE	95% CI	t-value	p-value
Intercept	<-0.01	0.04	$[-0.08, 0.07]$	-0.09	0.93
Connection	0.21***	0.06	$[0.09, 0.34]$	3.33	< 0.001
Time perception	0.02	0.05	$[-0.08, 0.12]$	0.37	0.71
Vastness perception	0.23**	0.07	$[0.09, 0.37]$	3.17	0.002
Physical sensations	0.14**	0.05	$[0.04, 0.25]$	2.62	0.009
Accommodation	-0.06	0.05	$[-0.16, 0.04]$	-1.11	0.27
Self-diminishment	< 0.01	0.05	$[-0.10, 0.10]$	< 0.01	> 0.99
Statistics	$F(6,475) = 27.38$, $p < 0.001$				
Fit	$R^2 = 0.257^{**}$, 95% CI[0.19, 0.31]				

Note. All variables were standardized before they were added to the regression.
* $p < 0.05$. ** $p < 0.01$, *** $p < 0.001$.

Bonding via Personally Transformative Raves Is Associated With Prosocial Behavior

Overall, participants donated more to the humanitarian charity ($M = £4.49$, $SD = 3.40$) than keeping money for themselves ($M = £3.14$, $SD = 3.71$; $p = 0.001$), both of which were allocated more money than the rave charity ($M = £2.37$, $SD = 2.96$; p 's < 0.004). Nonetheless, we found support for the hypothesis that personally transformative raves are associated with prosociality (measured in hypothetical charity donations) when individuals feel most bonded to the target group (H3, **Figure 6**).

Ravers donated to rave-based charities when they felt connected to other ravers and donated less when they reported weaker connections. Both the indirect path ($b = 0.05$ [$0.02, 0.09$], $p = 0.002$), from transformativeness to donations to a rave charity via bonding to other ravers, and total path ($b = 0.31$ [$0.22, 0.40$], $p < 0.001$) were significant, suggesting a significant role of the direct path from personal transformativeness to charity donations. However, we did not find support for the humanity model, in which both the indirect path and total path from transformativeness to donations to a humanitarian charity via bonding to other humanity were not significant ($b < -0.01$ [$-0.02, 0.01$], $p = 0.14$; $b = -0.06$ [$-0.15, 0.03$], $p = 0.16$).

We also further explored the same model, replacing choices in the simple economic game for actual past charitable giving to rave and humanitarian charities. Contrary to the prediction in our pre-registration, past donations to rave charities was not a significant outcome variable (indirect effect of transformativeness on past donations to a rave charity via bonding to ravers: $b = 0.001$ [$-0.01, 0.01$]), nor was past giving to humanitarian charities predicted by transformativeness via bonding to humanity (indirect effect: $b = -0.001$ [$-0.01, 0.01$]). However, logistic

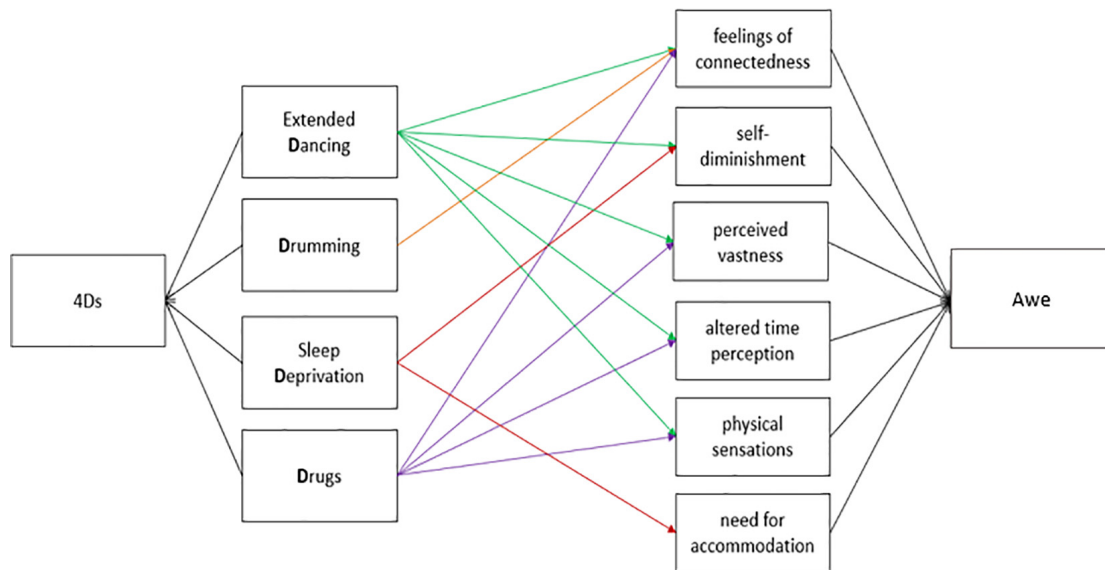


FIGURE 4 | Separate regressions of each of the 4D components onto each of the awe components (colored lines); only significant relations are shown.

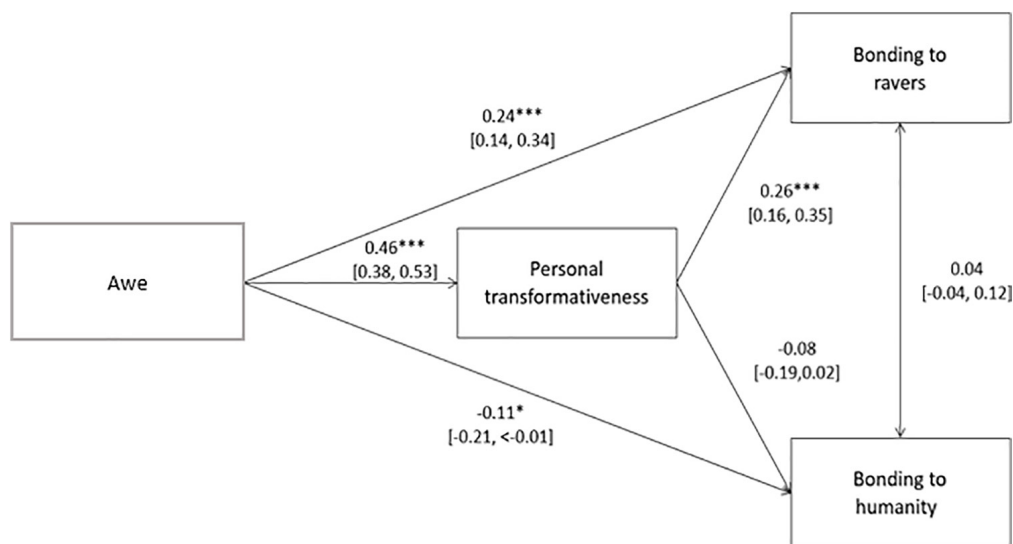


FIGURE 5 | Mediation model predicting bonding to ravers and humanity from awe via personal transformativeness. Standardized beta coefficients with 95% CIs. * $p < 0.05$, ** $p < 0.001$, *** $p < 0.001$.

regressions showed that bonding to ravers significantly predicted past charitable giving to rave based charities ($b = 0.38$, $SE = 0.14$, $p = 0.006$). The estimated odds ratio demonstrated an increase of nearly 46% [$\text{Exp}(B) = 1.46$] for having donated to a rave charity for every one unit increase of bonding to ravers. In contrast, bonding to humanity was not found to contribute significantly to past giving to a humanitarian charity ($b = 0.07$, $SE = 0.10$, $p = 0.47$). We found that the more recent the memorable rave participants reported on, the more they gave to the rave charity ($r(473) = -0.16$, $p = 0.001$), but there was no correlation between time passed since the

memorable rave and donations to the humanitarian charity ($p = 0.132$).

Exploratory Analyses: 4Ds at Rave > Awe > Transformation > Bonding > Charitable Giving

Finally, we combined the mediation models from the pre-registered hypotheses together in one model. The overall model (Figures 1, 7) incorporating the three mediation models had fit indices (RMSEA = 0.059; CFI = 0.969; SRMR = 0.040; see

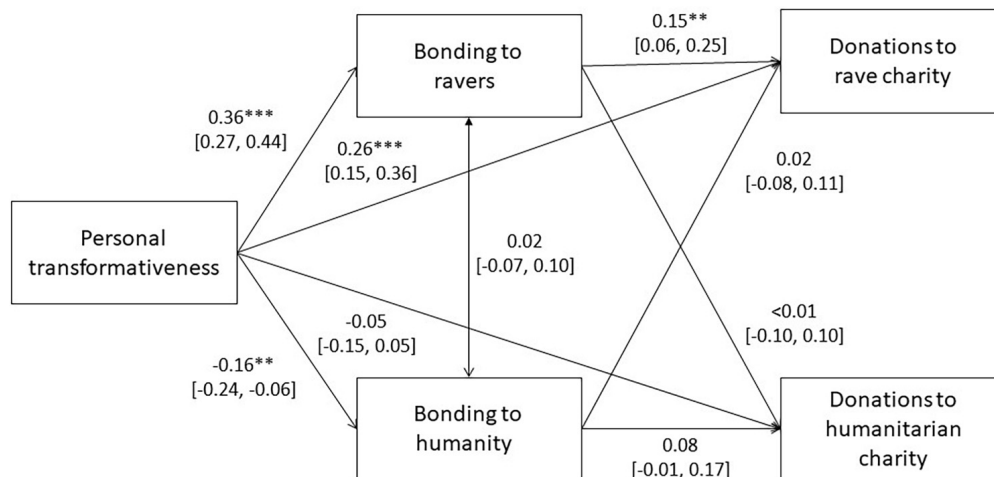


FIGURE 6 | Mediation model of prosocial donations. Standardized beta coefficients with 95% CIs. * $p < 0.05$, ** $p < 0.001$, *** $p < 0.001$.

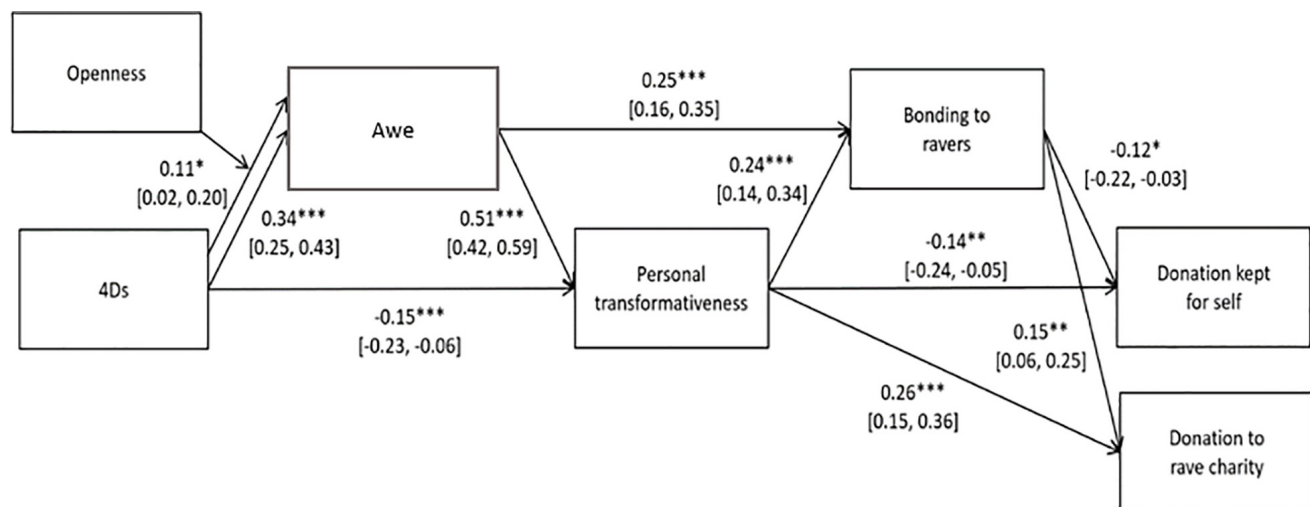


FIGURE 7 | Full structural equation model of the 4Ds at raves > awe > transformativeness > bonding > prosociality pathway. Standardized beta coefficients with 95% CIs. * $p < 0.05$, ** $p < 0.001$, *** $p < 0.001$.

Supplementary Material 9 and **Supplementary Table 16** for full statistics) within our pre-registered thresholds ($RMSEA \leq 0.08$, combined with $CFI > 0.90$ and $SRMR \leq 0.08$; Kline, 2011). This path model suggests that the 4Ds are associated with feelings of awe (especially for people with high trait openness), which in turn relate to personal transformation and a bonding to other ravers. Finally, this bonding, is associated with less selfish and more prosocial choices toward ravers in a simple economic game.

Further Exploratory Analyses

Finally, we found that illegal raves or free parties differed from legal raves in several important ways (**Table 5**). Of the 4Ds, drug taking was unsurprisingly higher at illegal raves. All subsequent variables in the model were also significantly higher at illegal

events (openness, awe, transformativeness, social bonding, and prosocial donations). Male participants reported significantly higher levels of trait openness and transformativeness than females ($p's < 0.004$) but there were no other gender differences after Bonferroni corrections (see **Supplementary Material 10**).

DISCUSSION

There is a long tradition of research on communal experiences that induce collective effervescence or *communitas*, such as those involving dance, drums, sleep deprivation and/or drugs ('the 4Ds'). Here we tested a series of pre-registered hypotheses to investigate how these mechanisms might be associated with feelings of awe in the context of contemporary raves and free parties, and how such personally

TABLE 5 | Comparing key variables between legal and illegal events.

Variable	Legality	N	M (SD)	t	df	p	95% CI of the difference
4Ds (Dance)	Legal	345	5.77 (1.29)	-1.891	306.35	0.060	-0.43; 0.01
	Illegal	136	5.98 (1.03)				
4Ds (Drums)	Legal	345	5.84 (1.26)	1.627	479	0.104	-0.04; 0.47
	Illegal	136	5.64 (1.34)				
4Ds (sleep Deprivation)	Legal	345	4.41 (1.66)	-1.51	479	0.132	-0.57; 0.07
	Illegal	136	4.65 (1.52)				
4Ds (Drugs)	Legal	345	4.19 (1.63)	-5.529	479	< 0.001*	-1.21; -0.57
	Illegal	136	5.08 (1.48)				
Awe	Legal	345	0.03 (0.75)	-3.391	479	0.001*	-0.41; -0.11
	Illegal	136	0.29 (0.77)				
Openness	Legal	345	0.68 (0.66)	-3.384	479	0.001*	-0.36; -0.10
	Illegal	136	0.92 (0.66)				
Transformativeness	Legal	344	-0.49 (1.65)	-4.089	271.8	< 0.001*	-0.94; -0.33
	Illegal	135	0.15 (1.48)				
Bonding (ravers)	Legal	345	3.08 (1.16)	-3.705	479	< 0.001*	-0.66; -0.20
	Illegal	136	3.51 (1.10)				
Donation (rave)	Legal	341	2.026 (2.73)	-3.786	201.34	< 0.001*	-1.88; -0.59
	Illegal	132	3.27 (3.36)				

*Bonferroni-corrected significance, $p < 0.005$.

transformative experiences may lead to social bonding and prosocial behaviors.

First, the 4Ds appeared to be an effective measure of mechanisms for inducing altered states of consciousness and feelings of awe. In support of previous research feelings of awe were particularly strong for people with open personalities (Yaden et al., 2019). Here we connect that association with a higher score on the 4Ds. In the wider literature, psychedelic use has been found to increase trait openness (MaClean et al., 2011; Erritzoe et al., 2019), but here we identify the significant role this trait may play in allowing people to perceive an event that could otherwise be quite exhausting to be awe-inspiring and personally transformative. It is also possible, however, that people's openness increased as a result of their experience with psychedelics, leading them to remember the event as more awe-inspiring and transformative. Experimental research is required to disambiguate these relationships.

Importantly, unless people reported elevated levels of awe, the 4Ds were negatively associated with personal transformation. This path of no personal growth could be considered a Durkheimian *anomie*. Presumably, ravers who dance to loud repetitive beats, stay up all night, and take excessive quantities of drugs without a feeling of awe, are quite simply exhausted. This is supported by exploratory regressions, which identify that loud or intense music ('drums') was especially negatively associated with transformativeness. Relatedly, the neuroscience literature has shown how emotionally intense experiences are associated with amygdala activity, i.e., encoding and consolidation.

Psychedelic drugs were particularly associated with feelings of awe, compared to MDMA or drugs in general. Drugs, as well as Dance, had particularly strong positive effects on awe compared to Drums or sleep Deprivation in this context. However, it was the 4Ds taken together that had the strongest association with awe. In turn, of the five awe subscales we explored,

perceptions of vastness, feelings of connectedness, and physical symptoms (e.g., having goosebumps) were most associated with transformativeness.

Awe experienced during a rave or free party - especially when illegal - appeared to take participants on a journey to irrevocable bonding with those around them. While previous research demonstrated a link between feelings of connectedness at the time of psychedelic experiences and bonding with nature and humanity up to five years later (van Mulukom et al., 2020), the present research included connectedness to one's more immediate social circle (other ravers), as well as associated prosocial behaviors. Direct, positive paths from connectedness and physical sensations and direct, negative paths from need for accommodation to identity fusion with ravers were also found. This supports recent research showing that visceral (but not detailed) flashbulb memories concerning Brexit referendum results led to personal transformativeness via processes of reflection about the meaning of the event (Muzzulini et al., 2021). Memory viscosity also includes physical experiences (e.g., feeling tense all over) when recalling the event (Talarico and Rubin, 2003).

Identity fusion is thought to consist of a visceral feeling of oneness with a group, such as resulting from the sharing of highly emotional, often dysphoric, experiences (Whitehouse, 2018). It is unsurprising that the need for accommodation was negatively associated with transformativeness here: this AWE-S subscale consists of items regarding the unsolved nature of an experience, whereas transformativeness is arguably the result of meaning making and reflection on meaning, processes shown to be involved in identity fusion (Jong et al., 2015).

Although personal transformativeness' role in identity fusion has now been well documented (Newson et al., 2016; Buhrmester et al., 2018; Whitehouse, 2018), the details about what makes some events more transformative than others has remained

elusive. We propose that feelings of awe may inspire a ritual state of liminality, connecting participants to parts of themselves and one another that are inaccessible in day-to-day life. One way that Dance, Drums, and perhaps Drugs, may contribute to creating awe-inspiring, liminal experiences is by inducing synchrony between ritual participants.

Synchrony is a powerful mechanism for creating a feeling of unity (Tarr et al., 2014; Lang et al., 2017), a potentially important aspect of inducing awe. Drumming and dancing clearly have synchronous elements so future understandings of the 4Ds would do well to consider synchrony's role in inducing awe in relation to the 4Ds. Furthermore, the distributed coordination observed in dancing associated with modern rave or club culture, i.e., patterns of coupled movement between individuals within a group rather than whole group unitary synchrony, has been linked to group affiliation in terms of both liking and conforming (Von Zimmermann et al., 2018). Variations in synchrony could also be a promising for further research in natural environments.

Links to Prosociality

We found that imagined donations to an ingroup were associated with awe-inspiring, transformative experiences induced by psychedelic consumption at raves in a complex, pre-registered multi-mediation model. These findings corroborate previous research demonstrating that awe is associated with prosocial outcomes. For example, the induction of awe (through a video clip or recall) has been associated with increased prosocial behavioral intentions (of generosity, or to help a person in need). It has been suggested that such prosocial effects may occur via a perception of 'small self' that is associated with awe (Shiota et al., 2007; Piff et al., 2015; Bai et al., 2017). More specifically, awe is considered to constitute "a shift in attention toward larger entities and diminishment of the individual self" (Piff et al., 2015, p. 884).

Some nuance may be required, however: While ego dissolution is typically equated with self-diminishment, we did not find a specific effect of self-diminishment on transformativeness and bonding, while we did find an effect of connectedness, in line with previous research (van Mulukom et al., 2020). While both ego dissolution and self-diminishment involve reduced focus on the self (e.g., resulting from the 4Ds), it may be that ego dissolution captures both self-diminishment and *self-expansion*. Rather than feel themselves 'shrink' (self-diminishment), participants' decreasing self-focus may have instead felt like they were becoming part of something larger, whether abstract (e.g., nature or God) or a larger group. Indeed, dispositional awe-proneness is associated with self-concepts that include more statements about membership to very large categories (Shiota et al., 2007).

In the current study, prosocial donations – past or imagined – were only found to a rave-based charity, and not to a humanitarian-based charity. The value of the economic game in this context was that it could be manipulated to specific real-world scenarios (rave and humanitarian charities (Pisor et al., 2020)). Coupled with extensive ethnographies describing

prosociality at, and following, raves, the measure seems relevant to test the theory (Tramacchi, 2000; St John, 2015).

Pro-social behavior in the economic game was linked to bonding and the personal transformativeness associated with particularly awe-inspiring raves where participants engaged in the 4Ds. Previous research has demonstrated that fusion is particularly aligned with extreme sacrificial behaviors, compared to more mild sacrificial behaviors (Paredes et al., 2020). If our prosocial outcome had been more extreme, e.g., protest or willingness to fight and die, the associations between fusion and behavioral choices may have been even stronger. Identity fusion and cocaine (an ego-inflating drug) have been found to interact among British football fans (Newson, 2021), such that highly fused fans who took more cocaine reported the most aggression toward their rivals. One explanation for the link is that cocaine-induced ego inflation leads to a heightened sense of agency and strength among highly fused people, who already feel imbued with their group's strength (Swann et al., 2009, 2012). We found peaceful associations between fusion and psychedelic drug use: prosocial choices in an economic game, at a cost to self.

Psychedelics and the Social Cure

The consequences of intense shared rituals – in terms of connectedness and prosocial behavior – have not previously been empirically tested in the context of raves or in relation to CSPs. A strength of the present research is that psychedelic use was reported at a culturally natural setting, i.e., organically occurring raves, as opposed to a commercial 'retreat'. Millière et al. (2018) called for caution regarding the "problematic conflation of temporary states of self-loss with 'selflessness' as a personal or social trait" (page 2). Our research offers a unique lens into the interpersonal nature of awe-based selflessness and connectedness to others. Furthermore, we offer an applied study that respects the value of 'set and setting' (Leary et al., 1963).

Our data, from a natural population, may also be regarded as tentative evidence of self-medication for the *communitas* and social connections the 4Ds, particularly psychedelic drugs, offer. This relates to the literature on improved social connection and wellbeing from expensive Westernized ayahuasca and similar retreats (e.g., Kettner et al., 2021). Future research could help to identify the features of an event that make it an awe-inspiring context, one that is ultimately capable of provoking transformative experiences that lead to powerful social connections in the form of identity fusion. Borrowing tools from the free party scene to create a ritual environment could be beneficial to commercial retreat providers and those managing therapeutic CSP settings to try and provide ritualized environments for participants, which are more potent for meaningful, lasting social bonds and altruistic behavior.

To effectively evaluate the therapeutic value of psychedelics in the future, natural environments must be considered, as therapeutic drug consumption has been convincingly argued as inherently social (Kettner et al., 2021). Indeed, social networks and identities are considered integral to both physical and mental health more generally (Jetten et al., 2012). Compounding

this, the plethora of psychedelic research has focused on individuals, leaving the intersubjective nature of altered states of consciousness and their pathway to shared experience and collective action less explored (Kettner et al., 2021).

Limitations

This study suffers from several limitations. First, the 4Ds are used here as a pilot into investigating mechanisms for altered states of consciousness in natural populations. The items need to be replicated across different contexts and the dimensions need further investigation. Second, we are limited by the nature of our cross-sectional mediation analyses: while our results largely support our predictions, they cannot be considered to indicate causality, which would require experimentation or longitudinal analyses (Maxwell and Cole, 2007). Nonetheless, with bootstrapped analyses and careful interpretation of the indirect effects, our results could be taken as evidence of the paths proposed, especially when triangulated with further studies (Preacher and Hayes, 2004).

Third, due to our recruitment strategy, this study is faced with population differences. The effects were stronger in our more natural sample (recruited via snowball sampling on drug forums and rave social media) than the less natural sample of Prolific users. This may simply have been because Prolific users were significantly less likely to report attending illegal parties, and hence consumed fewer drugs, leading to lower scores on all subsequent outcome variables. Nonetheless, the relationships between key variables were consistent, even for the Prolific users. For instance, some Prolific users reported very low (disagree) awe responses, which still related to transformativeness, suggesting that even a small amount of awe has a (small) effect on transformativeness.

Fourth, the results rely on retrospective self-reports, from a self-selecting sample. The sample is also WEIRD (Western, Educated, Industrialized, Rich, and Democratic) due to its Northern hemisphere sample. Nonetheless, our research is perhaps best framed with the WILD paradigm, i.e., research that is Worldwide, *In Situ*, Local, and Distinct (Newson et al., 2020). In particular, the rave cultural context mirrors many of the core features of communal entheogenic psychedelic rituals. We are keen for future research to seek convergent validity for the 4Ds in more diverse contexts, especially other organic rituals that employ psychedelics, e.g., shamanic rituals.

Fifth, our data regarding drug use may suffer from the confounding effects of different combinations of poly-drug use (e.g., the concurrent use of psychedelics and cannabis or alcohol). In natural settings, poly-drug use is a major potential issue. We found that many participants combined one or more drugs with alcohol, but no clear pattern emerged to this. As Ives and Ghelani (2006) point out, reporting polydrug use is an important first step and we have made this data freely available on OSF. Furthermore, we did not disambiguate between MDMA and 'pills': although either may be 'cut' with other illegal or legal substances, this is typically the case for pills and their effects should not solely be attributed to MDMA. However, this reflects the real world and can be understood in a wider context of literature where

psychedelic drugs are examined in controlled and laboratory settings.

Finally, our measure of 'sharedness' may have been too broad to accurately capture feelings of sharedness. Rather, the experience may have been with a smaller subset of the rave cohort, and bonding feelings then projected on to the wider group of ravers. Future research to quantify sharedness and disambiguate social targets is needed to disentangle this.

CONCLUSION

Crowd rituals, like raves, are about 'coming together' and, in this capacity, rave offers something of an alternative to materialism. It has long been noted that the absence of meaning that characterizes modern consumer culture leads to its members feeling unfulfilled, from which mass experimentation and cultural and religious diversity ensue (Wallace, 1956). Rave is one expression of dissatisfaction with the current era and, for people who perceive the event as awe-inspiring, transmutes as a meaningful act rather than a temporary hedonistic escape from reality (Hutson, 2000:37). Both Durkheim and Turner regarded ritual as fundamental to sociocultural revitalization and, in this respect, rave involves processes at both individual and societal levels. There are myriad different forms of human ritual to match as many cultures and, as rave culture emerges, so too do its ritual practices to fulfill its members' spiritual needs.

When physical connection is limited, e.g., during the COVID-19 pandemic, do we still have a need for physical proximity? How might the 4Ds and their associations with group synchrony help cohesion among young and vulnerable groups, who have been isolated during repeated lockdowns? What's more, how might awe-inspiring, group experiences and physical closeness have a trickle-down effect to the rest of society? We found that while bonding to ravers was associated with transformative, awe-inspiring experiences fueled by the 4Ds, bonding to humanity was not – how might the boundary between bonding targets be stretched to encompass wider celebratory groups?

Elements of the 4Ds appear in large crowds – from sports fans to festival goers to political activists. We suspect that the 4Ds have the potential for a more prolific role in group bonding for close knit or therapeutic communities, where there is more potential for long term bonding in stable groups, compared to relatively anonymous large crowds at raves. Our model suggests that the 4Ds have a powerful effect in how events may be perceived as ritual and transformative, leading to meaningful bonds that are also associated with real-world, prosocial behaviors.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: DOI 10.17605/OSF.IO/BZDE8.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Kent (004-ST-21). The patients/participants provided their informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

MN and VM conceptualized the study, prepared the pre-registration, ran statistical analyses, and wrote the manuscript. MN, FC, and RK collected the data. RK and MN prepared the data. VM led statistical analyses, prepared the code, and ran the

SEM. All authors discussed recruitment strategy and proofread the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpsyg.2021.719596/full#supplementary-material>

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MDMA-Assisted Therapy as a Means to Alter Affective, Cognitive, Behavioral, and Neurological Systems Underlying Social Dysfunction in Social Anxiety Disorder

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Social anxiety disorder (SAD) is a prevalent and often debilitating psychiatric disorder that can assume a chronic course even when treated. Despite the identification of evidence-based pharmacological and behavioral treatments for SAD, much room for improved outcomes exists and 3,4-methylenedioxymethamphetamine (MDMA) has been proposed as a promising adjunctive treatment to psychological interventions for disorders characterized by social dysfunction. A small randomized, placebo-controlled trial of MDMA-assisted therapy (MDMA-AT) for social anxiety in autistic adults offered encouraging results, but more research is sorely needed to explore the potential for MDMA-AT in treating SAD. This review aims to stimulate future study by summarizing research on disruptions in neurological, perceptual, receptive, and expressive systems regulating social behavior in SAD and proposing how MDMA-AT may alter these systems across four domains. First, we review research highlighting the roles of social anhedonia and reduced social reward sensitivity in maintaining SAD, with specific attention to the reduction in positive affect in social situations, infrequent social approach behaviors, and related social skills deficits. We posit that MDMA-AT may enhance motivation to connect with others and alter perceptions of social reward for an extended period following administration, thereby potentiating extinction processes, and increasing the reinforcement value of social interactions. Second, we review evidence for the central role of heightened social evaluative threat perception in the development and maintenance of SAD and consider how MDMA-AT may enhance experiences of affiliation and safety when interacting with others. Third, we consider the influence of shame and the rigid application of shame regulation strategies as important intrapersonal processes maintaining SAD and propose the generation of self-transcendent emotions during MDMA sessions as a mechanism of shame reduction that may result in corrective emotional experiences and boost memory reconsolidation. Finally, we review research on the role of dysfunctional interpersonal behaviors in SAD that interfere with social

functioning and, in particular, the development and maintenance of close and secure relationships. We discuss the hypothesized role of MDMA-AT in improving social skills to elicit positive interpersonal responses from others, creating a greater sense of belonging, acceptance, and social efficacy.

Keywords: MDMA-assisted therapy, social anxiety disorder, social functioning, shame, social anhedonia, social threat

INTRODUCTION

Social anxiety disorder (SAD) is the fourth most commonly diagnosed psychiatric disorder in the United States (1). Approximately 13% of the population in the U.S. will have SAD at some time in their life, with as many as 8% reporting SAD over the past year (1). SAD is characterized by a frequent and intense fear in social situations in which the person is afraid of being scrutinized by others and, as a result, avoids or experiences social situations with significant tension or discomfort (2). Epidemiological research has found that people with SAD report overall reduced quality of life, with negative consequences on their social and occupational lives, even at levels below the diagnostic threshold (3, 4). Indeed, behaviors associated with SAD have been shown to contribute to delayed and fractured relationships, reduced likelihood of partnering and having children, workplace absenteeism, lower worker productivity, and inability to maintain or initiate employment (2, 5, 6). SAD is often associated with the concurrence and development of other psychological disorders, particularly alcohol use disorder (7, 8) and major depressive disorder (MDD) (9). Although the exact nature of these relations remains unclear, SAD often occurs first and confers approximately a four-fold risk and five-fold risk for developing alcohol dependence (7) and MDD (10), respectively, relative to the general population. SAD may also confer greater risk for adverse physical health outcomes. SAD increases the risk for chronic social isolation and loneliness, robust longitudinal predictors for cardiovascular disease and increased mortality (11).

Among people with SAD, intense fears of being negatively evaluated in social situations often arise during adolescence (12) and the problem often goes unrecognized as something that could be treated (13). Evidence-based pharmacological (14) and behavioral treatments (15) for SAD have been identified, but much room for improved outcomes exists. Meta-analytic data on medication-based therapies suggests that SSRIs and SNRIs are associated favorable outcomes compared to placebo yet are also associated with higher dropout rates over the treatment course (14, 15). The efficacy of pharmacotherapies also appears dependent on continued adherence to medication, with as many as 25% of people reporting relapse after discontinuation of the drug. In terms of psychotherapies, cognitive-behavioral therapy has shown strong evidence for treatment efficacy and superior longevity to pharmacotherapy (15). Yet, in the case of both medication and psychotherapy a significant proportion

of patients remain considerably symptomatic at the end of treatment (15), with social anxiety often assuming a chronic course in spite of intervention (16).

Recent research has begun to explore whether certain drugs can be used to augment the effectiveness of psychological interventions for SAD. A recent systematic review of d-cycloserine as a means to augment psychotherapy for SAD found that it provides a small augmentation effect for exposure therapy in treating SAD (17). A second drug that has been investigated as an augmentation strategy in the treatment of SAD is 3,4-methylenedioxymethamphetamine (MDMA). A small randomized, placebo-controlled trial of MDMA-assisted therapy (MDMA-AT) for social anxiety in autistic adults ($N = 12$) found a large between groups difference in social anxiety symptoms at the primary endpoint in favor of MDMA-assisted therapy ($n = 8$; seven completed treatment) vs. psychotherapy plus placebo ($n = 4$; $d = 1.4$) after two doses of MDMA. Results from this trial suggest promise for the treatment of SAD in the absence of autism. Although autism spectrum disorder appears to confer greater risk of developing SAD relative to the general population, clinically elevated levels of social anxiety are found only in the minority of individuals with autism, demonstrating that SAD is a problem separable from autism itself, while still sharing some features (18). MDMA-AT has also been most extensively tested in the treatment of post-traumatic stress disorder (PTSD) and has shown to result in large effect size differences compared to placebo controls in Phase II and Phase 3 trials (18–21). In addition, both phase II (19) and the existing phase 3 study (20) suggest excellent safety and low abuse potential when MDMA is used under controlled conditions. However, little research has been conducted on its possible mechanisms of action in the context of treatment studies.

MDMA has been proposed as a particularly promising treatment adjunct for disorders characterized by social dysfunction, such as SAD (22). This may be due, at least in part, to its stimulation of hormonal responses related to oxytocin, vasopressin, prolactin, and cortisol (23–25), all of which have profound impacts on social behavior. These effects are largely downstream of primary effects of MDMA on serotonin, norepinephrine, and dopamine systems (26). MDMA also functions as a stimulant and results in subjective effects including, most relevant to this paper, altered responses to social stimuli and experience of social emotion, including heightened feelings of empathy, and feelings of love (27) and compassion (28).

MDMA-assisted therapy is typically delivered in the following format. Treatment begins with three preparatory sessions aimed

Abbreviations: MDMA-AT, MDMA-Assisted Therapy; SA, Social Anxiety; SAD, Social Anxiety Disorder.

at helping participants get ready for dosing sessions by providing information, answering questions, exploring relevant history, and teaching preliminary skills. This is followed by a dosing session, which is then followed by integration sessions aimed at helping the person make sense of what happened in the dosing sessions and how to generalize what they learned into their daily life. Studies typically have a total of 2–3 dosing sessions, each followed by three integration sessions.

Alongside the promise of MDMA-AT in augmenting current therapies for SAD to ameliorate social anxiety symptoms, evidence remains preliminary. One factor that may limit progress in this area is the lack of clear theorizing on potential processes of change that may occur in the context of MDMA-AT. A stronger theory will help identify potential processes of change that could guide research to improve integration between drugs and psychotherapy.

To address this gap in the literature, this review summarizes data on alterations in the affective, cognitive, and neurological systems related to social functioning in SAD and how MDMA-assisted therapy may alter these functions. We focus not on the immediate effects in dosing sessions, which we discuss in another paper (Luoma et al., manuscript submitted), but rather on downstream effects that may occur in the weeks or months after dosing sessions.

We discuss four overarching domains in which therapeutic processes of change may occur and result in long-term improvements in functioning in SAD. First, the potential role of MDMA-AT in reducing social anhedonia and enhancing social reward sensitivity in SAD. Second, the role of social threat perception and functioning of the ventral vagus complex and associated neurological structures in SAD and how MDMA-AT may result in sustained alterations in their functioning. Third, the role of shame and shame-regulation strategies, such as self-criticism, in maintaining elevated threat perception in SAD and how MDMA-AT may interrupt these patterns. Fourth, the potential role of MDMA-AT in changing interpersonal behavioral patterns observed in SAD that may maintain the disorder.

We present these domains as distinct for the purpose of presentation clarity; however, we view them as related and interdependent processes of change that reciprocally affect one another to affect overall social functioning in SAD. This conceptualization has guided terminology used throughout this paper in that we have chosen to use the term process of change, rather than mechanism, as it allows for the existence of bidirectionality, feedback loops, and concurrent change, whereas mechanism often implies a linear or causal pattern of variable interaction (29).

SOCIAL ANHEDONIA AND SOCIAL REWARD SENSITIVITY

People with SAD often have broad impairments in positive emotions, particularly in response to social situations (30, 31). For example, people with SAD experience diminished positive affect and increased negative affect in social interactions in

general (32), and reduced positivity in response to social acceptance and enhanced negativity in response to social rejection (33). The reduction in positive affect in response to social situations, infrequent social approach behaviors, and related social skill deficits observed in SAD has been termed social anhedonia (31). Relatedly, people with SAD show altered responses to social reinforcement, leading to alterations in the balance between approach goals related to seeking social connection and advancing socially and avoidance goals related to social threat (34, 35). An experimental study showed that due to greater hypersensitivity to social punishment, people with social anxiety may have greater difficulty adapting to increased social reinforcement after being rejected by someone (or perceiving they were) even when that person later becomes more rewarding (36). This overactivation of avoidance goals may be part of why people with SAD tend to interpret positive social stimuli in threatening ways (30) and show increased fear of positive evaluation from others (37). For example, people with SAD often react to positive feedback by expecting that their partner will expect more from them in the next interaction and that they will fall short of those expectations (38, 39). This tendency to interpret positive social events as threatening has been shown to partially mediate the relationship between social anxiety and decreased positive affect (40). Increasing the relative balance of approach vs. avoidance goals as it relates to social situations may be core to recovery from SAD. For example, increased approach behavior in the form of sharing positive emotions is associated with improvements in SAD symptoms during treatment (41) and experimental reductions in safety behaviors (i.e., reduced avoidance) among people with high social anxiety (SA) results in more enjoyment during social events (42, 43). Together, these results suggest that increased positive reinforcement in social situations and reduced experiences or perceptions of punishment are important in the treatment of SAD. In relation to MDMA-AT, various sources of evidence suggest that MDMA may make social interactions more rewarding and less punishing and that these effects may endure beyond the dosing session. This may help alter the ratio of approach- vs. avoidance-focused social goals that appear to maintain SAD. MDMA has been shown across multiple studies to affect the action of brain systems related to social bonding and positive reinforcement related to social encounters (22). At a subjective level, people ingesting MDMA report feeling peace, safety, and love (27) and a subjective sense of desire to be with others (44), which comports with observations that MDMA increases motivation to affiliate with others during active dosing. At a neurochemical level, MDMA has been shown to induce the release of oxytocin and prolactin, two hormones centrally implicated in the ability to form social connections (45, 46). MDMA also strongly affects 5-HT_{2A} receptors, which are important mediators of behavioral sensitization (47–49). A recent series of studies on mice indicate that the effects of MDMA on social behavior may extend beyond acute dosing. In a series of experimental studies, Nardou et al. (50) showed that mice exhibit a critical period through adolescence when they find social encounters with stranger mice reinforcing but then lose this preference as they age. Nardou et al. (50) also demonstrated that this critical window can be reopened

in adult mice by administering MDMA in the presence of another mouse. Furthermore, this increased sensitivity to social reinforcement extended for at least 2 weeks post-administration. They also revealed that this effect did not occur with cocaine administration, suggesting it was not simply the pairing of positive stimuli with the presence of another mouse that resulted in the effect. Additionally, they also established that the MDMA needed to be administered with another mouse present in order to achieve this enduring shift in social reinforcement, suggesting that the social context of MDMA administration is important. Another series of mouse studies by Curry et al. (51) showed increased social behavior toward unfamiliar mice after multiple treatments with MDMA, with this effect being greater when the mice received MDMA while in the presence of another mouse. Together, these results suggest that MDMA may enhance motivation to connect with others, enhance the likelihood that people find social interactions with strangers rewarding, and that this effect may extend beyond MDMA administration in a therapeutic, social context. These effects could have multiple therapeutic benefits in people with SAD. First, it could shift motivation to engage in social behavior that could potentiate extinction processes in post-dosing sessions. For instance, the only available placebo-controlled trial testing MDMA-AT on social anxiety symptoms in autistic adults (52) found that, out of the seven participants who completed a full course of MDMA-AT, two people reported initiating dating for the first time, and another two reported increased comfort exploring and expressing gender identity at the 6-month follow up. It is possible that temporary increases in the reinforcement value of social interactions could initiate a new pattern of behavior in which individuals with SAD seek out previously avoided social situations and have more frequent positive social experiences, resulting in a positive chain of events in which affiliative behavior toward others elicits reciprocal affiliative behavior toward oneself [e.g., (53)]. Over time, this new learning could reinforce social approach and result in a reduced perceived need to enact safety behaviors that interfere with effective social functioning thereby increasing perceptions of social efficacy.

HEIGHTENED SOCIAL THREAT

A heightened tendency to experience social stimuli as threatening has been posited to be *the* central mechanism in the development and maintenance of SAD (12). People diagnosed with SAD show heightened amygdala activity to stimuli related to social-evaluative threat, such as negative emotion expressions or critical comments about oneself (54–56). Essentially, people with SAD do not feel safe in their relationships with others. This appears to be particularly true when interactions involve greater threat of revealing their authentic self, such as in laboratory tasks focusing on closeness generation through reciprocal self-disclosure (57). In fact, those with higher social anxiety have been shown to self-disclose less often in social tasks when they have high expectations of being liked by another person, whereas this pattern is inverse for people with low social anxiety (58). Other examples of this pervasive sense of threat in interpersonal relationships is the greater discomfort with social touch among people higher in social anxiety (59), heightened

levels of interpersonal distrust (60), increased amygdala activity in response to emotional stimuli (61), and heightened loneliness in SAD youth (62). This heightened interpersonal-evaluative threat may account for at least some of the impairments in interpersonal functioning seen in SAD. The ability to feel safe around others and respond to social interactions in flexible, fluid, and contingent ways appears to be mediated through the same neuroanatomical systems. This system has been termed the social engagement (63) or social safety system (64) and involves the functioning of the parasympathetic nervous system and most centrally the vagus nerve and ventral vagus complex. The branch of the vagus nerve most fundamental in regulating social engagement enervates the heart as part of regulating global metabolism, slowing the body, and fostering a state of quiescence and potential for social engagement. The activation of this ventral branch of vagus nerve is thought to be indexed by higher heart rate variability, which refers to regular fluctuations in heart rate linked to the breathing cycle (65). Reduced high frequency heart rate variability at rest, which may be measured in a variety of ways we will not outline here, has been linked to a variety of anxiety disorders, social anxiety in particular (66), and also to perceived social connection (45, 46). High frequency heart rate variability is thought to measure the operation of the vagal brake, which refers to the action of the parasympathetic nervous system in downregulating physiological arousal in situations that are perceived as safe and in which rest is an adaptive response. Research suggests chronic under activation of the vagal brake in individuals with SAD, although it is unclear whether vagal nerve impairments play a role in the development of SAD or are better conceptualized as SAD sequelae. Nevertheless, people with social anxiety disorder demonstrate a rigid response style to social situations that involves the inability to inhibit threat-based responses in non-threatening situations (66) and which can be seen in decreased heart rate variability at rest compared to healthy controls (67). In addition to allowing the body to rest and regenerate, the ventral vagus and associated central nervous structures are also responsible for enervating muscles associated with flexible and responsive social engagement in the face, neck, and larynx. The result is that when the ventral vagus is active, our voice is more musical and face is more mobile thus facilitating better social engagement (64). Thus, in situations of increased sympathetic activity and decreased parasympathetic activity, peoples' ability to respond to social situations in a sensitive and synchronous manner is impaired. In sum, the tendency for people with SAD to experience heightened social threat appears to result in decreased operation of the social engagement system during social events, resulting in dysfunction in the operation of the vagus nerve, and thereby difficulties in non-verbal flexible social interaction. Behavioral evidence of social miscoordination can be seen in evidence that people with SAD demonstrate impairment in the non-verbal synchrony in social situations that is associated with greater warmth and rapport (68). Furthermore, people with SAD do not show increases in non-verbal synchrony that occur in healthy controls when engaging in closeness-generating conversations (69). Further indicators of social miscoordination in SAD include reduced reciprocal giving (70) and greater sensitivity to social punishment that may result in a greater difficulty adapting to

increased social reinforcement after being rejected by someone (36). People with SAD also show differential cortisol reactivity in a high self-disclosure context and evidence less of a decline in cortisol when self-disclosing compared to people lower in social anxiety (71). Different types of evidence indicate that when people with SAD attend to positive affiliative signals, this leads to a range of positive outcomes (72–74), suggesting that shifts in felt social safety, along with attendant shifts in the functioning of the social engagement system could mediate changes in social anxiety symptoms. In addition, several longitudinal studies combine in suggesting that close positive relationships and experiences of social mastery/belonging serve as protective factors against SA (30). For example, a prospective study of SA among adolescents found that SA decreases when positive friendship qualities (i.e., companionship and intimacy) increase (75). Other examples of the importance of attending to positive social stimuli can be found in research showing that people with SAD differed from healthy controls only in positive affective empathy, but not negative affective empathy (76). In other words, they could share in others' negative emotions in a laboratory task but were less able to vicariously share others' positive emotions. Improvement on an empathy accuracy task mediated treatment outcomes in group CBT for social anxiety; this was particularly the case for positive affective empathy relative to negative affective empathy (41). In addition, people high in social anxiety appear to underestimate intensity and duration of positive affect when exposed to a positive interpersonal vignette as compared to individuals low in social anxiety, and overestimate other-related disgust, internal shame, and guilt (77). This literature suggests that improvements in SAD are likely to be dependent upon the extent to which people experience a greater sense of safety in social encounters and that this change will be mediated through the social engagement system. MDMA-AT appears to help people feel safer with others. Anecdotal reports of early therapists using MDMA indicated that clients often report greater ease in relating in both close and more distant relationships for weeks or months afterwards (28). A qualitative analysis of reports from a clinical trial of MDMA-AT for PTSD found that reports of feeling safe were common, such as in the following quotes from participants,

... I think it allowed me to feel safe in my space... Now it was safe and I had my tools and weapons to be able to tackle the obstacles that I never had before; There's no words that's going to explain this but I have never in my life relaxed like I did during this... Maybe like what you would feel in your mommy's tummy or something, whatever being back in the womb, very safe, very warm [(78), p. 46].

Another possibility is that MDMA may potentiate changes in social safety through facilitating a greater focus on cues related to affiliation and intimacy and less of a focus on cues related to hierarchy and social rank. In most social situations, people with SAD may tend to focus on managing and attempting to improve a self-perceived low social rank, rather than on affiliation and intimacy (35). A focus on social rank, particularly in the context of perceived low social rank,

is likely to activate emotion systems linked to defensive arousal and deactivate those related to social engagement (79). This tendency to perceive affiliative cues as threatening can be seen in the fear and avoidance that people with SAD show to the positive evaluations of others (80) as well as their tendency to respond to positive evaluations with elevated arousal compared to healthy controls (81). MDMA has been shown to facilitate responding to positive social cues preferentially (82). Thus, MDMA may bolster internally experienced positive affect by shifting clients' focus toward positive aspects of social experiences (e.g., being accepted and feeling connected), exploring positively-valenced emotional experiences, and formulating social approach goals (relative to avoidance). As reviewed above, this effect may have its action through the influence of MDMA on the bonding-related hormones such as oxytocin and prolactin that may be linked to vagal tone (83). In addition, the serotonin system which MDMA strongly affects has been implicated in bonding. For example, experimental research on prairie voles shows that traumatic events reduce pair bonding in prairie voles, but this is reversed by selective serotonin reuptake inhibitors (84).

SHAME AND SHAME-RELATED COPING

Different types of evidence point to the significance of shame in maintaining heightened social threat perception in SAD. Shame is a self-conscious emotion characterized by the perception of being inferior, unlikable, or unacceptable and a desire to hide the undesirable self from others (85). Negative self-representations, negative interpretation biases, negative self-imagery, and social-evaluative thoughts characteristic of shame are observed at higher levels among individuals with SAD than healthy controls [see (12) for a review]. Indeed, shame is more highly correlated with SAD than other anxiety disorders (86) and predictive of social anxiety symptom severity (87). Decreases in shame-proneness, but not guilt-proneness, are associated with decreases in SAD symptoms (88). Shame is theorized to have evolved to prevent humans from behaving in ways that have a high negative social cost and could result in social devaluation by others and loss of social rank (e.g., cheating, stealing) (89, 90). When people are informed that social devaluation has occurred, or perceive that it could occur, shame is triggered to organize their behavior around mitigating their loss of social standing and reducing risk of ostracism (91). Studies have shown that self-reported shame elicited by social vignettes is highly correlated with actual ratings of social devaluation among individuals within and across distinct cultures (90). Experimental research has also shown that shame is elicited by predictive cues of social devaluation, such as being told one would be excluded by others, regardless of whether they acted in a morally transgressive way, suggesting the experience of shame is intimately tied to one's sense of threatened social cohesion rather than specific social behaviors (91). For individuals with SAD, negative attentional biases associated with increased social threat perception may result in an overestimation of the potential for social devaluation across social contexts (12), resulting in

more frequent and intense experiences of shame compared to people without SAD (92). Some clinical models of SAD treatment hold that the anxiety experienced by people with SAD is a secondary response to the anticipation of exposing the core shameful self to others (93, 94). Preliminary support for this idea is suggested by intensive longitudinal and experimental data. For example, a daily diary study of college students showed that social anxiety symptom severity predicted higher shame during significant social interactions among college students (95). Similarly, the likelihood of shame after receiving negative feedback following a speech task is more strongly predicted by trait social anxiety rather than ratings of state social anxiety immediately following that task (96). In this view, SAD is maintained because individuals with SAD develop a range of shame avoidance strategies that function to protect them from experiencing rejection, ostracism, and shame that may confirm predictions based on shame-based self-referential thinking (e.g., “I’ll make a fool of myself”). These avoidance behaviors, however, inadvertently prevent them from working through their core sense of shame and reinforce anxiety in social situations. Self-criticism is a key internal shame-avoidance strategy in SAD (95, 97). In moderate doses, self-criticism can serve an adaptive self-monitoring function that serves to identify discrepancies between an individual’s behavior and societal expectations, helping the person appropriately modify their actions to adhere to social norms. Among individuals with SAD, however, self-criticism appears to be applied frequently and inflexibly around social interactions (97) and incorporates a high level of negative self-evaluation (96, 98). For example, in a daily diary study, college students with higher social anxiety reported increased self-criticism following social events, regardless of the level of shame they experienced, whereas those low in social anxiety only endorsed self-criticism following high-shame interactions (95). This inflexible pattern of self-criticism is thought to perpetuate anxiety in social situations by reinforcing beliefs of low social rank and inferiority (79) and triggering defensive arousal associated with a sense of social threat. Indeed, an fMRI study showed that self-criticism was associated with increased activation in the lateral prefrontal cortex and dorsal anterior cingulate, areas of the brain associated with error processing and behavioral inhibition, but not areas associated with mindfulness and self-reassurance, such as the insula, suggesting a heightened attentional focus on identifying and correcting mistakes rather than general self-reflection (99). Over time, negative attentional biases in SAD may manifest in a general negative self-concept (100), greater access to negative self-related imagery in social situations (101) and heightened access to negative autobiographical memories (102), serving to maintain the shame-bound sense of self among individuals with SAD. Reductions in shame would have a broad range of positive effects for individuals with SAD. For instance, general decreases in shame should reduce the accessibility of negative self-imagery (103) and the tendency to engage in self-critical rumination in response to stressful social events (95, 96, 104), both of which appear to serve as maintaining factors in SAD. More broadly, if revealing the authentic self is less likely to trigger shame, then defensive self-focused attention may

also be reduced (105–107), resulting in a decreased need to regulate shame through avoidant, self-critical processes. Indeed, a study of emotion-focused therapy for social anxiety showed that decreases in shame expressed in-session were associated with reduced self-criticism the following week (92). MDMA-AT may help individuals with SAD reduce shame by facilitating experiences of compassion or kindness toward the self through neurochemical changes, as well as through modeling from the therapist in the dosing session. With respect to the former, two experimental studies with ecstasy (presumably containing MDMA in one study and tested to confirm MDMA in the other) demonstrated that ecstasy increases feelings of self-compassion and reduces self-criticism (108, 109). In addition, anecdotal reports of MDMA-AT sessions suggest that MDMA increases self-compassion and self-acceptance (28, 110). Research on SAD suggests that greater self-compassion is associated with decreased fear of positive and negative evaluation (111) and reduced social anxiety severity (112). In addition, MDMA appears to elicit self-transcendent emotions more broadly. The mostly commonly reported experience while taking MDMA is a blissful state characterized by feelings of pleasure, peace, and love (27). Love and compassion are self-transcendent emotions, a family of emotions that increase prosocial behavior (113, 114), perceptions of connectedness (115), and the tendency to transcend self-centered needs to focus on the needs of others (116). Self-transcendent emotions generated through loving kindness meditation have also been shown to increase social connectedness (117, 118) and reduce self-criticism (119). MDMA-AT also appears likely to strengthen the bond between therapist and client and boost feelings of safety in dosing sessions, potentially laying the foundation for reproducing these types of safe interactions with others following participation in MDMA-AT. MDMA-AT participants often report feeling very safe with therapists during dosing sessions (78) and the tendency for MDMA to elicit expressions of warm and positive emotions toward therapists is also likely to elicit reciprocal responding from therapists (120, 121). Furthermore, the tendency for MDMA to strengthen emotional responses to positive social stimuli (44, 122) is likely to make therapists’ responses of compassion and warmth more salient at a visceral level. If the core fear of people with SAD is that the exposure of a seemingly flawed and inferior self will result in rejection and shaming from others (94), then this enhanced therapeutic bond should potentiate corrective interpersonal learning experiences by both encouraging the person to be authentic and thereby reveal this core defective self, while also resulting in a prediction error when the person experiences acceptance and caring as a response, rather than the expected ridicule or rejection. This could enhance memory reconsolidation of shameful memories contributing to the person’s core sense of shame, thereby reducing personally felt shame as well as the fear of shame previously resulting in shame regulation strategies (123). In sum, when used in a supportive therapeutic relationship, MDMA may reduce shame through the facilitation of self-transcendent emotions, particularly compassion, and by enhancing the therapeutic bond to potentiate corrective interpersonal learning. Reductions in shame should then result in reduced experiences of social

evaluative threat and reductions in the defensive, avoidant, and preparatory behaviors that are central to maintaining SAD.

DYSFUNCTIONAL SOCIAL BEHAVIOR

SAD has been associated with a variety of social behaviors that function to decrease anxiety in social situations but inadvertently induce discomfort in others and evoke desires for social distance from people with SAD (12). These interpersonal behaviors are likely to contribute to the maintenance of SAD by evoking responses in others that further reinforce the person's perceived low social status and their perceptions of defectiveness and social inadequacy [e.g., (124)]. In addition, these behaviors have been shown to interfere with the development and maintenance of the kinds of close and secure relationships that are essential to adaptive functioning (125, 126). Since people with higher levels of social anxiety have been shown to preferentially benefit from the presence of close others compared to those with lower levels of social anxiety (127), behavior that blocks the development of these close secure relationships may foster an overarching sense of social disconnection in some that further contribute to heightened arousal and reduced activation of the social engagement system. Studies informed by ethological models of social anxiety (79) frame social anxiety as a mechanism that evolved to de-escalate competition between individuals in part *via* safety behaviors such as submissive gestures like gaze aversion, slouched posture, and constricted vocal tone. Consistently, one study (128) showed that socially anxious male participants demonstrated a higher number of submissive behaviors, specifically higher vocal tone and collapsed posture, than their less anxious male counterparts while engaged in a semi-structured role-play designed to elicit competitive threat. These submissive behaviors were positively correlated with both state shame and social anxiety. In addition, Zimmerman et al. (129) found that submissive behaviors mediated the relation between trait social anxiety and internalized shame among socially anxious men. These submissive displays are inconsistent with desired behavioral norms in Western society that have historically prioritized dominance and status as the primary markers of success, particularly for men. Although behaviors such as polite smiles, directing gaze downward, restricting speech in conversation, and speaking softly may serve to reduce anxiety in the moment, they have been associated with negative perceptions from observers and decreased willingness among peers to re-engage the individual in conversation in a lab setting, particularly in ambiguous social tasks (130–132). Perhaps the most extreme behavior in the repertoire of individuals with SAD to down-regulate anxiety is to avoid social situations altogether (133), resulting in fewer opportunities to build relationships with others and inadvertently confirming perceptions of one's lack of social value. Thus, these interpersonal deficits may both impair the development of new relationships and interfere with the development of greater intimacy and safety in existing relationships, thus perpetuating perceptions of social threat due to lack of a close and connected relationships. Furthermore, research suggests that SAD severity may be associated with

reduced prosocial interpersonal signals. One example is the reduced frequency of genuine smiles in social interactions. Genuine smiles have been robustly demonstrated to be perceived as signals of generosity (134), competence (135), and intrinsic engagement and motivation by others (136). In one study, people with SAD showed less smiling during social encounters compared to controls and this predicted less interest in future interactions from conversational partners (125). This lack of smiling in people with SAD is likely to result in lower liking and pleasure in conversational partners, which has been confirmed in a study that found that conversational partners low in social anxiety did not experience boosts in positive affect when paired with individuals high in social anxiety and that this lack of positive affect was correlated with SAD partner's lack of smiling (137). The heightened sense of social threat in people with SAD also leads to a tendency to conceal their true feelings, a phenomenon termed expressive suppression (138). The behavior of masking one's true feelings has been demonstrated to lead to negative reactions from others in social encounters (139–141). Furthermore, trait tendencies toward expressive suppression have been shown to predict negative interpersonal outcomes over time (126, 142) including reduced social support (143) and difficulty forming new relationships (126). Fortunately, expressive suppression has been shown to decrease with successful treatment of SAD (138), suggesting that improvements in expressive suppression may play an important role in recovery from SAD. These interpersonal deficits in SAD are also likely to lead to subjective feelings of inauthenticity and perceptions from others that the person is being inauthentic. Authenticity refers to whether a person is expressing their “true” or “core” self in their behavior or whether the person is behaving in a way that is true to what they really experience (144). Authenticity has been associated with higher personal (145–147) and interpersonal well-being (148, 149). People with SAD have been shown to experience lower self-rated authenticity in dyadic interactions as well as being rated by conversational partners as less authentic (150). Furthermore, people with SAD have also been shown to exhibit more inauthentic opinions (151), with this tendency predicting lowered self-concept clarity. This suggests that people with SAD who chronically express opinions and attitudes based on what they believe others wish to hear, rather than their own genuine viewpoint, tend to become confused about their own opinions and attitudes, potentially contributing to this uncertain and inadequate sense of self found in SAD. An individual's early social context is theorized to play a significant role in the development of safety behaviors in SAD by informing the person's sense of social-evaluative threat and level of anxiety across social situations (12). For instance, parenting styles associated with overcontrol or overprotection (152–154), exposure to adverse social experiences with peers, such as bullying, social ostracism, or peer victimization (152, 155, 156), early relational traumatic experiences (154, 157, 158) and strong societal expectations to adhere to strict cultural norms (159) contribute to the development of social anxiety and may also play a maintaining role (12). Other evidence suggests a bidirectional relation between social anxiety and social victimization and rejection, potentially due to poorer social

performance secondary to increased use of safety behaviors (106, 160, 161). This may particularly be the case for children that display behaviors associated with inhibited temperament (e.g., excessive crying, shyness around strangers). Research has shown that inhibited or avoidant temperament in as early as infancy can elicit protective parental behaviors and negative interactions with same-aged peers (162, 163), that may increase the individual's threat perception of social interactions and exacerbate social-evaluative anxiety over time. A number of studies suggest that changes in safety behaviors and other forms of interpersonal expression may play an important role in recovery from SAD. For example, in one study, people with SAD engaged in an interaction with an unknown individual. They were randomly instructed to either interact normally or to reduce safety behaviors in a way intended to increase authenticity. Results showed that increases in authenticity due to reduced safety behaviors led to increased positive affect in the person with SAD, more positive perceptions of their partner's response, and a greater desire to interact with their partner again (42). Another experimental study showed that people with SAD assigned to a safety behavior reduction intervention prior to a conversation showed increases in both perceived and actual positive interpersonal outcomes, reduced self-judgments, and more social approach behavior compared to the control condition (164). Together, these results show that both authenticity and positivity can be increased in social interactions among people with SAD and that increases in authenticity have important personal and interpersonal benefits. This also suggests that it may be important for people with SAD to expose their true selves to social scrutiny and that authenticity may be an important treatment target for people with SAD. In sum, the social context of people with SAD appears to play an important role in maintaining the disorder. In addition, it appears that people with SAD contribute to their negative social context by engaging in various problematic social behaviors including reduced smiling, expressive suppression, and inauthenticity that may result in negative reactions from others and thereby confirm perceptions of low social status. Furthermore, research suggests that the behavior of close others may affect the outcome of CBT for SAD (165). Thus, interventions that help increase feelings of social safeness, increase positivity in social interactions, and reduce social threat may improve outcomes for SAD *via* changes in spontaneous interpersonal behavior and improved responses from others signaling social inclusion and liking. Increases in social reinforcement might result in more positive emotion expressed during social situations, such as genuine smiling. Increased safety and reduced shame due to MDMA-AT would presumably result in a decrease in safety behaviors or expression suppression that have been shown to impede relationship development and intimacy. Furthermore, a qualitative study of people in MDMA-AT for PTSD, Barone et al. (110) found that 12 out of 19 of the interviewees reported subjective improvements in relationships and social skills as a result of MDMA-AT. In addition, research shows that people taking MDMA feel more authentic (166) and experience enhanced

positive emotions (27) that might lead to shifts in interpersonal behavior that alter their social context, resulting in a beneficial feedback loop.

DISCUSSION

Social anxiety disorder is a debilitating psychological problem with heavy costs to the individual and society at large. Although effective behavioral and pharmacological interventions exist, many people struggling with SAD experience ongoing symptoms following treatment (16, 167) or do not present for treatment (5) indicating room for innovation in SAD treatment strategies. We believe MDMA-AT is particularly well-situated to be a novel, efficient, and effective intervention to help individuals with SAD alleviate psychological suffering and improve social functioning. In this paper, we put forth four domains where MDMA-AT may have lasting effects in altering processes hypothesized to maintain SAD beyond the dosing session: social anhedonia and decreased social reward, heightened social threat perception, increased shame and self-criticism, and dysfunctional interpersonal behavior. Evidence considered in this review for the role of MDMA in facilitating these changes was largely from basic scientific research using non-human animals and studies assessing humans who ingested MDMA outside the context of psychotherapy. Future clinical research examining the effectiveness of MDMA-AT will be necessary to test the hypothesized effectiveness of MDMA-AT for SAD beyond the single study conducted to date (52), as well as to directly test the respective roles of enhanced social reward sensitivity, decreased social threat perception, reduced shame and self-criticism, and alterations in interpersonal behavior in facilitating MDMA-AT treatment outcomes. It is our hope that by understanding the relevant processes of change in MDMA-AT for SAD, therapists may be better equipped to tailor in-session interventions to fit the individual, thereby augmenting treatment outcomes and facilitating greater and more lasting changes in social functioning and quality of life.

AUTHOR CONTRIBUTIONS

JL and ML contributed to all aspects of the manuscript from initial conceptualization, drafting, and editing the manuscript. Both authors agree to be accountable for the work.

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Psychedelics, Sociality, and Human Evolution

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Our hominin ancestors inevitably encountered and likely ingested psychedelic mushrooms throughout their evolutionary history. This assertion is supported by current understanding of: early hominins' paleodiet and paleoecology; primate phylogeny of mycophagical and self-medicative behaviors; and the biogeography of psilocybin-containing fungi. These lines of evidence indicate mushrooms (including bioactive species) have been a relevant resource since the Pliocene, when hominins intensified exploitation of forest floor foods. Psilocybin and similar psychedelics that primarily target the serotonin 2A receptor subtype stimulate an active coping strategy response that may provide an enhanced capacity for adaptive changes through a flexible and associative mode of cognition. Such psychedelics also alter emotional processing, self-regulation, and social behavior, often having enduring effects on individual and group well-being and sociality. A homeostatic and drug instrumentalization perspective suggests that incidental inclusion of psychedelics in the diet of hominins, and their eventual addition to rituals and institutions of early humans could have conferred selective advantages. Hominin evolution occurred in an ever-changing, and at times quickly changing, environmental landscape and entailed advancement into a socio-cognitive niche, i.e., the development of a socially interdependent lifeway based on reasoning, cooperative communication, and social learning. In this context, psychedelics' effects in enhancing sociality, imagination, eloquence, and suggestibility may have increased adaptability and fitness. We present interdisciplinary evidence for a model of psychedelic instrumentalization focused on four interrelated instrumentalization goals: management of psychological distress and treatment of health problems; enhanced social interaction and interpersonal relations; facilitation of collective ritual and religious activities; and enhanced group decision-making. The socio-cognitive niche was simultaneously a selection pressure and an adaptive response, and was partially constructed by hominins through their activities and their choices. Therefore, the evolutionary scenario put forward suggests that integration of psilocybin into ancient diet, communal practice, and proto-religious activity may have enhanced hominin response to the socio-cognitive niche, while also aiding in its creation. In particular, the interpersonal and prosocial effects of psilocybin may have mediated the expansion of social bonding mechanisms such as laughter, music, storytelling, and religion, imposing a systematic bias on the selective environment that favored selection for prosociality in our lineage.

Keywords: drug instrumentalization, evolution of religion, hominin evolution, niche-construction theory, sociality, socio-cognitive niche, psilocybin, psychedelics

INTRODUCTION

Early hominins were omnivores that relied substantially on forest floor foods, including mushrooms (Sayers and Lovejoy, 2014). The presence of mycophagy and self-medication among both primates (Huffman, 1997; Hanson et al., 2003) and Paleolithic humans (Hardy et al., 2013; O'Regan et al., 2016) suggests hominins also incorporated fungi with bioactive properties in their diet. It is likely that psychedelic mushrooms from the genus *Psilocybe* were ingested by our ancestors since the Pliocene (beginning 5.3 million years ago [mya]), when semi-arboreal hominins intensified foraging activity on the ground (see White et al., 2009). Exposures to psychedelic fungi by australopithecines and early *Homo* during the Pleistocene (beginning 2.5 mya) are implied by their presence in African grasslands (Guzmán et al., 2014), especially growing on dung of ungulates [an important target of hominin scavenging and hunting for millions of years (Domínguez-Rodrigo and Pickering, 2003)]. Moreover, psilocybin-containing mushrooms are found on all continents (except Antarctica) and across most ecological zones (Guzmán et al., 1998; Guzmán, 2005; Froese et al., 2016), and thrive on landscapes affected by anthropic activities [e.g., woodland clearings and grazing pastures (Stamets, 1996)], indicating their widespread availability as *Homo* spread across Africa, into Eurasia, and eventually across the globe (see Antón et al., 2014)¹.

Typical psychedelics such as psilocybin and lysergic acid diethylamide (LSD) modify fundamental brain processes that normally serve to constrain neural systems central to perception, emotion, cognition, and sense of self (Swanson, 2018). It is well established that such effects are generated primarily by the interaction of these substances with the serotonin (5-hydroxytryptamine; 5-HT) system, binding the 5-HT_{2A} receptor as partial agonists (Nichols, 2016). Psychedelic stimulation of 5-HT_{2A} receptors increases excitability of neocortical pyramidal neurons, augmenting extracellular glutamate release in the prefrontal cortex, and thereby disrupting cortical rhythmicity and large-scale brain networks (Carhart-Harris et al., 2014; Varley et al., 2020; Vollenweider and Preller, 2020). This alteration of distributed neural processes manifests as increased synaptic plasticity and entropy, as well as reduced integrity of discrete brain networks (e.g., functional disintegration of the default-mode network [DMN]) and reduced segregation between networks (e.g., increased functional connectivity between the DMN and dorsal attention network) (De Gregorio et al., 2018; Preller et al., 2019, 2020; Madsen et al., 2021). Such changes in brain activity and connectivity lead to a flexible, functionally more connected brain during the psychedelic state (Petri et al., 2014; Tagliazucchi et al., 2016; Mason et al., 2020). Further important mechanisms of action of psychedelics involve reduced thalamic filtering of interoceptive and exteroceptive

information, which sustains an increased information flow to particular areas of the cortex (Vollenweider and Preller, 2020); and sensory bottom-up overflow and relaxed high-level priors (e.g., models related to self or social identity) as formulated by the relaxed beliefs under psychedelics (REBUS) model (Carhart-Harris and Friston, 2019; for further contextualization see Noorani and Alderson-Day, 2020).

The present paper suggests that these and other psychopharmacological properties of psilocybin could have had direct effects on the adaptation of early humans to their environment by enhancing their ability to live in highly social cooperative communities and participate in collaborative activities with shared goals and intentions. This human niche expanded the core of hominin sociality through collective intentionality, hyper cooperation, cultural transmission and innovation, teaching, and more recently, language (Boyd et al., 2011; Sterelny, 2012; Gamble et al., 2014; Tomasello, 2014). The emergence of these distinctively human capabilities occurs across our evolutionary history and involved a pattern of socio-cognitive niche construction predicated on a cumulative and ratcheting culture alongside substantive neurological and behavioral plasticity (Iriki and Taoka, 2012; Whiten and Erdal, 2012; Fuentes, 2015). In this context, psilocybin may have been harnessed to increase adaptability and fitness through its capacity to modulate the 5-HT_{2A} receptor mediated active coping strategy (Carhart-Harris and Nutt, 2017), which provides elevated cortical plasticity, enhanced rate of associative learning, and elevated capacity to mediate psychological transformation (Brouwer and Carhart-Harris, 2021).

Our model emphasizes effects of incidental ingestion of psilocybin-containing mushrooms as an environmental factor affecting hominin populations across millions of years of evolution. Eventually, psychedelic consumption was institutionalized in many pre-modern human societies in ritual activities focused on healing, divination (i.e., for obtaining otherwise inaccessible information), and socialization (e.g., in initiations) (Dobkin de Ríos, 1984; Furst, 1990; Schultes et al., 2001; Rättsch, 2005; Quirce et al., 2010; Leptourgos et al., 2020). In many instances, only male shamans ingested psychedelics (Harner, 1973). But in some cases they were also consumed by the general population (e.g., among the Huichol of Mexico, the *híkuri* cactus, *Lophophora williamsii*, is used by men, women, and children: Myerhoff, 1974). Hunters and gatherers likely learned about hallucinogenic plants as part of their detailed environmental knowledge (see e.g., Veile, 2018), and smaller scale societies placed high cultural value on the personal revelations produced (Boyer, 2019), which is attested to in the recurring mythological roles ascribed to the these mind-altering materials (Guerra-Doce, 2014, 2015).

Given the robust alterations of perception and consciousness produced by psychedelics and their medicinal and religious importance in some traditional cultures, it has been hypothesized that their ingestion influenced human evolution. McKenna (1992) proposed that psilocybin's effects stimulating visual acuity, sexual activity, and ecstatic/visionary experiences influenced hominins' foraging, sensitivity to community, as well as religious and spiritual concerns. He also argued the

¹We focus on psilocybin mushrooms as likely candidates for early psychedelic consumption in our lineage for the reasons enumerated here and because they require no preparation whatsoever, being bioactive in their natural state. Psychedelic plants in general were also ubiquitous and, in some instances, readily available (though certain plants required further processing to extract psychoactive secondary compounds) (Rättsch, 2005; Wink and van Wyk, 2008; Pennacchio et al., 2010; Alrashedy and Molina, 2016).

presence of psychedelics in the early human diet drove the rapid reorganization of the brain's information-processing capacities by catalyzing the emergence of self-reflective consciousness and language. These hypotheses about human origins have received little attention and thus still need to be examined further. Moreover, they require additional development so that they can be empirically tested (e.g., using cross-cultural research methods and experimental approaches). The aim of this paper is to contribute to this task by formulating an evolutionary model of the adaptive utilization of psychedelics that properly integrates current anthropological and neuropsychopharmacological knowledge on these substances with the human evolutionary behavioral sciences.

We recognize that a simplistic version of McKenna's account of human evolution implying that psilocybin use by itself led inevitably to the emergence of the unique cognitive, communicative, and cooperative patterns characteristic of modern human populations is most certainly false. Hominin entry into the socio-cognitive niche cannot be explained in terms of a single causal factor, a critical adaptive breakthrough (e.g., bipedality, tool-use, cooking, or even psychedelic use), but instead through positive feedback loops among various aspects of hominin life, an adaptive complex involving novel or greatly exaggerated features of our lineage (Sterelny, 2012). From this multifactorial and coevolutionary viewpoint, we propose psychedelics acted as an *enabling factor* in human adaptation and evolution. This means psychedelic use may have established positive feedback loops with core features of the evolving hominin lifeway, in part generating the coevolving dynamic that came to structure human evolution. This proposal is based on two premises:

- (a) Psychedelics are serotonin analogs that preferentially activate the 5-HT_{2A} receptor subtype (Nichols, 2016), and thereby have effective medicinal applications in the treatment of stress-related conditions (Vollenweider and Preller, 2020) and significantly modulate aspects of creativity (Girn et al., 2020) and sociality (Preller and Vollenweider, 2019) that could have enhanced adaptability and fitness, especially in a knowledge-using, socially interdependent lifeway; and
- (b) Psychedelic use can amplify symbolic behavior and a predisposition for collective rituals and synchronicity (e.g., by stimulating deployment of rhythmic, hermeneutical, and rhetorical activity to endure, make sense of, and communicate ecstatic and visionary experiences; Doyle, 2011) that could have transformed the social environment, and thus local selection pressures, through cultural niche construction.

While we are definitely not proposing that psychedelics are the "missing link" in hominin evolution, we do propose that the dietary incorporation of psilocybin would have enhanced the survival and reproductive prospects of our ancestors through its incidental effects on adaptive stress-coping and enhancement of socio-cognitive dynamics. Moreover, the integration of psilocybin into ancient diet, communal practice,

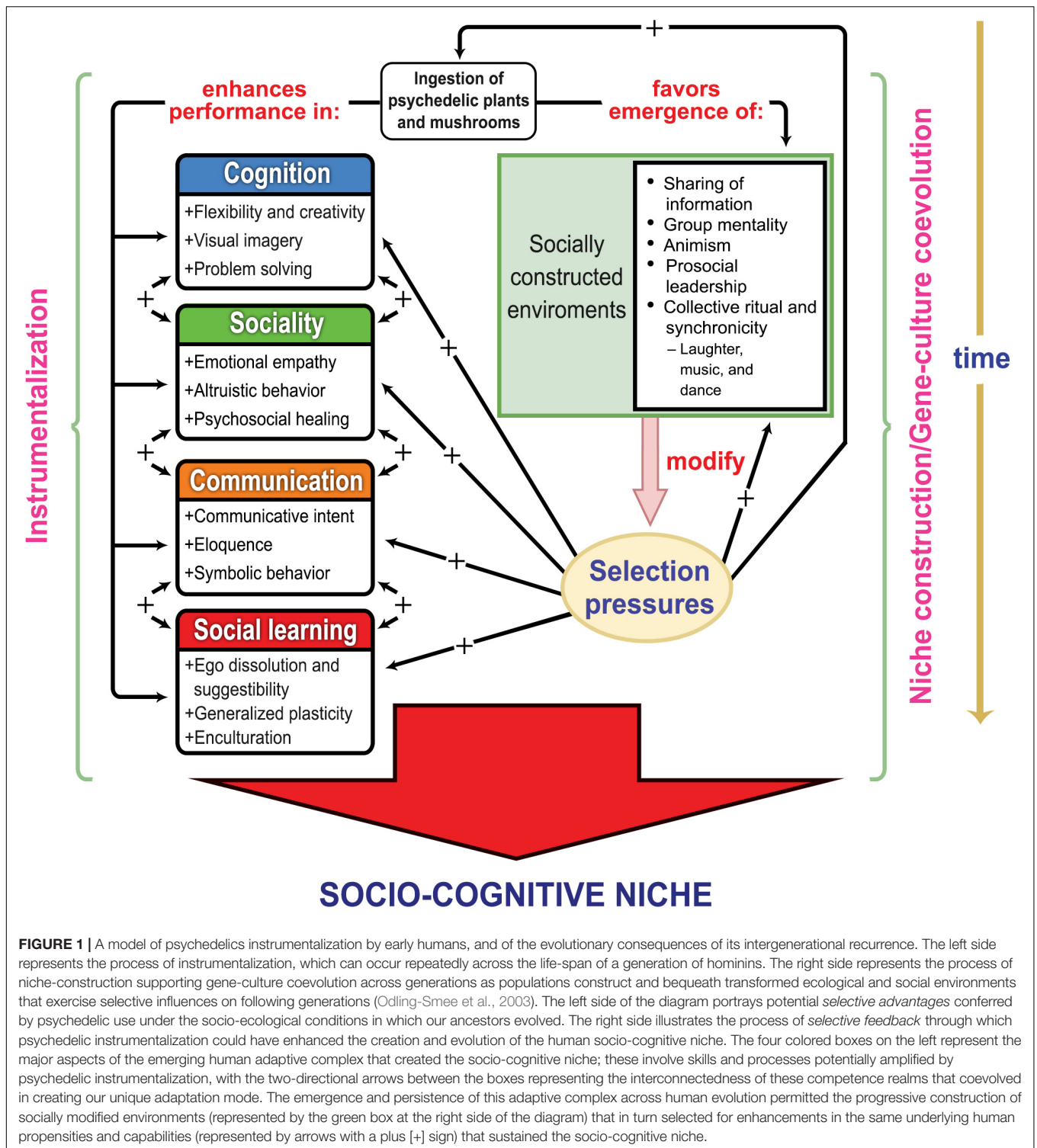
and proto-religious activity could have sustained feedback loops in which increases in social cognition and symbolic behavior engendered by psychedelic use selected for yet further increases in such capacities by increasing the richness and complexity of the social and semiotic environment. Psychedelics thus may have helped hominins both create and respond to a socio-cognitive niche, as hypothesized in **Figure 1**.

This article presents evidence for this claim. First, the main characteristics of the human socio-cognitive niche are described. Then, we examine interdisciplinary evidence supporting the hypotheses that psychedelic ingestion has deep hominin roots and that psilocybin instrumentalization conferred adaptive benefits and contributed to the human evolutionary trajectory involving advancement into a socio-cognitive niche (Barrett et al., 2007; Whiten and Erdal, 2012). The model of adaptive utilization of psychedelics presented is informed by a homeostatic perspective (Forbey et al., 2009) and the drug instrumentalization paradigm (Müller and Schumann, 2011) to explain potential selective advantages bestowed by psychedelics to hominins. The model also incorporates niche-construction (Laland et al., 2016) and gene-culture coevolutionary (Richerson et al., 2010) processes to specify how dietary and societal incorporation of psychedelics may have become evolutionarily significant by imposing a systematic bias on the selective environment that supported development of a socio-cognitive niche. The interpersonal and prosocial effects of psychedelics could have mediated expansion of social bonding mechanisms such as laughter, singing, dancing, storytelling, and religion that, in turn, accelerated the rate at which key biological components of social cognition and religiosity spread in our lineage.

THE HUMAN SOCIO-COGNITIVE NICHE

Modern humans have complex languages, sophisticated technology, intricate stores of cultural knowledge and beliefs, and an advanced theory of mind (Richerson and Christiansen, 2013; Tomasello, 2014). Early hominins may have lacked these traits (Silk, 2007), but specific selection pressures led to their acquisition in the *Homo* lineage (Schwartz and Tattersall, 2015). To explain this constellation of zoologically unusual features it has been argued that we evolved to specialize in the cognitive niche (Tooby and Devore, 1987; Cosmides and Tooby, 2001; Barrett et al., 2007; Pinker, 2010; Bertolotti and Magnani, 2017). A niche is the structural, temporal, and social context in which a species exists, defining its mode of adaptation (Fuentes, 2015). Therefore, the concept of the "cognitive niche" implies that it is mainly by thinking that humans succeed in adapting to a wider range of environments than other animals (Boyd et al., 2011). From this viewpoint, "improvisational intelligence" was selected in our lineage because the costs required to sustain it were outweighed by the benefits of the numerous solutions such intelligence could generate (Morgan, 2016).

Crucially, however, the human niche is not only about being smart: this way of life also has a cooperative core that



nurtures a “deep social mind,” a way of thinking characterized by profound mental intermingling and group-mindedness (Whiten and Erdal, 2012). This novel form of socially infused thinking (Tomasello, 2014) entails unique cognitive skills and motivations for collaborating and communicating with others, such as an altruistic and egalitarian orientation and

the capacity to mindread in order to enhance interpersonal coordination (Bernhard et al., 2006; Fehr et al., 2008; Heyes and Frith, 2014). Functioning in this socio-cognitive niche thus required not just intelligence and technological know-how, but more importantly the capacity for cooperation among non-kin and social learning, eventually mediated by

language (Barrett et al., 2007; Whiten and Erdal, 2012). Equipped with this suit of adaptations to richly cooperative social lives (Sterelny, 2014), humans expanded across the globe, successfully adapting to a diverse range of habitats (Antón et al., 2014). We became a ‘generalist specialist,’ not only occupying and utilizing a diversity of environments, but also specializing in our adaptation to some of these environmental extremes (Roberts and Stewart, 2018).

Current understanding of the cognitive niche emphasizes that humans’ uniquely developed ability to learn from others was absolutely vital for their ecological success because it enabled the gradual accumulation of information and technologies across generations and the development of well-adapted bodies of local knowledge and complex social arrangements beyond the individual capacity to invent alone (Boyd et al., 2011; Richerson and Christiansen, 2013; Sterelny, 2014). Therefore, as has been cogently argued by Boyd et al. (2011) and Whiten and Erdal (2012), and empirically shown by Morgan (2016), the cognitive niche is eminently a social and cultural niche. We adapt not through intelligence alone but primarily through the skills, values, ideas, information, and expected modes of social interaction acquired from others in distinctively prosocial and culturally scaffolded milieus. The expansion of sociality and inter-generational cultural learning in our lineage was thus crucial for the reliable preservation of various types of expertise and the expansion of cognitive capital via cumulative cultural evolution (Sterelny, 2012, 2014).

The human socio-cognitive (or cultural) niche is simultaneously selection pressure and adaptive response (Downey and Lende, 2012). It was built and reshaped by hominins, who consequently modified the evolutionary pressures acting on them, on their descendants, and on unrelated populations sharing the same landscape (Laland and O’Brien, 2011). The various aspects of social cognition and behavior of the cognitive niche are dynamic components that established reinforcing relationships among themselves (e.g., mindreading and culture create, and in turn, are sustained through sociality), embodying an interconnected, adaptive complex that sustains our unique survival mode (Whiten and Erdal, 2012). Hence, the emergence of *Homo* was characterized by an auto-catalytic niche construction process; an iterative dynamic whereby increasing cognition, dietary quality, and cooperative behavior resulted in lowered extrinsic mortality risk and favored changes in brain size, body composition, life-history parameters, and behavioral and communicative complexity (Kaplan et al., 2000; Antón and Snodgrass, 2012; Fuentes, 2015).

The socio-cognitive niche theory invokes the undeniable practical advantages of increased cognition, sociality, communication, and social learning in order to explain the evolution of human uniqueness. Our model and the supporting evidence reviewed below suggest that the instrumentalization of psilocybin could have enhanced performance on each of these interrelated competence domains (see left side of **Figure 1**), potentially increasing the adaptability and fitness of our ancestors. The psychedelic instrumentalization model also proposes that psilocybin consumption had niche-constructing effects that imposed a systematic bias toward a socio-cognitive

niche across the human evolutionary trajectory (see right side of **Figure 1**).

ANCIENT HOMININ DIETS AND THE ECOLOGY OF PSILOCYBIN-CONTAINING FUNGI

Hominin encounters with macroscopic fungi growing on the soil surface must constitute a very ancient and continual phenomenon that demanded behavioral adaptations. Fungi are widely distributed across ecozones and comprise not only valuable foods and medicines, but also highly toxic and even quickly fatal substances. Sporocarps (fungal fruitbodies) are much more abundant in the forest understory than in the middle and upper canopies where most primate species tend to live (Hanson et al., 2003). Once our hominin ancestors habitually foraged on the floors of forests and in meadows, especially in tropical areas, they recurrently encountered mushrooms. By necessity, they experimented with mycophagy and found out which species could be safely eaten as food or carefully exploited as medicine. Likewise, when psilocybin containing fungi were consumed in large enough quantities they caused dramatic alterations in perception and consciousness, drawing attention to their properties and their positive and negative effects on well-being. As a consequence, memories (and eventually cultural traditions) were formed regarding the identification of these species and the resulting effects of their ingestion. As has been hypothesized for non-human primate self-meditative behaviors (see Huffman, 1997), traditions of medicinal use of psychedelic mushrooms may have started as a result of ill, hungry hominins trying new foods during periods of extreme food scarcity, and upon recovery, associating their improved health with the new dietary item. Subsequently, local enhancement (i.e., naïve individuals having their attention drawn to species used by others) and social learning could have played a role in spreading the behavior through the group.

While incontrovertible direct evidence of psychedelic mushroom ingestion by ancient humans (e.g., dental calculus containing psilocybin mushroom tissue or spores) is lacking, there is direct evidence of the ingestion of edible mushrooms (O’Regan et al., 2016) and medicinal plants (Hardy et al., 2013) derived from analysis of dental calculus recovered from remains of humans from the Upper Paleolithic. There are 22 primate species known to eat fungi (Hanson et al., 2003), and African great apes, in particular, are known to ingest a variety of non-nutritional plants to “treat” homeostatic challenges [e.g., to aid in the control of intestinal parasites and/or provide relief from related gastrointestinal upset (Huffman, 1997)]. It thus seems highly unlikely that our hominin ancestors ignored the widespread coprophilic species of psilocybin containing mushrooms conspicuously growing on ungulates’ dung (e.g., the pantropical *Psilocybe cubensis*), especially since Plio-Pleistocene hominin activities of scavenging, hunting, and eventually domestication of bovines placed this psychedelic within the sphere of daily activities (see van Ginneken et al., 2017 for evidence and discussion regarding the similarity of migration

routes of early bovines and early hominins and its implications for understanding our ancestors' pan-African dispersal). As will be shown below, the likelihood of intentional and repeated use of psilocybin is supported by its low toxicity and by its close resemblance to the neurotransmitter serotonin, which opened up the possibility for its exploitation as a “treatment” for a significant homeostatic challenge recurrent in a socio-cognitive niche – serotonin depletion.

TRADITIONAL PSILOCYBIN MUSHROOM INGESTION AND THE ANTIQUITY OF RITUAL PSYCHEDELIC USE

Frost (2017) reviews reports from Mesoamerican transegalitarian agricultural societies during the early contact period with the Spanish, illustrating a range of uses for psilocybin mushrooms that involve healing, spiritual, ritual, social, festive, and divinatory practices, some still reported in the 20th century (e.g., Estrada, 1989) among the Mazatecs of Oaxaca in southern Mexico. The Nahuatl, for instance, used these fungi in the rituals performed by Mexica (Aztec) clergy, and on a local, personal level through the assistance of medicinal/divinatory aid of *ticitls* (shamanistic healers). In the context of the official religious system, psychedelic mushroom consumption characterized notions of hospitality and ostentatiousness amongst the Mexica elite, and involved intricate ritual performances that included call and response, chanting, and dancing, as described in Hernando de Alvarado Tezozómoc's *Crónica Mexicana* (written circa 1598) (Frost, 2017). Modern-day Mazatecs employ psilocybin mushrooms mainly to find lost items, discover hidden truths, or diagnose an ailment in the context of nocturnal rituals in which it is common for both healer and client/patient to consume the mushrooms (Estrada, 1989). This ceremony involves whistling, humming, chanting, singing, percussive artistry, ventriloquism, and dancing. To our knowledge, there are no documented foraging societies that use psilocybin fungi. This may be due, in part, to the fact that mushrooms grow mainly during the rainy season, a particularly

difficult time for ethnographers to accompany the already challenging nomadic lifestyle of foragers. Possible evidence of the use of psilocybin-containing mushrooms among early Neolithic farming and herding communities may be present in rock carvings and paintings [e.g., in Africa (Samorini, 2020) and Spain (Akers et al., 2011), also see Winkelman (2019a) for review].

The utilization of psilocybin mushrooms or other psychedelic plants is documented in the ethnographic and historical literature from all cultural regions of the globe except the Insular Pacific (see **Table 1** for examples). It is likely that psychedelics have been used ritually for millennia, and that this behavior has deep hominin roots. Evidence regarding the evolution of human hepatic enzymes suggests significant selection pressures were exerted on hominin populations by frequently encountered environmental chemicals, including fungal and vegetal secondary metabolites that act as stimulants, narcotics, and hallucinogens (Sullivan and Hagen, 2002; Sullivan et al., 2008). Drug consumption is not an evolutionary novelty; rather, ancient and recent exposures resulted in evolved countermeasures to tolerate them to some degree and safely metabolize them. Evidence of humans' relationships with psychedelics during more recent times (the Holocene) is found in the archeological and paleoethnobotanical record (Guerra-Doce, 2015; Fitzpatrick, 2018; Miller et al., 2019; Samorini, 2019; Robinson et al., 2020). While the presence of psychoactive plant remains in archeological contexts does not establish their use as drugs, it is highly probable in many instances given known ethnographic analogies, artifactual associations, and iconographic interpretations (Guerra-Doce, 2014; Winkelman, 2019a; Domnauer, 2020).

HOMEOSTASIS OF INGESTIVE BEHAVIORS AND THE DRUG INSTRUMENTALIZATION PARADIGM

Natural landscapes are a diverse combination of plant species that are literally nutrition centers and pharmacies with a wide range of primary (nutrient) and secondary (pharmaceutical) compounds

TABLE 1 | Selected societies from all over the world that employ psychedelics acting on the serotonergic system.

Region	Subregion	Culture	Species employed	Common name	Main psychoactive principles	References
Africa	West Africa	Fang	<i>Tabernanthe iboga</i>	eboka	ibogaine, ibogamine	Rätsch (2005)
Africa	Eastern Africa	Maasai	<i>Acacia nilotica</i>	olkiloriti	dimethyltryptamine (DMT), tetrahydroharman	Sobiecki (2002)
Middle East	Middle East	Iran	<i>Peganum harmala</i>	haoma	harmine, harman	Flattery and Schwartz (1989)
Asia	East Asia	Chinese	<i>Gymnopilus junonius</i>	xiàojūn	psilocybin, psilocin	Zhang and Greatrex (1987)
Europe	Southeastern Europe	Greeks	<i>Claviceps</i> spp.	kykeon	ergometrine, ergotamine	Samorini (2019)
North America	Arctic and Subarctic	Ojibwa	<i>Lophophora williamsii</i>	peyote	mescaline, pelotone	Barnouw (1950)
Middle America and the Caribbean	Central Mexico	Mazatec	<i>Psilocybe</i> spp.	ndi xi tjo	psilocybin, psilocin	Estrada (1989)
South America	Amazon and Orinoco	Tukano	<i>Banisteriopsis caapi</i> + <i>Diplopterys cabrerana</i>	yagé	harmine, harmaline + DMT	Jackson (1983)
South America	Southern South America	Mataco	<i>Anadenanthera colubrina</i> var. <i>cebil</i>	cebil	DMT, 5-MeO-DMT	Dijour (1933)

vital to the health of plants and herbivores (Villalba and Provenza, 2007). Animals generally avoid secondary metabolites (which typically have negative physiological and behavioral consequences following their ingestion) while selecting nutrient-rich foods. However, a homeostatic perspective suggests that dietary selection is not guided simply by avoidance of plant secondary metabolites, but, in some cases, by their selection to ameliorate other challenges (Forbey et al., 2009). From this view, food selection is a quest for substances (whether nutrients or drugs) that provide homeostatic utility for the organism (Villalba and Provenza, 2007). Hence, potentially toxic secondary metabolites in fungi and plants might be actively selected by animals to achieve homeostasis. Evidence shows animals exploit the biological activity of secondary metabolites to mitigate the costs of infection by parasites, enhance reproduction, moderate thermoregulation, avoid predation, and increase alertness (Rodríguez and Wrangham, 1993; Huffman, 1997; Forbey et al., 2009).

Similarly, drug instrumentalization theory proposes that non-addictive drug use can be explained in functional terms as a purposeful adaptive process. It proposes humans and many animal species seek and consume psychoactive substances because the subsequent effects on mental states can be utilized to improve performance of goal directed behaviors (Müller and Schumann, 2011; Müller, 2020). From this viewpoint, repeated, non-addictive drug use should be modeled as a two-step process: (1) the seeking and consumption of a psychoactive drug in order to change the present mental state into a previously learned mental state, which then allows for (2) better performance of other, previously established behaviors and enhanced goal achievement (Müller and Schumann, 2011). Some instrumentalization goals proposed by the researchers include: improved social interaction; improved cognitive performance and counteracting fatigue; facilitated recovery and coping with psychological stress; and facilitation of spiritual and religious activities.

According to the homeostatic perspective, the probability of secondary metabolite exploitation is determined by the relative difference between the cost of a challenge and the toxicity of the secondary metabolite in question; the ultimate “goal” for the animal being to regulate homeostasis, achieving a balance between minimizing the cost of a challenge and minimizing toxicity (Forbey et al., 2009). We review next substantial evidence that psilocybin possesses very low toxicity and generates very few and unimportant negative side effects. This quality, in combination with the relatively high costs of the challenge it could potentially ameliorate (i.e., serotonin depletion) and the adaptive behaviors it could facilitate (discussed afterward), made psilocybin a prime candidate for instrumentalization in our lineage.

TOXICITY OF PSILOCYBIN AND ASSOCIATED COSTS

Hagen et al. (2013) propose that plant neurotoxins currently used as drugs illustrate the necessity of their characterizations

in terms of acute drug toxicity because of their fitness costs; however, the situation of psychedelics is dramatically different. Although there is a general public perception that psychedelics are dangerous, from a physiologic viewpoint they are one of the safest classes of central nervous system drugs (Nichols, 2016). Psilocybin, in particular, is exceptionally harmless. This is reflected by its high therapeutic index, 641, which is indicative of very low toxicity (Tylš et al., 2014). van Amsterdam et al.’s (2011) review of literature on psilocybin risks found that in spite of moderate acute toxicity, psilocybin has low chronic toxicity and negligible public health risk. Other public health assessments have similarly concluded that psilocybin mushrooms are the safest of all common recreational drugs (Gable, 2004; Nutt et al., 2010; Studerus et al., 2011). Moreover, psilocybin is not neurotoxic, its lethal to psychoactive dose ratio is estimated at 1000:1, it has little or no potential for creating dependence, and there is no evidence of long-term cognitive impairment (Johnson et al., 2008; Tylš et al., 2016).

Even though some adverse physical effects may occur during psychedelic action, most commonly dizziness, nausea, drowsiness, paraesthesia, blurred vision, and dilated pupils, they are relatively unimpressive even at doses yielding powerful psychological effects (Johnson et al., 2008). Higher doses are more likely to cause anxiety or fear due to feelings of ego dissolution or lack of control (Johnson and Griffiths, 2017), as well as paranoid and delusional thinking (Carhart-Harris et al., 2016b), but even exceptional overdoses don’t lead to enduring harms (Haden and Woods, 2020). Side effects such as derealization, depersonalization, long lasting unpleasant experiences (bad trips), and psychotic reactions can also occur (Strassman, 1984); however, psychological interventions are mostly sufficient and the risk of prolonged psychosis (lasting longer than 48 h) in otherwise healthy subjects after a single dose of psilocybin is rare; and in most cases, prolonged negative effects are associated with personality predispositions (Johnson et al., 2008). A large population study of 130,000 adults in the United States found no link between the use of psychedelics and suicidal behavior or mental health problems (Johansen and Krebs, 2015). Typically, when psychedelics are administered in a supportive, controlled environment (ritual or clinical setting) no severe acute or chronic adverse effects occur, and no overdose deaths have been reported after ingestion of typical doses of LSD, psilocybin, or mescaline (Nichols, 2016).

The notable potential cost of psychedelic ingestion involves the loss of cognitive structuring, opening the possibility for errors in judgment, false perceptions, distortions, and illusions that could undermine an individual’s capacity for alertness, strategic thinking, and decision-making. This specific cost (excessively “relaxed beliefs”; see Carhart-Harris and Friston, 2019), coupled with the rapid onset of mental tolerance and lack of hedonic reward (craving or withdrawal) help explain why psychedelic use is normally episodic and not compulsive, with chronic use being relatively unusual (Nichols, 2004, 2010). The ontologically shocking effects of psychedelics and their meaning-enhancing properties is likely why their use commonly occurs in engineered social contexts (e.g., in intense and immersive shared experiences consisting of multimodal performances of music, ritual, and

dance: Sterelny, 2018; Winkelman, 2021c; also see St John, 2006). These factors of set (i.e., intentions, mood state, and expectations) and setting (i.e., context of ingestion, involving all sensory modes, social environment, and the set of those present) provide for protection of the psyche and integration of the experience (Dobkin de Ríos, 1984; Hartogsohn, 2016; Lifshitz et al., 2018). It seems human ancestors learned to employ psychedelics in specific contexts and in conjunction with certain “protective” behaviors that allowed them to minimize and endure negative effects (costs) and maximize and counter exploit certain qualities to maintain homeostasis and manage the challenges of group living.

PSYCHEDELIC SELF-MEDICATION AS A “TREATMENT” FOR SEROTONIN DEPLETION

From a homeostatic perspective, increased fitness can potentially result from consumption of psychoactive plants containing compounds that chemically resemble endogenous signaling molecules, especially when internal signaling functions are compromised [e.g., due to deficiencies in dietary precursors in marginal environments (Sullivan and Hagen, 2015)]. Our proposal is that the incidental ingestion of psilocybin and other psychedelic secondary metabolites that have very low toxicity and structurally resemble the neurotransmitter serotonin (5-hydroxytryptamine; 5-HT) provided a “treatment” for 5-HT depletion, a costly challenge likely recurring throughout advancement into a socio-cognitive niche (see e.g., Young and Leyton, 2002; Wood et al., 2006). Consequent to this self-medicative behavior was the development of cultural traditions of psilocybin use to ritually and symbolically exploit its salutogenic, sociality expanding, and cognitive enhancing effects (see below).

Hominin evolution occurred in settings of strong climatic and environmental variability (Potts, 2013) and involved an increasing interdependence and reliance on intelligence, cooperation, and learning from others (Sterelny, 2012). This dynamic inevitably placed a higher strain on the serotonergic system given its involvement in facilitating stress relief and mental flexibility (Carhart-Harris and Nutt, 2017; Nilsson et al., 2019) by regulating perception, cognitive function, mood, memory, and social behavior (Berger et al., 2009; Friedman, 2018; Tricklebank and Daly, 2019).

Humans cannot produce the amino acid tryptophan, precursor in the biosynthesis of 5-HT, and must obtain it through their diet (Friedman, 2018). Given early hominins’ diets low reliance on tryptophan-rich foods such as seeds, nuts, red meat, and fish (Hublin and Richards, 2009; Ungar and Sponheimer, 2011) they certainly faced deficits of this essential amino acid with the potential to perturb homeostasis through lowered levels of 5-HT. Under such circumstances, tryptamine psychedelics (e.g., DMT, psilocybin) could have provided an ideal substitute for a fundamental bioactive compound that is hard for the body to produce, effectively mimicking 5-HT’s structure and function (Nichols, 2016). Self-medication with psilocybin mushrooms would have ameliorated the costs associated with

impairment of serotonergic neural signaling, involving depressed mood (Jenkins et al., 2016), increased stress vulnerability (Sachs et al., 2015), and cognitive inflexibility (Kanen et al., 2020).

5-Hydroxytryptamine moderates anxiety and stress, promotes patience and coping, and under conditions of increased environmental volatility, opens a window of plasticity for greater adaptation (Branchi, 2011; Miyazaki et al., 2012; Carhart-Harris and Nutt, 2017). Therefore, the brain displays two different serotonin-mediated responses to adversity: a default response involving a passive coping strategy (i.e., tolerating a source of stress) mediated by 5-HT_{1A} receptor signaling; and an active coping strategy that provides an enhanced capacity for change that is mediated by 5-HT_{2A} receptor signaling (Carhart-Harris and Nutt, 2017). Interestingly, serotonergic psychedelics preferentially engage the 5-HT_{2A} receptor signaling pathway, functionally modulating its activity (Nichols, 2016; Carhart-Harris and Nutt, 2017). Psilocybin thus stimulates a system that evolved to mediate rapid and deep learning when faced with environmental demands for change (Brouwer and Carhart-Harris, 2021). From the homeostatic and drug instrumentalization perspective developed here, this capacity of serotonin-mimicking psychedelics to enable a hyper-plastic state that can aid psychological transformation when (actual or perceived) environmental pressures demand it (Brouwer and Carhart-Harris, 2021) helps explain why ritualized psychedelic consumption became central to group healing, decision-making, management of ecological relations, and creation of individual and social identity in many premodern societies (Rätsch, 2005; Guerra-Doce, 2014, 2015; Kennedy, 2014).

The negative impact of 5-HT depletion on fitness likely increased as hominization ensued given an escalating dependence on cognitive skills for an intensively cooperative and collective life (Dunbar, 2014; Gamble et al., 2014). Under these conditions of demands for functioning in a socio-cognitive niche, higher-order executive tasks such as social learning, working memory, and behavioral flexibility became increasingly important; this generated an increased demand for sufficient levels of 5-HT to modulate the function of the prefrontal cortex, on which these skills critically depend (see Puig and Gullledge, 2011). Considering the costly nature of 5-HT production, its key role in hominin adaptive brain function and behavior, and the increasing selection pressures for sophisticated social cognition skills for participation in the socio-cognitive niche, it is reasonable – perhaps inevitable – that early hominins actively pursued available exogenous chemical analogs of 5-HT.

Importantly, as meat became a more pervasive item in later hominins’ diet, it is likely that tryptophan deficits were less common since it is present in high quantities in most protein-based foods (Friedman, 2018). This means that if psychedelics were initially used among hominins and archaic human species to “treat” 5-HT depletion, reliance on this self-medicative behavior may have become less important as our human ancestors’ diet progressively included seeds and nuts, as well as larger quantities of meat from large animals and fish. Thus, while psychedelics may have entered hominin evolution via their role as a “treatment” for 5-HT depletion, once full “migration” into a socio-cognitive niche was complete (which involved establishment of a foraging

strategy extended to large mammalian prey) their ingestion was likely sustained because of the additional adaptive benefits their ritual and symbolic instrumentalization could confer to humans properly (see below). In other words, while tryptophan deficiency was likely no longer an issue among hunter-gatherer societies or prehistoric horticultural/agricultural societies, the premium placed on cognitive and social functions by the socio-cognitive niche meant there was still a place for counter exploiting psychedelics' effects in our lineage.

PSYCHEDELIC INSTRUMENTALIZATION IN THE HUMAN SOCIO-COGNITIVE NICHE

Entry into the socio-cognitive niche involved increasing cognition, sociality, communication, and social learning. **Figure 1** summarizes a model of how these major aspects of the emerging human adaptive complex were potentially enhanced by incidental psychedelic ingestion and periodic psychedelic instrumentalization. The model suggests psilocybin would have amplified the requisite capacities for increasingly complex social interaction and a suite of cognitive abilities supportive of the socio-cognitive niche, including aspects of creativity, non-verbal and linguistic expression, and suggestibility (left side of **Figure 1**). These effects could have facilitated general problem solving, cooperative foraging, ritual healing, conventional representation and symbolization (including myth and identity formation), and enculturation practices (e.g., rites of passage). The following sections integrate current understanding of the socio-cognitive niche with recent psychedelic research (mainly controlled experimental studies in humans, both in clinical populations and healthy volunteers) to illustrate how psychedelics could have been adaptively employed by our ancestors. We focus on four interrelated psychedelic instrumentalization goals: management of psychological distress and treatment of health problems; improved social interaction and interpersonal relations; facilitation of collective ritual and religious activities; and enhanced group decision-making.

Management of Psychological Distress and Treatment of Health Problems

Foraging is not a safe activity; it leads to significant mortality and morbidity. Even cooperative hunting, for example, is accident prone, attacks by wounded animals being paramount (Klein, 1999). Human ancestors suffered from infectious pathogens (e.g., bacteria, viruses, parasites) and social stress management imposed pressure on their time budget as group size increased (Gamble et al., 2014). We suggest under these conditions of disease and stress, psychedelic use could have improved stress management, healing, and well-being. Psychedelics can facilitate adaptive stress coping via upregulation of 5-HT_{2A} receptor functioning (Carhart-Harris and Nutt, 2017), bringing about a "pivotal mental state" characterized by an enhanced rate of associative learning and the potential for the mediation of stress through psychological or cognitive transformations

(Brouwer and Carhart-Harris, 2021). These effects in enhancing active coping strategies illustrate a core aspect of psilocybin's potential contributions to hominin adaptability and fitness.

Psychedelic abatement of psychological distress can aid in the treatment of mental illness. In contemporary clinical contexts, psychedelics have effective psychiatric applications, particularly in the treatment of stress-related disorders (dos Santos et al., 2016; Garcia-Romeu et al., 2016; Carhart-Harris and Goodwin, 2017; Johnson and Griffiths, 2017; Goldberg et al., 2020a; Luoma et al., 2020; Reiff et al., 2020; Vollenweider and Preller, 2020; Carhart-Harris et al., 2021; De Gregorio et al., 2021a; Inserra et al., 2021). Winkelman and Sessa's (2019) edited volume contains reviews of clinical evidence showing the therapeutic effectiveness of psychedelics in the treatment of various health conditions, including anxiety, trauma, treatment-resistant depression, as well as personality, inflammatory, and autoimmune conditions (also see Szabo, 2019; Thompson and Szabo, 2020). The immersive experiences engendered by high doses of psychedelics are often attributed deep personal meaning, and a growing body of theoretical and empirical work shows they can have persisting beneficial effects on well-being and psychosocial functioning (Kuypers et al., 2016; Sweat et al., 2016; Bouso et al., 2018; Haijen et al., 2018; Carhart-Harris and Friston, 2019; Kuypers, 2019; Mason et al., 2019, 2021; Preller and Vollenweider, 2019; Barrett et al., 2020; Girn et al., 2020; Goldberg et al., 2020b; Yaden and Griffiths, 2020). There are also hints that lifetime psychedelic use is associated with markers of physical health (self-reported overall health, body mass index, and heart condition and/or cancer in the past 12 months: Simonsson et al., 2021).

Most pre-modern societies considered illness to be caused by supernatural and spiritual agents (Schultes et al., 2001; Rätsch, 2005); psychedelics can contribute to cures because they produce spiritual experiences and a sense of control over preternatural realms (Dobkin de Ríos, 1984; Furst, 1990; Winkelman, 2010). Many shamanistic healing traditions use psychedelics to facilitate an experience of contact between the ritual specialist and supernatural beings/realms, inducing visions that provide knowledge about the causes of the condition afflicting the patient and proper treatment, or allowing healers to confront and combat a disease through symbolic battles with its cause (Rivier and Lindgren, 1972; Harner, 1973; Dobkin de Ríos, 1984; Ferreira Júnior et al., 2015).

Psychedelics' imagery-inducing (de Araujo et al., 2012), meaning-enhancing (Hartogsohn, 2018), and contextual effects (Carhart-Harris et al., 2018b) can play an important role in boosting imagination, the placebo effect, and hypnotic suggestibility, thereby favoring salutogenesis through psychoendoneuroimmunological processes (Ray, 2004). Psychosocial healing is a component of human cooperation that comprises empathy, mirroring, emotional contagion, self-regulation, and mentalizing; it also recruits symbolic processes requiring shared meanings of symbols (Kohrt et al., 2020). Thus, besides the psychedelic substance, other ritual elements (e.g., cultural expectations, mimetic enactments, verbal displays, songs, and dances) also serve an important function in enabling healing (Winkelman, 2008, 2019b, 2021a,c; Uthaug et al., 2021).

The fact that psychedelics induce an experience of well-being may have favored learning of their use by humans (Johns, 1990). Rodríguez et al. (1982) suggest hallucinogenic plants were initially used for the treatment of diseases due to their antiparasitic properties. As argued by Ferreira Júnior et al. (2015), the overlap between medicinal and hallucinogenic uses may indicate that the initial consumption of a plant for medicinal purposes lead to the discovery of its use as a hallucinogen. This is consistent with our view that psychedelics were initially ingested because they could provide homeostatic utility.

Improved Social Interaction and Interpersonal Relations

Humans, like all primates, are intensely social. The human niche encompasses face-to-face interactions within social groups, interactions among social groups, and complex social dynamics at both group and larger community levels (Fuentes, 2015). Human ancestors faced the adaptive problem of maintaining the cohesion of large social groups in the face of the centrifugal forces created by the stresses of group living. Primates solve this problem by developing intense forms of commitment to each other through close physical proximity and the use of touch (e.g., licking and other social grooming behaviors [Dunbar, 2010]). Hominins evolved larger group sizes (100–200 individuals) by developing indirect ways (i.e., without physical contact) of triggering endorphin activation that produces community bonding (Dunbar, 2014; Gamble et al., 2014). In sequential order, these extended grooming behaviors involved laughter (a form of chorusing), singing (without words), dancing, storytelling, and more recently, religion – activities that stimulate the endogenous opioid mechanisms that enhance the sense of being bonded with others involved (Pearce et al., 2015; Tarr et al., 2015; Dunbar et al., 2016; Charles et al., 2020). The enhanced emotional ties provided human groups with a higher degree of cohesiveness and stability through time, enhancing various forms of cooperation.

We propose that in this context, psychedelics' effects were harnessed to modulate the strength and quality of social bonds. Ingestion of psilocybin induces euphoria, involuntary grinning, uncontrollable laughter, giddiness, playfulness, and exuberance (Preller and Vollenweider, 2016); it also enhances engagement with music (Kaelen et al., 2018) and eloquence (Doyle, 2011). This means psilocybin ingestion would have amplified sociality long before the emergence of religious rituals. Once archaic humans developed religious and spiritual concerns (see following section on *Facilitation of collective ritual and religious activities*), psilocybin would have become even more useful given its intrinsic ability to produce mystical-type experiences involving the dissolution of self-boundaries and a sense of unity with others (Griffiths et al., 2006, 2011). Therefore, psychedelic use increased participation in the emerging niche in which sociality enhancing experiences such as playing and laughing, singing and dancing, fantasizing and telling stories, and participating in religious rituals became commonplace activities. Collective use of psychedelics may have thus enriched social life and bolstered hermeneutical and rhetorical activity, enhancing management of group tension (through emotional catharsis) and strengthening

social bonds (by triggering the endorphin system), ultimately facilitating complex sociality and communication in the ever-larger human groups.

Recent studies show that psychedelics can modify a range of social behaviors and cognitive processes, having pro-social effects (Table 2; also see Preller and Vollenweider (2019) for a recent review of experimental and controlled studies in humans). Psilocybin has been shown to modulate different objective measures of social cognition; most importantly, it increases empathy for positive emotions (Pokorny et al., 2017) and reduces recognition and processing of negative emotional faces (Schmidt et al., 2013), which facilitates social approach behaviors and thus social interaction (Preller and Vollenweider, 2019). Psilocybin also increases altruistic behavior: employing the Ultimatum Game, Gabay et al. (2018) found that it reduced costly punishment by increasing the participants' concern for the outcome of interacting partners. Furthermore, psilocybin shifts emotional biases away from negative toward positive stimuli (Kraehenmann et al., 2016), and a single high-dose experience can engender measurable and long-lasting changes in socially oriented aspects of personality, such as increases in the dimensions of Openness and Extraversion (MacLean et al., 2011; Bouso et al., 2018; Erritzoe et al., 2018).

The unusually high level of intragroup tolerance and cooperative communication of modern humans is explained by selection for prosociality (or against aggression), a process that has been described as self-domestication (Benítez-Burraco et al., 2020). Selection likely modulated tolerance with increased brain 5-HT levels (Hare, 2017; Raghanti et al., 2018), which is consistent with the scenario developed here in which serotonergic psychedelics provided homeostatic utility by substituting for 5-HT under circumstances in which endogenous biosynthesis and thus signaling functions were compromised. Changes in social cognition also relied on decreases in emotional reactivity supported by shifts in the hormonal and subcortical profiles (e.g., amygdala reactivity) linked to temperament, which then allowed cognitive skills to be expressed in new social situations (e.g., in teaching contexts) (Hare and Tomasello, 2005; Hare, 2017). It is thus noteworthy that a single dose of psilocybin decreases amygdala reactivity to negative stimuli and increases positive mood state (Kraehenmann et al., 2016; also see Rocha et al., 2019). Such shifts in affect and the neural correlates of affective processing can endure for several weeks beyond acute drug effects (Barrett et al., 2020). This suggests that psychedelics increased social tolerance and cohesion by inducing socially desirable mood changes from reduced neural responses to negative stimuli (Kometer et al., 2012; Mueller et al., 2017; Barrett et al., 2020; Vollenweider and Preller, 2020).

Recent work with rodents has unveiled a mechanism of action potentially underlying the prosocial effects of psychedelics. De Gregorio et al. (2021b) have demonstrated that repeated administration of low doses of LSD in mice enhances social interaction by potentiating 5-HT_{2A} and AMPA receptor neurotransmission in the medial prefrontal cortex via an increasing phosphorylation of the mTORC1 (a protein involved in the modulation of social behavior). Moreover, psilocybin has been found to increase striatal dopamine concentrations

TABLE 2 | Evidence for enhanced social and interpersonal capacities during and after psychedelic exposure.

Potentially adaptive effect	Study	Summary of results	Subject population	Total number of subjects
Enhanced social approach behaviors and social interaction	Kometer et al. (2012);	↑ positive mood states, ↓ recognition of negative facial expression, and ↑ behavior toward positive relative to negative cues	Healthy subjects	17 (6 females)
	Dolder et al. (2016);	LSD ↑ happiness, trust, closeness to others, emotional empathy, and sociality	Healthy subjects	40 (20 females)
	Pokorny et al. (2017)	↑ explicit and implicit emotional empathy	Healthy subjects	33 (15 females)
Enhanced social connectedness	Watts et al. (2017)	↓ disconnection (from self, others, and the outside world), ↓ avoidance of difficult emotions and memories, and ↑ acceptance	Patients with treatment-resistant depression	20 (6 females)
Enhanced emotional self-control and tolerance	Barrett et al. (2020)	↓ negative mood, ↑ positive mood, and ↓ amygdala response to negative affective stimuli; reflecting ↑ top-down control of emotionally conflicting information	Healthy subjects	12 (7 females)
Enhanced prosocial attitudes/behaviors and healthy psychological functioning	Griffiths et al. (2018)	Positive changes on longitudinal measures of interpersonal closeness, gratitude, life meaning/purpose, forgiveness, and altruistic behavior	Healthy subjects	75 (45 females)
Positive personality changes	MacLean et al. (2011);	↑ Openness (sustained 1 year after the session)	Healthy subjects	52 (30 females)
	Erritzoe et al. (2018);	↓ Neuroticism and ↑ Extraversion (sustained at 3-month follow-up)	Patients with treatment-resistant depression	20 (6 females)
	Netzband et al. (2020)	Ayahuasca ↑ agreeableness and ↓ neuroticism (sustained in a 6-month follow up)	Patients with depression, anxiety, or post-traumatic stress disorder	24 (9 females)

In all studies, psilocybin was the substance administered, unless otherwise stated.
 ↑, increased; ↓, decreased.

in humans, a mechanism partly underlying euphoria and depersonalization phenomena (Vollenweider et al., 1999). Striatal dopamine promotes social living and increases reward emanating from social interactions (Rilling and Sanfey, 2011). The human striatum exhibits a unique neurochemical profile involving high dopamine levels, consistent with humans' distinctive ultrasociality (Raghanti et al., 2018). This suggests psilocybin instrumentalization could have favored a dopamine-dominated striatum personality style, which is associated with enhanced sensitivity to social cues that promote social conformity, empathy, and altruism (see Raghanti et al., 2018).

Facilitation of Collective Ritual and Religious Activities

Rituals are socially stipulated, conventional behaviors that are critical for group social interaction; they also drive cultural transmission within and between generations (Legare and Nielsen, 2020). Rituals are very diverse and complex, but often involve synchronic movement, causally opaque action, and both euphoric and dysphoric arousal (Whitehouse and Lanman, 2014; Boyer and Liénard, 2020). Ritualized behaviors in the animal kingdom have the basic function of enhancing coordination and cooperation (Winkelman, 2009, 2019b,c). In humans, they also have other social, psychological, and instrumental functions involving, for instance, signaling commitment to others, binding group members together, and reducing individual and collective anxiety (Boyer and Liénard, 2020; Legare and Nielsen, 2020; Nielsen et al., 2020). In traditional cultures, rituals often have goals related to survival and reproductive success such as curing an illness, harming a rival, or ensuring success in hunting (Rossano, 2020). They are particularly crucial during times

of transition, risk, and uncertainty in the human lifespan (Legare and Nielsen, 2020).

Religion comprises symbolically and emotionally laden beliefs and practices (e.g., rituals) regarding superhuman powers, and the institutions that maintain and transmit such beliefs and practices (Bulbulia et al., 2013). A wealth of ethnographic and experimental evidence suggests that religions forge solidarity and cooperation through various mechanisms and at different levels of social complexity (Katz, 1984; Boehm, 1993; Winkelman, 2013b, 2021b; Norenzayan et al., 2016; Skoggard et al., 2020). Early religious forms developed in the context of intense and immersive experiences of music, ritual, and dance (Dunbar, 2017, 2020), likely in combination with psychedelics (Sterelny, 2018; Winkelman, 2019b,c, 2021a,c) and other mind-altering techniques (Rossano, 2007, 2009). Dunbar (2017, 2020) suggests these shamanic type religions based on trance-dancing evolved sometime between the appearance of archaic humans (i.e., Heidelbergians) around 500,000 years ago and the appearance of anatomically modern humans (*Homo sapiens*) around 200,000 years ago as one of a series of behaviors that humans developed to enhance social bonding by triggering the endorphin system.

Foragers mainly utilize psychedelics in shamanic rituals (Harner, 1973; Dobkin de Ríos, 1984; Winkelman, 2010, 2013a) indicating a key aspect of psychedelic instrumentalization was incorporation into prosocial contexts involving synchronic activities (e.g., ritual, drumming, dancing, and singing) that were the precursors to shamanism (Winkelman, 2011a,b, 2019b, 2021c). The prosocial and interpersonal effects of psychedelics (see Table 2) likely supported the “collective effervescence” (*sensu* Durkheim, 1995) and the sense of “communitas” (*sensu* Turner, 1969) during our ancestors' rituals, religious ceremonies,

and secular celebrations, thus aiding activities that allowed individuals to reaffirm their common identity and their connectedness within the social order. Recent work by Kettner et al. (2021) lends support to this hypothesis, showing that *communitas* – an intense sense of togetherness and shared humanity – mediates enduring increases in psychological well-being and social connectedness following psychedelic use in ceremonial retreats.

Since pre-modern societies typically conceptualized psychedelics as entheogens [i.e., as gateways to a spiritual or religious experience and/or communication with the spirit worlds (Winkelman and Hoffman, 2015)] that provide sacred knowledge and power, they have to be understood as a source of inspiration of primordial magico-religious impulses. Importantly, controlled studies show that psychedelics reliably produce mystical-type experiences involving self-loss and a sense of awe and connectedness (Griffiths et al., 2006, 2011, 2018), as well as a range of anomalous experiences (e.g., synaesthesia, out-of-body and near-death experiences, entity encounters; see Luke, 2020; also Strassman, 2001; Winkelman, 2018) that are commonly interpreted as spiritual interactions in pre-modern cultures. Psilocybin occasioned mystical experiences produce enduring beneficial changes, such as trait-level increases in prosocial attitudes and behaviors (Griffiths et al., 2018) and in the personality domain of Openness (MacLean et al., 2011). Moreover, both psychedelic mystical experiences and entity encounters have profound and sometimes lasting effects on beliefs and worldviews (Griffiths et al., 2011, 2019; Davis et al., 2020; Lutkajtis, 2020).

Generally, in traditional smaller scale societies psychedelics are employed in socially oriented settings including healing rituals, rites of passage, initiation into secret societies and cults, and multi-group gatherings (Dobkin de Ríos, 1984; Rätsch, 2005). In these contexts, psychedelic use is carefully programmed and orchestrated by the ritual specialists to produce experiences of a confirmatory nature (Noorani and Alderson-Day, 2020), in the sense that they reinforce a set of socially situated expectations established before entering the altered state (e.g., that a cure will be effected through shamanistic magical intervention, or that initiatic contact with the ancestors will be achieved). Cross-culturally, ritual specialists leverage collective, socially bonding mythic narratives and coordinated, mixed modality performances of entrained ritual or dance to provide structuring during ego-dissolution and to evoke culturally expected visions through expressive dimensions of ritual (Dobkin de Ríos, 1984; Winkelman, 2002, 2015, 2021c; Rodríguez and Quirce, 2012). Thus, for instance, among the Tukano from the Colombian Amazon, psychedelic yagé (*Banisteriopsis caapi* + *Diplopterys cabrerana*) is administered during the Yuruparí dance rites, an ancestor ceremony for initiation of young men into adult male society (Hugh-Jones, 1979; Jackson, 1983). This intense, self-defining experience involves dancing that is interspersed with periods during which tobacco, coca, manioc beer, and yagé are consumed and myths are chanted in unison. During this ritual, young boys are supposed to enter into controlled and voluntary contact with the beginning and source of life, the (other-)world of myth, in order to gain visionary knowledge by assuming the

identity of the *He* People or first ancestors (Reichel-Dolmatoff, 1971; Hugh-Jones, 1979).

Traditional enculturation rituals such as the one just described involve a “socialization of hallucinations” that involves the education of attention, the categorization of perceptions, and the shaping of emotions and expectations (Dupuis, 2021). Crucially, as argued by Dupuis (2021: 10), “Insofar as psychedelics are able to produce perceptions whose phenomenological content is strongly influenced by culture, their noetic property may enhance the significance and attribution of the reality of cultural worldviews as metaphysical, ontological, or supernatural claims. . . these two properties make hallucinogenic substances powerful potential vectors of cultural transmission.”

Current neuroscientific understanding of the effects of psychedelics suggests they can potentially facilitate ritual activities aimed at socialization and enculturation (such as rites of passage and initiation cults). Brain action of psychedelics involves a temporal dampening effect on activity and integrity of the default-mode network (DMN) that decreases top-down inhibition, liberating sensory and cognitive bottom-up information flow, thereby increasing the richness of subjective experience (Carhart-Harris et al., 2012, 2014; Carhart-Harris and Friston, 2019). DMN roles in self and social cognition (Spreng and Andrews-Hanna, 2015; Fingelkurts et al., 2020) are also compromised, with an inhibition or reduction of personhood and agency that leads to enhanced cognitive flexibility and emotional lability (Carhart-Harris and Nutt, 2017; Carhart-Harris and Friston, 2019). In this liminal state, suggestibility, sensitivity to context, and imagery are all heightened (Carhart-Harris et al., 2015, 2018b; Kometer and Vollenweider, 2016). Moreover, this “pivotal mental state” (Brouwer and Carhart-Harris, 2021) involves a generalized malleability, in the form of enhanced synaptogenesis and neural plasticity (Ly et al., 2018), as well as low-level learning and extinction learning (Carhart-Harris and Nutt, 2017) that can further aid self-actualization and self-editing. This destabilizing process is contained within ritual to create new meaning, mediate identity formation, and facilitate the programming of the individual into cult beliefs and cultural patterns.

Enhanced Group Decision-Making

Hominins developed an egalitarian political system in which interdependence and the availability of lethal weapons (e.g., wooden spears and lithic points) made possible group control of leaders; consequently, group success came to depend greatly on the ability of leaders to persuade (Gintis et al., 2015). Undermining the ability of dominants to exploit others helped our ancestors replace hierarchical social dominance with a more equitable sociopolitical structure based on knowledge, conflict resolution, generosity, and status leveling mechanisms (Boehm, 1993). According to Gintis et al. (2015), the heightened social value of nonauthoritarian leadership entailed enhanced fitness for such leadership traits as the ability to form and influence coalitions and intelligence. This emerging sociopolitical system thus selected for increased cognitive and linguistic ability, which enhanced prosocial leadership skills. In this context, non-authoritarian, charismatic leaders such as shamans and other

leaders with supernatural abilities flourished, specializing in palliating or preventing misfortune, providing prosocial services based on knowledge and expertise related to ritual and medicinal functions (Boyer, 2019; Garfield et al., 2020). This type of leaders played an outsized role in numerous domains beyond healing, particularly in group decision-making and problem-solving contexts (e.g., conflict and intergroup mediation, guiding hunting and group movement [Winkelman, 2010, 2013b, 2021a]).

Comparative ethnographic evidence reveals that one of the main shamanistic uses of psychedelics is for divination, i.e., for procuring otherwise unattainable information (Dobkin de Ríos, 1984; Schultes et al., 2001; Rättsch, 2005). Divination practices are required for important collective decisions in many small-scale societies (Boyer, 2020). Ingestion of a vision-inducing material is a common method to gain privileged nonempirical knowledge for decision-making (Sutton and Anderson, 2010). Psychedelic supported divination is employed for purported communication with ancestors or supernatural entities to solve diverse problems and social quandaries, to diagnose and treat illnesses, to have foreknowledge of the future, or to plan and organize subsistence-related activities (e.g., making sure that a hunting expedition will be successful) (Reichel-Dolmatoff, 1971; Dole, 1974; Myerhoff, 1974; Dobkin de Ríos, 1984; Furst, 1990; Ott, 1993). Therefore, in smaller scale societies, psychedelic use is intimately linked with strategizing and decision-making through its central role in diagnostic, forecasting, and interventionist forms of divination.

Psychedelics can afford genuine epistemic benefits even if there is no transcendent reality or all-knowing otherworldly agents (Winkelman, 2013b; Letheby, 2019). Psychedelics can offer new knowledge of old information, allowing appreciation of already known (or otherwise knowable) facts in deep, vivid, affectively and motivationally significant ways (Letheby, 2019). These knowledge-gains seem to be supported by several related psychedelic-enhanced mechanisms that include curious behavior, explorative search, structure and fact-free learning, and insight and perspective change (Carhart-Harris and Friston, 2019). Such effects were likely useful for early humans under circumstances in which immediate decisions had to be made and/or actions taken promptly despite incomplete information. Our ancestors might have been particularly drawn to the rapidly ensuing boost in cognitive flexibility, imagination, and optimism, as well as to the visual intensifications and complex imagery linked to intuitive realizations that psychedelics can facilitate (see **Table 3** for a summary of behavioral and neuroimaging evidence of potentially fitness-enhancing effects of psychedelics on cognition).

Psychedelics modulate aspects of creative thought, inducing a hyper-associative, imagistic mode of thinking that operates with little logical constraints and involves making connections between relatively unrelated words and images (Girn et al., 2020). Psychedelics thus augment semantic activation (Spitzer et al., 1996; Family et al., 2016) and access to novel mental representations (Baggott, 2015), spurring unconventional associations and conceptual links that give rise to unusual thoughts. In fact, naturalistic psilocybin use has been associated with sub-acute enhancements in divergent thinking (Mason et al., 2019) and creative problem-solving ability (Sweat et al., 2016). Since reasoning about causally opaque events

TABLE 3 | Evidence for enhanced cognitive capacities during and after psychedelic exposure.

Potentially adaptive effect	Study	Summary of results	Total number of subjects
Enriched state of consciousness	Lord et al. (2019)	Psilocybin ↑ the repertoire of brain functional network states, ↑ brain integration and neural signal complexity	15 (5 females)
Enhanced cognitive flexibility	Carhart-Harris et al. (2016a)	LSD ↑ cognitive flexibility and optimism for up to 2 weeks afterward	20 (4 females)
Heightened creativity	Family et al. (2016);	LSD ↑ indirect semantic activation, facilitating retrieval of distant associations	10 (1 female)
	Sweat et al. (2016);	Naturalistic psychedelic use associated with ↑ creative problem-solving ability	68 (38 females)
	Mason et al. (2021)	Acutely, psilocybin ↑ ratings of (spontaneous) creative insights and ↓ (deliberate) task-based creativity. 7 days after psilocybin, novel ideas ↑	60 (25 females)
Enhanced mental imagery	de Araujo et al. (2012)	Ayahuasca ↑ the intensity of recalled images to the same level of natural image	10 (5 females)
Enhanced ability to attribute meaning/value	Studerus et al. (2010)	Psilocybin alters the sense of meaning in percepts, e.g., 'things around me had a new strange meaning'	327 (140 females)
Enhanced insightfulness and self-awareness	Kometer et al. (2015)	Psilocybin ↑ retrieval and reattribution of autobiographic memories	50 (22 females)

All studies were performed with healthy volunteers.

↑, increased; ↓, decreased.

or outcomes – those lacking a known causal explanation – is a pervasive feature of human cognition (Legare and Nielsen, 2020), it seems fitting that certain individuals (particularly ritual leaders) in numerous cultures adopted psychedelics as instruments for inspiration and envisioning, since they provide a state of consciousness that can potentially facilitate creative generation addressing knowledge gaps.

This psychedelic-induced 'primary process thinking' (Kraehenmann et al., 2017) involves an increased excitability of the visual pathway (Kometer et al., 2013; Kometer and Vollenweider, 2016; Timmermann et al., 2019) and engagement of an intrinsic representational system also manifested in phantasy, daydreaming, night-time dreaming, and mystical visions (Horváth et al., 2017; Fox et al., 2018). This mode of visual mentation that likely preceded our rational, language-based consciousness supports information integration, decision making processes through presentational symbolism (involving, e.g., simulation of alternative mental scenarios), and learning (Winkelman, 2010, 2017). For millions of years, this image-based cognitive modality provided hominins with a meta-cognitive system for representation of complex relations, problem-solving, and strategic planning (Lohmar, 2010) despite it being less analytically advanced than the (logical, rule-based, and reflective) secondary process thinking (Carhart-Harris et al., 2014).

Cognitive enhancement properties of psychedelics likely derive from their modification of neural signaling, increasing system level complexity and flexibility and interconnectedness of distinct networks (Tagliazucchi et al., 2016; Lord et al., 2019). This brings about an enriched state of consciousness that spontaneously transitions between states with greater freedom and less predictably (Carhart-Harris et al., 2014; Carhart-Harris and Friston, 2019). Hence, psychedelic brain states exhibit higher signal complexity (entropy) and higher cognitive flexibility, but lower cause-effect information (Gallimore, 2015). This degradation of the brain's ability to impose the habitual organization and categorization schemas involves a temporal disabling of the functioning of the DMN that decreases top-down inhibition and liberates bottom-up information flow to specific cortical areas, particularly via intrinsic sources such as the limbic system (Carhart-Harris and Friston, 2019; Vollenweider and Preller, 2020). According to Carhart-Harris and Friston (2019), this broadens the volume and breadth of available sensory and mnemonic content and increases the potential for 'out of the box' ideas, novel insights, and new perspectives. During the psychedelic state, there is also increased communication across the entire brain, which likely engages audiovisual synaesthesia and associative processing (Petri et al., 2014); and the altered integration of sensory perceptions facilitates novel experiences of self and environment, helping to reduce rigid or overly entrenched thinking patterns (De Gregorio et al., 2021a). All of this implies that psychedelic-assisted divination practices could provide access to new and unusual perspectives and innate and unconscious knowledge useful for construing judgments regarding the unknown, thereby constituting an active rhetorical coping and self-editing strategy against inevitable uncertainty.

Crucially, divination is a ritual and a tradition involving an ongoing dialog with more-than-human agents (Curry, 2010; Espírito, 2019). Cross-culturally, the belief that such supernatural agents have information people lack is widespread (Boyer, 2020). Psychedelics' capacity to engender convincing experiences of travel to alternative worlds involving communication with autonomous entities (Winkelman, 2018; Luke, 2020) – apparently allowing a ritual specialist to channel those agents' knowledge – likely made its ingestion a seemingly reliable procedure for obtaining inscrutable information. The robust dishabituating effects of psychedelics on behavior and their persistent rhetorical features (glossolalia and graphomania) that make discourse more attention-grabbing (Doyle, 2011) provided credible costly signals of purported direct interaction with superhuman agents, a persuasive demonstration that the diviners were not the authors of the statements they uttered. All of this reinforced "ostensive detachment," leading people to deem such divinatory statements as less likely to be influenced by anyone's intentions or interest, ultimately favoring efficient coordination (see Boyer, 2020).

Consequently, incipient psychedelic divination practices were mostly functional, likely taking advantage of dishabituating, creative generation, and alternative noetic and epistemic pathways in instrumental ways; at the same time, given the way they supported ostensive detachment (e.g., by reinforcing the notion that the information in question was provided by the spirits; see Winkelman, 2004), they were capable of overriding

individual and collective paralysis, facilitating adaptive strategic thought and group decision making.

DISCUSSION

Psychedelic Ingestion and Shamanistic Leadership in the Socio-Cognitive Niche

Shamans and other leaders with supernatural abilities that often employed psychedelics used their knowledge to both provide benefits and impose costs on others. Shamans had ritual and medicinal functions relying on special knowledge and supernatural qualities that generated fear (e.g., an alleged capacity to magically kill others). Thus, according to Garfield et al. (2020) shamanism appears to be a distinct form of leadership that combines a strategy of inducing fear, similar to the dominance strategy, but is based on knowledge and expertise, similar to the prestige strategy. Shamans thus attained influential positions of leadership through their charisma and knowledgeability, social unification, healing competence, and use of supernatural powers to cause harm (Winkelman, 2010, 2021a). Artistic performance (often involving displays that incorporate superhuman abilities) is also implicated in this style of leadership (Singh, 2017).

How do we know that psychedelics were not frequently used by shamans in a Machiavellian way to mislead other community members to their own advantage (and to the detriment of their followers)? The anthropological record shows that while there are some shamans who have abused their positions, there are also those who do not act solely for personal gains, but who go about their functions without regard for material or political considerations (Ripinsky-Naxon, 1993). For instance, according to Sieroszewski (1900), who spent over a decade with the Yakuts (whose shamans employ the *Amanita muscaria* mushroom; a GABAergic hallucinogen), the "great" shamans were clearly distinct from the "middling" and the "mocking" or deceitful shamans, in the sense that they had not only material gain in view but the alleviation of the griefs of their fellow people, which was evident in the way they undertook their duties: with genuine conviction, negligence of personal danger, and inspired by the high ideal of sacrifice. Such shamans, he argued, always exerted an enormous influence over their audience.

Shamans are performers of the first order, enacting struggles with spiritual forces or magical flights to other realities, singing, dancing, and composing poetry (Estrada, 1989; Cardeña and Beard, 1996). Importantly, the shaman's exhibition of power is carried out in service of the community, usually in public rituals (Langdon, 1992; Winkelman, 2021a) – the reactions of the audience enhancing the shamans' prestige and efficacy (Cardeña and Beard, 1996). This public scrutiny and the ambiguous position of shamans in society (associated with the fact that they may use their power in negative ways, especially when directed against enemies outside of the social group) meant, as exemplified among the Aguaruna (whose shamans employ the psychedelic brew ayahuasca), that if results (e.g., of a healing session) are not forthcoming, the shaman himself may be suspected of, and punished for, sorcery (Brown, 1989). While shamans are known to engage in shamanic rivalries, wars, and duplicity

(see e.g., Hugh-Jones, 1996), ethical training is a key element of the shaman's education (Harner, 1980; Dow, 1986; Walsh, 1990; Krippner, 2002). Thus, shamans were dedicated to ending suffering, even if it required them to forgo their own comfort (see e.g., Dow, 1986), and had a personal interest in maintaining a good reputation (even if just for self-preserving reasons).

To be clear, shamanism includes a number of tricks of the trade such as sleight-of-hand, ventriloquism, surreptitiously using informants to obtain information about the patient, and the prototypical "sucking" cure (Eliade, 1972), which may be construed as involving deceit. However, these activities can be more properly considered as a form of "truthful trickery," in the sense that they are procedures that engender a sense of mastery on the part of the client (e.g., specific techniques such as ventriloquism are used by shamans to indicate the presence of spirits) (Cardena and Beard, 1996). Moreover, the use of acting and the employment of illusions (e.g., the use of masks and costumes) intentionally seek to affect the thoughts, feelings, or perceptions of the audience, bringing about emotional arousal and the evocation of faith, hope, and trust that ultimately enhance client expectations (Krippner, 2002). Hansen (2001) has compiled dozens of examples of shamanic trickery from the anthropological literature, adding that they may promote healing. As Cardena and Beard (1996) argue, therapeutically speaking, pretense, role-playing, and performed illusions can go a long way in impressing onlookers, much more so than words alone. Undoubtedly, illusory cures can have concrete and real effects, as demonstrated by the placebo effect (Oken, 2008). The use of psychedelics to enhance suggestibility could have conferred a number of selective advantages in enhancing the ritual-induced placebo and hypnotic effects (see Rossano, 2007, 2009), as well as through inducing shared world views, and enhancing stress-reducing spiritual adaptations.

Therefore, while it may be concluded that shamans engage in deception and, perhaps, self-deception, as maintained by Warner (1980), a valid alternative perspective, as presented by Cardena and Beard (1996: 33) is that shamans "give concrete form and shape to a vague, ungraspable disease, and that by this and other means the expectations of a possible cure are enhanced." Shaman's adroit maneuvering and use of legerdemain is thus justified by their cause: promoting individual and community health and well-being (Hansen, 2001). So, for instance, sleight-of-hand involving object extraction can be construed as the enactment of a spiritual struggle through which the shaman is able to remove a noxious influence on the patient's welfare (Turner, 1964). Likewise, shamanic rituals in which psychedelics are consumed by the shaman and others to supposedly contact spirit worlds are an effective way to produce a community of experience, acting as a vector of affiliation to the social group and favoring the efficient transmission of metaphysical propositions relating to the supernatural realm (Dupuis, 2021).

It has been argued that human social evolution involved two key steps: first, early humans began to cooperate more and across wider interdependent networks; and second, humans became more group-minded, conforming to social norms in culturally marked groups and punishing norm-violators (Sterelny, 2007; Tomasello et al., 2012; Jensen et al., 2014). In this context of

interdependence and mutualistic collaboration brought about by an obligate collaborative foraging lifeway, individuals had a direct interest in the well-being of their partners. This led to humans' tendency to socially select others with regard to their cooperative behaviors, involving reputation-based social selection (including a concern for self-reputation as a cooperator) (Tomasello et al., 2012; Tomasello, 2014). In this context of joint intentionality and social selection against cheaters, it is hard to imagine that shamans using psychedelics to malignantly delude others could rise to positions of authority and succeed in maintaining power. Only shamans with exceptional abilities relative to others gain status (Garfield et al., 2020), and this involves providing benefits to the community as well as imposing reasonable costs (people accept this costs because they entail assurance of supernatural protection from a powerful figure). This capacity is directly related to their cognitive capital, involving medicinal and ritual knowledge. So, shamans that only imposed costs (e.g., threatening to harm others) without providing benefits (e.g., healing others) could not have gained status and would have likely been deemed cheaters deserving of shunning, ostracization, or even death. Concomitantly, the concern for self-reputation as a cooperator would have likely disincentivized free-riding or cheating strategies from psychedelic-using shamans since anyone with a poor reputation would have been avoided in the first place.

Moreover, an ability to mediate and resolve conflict (i.e., social unification capacities), healing abilities, and artistic prowess are hard-to-fake, costly behaviors that are interpreted as signaling commitment to the group's well-being. Individuals using psychedelics, pretending to be able to provide benefits to the community (but in effect acting in the detriment of their followers) would have found it very difficult to fake these qualities convincingly, making deception by shamans much less likely. To gain prestige and maintain authority shamans needed to show charisma and ostensibly display their capacity to enter into contact with supernatural realms and powers, but they also were required to demonstrate to others their specialized knowledge by effectively healing and resolving social conflicts. In this way, the potential threat posed by fake, ineffective, or effectively damaging shamans was likely not much of an issue among the simple, smaller scale foraging societies that emerged over the course of the Pleistocene, given the scrutiny of followers (involving social selection based on reputation as a good collaborator); the special incentives for helping partners altruistically in a cooperative foraging context (which enhances the ability to suppress selfishness); and the difficulty of convincing others of having prosocial intentions without "tangible" or persuasive outcomes regarding healing and/or social unification.

Psychedelic Instrumentalization as an Enabling Factor in the Construction of the Socio-Cognitive Niche

The evolutionary scenario put forward suggests that dietary incorporation of psilocybin, and its eventual integration into communal practice and proto-religious activity may have helped hominins respond adaptively to the socio-cognitive niche. Given that the socio-cognitive niche: (a) is simultaneously

selection pressure and adaptive response (Downey and Lende, 2012); and (b) was partially constructed by hominins through their metabolism, their activities, and their choices (Laland et al., 2016), a second key aspect of this model is that psychedelic instrumentalization had niche-constructing effects that concomitantly aided in the creation and evolution of the socio-cognitive niche (right side of **Figure 1**). We hypothesize that the presence of psychedelics in the hominin social environment had significant consequences on the selective regime that drove hominin cognitive and behavioral evolution because it facilitated the construction of the adapted social environments that in turn selected for enhancements in the same underlying human capabilities that sustained the socio-cognitive niche. Interpersonal and prosocial effects of psilocybin would have mediated the expansion of social bonding mechanisms such as laughter, singing, dancing, storytelling, and religion, generating feedback and an ecological inheritance (see below for definitions of these concepts) that systematically biased the human evolutionary trajectory toward a socio-cognitive niche.

Niche construction is a process whereby organisms actively construct their environments and consequently change the conditions that effect selection (Odling-Smee et al., 2003). This implies that the products of an organism's behavior are part of its selective environment. If organisms evolve in response to selection pressures modified by their ancestors, there is feedback in the system (Odling-Smee et al., 2003). So, for example, in the case of humans, fire use created selection for biological adaptations to cooked food (Wrangham, 2009); increased and diversified "tool" use favored neurobiological changes sustaining innovation and instruction-learning (Iriki and Taoka, 2012; Stout and Chaminade, 2012); and, more recently, dairy farming selected for lactase persistence (Tishkoff et al., 2007). The niche construction perspective thus recognizes human activities as directing human evolution (Odling-Smee et al., 2003; O'Brien and Laland, 2012). It also emphasizes the interactions between genetic and cultural processes over evolutionary time (Richerson et al., 2010). From this viewpoint, acquired characteristics and byproducts can become evolutionarily significant through evolutionary niches and ecological inheritance, which involves the passing on to descendants of inherited resources and conditions, and associated modified selection pressures (Laland et al., 2014, 2016)².

Consequently, psychedelic instrumentalization can be modeled as an enabling factor in the hominization process, as a socially learned and culturally evolved trait (initially an individually learned self-meditative behavior) that assisted in the construction of the socio-cognitive niche. We argue this is the case because if early enhancements in the tendency to develop social links and cooperate in groups, in creativity, in

non-verbal and linguistic expression, or suggestibility were actually produced by psychedelics (as suggested in the section on *Psychedelic instrumentalization in the human socio-cognitive niche*) they would have transformed the social environment, and thus the selection pressures, for ancient hominins. Psychedelic use could have sustained a feedback loop: it increased social cognition and symbolic behavior and thereby selected for yet further increases in such capacities by increasing the richness and complexity of the (constructed) social and semiotic environment.

In this way, the acquisition of enhanced cognition and sociality by members of the population that instrumentalized psychedelics would have intensified the selection pressures on members of descendant generations to develop visual representations, intelligence, and cooperation skills. Through a Baldwin effect [a non-Lamarckian way for environmentally induced somatic modifications, resulting from either learning or physiological adaptation, to become heritable changes (Jablonka and Lamb, 1998; Weber and Depew, 2003)], selection for genetic variants that make the acquisition of creativity and sociality faster, more reliable, and less dependent on environmental signals (such as the ritual consumption of psychedelics) would have eventually occurred.

Early humans learned by doing in an environment seeded with informational resources (indexical, iconic, and eventually symbolic) without explicit instruction and without formalized institutions (Sterelny, 2012, 2014). Our ancestors integrated these diverse semiotic elements in their collaborative efforts to interact with, and modify, their local physical and social ecologies, producing alterations in those ecologies that created new potentials for evolutionary dynamics (Fuentes, 2015). Semiotic elements, as well as artifacts and modified aspects of the landscape, contributed to a legacy of changed selection pressures (bequeathed generation through generation) that scaffolded the development and selection of adaptive traits. Thus, if psilocybin systematically increased the frequency of laughter, music-making (including dancing), ritualization, and prosocial leadership in ancient populations – thus enhancing the strength and quality of social bonds and decision-making, and consequently modifying the conditions for selection – then psilocybin could have ultimately influenced human evolution because such (ecologically and culturally inherited) communally held aspects of culture could exercise influences that selected in turn for genetic variants enhancing sociality, cognition, and communication skills.

As discussed above, construction of the socio-cognitive niche entailed expansion of a set of informal religious activities or "wild traditions" (*sensu* Boyer, 2019) involving leaders with supernatural qualities (shamans, in the broad sense; Garfield et al., 2020) that ritually induced altered states of consciousness (involving interactions with presumed superhuman powers and supernatural entities) to provide prosocial services of healing and divination (Winkelman, 2010, 2021c). These magico-religious activities were rooted in dancing, singing, and enactment that both induced alterations of consciousness and further served as a means for enhancing peace-making, affiliation, and imagination in community-wide nighttime

²The niche construction perspective involves a triple-inheritance system comprised by genetic inheritance plus ecological inheritance and cultural inheritance (in humans and other cultural animals), which means that there are several relevant extra-genetic factors involved in evolutionary processes (for a diagrammatic explanation of this process see Figure 6.1 in Odling-Smee et al., 2003).

healing and social effervescence rituals (Dunbar, 2017, 2020; Sterelny, 2018; Winkelman, 2021a). Psilocybin has a capacity to amplify these ecstatic and visionary thinking modalities through inducing ego-dissolution (Lebedev et al., 2015); a sense of connectedness (Carhart-Harris et al., 2018a); increased elementary and complex imagery (Kometer and Vollenweider, 2016); and entity-encounter occurrences (Lutkajtis, 2020). In an attempt to endure, make sense of, and communicate such intense, self-defining experiences humans often deploy rhythmic, hermeneutical, and rhetorical activity (Doyle, 2011, also see Munn, 1973 and Sterelny, 2018). Consequently, it is likely that repeated exposures to psilocybin mushrooms in ancestral human populations constituted an important influence on the origins and development of ancient religiosity, which comprised animism, belief in an afterlife, and shamanistic concepts (see Peoples et al., 2016 for a reconstruction of ancestral character states of religion; also Winkelman, 2010, 2013a, 2021b).

This means that early instantiations of animistic thinking and proto-shamanistic behavior prompted by psychedelic-induced altered states of consciousness (ASC) could have created contexts that effected subsequent selection enhancing human religiosity. If psychedelics engendered mental states that had adaptive effects on health, social bonding, and decision-making, this would have led to subsequent selection (both genetic and cultural) for the ability and motivation to alter consciousness through alternative (non-drug) means, and particularly in ways that most effectively functioned to promote salutogenesis, sociality, and creativity.

Accordingly, humans across the world and through time deployed various techniques to mimic, supplement, or amplify psychedelics' effects, which involve stressing the cognitive system through sleep deprivation, temperature extremes, sensory overload, exhaustion, and emotionally charged, intense experience (Baumard and Boyer, 2013; Winkelman, 2013c). Ritual chanting, music, and dance were developed to induce euphoria and ecstasy (i.e., ASC) (Nettl, 1956; Winkelman, 1992, 2019b; Becker, 2004), enhancing health and well-being (Winkelman, 2008; MacDonald, 2013), social bonding (Savage et al., 2020), and creativity (Passanisi et al., 2015) even in the absence of psychedelic ingestion. Concomitantly, mythological narratives and religious beliefs were elaborated that enabled individual integration (McNamara, 2009) and collective accommodation (McKay, 2018; Sterelny, 2018) of the profound, and often unsettling, visionary experiences encountered in ASC. We think this niche-construction dynamic, which involves a combination of cultural and biological selection, helps explain why psychedelic use is not ubiquitous while institutionalized ASC (Bourguignon, 1973), music (Mehr et al., 2019), and religion (Norenzayan, 2010) are cross-cultural universals.

So, while psychedelic instrumentalization may have been an important ancient feature of human social and cognitive lives, it is now largely absent from most human cultures. Perhaps it suffered a fate similar to that of hunting and stone tool making (both also being mostly absent in modern human societies, having been replaced by agriculture and the use of metal tools) because safer, more effective and/or convenient (albeit perhaps less powerful) means to access ASC and support health, social bonding, and

decision-making (e.g., music and religion) are now an integral part of the human niche.

CONCLUSION AND FUTURE DIRECTIONS

This article presents a model of adaptive utilization of psychedelics based on homeostatic and instrumentalization perspectives that explain potential selective advantages bestowed by psychedelics to hominins and archaic humans. Psilocybin ingestion could have provided homeostatic utility to our ancestors as a "treatment" for 5-HT depletion – a recurrent adaptive problem throughout advancement into a socio-cognitive niche. We show that, afterward, psychedelics could have increased adaptability and fitness in the context of this obligatorily cooperative, social-learning-dependent lifestyle because they could be harnessed as "instruments" to enhance performance of non-drug-related behaviors, particularly: to manage psychological distress and treat health problems; to improve social interaction and interpersonal relations; to facilitate collective ritual and religious activities; and to enhance group decision-making.

Niche-construction and gene-culture coevolutionary processes explain how dietary and societal incorporation of psychedelics may have become evolutionarily significant. The suggestion put forward is that psychedelics supported the elaboration of socially constructed environments – involving collective rituals, synchronic activities, and guidance by prosocial leaders – that could persist even if psychedelic instrumentalization was no longer an active part of the hominin behavioral repertoire. This means that psychedelic instrumentalization acted as an enabling factor in the development of the human socio-cognitive niche by mediating the expansion of ritual alterations of consciousness, healing, social bonding, and decision-making activities that, in turn, accelerated the rate at which key biological components of sociality, cognition, and communication skills spread in our lineage.

A topic worthy of further attention concerns psychedelics' role in human brain evolution. Considered in the context of the changes in brain size and complexity that accompanied entry into the socio-cognitive niche, the ability of psychedelics to act as "psychoplastogens" (i.e., to rapidly promote induced synaptogenesis and neural plasticity: Ly et al., 2018) could have aided release of energetic constraints on encephalization, similar to how increased consumption of meat and energy-dense plant foods (e.g., fruit, tubers) was necessary for humans to overcome the metabolic constraints on brain expansion (Aiello and Wheeler, 1995; also see Milton, 2003). The presence of psychedelics in the early human diet may have also favored positive selection for exaggerated cortical plasticity – which apparently is a uniquely human derivation (Krubitzer, 2009) – and for the expansion of key functional networks involved in the enhancement of cognitive functions in humans compared to other primate species. Through their agonist action at 5-HT_{2A} receptors, psychedelics elevate synaptic efficacy and

neuroplasticity (Ly et al., 2018) and functionally modulate the activity and connectivity of the frontoparietal network and the DMN (Carhart-Harris and Friston, 2019; Vollenweider and Preller, 2020), enhancing (potentially in the long-term) cognitive functioning (Cini et al., 2019) and sociality (Preller and Vollenweider, 2019). It has also been shown that psychedelic effects can reduce symptoms of autism (Sigafoos et al., 2007) and mimic certain aspects of psychosis (Carhart-Harris et al., 2016a). Intriguingly, the rapid evolutionary cortical expansion and reorganization in the human brain is most pronounced in higher-order cognitive networks (especially the frontoparietal network and DMN), and runs parallel (most pronouncedly in the DMN) with high expression of human-accelerated genes (HAR genes) involved in synapse and dendrite formation (Wei et al., 2019). Moreover, HAR and DMN genes show significant associations with individual variations in DMN functional activity, intelligence, social behavior, and mental conditions such as schizophrenia and autism (Wei et al., 2019).

An important matter that remains to be properly addressed concerns the question of why psychedelics affect our minds in the way they do. The homeostatic and drug instrumentalization perspective we have developed suggests that despite being chemical defenses designed to deter consumption (mainly by insects), psilocybin and other psychedelics were likely exploited by humans because of their chemical resemblance to endogenous signaling molecules that are fundamental but hard for the body to produce (in this case, 5-HT). Therefore, we surmise that the answer to the question of why psychedelics affect our minds in the way they do involves the coevolutionary chemical arms races between plants (fungi) and insects that selected for secondary metabolite synthesis of compounds that can similarly affect the nervous systems of insects and humans through common intercellular signaling pathways that plants, humans, and mushrooms share (Kennedy, 2014). This created the opportunity for what Schultz (2002) has referred to as “phylogenetic espionage” between plants, animals, and mushrooms, involving the capacity of animals to adaptively exploit potentially toxic fungal and vegetal secondary compounds. Moreover, animals typically engage in self-medicative and drug instrumentalization behaviors to solve adaptive problems directly related to their way of life (Forbey et al., 2009; Müller, 2020). Therefore, the answer to this question also resides in the specifics of the human lifeway, which placed a premium on social tolerance and cognitive flexibility (both regulated by 5-HT; Tricklebank and Daly, 2019) making the ingestion of 5-HT-mimicking psychedelics potentially beneficial and adaptive.

While observational evidence shows non-human mammals using plants for their psychoactivity (Siegel, 2005; Forbey et al., 2009) most animals are not particularly fond of mind-altering materials. Although self-medicative consumption of pharmacologically active plants occurs among animals (Huffman, 1997; Villalba and Provenza, 2007), only humans intentionally and periodically self-administer psychoactive compounds in the context of shared intentionality (i.e., coordinating their behavior and intentional states in cultural and conventional ways, e.g., in entrained ritual or dance) and manifest a propensity to employ non-pharmacological techniques to produce ASC

(which likely indicates a derived preference for mind-alteration). Humans also possess an exceptional culturally accumulated knowledge about the toxic and intoxicating properties of plants, an ethnobotanical lore closely interwoven with mythology and under the purview of leaders with ritual/medicinal functions and supernatural qualities (Rätsch, 2005; Wink and van Wyk, 2008; Kennedy, 2014; Garfield et al., 2020). This shows that human ancestors – in a taxonomically distinctive way – constructed a niche that functionally and adaptively integrated certain mind-altering substances (i.e., hallucinogens, stimulants, and narcotics) into culture.

Importantly, archaic humans manifested derived traits such as advanced mindreading capacities, a propensity for shared rhythmical movement and sound, and early precursors of storytelling through mimesis (Sterelny, 2018; Dunbar, 2020). These are expected to have greatly enhanced the value of the “psychedelic experience” (Winkelman, 2021c) and its emotional, aesthetic, and hermeneutical appeal, thus explaining motivation for continued use of psychedelics in humans despite the fact that they do not have rewarding effects in animal models (see Heal et al., 2018). Although there is certain level of recreational abuse of psychedelics in humans (Murnane, 2018), psychedelics seem to have very little appeal to nonhuman primates and rodents and are considered to be a false negative of self-administration procedures (Calvey, 2019). Motivation to consume psilocybin is specifically related to visual effects, positive mood, insight, positive social effects, increased awareness of beauty (both visual and music), awe/amazement, meaningfulness, and mystical experience (Carbonaro et al., 2020). Hence, the nature of the reinforcement in humans seems to be intimately related to our enriched intersubjective, social, and symbolic life, and to the cognitive capacities that sustain that life, involving “perceptions of greater awareness, increased understanding, or profound insights that would have no counterpart in lower species with a less developed frontal cortex” (Nichols, 2004: 138).

In spite of this situation, it is unclear if psychedelic use was established relatively early in hominin life and thus may help explain the evolution of the socio-cognitive niche (as suggested here); or alternatively, if it emerged relatively late in human life (and was able to coincidentally or accidentally enhance cognition and sociality), in which case the focus should be instead on their coevolutionary interaction after independent origins. Evidence reviewed above concerning early hominins’ paleodiet and paleoecology, primate phylogeny of mycophagical and self-medicative behaviors, and the biogeography of psilocybin-containing fungi supports the former scenario. But, in all probability, exactly when our ancestors first deliberately employed consciousness-altering substances in rituals will forever remain uncertain. Nonetheless, more empirical research should enable us to properly evaluate the possible role and impact of the consumption of psychedelics in human adaptation and evolutionary history.

Moving forward, we think that research should seek to test some of the predictions that follow from the model, in an attempt to falsify them. For instance, the psychedelic instrumentalization model does not necessitate nor predict that psychedelic use is universal, or even widespread among cultures; but it does predict

that psychedelic use should be more prevalent among foragers than agriculturalists (because it is assumed that psychedelic use is a relatively ancient behavior associated with simpler foraging societies and their shamanistic practices, which tend to disappear as agriculture intensifies; see Winkelman, 2021a). Systematic cross-cultural research methods could be used to test this prediction by empirically determining the frequency of psychedelic use as a function of subsistence type and political integration in a worldwide sample of societies that has been randomly selected through established probabilistic sampling procedures. Another *a priori* hypothesis that can be tested against the available cross-cultural evidence (e.g., from sources such as eHRAF) is that psychedelic use is mainly associated with specific functional contexts (i.e., healing, social bonding/socialization, and decision-making rituals). This notion is suggested by a qualitative reading of the anthropological record, but has yet to be confirmed by more systematic studies. Such cross-cultural similarities related to functionality, if verified, would suggest selection by biological and/or cultural evolution.

Moreover, the model predicts that psilocybin (and other serotonergic psychedelics) can substitute for 5-HT under conditions of tryptophan depletion, thereby ameliorating the costs associated with impairment of serotonergic neural signaling (involving, e.g., depressed mood, increased stress vulnerability, and cognitive inflexibility). This prediction can be subjected to a critical test by employing established experimental procedures for modifying peripheral and central 5-HT levels (that manipulate tryptophan levels, acutely or chronically, by depletion or supplementation; see Jenkins et al., 2016) in conjunction with the administration of different doses of psychedelic substances. For instance, it has been shown that tryptophan depletion produces significant reductions in the level of cooperation shown by participants in the context of a mixed-motive game, the Prisoner's Dilemma (Wood et al., 2006). It is predicted that administration of psilocybin should revert the deficits in cooperation observed under such experimental conditions.

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- Obtaining negative results from these empirical tests would imply that the hypothetical scenario proposed here is unlikely.
- Besides advocating for the relevance of an evolutionary perspective in the task of explaining and therapeutically harnessing the effects of psychedelics, it is hoped that this article will help encourage the incorporation of psychedelics into theoretical and empirical efforts directed at further advancing our understanding of the evolution of human behavior.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

JR presented the idea of psychedelic instrumentalization in the socio-cognitive niche in a manuscript sent to MW. Both authors contributed to all aspects of the current manuscript.

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The Power of Social Attribution: Perspectives on the Healing Efficacy of Ayahuasca

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During the last decades, ayahuasca gained much popularity among non-Indigenous and out-of-Amazonia based populations. In popular culture, it has been advertised as a natural remedy that was discovered by Indigenous peoples ante millennia and that has been used for shamanic healing of all kinds of ailments. This “neo-shamanic,” and often recreational, use of ayahuasca, however, has to be distinguished from traditional Indigenous praxes on the one hand, and, on the other hand, from medical investigation in the modern world. The former, Indigenous use mainly understands ayahuasca as an amplifying power for interacting with non-human beings in the animal, plant, or spirit realms. Within this paradigm, efficacy is not dependent on the drug, but on the correct communication between the healer (or sorcerer) and the non-human powers that are considered real and powerful also without resorting to ayahuasca. The latter, modern mode of understanding, contrastingly treats the neurochemical processes of MAO inhibition and dimethyltryptamine activity as trigger mechanisms for a series of psychological as well as somatic responses, including positive outcomes in the treatment of various mental conditions. I argue that there is an ontological incommensurability occurring especially between the Indigenous and medicinal concepts of ayahuasca use (with recreational use in its widest understanding trying to make sense from both sides). Modern medical applications of ayahuasca are so fundamentally different from Indigenous concepts that the latter cannot be used to legitimate or confirm the former (and vice versa). Finally, the deep coloniality in the process of appropriation of the Indigenous by the modern has to be questioned and resolved in any case of ayahuasca application.

Keywords: ayahuasca, constructivism, indigenous knowledge, stereotypes, colonialism, appropriation

INTRODUCTION

In recent times, ayahuasca has been in use by at least three large and overlapping groups: traditional Indigenous and Mestizo people within their communities, neo-shamanic and recreational users all over the world, and patients of mental health facilities in the realm of modern medicine and psychiatry. In this perspective paper, I will show that although all these forms of use are

legitimate and meaningful, they are still situated in a deep colonial structure of power relations and appropriation. For example, in neo-shamanic and medical use, traditional healers are often employed, who are then missed in their original communities. In addition, it seems that the efficacy of ayahuasca in both neo-shamanic and medical use draws primarily from ascriptions of alterity to the substance: why do modern users so often resort to constructed images of Indigeneity, naturalness, and ritual when drinking or administering ayahuasca, while at the same time its efficacy is ascribed to its pharmacology, or to “doing ayahuasca”? In order to answer this question, I will compare traditional Indigenous concepts with neo-shamanic or recreational, and modern medical concepts of attributing efficacy to this substance.

From the first half of the 20th Century on, reports of Westerners concerning ayahuasca placed it as a “medicine” within the construction of “ayahuasca shamanism,” that is a health-related use of this substance, although Indigenous or Mestizo people then mainly used ayahuasca for divination, (counter-)witchcraft, warfare, and communal religious rituals (Gow, 1994; Bianchi, 2005; Brabec de Mori, 2011). The idea that ayahuasca was used for “curing,” although not yet literally for medical purposes, probably dates back to the rubber boom and its exploitation and genocidal mistreatment of Indigenous populations that had to be “healed” in a political-metaphysical sense of empowerment and reconciliation (Taussig, 1987; Byrne, 2017). Indigenous medical concepts are much older and deeply rooted in an animist worldview and complex techniques of contacting, socializing with, and dealing out reciprocities with non-human spirits, animals, or other entities; techniques that completely lack any necessity of ayahuasca use.

Despite the constructed quality of “ayahuasca shamanism,” it seems impossible to shed off implicit assumptions in contemporary Western or “modern” applications about ayahuasca’s “mythical,” “spiritual,” “shamanic,” “ritual,” “Indigenous,” “entheogenic,” “ecological,” and similar qualities that are ascribed to this complex (see Gearin, 2015; Fotiou, 2020a,b). Especially neo-animist renderings of “mother ayahuasca” or “teacher” and “master plants” are impressively popular among Westerners. I argue, therefore, that ayahuasca’s distinctive successes in both popular culture and medical investigation are indebted mainly to said social attributions of healing power grounded in intrinsic assumptions of Alterity.

I use the term “social attribution” to denote the *discourse about* a specific item, in this case, ayahuasca, and what it is assumed to do to its users.¹ Different forms of discourse shape differing opinions about the item and thus inform different certainties about its qualities. In all cases discussed here, ayahuasca as a substance is constituted by basically the same, or similar, human pharmacology, but the qualities that are attributed to this substance show significant variation.

¹ Attribution theory was used in social psychology to understand “folk psychological” judgments of one person about another but has been mostly substituted by discourse analysis (Potter and Edwards, 1990). Attribution theory is nowadays used in organizational sciences for example to describe how laypeople perceive certain brands (Al-Sharif, 2020).

In the following, I will describe three modes in which ayahuasca is used. Quite naturally, when one constructs categories, exceptions from the rule will be found: there are many instances where the three modes overlap and interact, and in addition, though very rarely, some people may use ayahuasca in other modalities than described here.

SOCIAL ATTRIBUTIONS IN INDIGENOUS TRADITIONAL USE

It is difficult to present Indigenous concepts around ayahuasca in a nutshell, so I will exemplarily explain traditional ayahuasca use among the Peruvian Shipibo-Konibo. This is where I conducted systematic fieldwork from 2000 to 2006, continued through visits until 2019. I describe the healing-sorcery practices as observed among Shipibo-Konibo healers (*médicos*) who in the early 2000s worked among their communities, but not (yet) with tourists or visitors.

In traditional Shipibo medicine, an apprentice would embark on lengthy “diets” (*samá*; cf. Illius, 1987; LeClerc, 2003; O’Shaughnessy and Berlowitz, 2021) that do not involve the intake of ayahuasca but of other plants, and seldom animal or inorganic substances. These are ingested before and during a span of time when the apprentice would retire from much of social contacts and follow a set of alimentary and social taboos. Note here, that “diets” are also prescribed for patients after a curing session (in order not to disturb the songs that are thought to linger in the body), or for healing processes that apply any plant preparations. “Diets” are likewise essential for many forms of learning, e.g., for becoming a good hunter, for producing precious artwork, for toddlers to walk and talk more quickly, for being a good soccer player or musician, and so on. During a “diet” devoted to becoming a healer-sorcerer, however, the apprentice should make contact with the humanoid entities of the plant ingested, who are called “owners” (*ibo*) or “spirits” (*yoshin*), in dreams or wake-state visions. From these, the disciple obtains their powers which often take the forms of songs. Between “diets,” the apprentice would accompany his² teacher in curing sessions and thereby practice working with him and learn to apply what he obtained from his “diet.” There was no formal initiation, so at some point the apprentice would start conducting healing or sorcery sessions on his own, thus stepping into the competitive ring of healer-sorcerers. Illness was understood as a reciprocal process, stemming from a source, which, in order to heal, has to be tricked, seduced, or overthrown. In cases when a competing specialist would be held to be the original causer of an illness, from the others’ perspective, “my healer” is “his sorcerer” (Brabec de Mori, 2017).

Efficacy is attributed to the power of a healer from close kin who accomplished many lengthy “diets,” has vast social relations with animals, plants, and spirits, and knows a great repertoire

²I use the male form here, because in traditional Shipibo ayahuasca use, only men would embark on these duties. Female participation was extremely rare but has rapidly been growing since around 2000.

of magical songs – the main means of interacting with his non-human allies, and their foes. The correct use of melodies, language, codes, and metaphors was crucial. The powerful voice (see Brabec de Mori, in print) would be obtained through “diets,” too. I repeat that the use of ayahuasca was totally optional, restricted to the specialist himself, and the most powerful healer-sorcerers, the *meraya*, did not use it at all.

It is important to note that in order to accomplish “diets,” and to be instructed by a teacher, one had to “stand firmly on both legs,” as one specialist put it. Therefore, the intake of ayahuasca was (ideally) socially restricted to healthy, psychologically and socially established well-trained individuals, because, as indicated above, only they would drink the brew, while patients or laypeople would never touch it – “why should I drink this, I am not a healer!”

Among all the Indigenous healers I worked with, high-intensity hallucinations were avoided. Most healers would drink fairly low doses in order to only “open up the world” (*nete kepentí*). They would retain control of their condition in order to channel their songs’ power toward the patient. Finally, vomiting was not a topic. During around 100 ayahuasca sessions I witnessed among traditional Shipibo healers, no single one would ever vomit. Ayahuasca was considered a delicate tool to more easily reach the spirit world, nothing more, nothing less.

SOCIAL ATTRIBUTIONS IN NEO-SHAMANIC AND RECREATIONAL USE

In Indigenous use prior to the ayahuasca boom, the healer would take the substance, but not the sick. This constitutes the most prominently marked difference between Indigenous and modern understandings of ayahuasca: ayahuasca had to – by itself, as a substance – show therapeutic effect, and clients would be those who had to go through the hallucinatory experience. Thus, a “psychologization” of the whole process took place (Brabec de Mori, 2013; Labate, 2014). Remarkably, Indigenous thought attributes efficacy to the healer’s power, knowledge, and experience, while Westerners cannot but attribute efficacy to the substance-as-ingested.

The appearance of Western researchers and later drug and healing tourists and visitors triggered a transformation in Amazonian Indigenous and Mestizo “traditions” toward communal ayahuasca-drinking sessions that became known as “ceremonies.”³ This newly invented style of ayahuasca use was then exported to North America and Europe, and practically all over the world. Nowadays, a multitude of neo-shamans who either learned from the first generation of out-of-the-Amazon *ayahuasqueros*, or who created their own eclectic ayahuasca ceremony styles, offer their services to a growing general public. Most of these sessions are held exclusively for “white” or other non-Indigenous, non-local people. There is much work about

these forms of ayahuasca use in the Amazon and beyond (see Gearin, 2015; Labate et al., 2016; Fotiou, 2020b). I will restrict my analysis here to my fieldwork among White neo-shamans in Shipibo territory, and to phenomena that I consider most distinctive.

In these neo-shamanic contexts, the importance of “diets” is varied, in some cases they are completely omitted (most often in foreign contexts), or they are recommended because the brew would cause stronger hallucinogenic effects after fasting. In the latter cases, the diet has to be held before the ayahuasca session, while in Indigenous use, it should follow the treatment. For “becoming a shaman,” the diet is usually prescribed very much in the Indigenous sense, but most often “mixed” with ayahuasca ingestion, or thought to “strengthen” one’s control of ayahuasca hallucinations. Diets are rarely considered important for anything beyond the ayahuasca complex.

Another main distinction is a certain “white-washing” of the practice: “shamans” are considered “good,” and ayahuasca use is by definition beneficial. Sorcery is not considered inherent (see Fotiou, 2010), and not connected to emotion control or psychological stability. Quite on the contrary, as I observed among “shaman apprentices” in Ucayali, many of them have a history of minor mental disorder or at least some issues with mental or social instability, not by any means “standing firmly on both legs.” Many are seekers, with “alternative” world-views, lacking or avoiding well-defined integrated professional or family life (of course there are some exceptions here). Therefore, ayahuasca by itself and its use are considered to be beneficial to health, spiritual growth, inspiration, and general well-being, promising a possible solution for preconditions like mental problems or social instability.

This results in a very different kind of people drinking ayahuasca compared to Indigenous traditions: mainly people with a background of experience-seeking, of spiritual, psychological, ecological, or socio-economic discontent, or with diagnosed health problems tend to attend such ceremonies (Wolff and Passie, 2018). The attribution of efficacy goes to the substance itself, which is often worshipped as “mother,” “teacher,” or “master,” and to a complex of alleged authenticity in terms of eco-harmony, purity, shamanism, spirituality, and indigeneity, say: colonial style exoticism. Local ayahuasca ceremonies I observed in Central Europe are highly ritualized and exoticized, and immense healing power is attributed to the substance and its immediate effects: heavy vomiting, physical suffering, and harrowing, dreadful visions are seen as necessary for a cathartic experience which in turn is considered foundational for achieving spiritual, mental, or physical well-being.

I could also observe that many White shaman apprentices in Peru were surprisingly uninterested in the lived world of the “non-ayahuasca-drinking” locals, who still constitute the vast majority of Indigenous or Mestizo populations, and their situation of marginalization and often extreme and illness-causing poverty. One shaman apprentice even believed that “they are happy living in that way.” There are many people who do care, of course, but I was harshly surprised that this attitude occurred among all (randomly selected) White shaman

³The term “ceremonies” recently appeared in the 1990s and has been exclusively used for sessions involving visitors; the same happened with the term “shaman” (for a critical discussion, see Martínez González, 2009).

apprentices I interviewed in hostels and “albergues” during my fieldwork in 2019.

SOCIAL ATTRIBUTIONS IN WESTERN THERAPEUTIC AND CLINICAL USE

There is strong and growing support for a general efficacy of so-called “psychedelic,” hallucinogenic drugs including LSD, MDMA, mescaline, psilocybin, ketamine, and others, in the context of treating a variety of non-psychotic mental conditions including, for example, recurrent depression, anxiety and obsessive-compulsive disorders, and drug addiction. Ayahuasca, too, seems beneficial in therapies of various mental disorders (most solid in addiction treatments, see Bouso and Riba, 2014; Palhano-Fontes et al., 2019).

Pioneer studies on the chemistry and human pharmacology of the substance were mostly undertaken in un-controlled settings, they had to deal with the difficult accessibility of the material (Rivier and Lindgren, 1972), or create alternatives to circumvent the problems of remoteness and prohibition (Ott, 1994). Similar problems appeared for investigations about the efficacy of ayahuasca on health-related conditions, though they still have to be acknowledged as most seminal in the field (Grob et al., 1996; Riba et al., 2001). Until today, many studies about the effects of ayahuasca on human health have to be conducted “in the wild” in (more or less legal) ayahuasca ceremonies. Uthaug et al. (2021), for example, “visited 6 ayahuasca retreats, hosted by a single organization, all taking place at several locations in Europe...” The same authors clearly state that “Only ‘students of the ayahuasca school’ (linked to the host organization) were invited to participate in the present single-blind, placebo-controlled study.” That means that the population under study were exclusively European ayahuasca users who had previously decided to devote themselves to “studying” with the “host organization,” which – though un-attended by the authors – carries a strict dogma of ayahuasca’s properties, and students probably feel obliged to reproduce these. Similar limitations (acknowledged by the authors) apply to the “global ayahuasca project” (Sarris et al., 2021) that based its analysis on 11,912 online survey responses by people from all over the world who, obviously, were mostly involved with groups of regular, and biased, ayahuasca users.

Although most clinical studies are methodologically well designed and solid, there is a strong bias to be observed when reviewing the literature, that either researchers, the studied population, or both underlie the abovementioned assumptions that ayahuasca *per se* was a medicine. For example, in Labate and Cavnar’s (2014) influential book *The Therapeutic Use of Ayahuasca*, where some of the finest scientists working on the human pharmacology of the substance contributed chapters, the foreword reproduces ethnographic myths, and rather naïvely states, without any reference, that among Indigenous people “ayahuasca is considered a medicine: the great medicine. Practically, in today’s world, the shamanic model incorporates easily-transferable features, including group structure, attention to set and setting, import of intention, and proper preparation

for and integration of the experience” (Grob, 2014: x–xi). In my perspective as a critical ethnographer, this attitude is way colonial. It does not listen to but models a Western imagination of, Indigenous people’s opinions. Most chapters in Labate and Cavnar’s book, and many studies on ayahuasca as a therapeutic tool, cling to un-referenced and never tested assumptions that this substance would have been used by Indigenous people during millennia for the purpose of (spiritual) healing – although this “healing” was recently constructed during the second half of the 20th Century.

A psychedelic experience may, on the contrary, also be disturbing or frightening and even cause lasting mental health problems. This seems to occur very rarely and mostly through triggering pre-existing latent disorders, and could be statistically counterbalanced by positive effects in others (Krebs and Johansen, 2013). Heise and Brooks (2017) report acute intoxication crises after ayahuasca ingestion that were brought to US poison control, including three fatalities. Dos Santos et al. (2017) registered diagnosed psychotic episodes from published literature. Gearin and Calavia Sáez (2021: 147) found that personality disorders, especially “narcissism and related problems of the self” may be exacerbated by ayahuasca use. Although cases of less severe adverse effects may have escaped these studies, an overall beneficiary effect seems evident as such.

In stark contrast to the Indigenous concept, the drug is now ingested by the patients, that is, exclusively by people with diagnosed mental health conditions. The (hopefully) psychologically and socially stable therapist, on the contrary, does not drink the brew together with the client. In most countries, healthy individuals are not allowed to drink ayahuasca while ill people may obtain a legal exception.

In sum, I do not doubt that ayahuasca, along with other hallucinogens despite some counterindications may be very useful in treating certain mental disorders. However, the power of social attributions remains un-attended in many studies (but see e.g., Talin and Sanabria, 2017), and expectations abound – even among the researchers themselves who are often quite fond of their own visionary experiences obtained through the brew, possible leading to a sense of mission, which is rather unsettling in terms of good scientific practice (cf. Grob, 2014: xiii).

OUTLOOK

People form general beliefs fed by their social environment, in this case, people (including scholars) believe that ayahuasca has intrinsic natural, medical, spiritual, ecological powers that had been suppressed through the Western world’s (often radical) secular, disenchanted life-world history. People with such a general belief are then seeking and creating situations that trigger certain experiences, which in turn enable them to form a personal (or scientific) account, including mental states and personal development, that strengthens the general belief (Van Leeuwen and Van Elk, 2018).

This should not be misunderstood as a generalizing critique on the use and study of ayahuasca and other hallucinogens for therapeutic applications. I do suggest, however, that there

are more contextual (e.g., ritualization) and psychological (e.g., beliefs) factors to be understood than hitherto recognized. Furthermore, I think that the three modes of ayahuasca use I briefly presented here are ontologically different. Social attributions of efficacy range from interaction with spirits (requiring an animist ontology, see Descola, 2013), to worshipping neo-indigeneity and ecology (requiring a colonial world and ecological doom), to a substance that is therapeutically effective (a naturalist ontology). Therefore, it is not enough to heed some “cultural” factors. For serious medical studies, research designs have to be separated from Indigenous concepts, and, if possible, from ideologically biased recreational (in the widest sense) applications of ayahuasca. This is difficult indeed, given that many authors are themselves involved in some form of ayahuasca ritual circles, churches, or freelance use.

Finally, the implicit coloniality in virtually all forms of ayahuasca use should largely be recognized, and strategies have to be developed to find a way of fair use of ayahuasca in an anti-colonial sense. Those regions where ayahuasca originated

and where most ayahuasca centers are located are among those hardest hit by COVID-19 death tolls. How can this be?

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

BB was the sole author and responsible for all the content and manuscript redaction.

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Psychedelic Experiences During the Early COVID-19 Pandemic: Findings From an International Online Survey

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Introduction: The current corona virus disease (COVID-19) pandemic has caused a serious global health crisis that has affected large parts of the public and private life worldwide, including the use of psychoactive substances. In this study, we investigated the effect of the COVID-19 pandemic on the use of serotonergic psychedelics, i.e., the settings in which people use psychedelics, the motives of usage, and the subjective quality of psychedelic experiences.

Methods: The study was part of an international, cross-sectional, internet-based survey ($N = 5,049$) available in five languages (English, German, Spanish, Italian, and Korean) carried out during the early phase of the pandemic from April to August 2020. Participants were asked to retrospectively rate settings and motives of psychedelic substance use before the pandemic and in the last 4 weeks during the pandemic, as well as changes in psychedelic experiences.

Results: Of $n = 1,375$ participants that reported the use psychedelics in 2019 or 2020, $n = 642$ (46.6%) also took psychedelics during the pandemic. During the pandemic, participants used psychedelics significantly less often in settings that were outside their home. Top motives to use psychedelics were comparable before and during the pandemic, but participants consumed less out of curiosity, to celebrate, or because friends took it, and more out of boredom. An increase in positively connoted, often pro-social experiences was observed. Two thirds of participants who used psychedelics during the pandemic claimed that psychedelics had helped them to deal better with the corona pandemic at least slightly.

Discussion: Changes in setting and motives were mostly in line with restrictions caused by control measures to contain the spread of the virus. The unexpected increase in positively connoted experiences possibly reflects a favorable interaction of environmental macro- and individual micro-contexts during the pandemic (e.g., by reducing the use in more uncontrolled recreational settings or by encouraging a strong self-selection of

substance users due to the expectation of “bad trips”). Increased pro-social feelings under psychedelics might reflect a desire for social interactions in times of social distancing and pandemic-related stress and anxiety.

Keywords: corona, pandemic (COVID-19), SARS-CoV-2, drug use, psychedelic, experience, survey, setting

INTRODUCTION

Beginning at the end of 2019 and reaching its first peak in most countries in early 2020, the current corona virus disease (COVID-19) pandemic has caused a serious global health crisis affecting large parts of public and private life worldwide (1). Profound changes in living conditions have resulted not only from the infectious disease caused by the new severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2), but also from the extensive measures implemented to contain the spread of the virus (2). Most countries have introduced measures restricting the freedom of movement, social contacts, and other aspects of public life (3). Those far-reaching changes in daily life have been associated with increased mental health problems, including symptoms of depression, anxiety, stress, and insomnia (4–6).

Many of these pandemic related measures have also affected drug use, drug supply, and drug markets (7). A large international online survey on drug use that was conducted during the early phase of the COVID-19 pandemic revealed that the frequency of drug use, during the pandemic compared to before the pandemic, varied across substances: While the consumption of stimulants more commonly used at parties and in other social contexts, like 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) and cocaine, had declined, the use of tetrahydrocannabinol (THC)-containing cannabis products and prescription benzodiazepines had increased (8). It has been suggested that the latter changes in substance use might reflect a maladaptive coping strategy in the face of challenges imposed by this worldwide public health crisis (9, 10). As drug markets appeared to rapidly adapt, e.g., by shifting from face-to-face to online sales, local drug supply underwent constant changes during the pandemic (7). The impact of the COVID-19 pandemic on drug markets, however, varies greatly across countries, possibly depending on the respective measures implemented to contain the spread of SARS-CoV-2, and the extent to which those measures affect the pre-pandemic routes of production and trafficking (11).

In this context, serotonergic psychedelics represent a substance group for which relatively little is known about how it is affected by the pandemic. This group of psychoactive substances includes substances like lysergic acid diethylamide (LSD), psilocybin, and mescaline, which share psychedelic properties and serotonin (5-HT_{2A}) receptor agonism as mechanism of action (12). The use of serotonergic psychedelics has been controversially discussed over the last decade. While it received considerable positive attention as a potential treatment tool for specific mental disorders, potential risks for mental health associated with psychedelic substance use have also been critically emphasized (13–15). Part of this discrepancy may be resolved by emphasizing the role of extra-pharmacological,

contextual factors that are known to strongly affect the quality of psychedelic experiences (16). Those contextual factors include individual characteristics of the user (“set”) and aspects of the environment in which the experience is taking place (“setting”) (17, 18). The specific characteristics of the terms “set” and “setting” are not uniformly defined but represent broad concepts according to which non-pharmacological context factors can be classified. The substance users’ “set” has been described to include stable individual characteristics like personality traits, as well as transient features of mood, motivation, intentions, or personal preparation for use (19). The term “setting” encompasses all characteristics of the substance users’ “physical, social, and cultural environment” [(19), p. 1]. Unfavorable contextual conditions, i.e., unfavorable set and setting variables, have previously been associated with an increased likelihood of adverse reactions or challenging experiences during psychedelic substance use (13, 20).

While the significance of context has frequently been described, few studies have systematically explored different types of contexts. Most contemporary clinical research trials carefully design the context to increase the likelihood of experiences that are considered as helpful, e.g., through patient selection, detailed preparation of participants, provision of a safe environment, and social support (21). Investigating conditions that might be unfavorable for participants appears, on the other hand, to be highly unethical. While these interventions usually address the immediate environment during substance use (or “micro-context”), it has been emphasized that the context is not only characterized by aspects of the micro-context but also by “the wider social, cultural, and economic milieu” in which the substance use is embedded (“macro-context”) [(22), p. 5]. Given the temporal stability of social, cultural, and economic environments, an exploration of intraindividual changes concerning these factors is hardly feasible. To our knowledge, no study has yet investigated how changes in environmental macro-contexts affect the quality of psychedelic experiences.

In view of the abovementioned restrictions and changes in everyday life and their reported impact on mental health in general, we interpret the COVID-19 pandemic as such a global and profound macro-contextual change. Most groups of psychoactive substances like alcohol, opioids, sedatives and stimulants reliably induce pleasant transient mood states, e.g., feelings of euphoria and/or anxiolysis, that might be associated with maladaptive coping mechanisms and increased addiction potential in the face of the pandemic (9, 23). In contrast, psychedelics were expected to be less attractive as coping tools during a global public health crisis. Thus, we aimed to explore the effect of the COVID-19 pandemic on different aspects of (serotonergic) psychedelic use. Using an international,

cross-sectional, internet-based survey during the early COVID-19 pandemic, we examined the effects of the pandemic on (1) the setting in which participants would use psychedelics, (2) the motives to use psychedelics, and (3) the quality of psychedelic experiences. Due to the sensitivity of psychedelic experiences to extra-pharmacological, contextual factors, it was expected that an increase of aversive environmental conditions during the COVID-19 pandemic would be associated with an increase in unpleasant and challenging psychedelic experiences.

METHODS

Procedure

Study data were collected as part of the larger, anonymous, internet-based “Corona Drug Survey.” This cross-sectional survey investigated how psychoactive substance use was affected by the COVID-19 pandemic. The survey was online between April 30, 2020 and August 4, 2020 and available in five languages (English, German, Spanish, Italian, Korean). The study was approved by the Ethics Committee of the Charité—Universitätsmedizin Berlin, Germany (EA1/109/20).

Inclusion and Exclusion Criteria

Eligible participants had to be at least 18 years old, fluent in one of the five languages available, and had to have used at least one of the following substances in 2019 or 2020: alcohol, nicotine, cannabis, benzodiazepines, cocaine, amphetamine, ecstasy, psychedelics, dissociatives, opioids, gamma-hydroxybutyric acid (GHB)/gamma-butyrolactone (GBL), or new psychoactive substances (NPS). The present analysis included data of participants that reported to have taken serotonergic psychedelics (5-HT_{2A} receptor agonists). This section included the following substances: lysergic acid diethylamide (LSD), psilocybin, ayahuasca, N,N-dimethyltryptamine (DMT), 5-methoxy-DMT (5-MeO-DMT), mescaline, 2,5-dimethoxy-4-bromophenethylamine (2C-B), new psychedelics [e.g., 1-propionyl-LSD (1P-LSD)], or other (serotonergic) psychedelics. Data on other substances sometimes referred to as psychedelics [e.g., ketamine or 3,4-methylenedioxymethamphetamine (MDMA)], as well as data of non-psychedelic substances will be published elsewhere.

Recruitment of Participants

Participants were recruited via online postings and advertisements on various Internet websites (e.g., www.reddit.com), e-mail announcements, and articles in online magazines (e.g., “VICE”). Interested participants could inform themselves about the goals of the survey on a project landing page. If they wanted to start the survey, participants were redirected to the survey that was hosted on the secure online platform “SoSci Survey,” a German survey tool (www.soscsurvey.com) (24). Participants then filled out the questionnaire described below. If participants omitted questions of the survey, they were asked to answer the missing questions at the end of each page. However, participants could nevertheless choose to skip the missing items, which resulted in varying sample sizes across the items.

Design of Online Survey

Demographics

Participants were asked for their age, gender, country of origin, level of education, work situation, housing situation (household size and number of children living in the same household), and frequency of psychedelic and other drug use.

Effects of the COVID-19 Pandemic on the Participants' Personal Lives

The survey included questions about how the COVID-19 pandemic affected the participants' personal lives. This section included questions about lifestyle restrictions associated with the pandemic, personal experiences of quarantine, changes in the work situation, changes in price and quality of psychedelic drugs, as well as the personal evaluation of the current situation (e.g., worries and concerns, as well as confidence to be able to cope with the situation). Furthermore, participants were asked about positive changes (e.g., new hobbies, more free time) associated with the pandemic using a multiple-choice list of options. Increase in psychopathological symptoms during the pandemic was measured with a modified version of the 9-item short version of the symptom check list (SCL-9) (25). Respondents were asked to directly indicate the change in severity of each symptom on a five-point Likert scale from “much less” to “much more.” Please note that not all versions represent published translations but were translated from German by our translators.

Setting and Motives to Use Psychedelics

Participants were asked how the dosage of psychedelics changed in the last 4 weeks compared to before the COVID-19 pandemic on a five-point Likert scale from “much lower” to “much higher.” For both periods separately [before the pandemic/ in the last 4 weeks (during the COVID-19 pandemic)] participants were asked to indicate the settings in which they had consumed, and their motives to consume using pre-set multiple-choice lists (see **Figures 2, 3**).

Quality of Psychedelic Experiences

If participants reported to have taken psychedelics in the last 4 weeks (during the COVID-19 pandemic), they were presented with a list of 14 common phenomenological aspects of psychedelic experiences. They were asked to indicate on a five-point Likert scale ranging from “much less” to “much more” what kind of experiences they had in the last 4 weeks compared to before the COVID-19 pandemic (see **Figure 4**). A complete overview of items and questions from the survey is available in the supplement of this article.

Analyses

Data quality was assessed and participants that showed indicators of poor data quality were excluded before data analysis: Data sets were excluded if participants did not answer at least one question regarding their experiences with psychedelics. Furthermore, data were excluded if participants choose mutually exclusive response options (e.g., indicating that they took psychedelics for the first time during the COVID-19 pandemic but simultaneously reporting substance use before the pandemic). Lastly, data sets

TABLE 1 | Sample description.

	Before the pandemic		In the last 4 weeks (during pandemic)				P ^a
	User		User		Non-user		
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	
Sample size	1,332	(96.9) ^b	641	(46.6) ^b	734	(53.4) ^b	
Age in years (range)	26.6	(18-67)	26.6	(18-62)	26.4	(18-67)	0.574
Gender							0.417
Female	471	(35.4)	220	(34.3)	274	(37.3)	
Male	811	(60.9)	392	(61.2)	437	(59.5)	
Non-binary	33	(2.5)	20	(3.1)	15	(2.0)	
Education (at time of survey)							0.586
University degree	612	(46.0)	297	(46.3)	334	(41.9)	
Secondary school degree	561	(42.1)	273	(42.6)	308	(45.6)	
Vocational training	111	(8.3)	54	(8.4)	59	(8.0)	
No degree	48	(3.6)	17	(2.7)	33	(4.5)	
Work situation (before COVID-19 pandemic)							0.050
Employed	531	(39.8)	276	(43.1)	272	(37.1)	
Freelancer/Self-employed	271	(20.4)	126	(19.7)	150	(20.4)	
Temporary employment	83	(6.2)	34	(5.3)	50	(6.8)	
Seeking work	168	(12.6)	67	(10.5)	105	(14.3)	
Unpaid domestic work/ Parental leave	20	(1.5)	13	(2.0)	9	(1.3)	
Student employment	231	(17.3)	116	(18.1)	129	(17.6)	
Retired	15	(1.1)	5	(0.8)	10	(1.4)	
Household size							0.381
No other person	179	(13.4)	97	(15.1)	91	(12.4)	
1 other person	226	(17.0)	120	(18.7)	116	(15.8)	
≥2 other persons	927	(69.6)	424	(66.2)	527	(71.8)	
Children living in household							0.100
None	1,060	(79.6)	501	(78.2)	598	(81.5)	
1 child	147	(11.0)	70	(10.9)	78	(10.6)	
≥2 children	123	(9.3)	69	(10.8)	57	(7.8)	
Psychedelic substance use							
LSD	1,147	(86.1)	445	(69.4)			
Psilocybin	739	(55.5)	205	(32.0)			
2C-B	324	(24.3)	85	(13.3)			
DMT	307	(23.0)	76	(11.9)			
New Psychedelics	248	(18.6)	66	(10.3)			
Mescaline	156	(11.5)	32	(5.0)			
Ayahuasca	117	(8.8)	21	(3.3)			
5-MeO-DMT	63	(4.7)	13	(2.0)			
Other	24	(1.8)	6	(0.9)			
Other substances used in 2019 or 2020							0.276
Alcohol	1,245	(93.5)	594	(92.7)	691	(94.1)	
Cannabis	1,244	(93.4)	592	(92.4)	691	(94.1)	
Nicotine	958	(71.9)	445	(69.4)	535	(72.9)	
MDMA	798	(59.9)	386	(60.2)	427	(58.2)	
Cocaine	727	(54.6)	334	(52.1)	410	(55.9)	
Amphetamines/ Methamphetamines	513	(38.5)	255	(39.8)	273	(37.2)	
Dissociatives	484	(36.3)	254	(39.6)	244	(33.2)	
Benzodiazepines	332	(24.9)	172	(26.8)	167	(22.8)	
Opioids	164	(12.3)	87	(13.6)	81	(11.0)	
New Psychoactive substances	160	(12.0)	86	(13.4)	77	(10.5)	
GHB/GBL	101	(7.6)	47	(7.3)	58	(7.9)	

User/Non-User refers to use of psychedelics in the specified time periods.

Unless otherwise stated, percentages refer to the respective sub-sample.

^aRefers to comparison between users and non-users, ^bpercentages from total sample size of *n* = 1,375.

TABLE 2 | Frequencies of psychedelic substance use.

Before the pandemic (per year)			In the last 4 weeks (during pandemic)		
	<i>n</i>	(%)		<i>n</i>	(%)
No use ^a	43	(3.1)	No use	734	(53.4)
1-4 days	678	(49.3)	1 day	291	(21.2)
5-14 days	293	(21.3)	2-4 days	239	(17.4)
15-24 days	119	(8.7)	5-9 days	61	(4.4)
25-49 days	72	(5.2)	10-14 days	21	(1.5)
50 days or more	170	(12.4)	15 days or more	29	(2.1)

Percentages from total sample size of $n = 1,375$ indicate frequency of substance use for the psychedelic substance that participants reported they had used most often.

^a $n = 43$ participants reported first time use of psychedelics during the last 4 weeks.

were excluded if their relative speed index was above the recommended cut-off of 2.0 (26).

A detailed sample description was performed to verify macro-contextual changes (i.e., changes in the social, cultural, and economic milieu) associated with the COVID-19 pandemic during the last 4 weeks.

Changes in the micro-context (i.e., setting and motives) before and in the last 4 weeks (during the COVID-19 pandemic) were analyzed using McNemar's test for paired samples.

In participants that reported psychedelic use in the last 4 weeks (during the COVID-19 pandemic), changes in the quality of psychedelic experiences were analyzed using single-sample *t*-tests and changes were correlated with reported pandemic-related restrictions, concerns, and psychopathology using Spearman's rank correlation coefficient. Statistical significance was set to $p < 0.05$, Bonferroni-corrected for multiple comparisons.

Lastly, it was explored whether participants that had taken psychedelics during the pandemic differed from participants that had not taken psychedelics during the pandemic but before the pandemic. Based on data level, group comparisons were performed using *t*-tests, Mann-Whitney *U*-tests, or chi-squared tests. As these analyses were exploratory, no Bonferroni-correction was applied.

All statistical analyses were performed using PASW Statistics 18 (27).

RESULTS

General Sample Description

Of the total number of 5,049 participants of the Corona Drug Survey, 1,588 (31.5%) reported the use of psychedelic drugs in 2019 or 2020. Of those, 213 datasets (13.4%) were excluded because of quality reasons, yielding a total sample size of $n = 1,375$ participants.

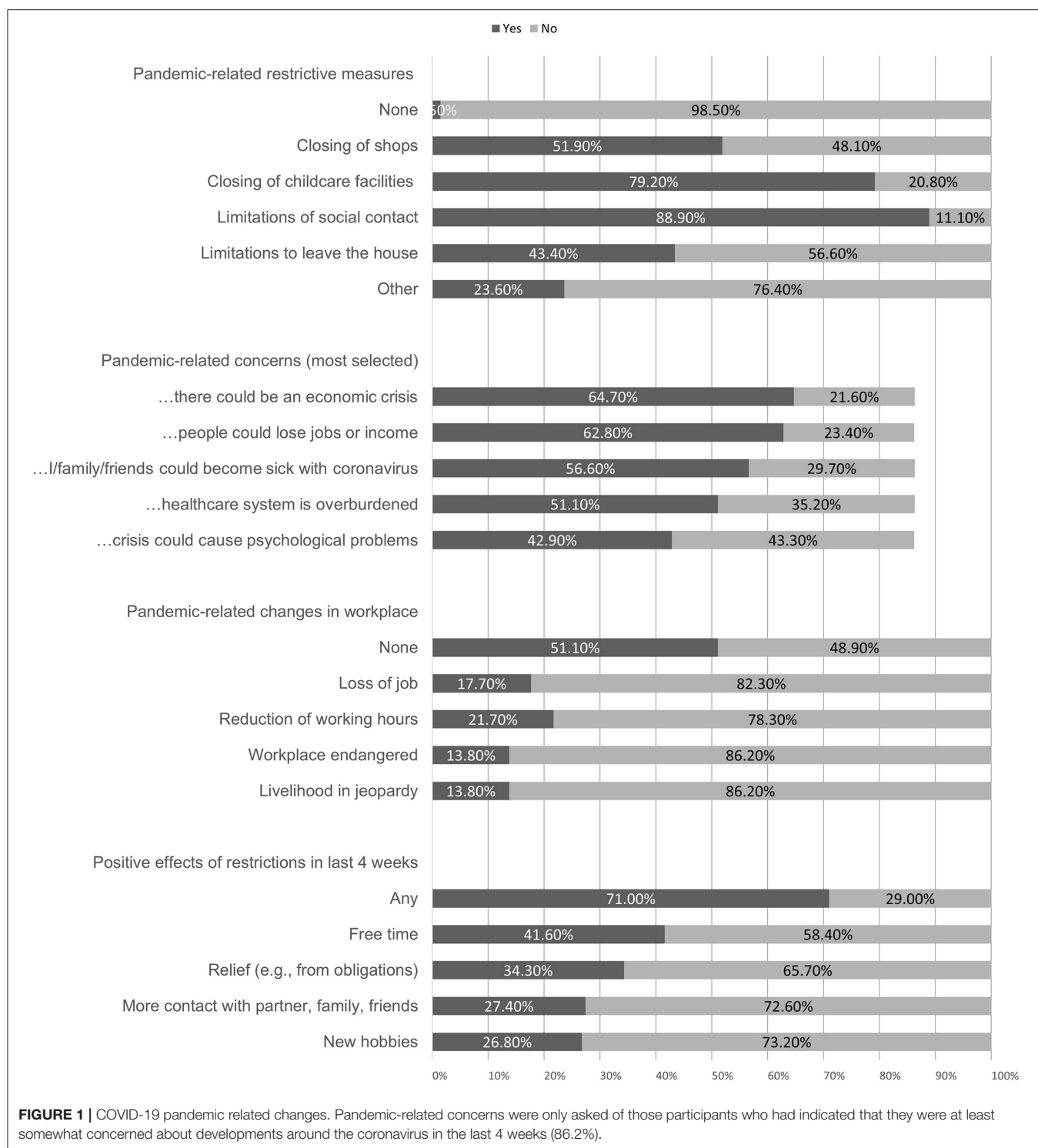
Participants from 53 different countries completed the survey. Most participants originated from Germany (29.0%), Mexico (17.6%), Colombia (12.6%), Argentina (6.3%), USA (5.5%), India (3.7%), UK (3.6%), Bolivia (3.8%), and Italy (2.5%). The questionnaire was completed in the following languages Spanish (43.3%), English (29.5%), German (24.4%), and Italian (2.8%). A detailed sample description is provided in **Table 1**.

The majority of participants ($n = 1,332$; 96.9%) reported that they had used psychedelics before the COVID-19 pandemic, 641 participants (46.6%) reported that they had taken psychedelics in the last 4 weeks (during the pandemic), 43 participants (3.1%) reported that they had used psychedelics for the first time since the beginning of the COVID-19 pandemic. The three psychedelic substances most used before the pandemic were LSD, psilocybin, and 2C-B. Most of the participants reported that they also consumed other substances in 2019 or 2020 (see **Table 1**). Frequencies of psychedelic substance use are presented in **Table 2**. For $n = 1,332$ participants that had used psychedelics already before the pandemic, median frequency of monthly use for the participants' most commonly used psychedelic changed from 0.30 times per 4 weeks before the pandemic (estimated from yearly median 3.95) to 0.91 times in the last 4 weeks during the pandemic.

Effects of the COVID-19 Pandemic on the Participants' Personal Lives (Macro-Contextual Changes)

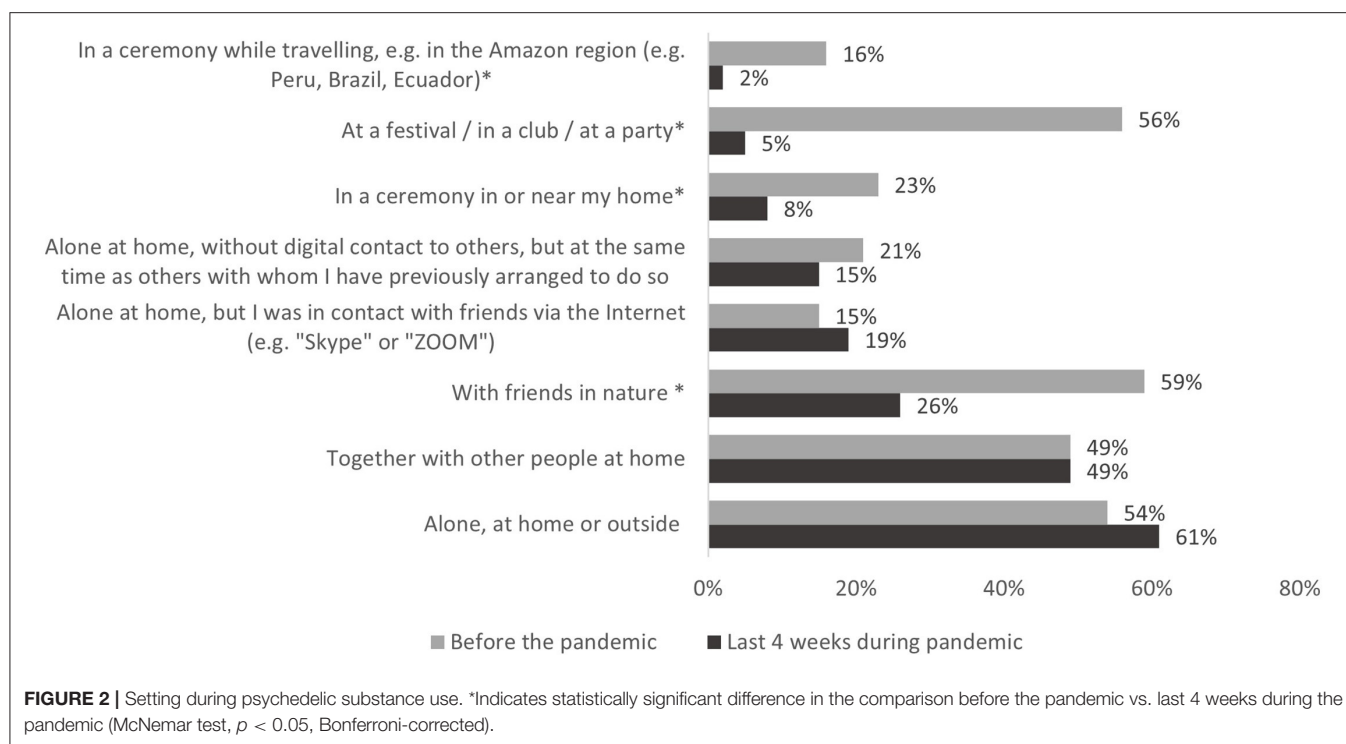
Almost all participants ($n = 1,354$; 98.5%) stated that they had faced some form of restrictive measures in their surroundings due to the pandemic. Most participants (67.0%) reported to adhere to these measures rather well or very well. Only few people reported to adhere to the measures not at all (1.5%) or not very well (5.5%). A little more than half of the participants (57.4%) indicated that they had been in quarantine at least temporarily during the last 4 weeks; 16.2% had experienced cold symptoms themselves during the last 4 weeks; 3.9% had already been tested for COVID-19, and 0.2% had received a positive test result. **Figure 1** gives an overview of pandemic-related changes reported by the subjects.

Most participants (65.1%) felt that they had restricted their lifestyle in the last 4 weeks compared to before the pandemic significantly; 86.6% left their house less frequently; 71.8% felt at least partially socially isolated. Most participants (86.2%) were at least somewhat concerned about the COVID-19 pandemic, 8.1% were very significantly concerned. Most common concerns are presented in **Figure 1**. Half of the participants (54.8%) were a little or very confident that



they would be able to cope with the current crisis by themselves, 18.6% were not or barely confident they could cope with it. Participants reported a slight increase in psychopathological symptoms as measured with the SCL-9 (mean of 3.35 on a scale from 1 to 5 from “much less” to “much more”).

A little more than half of the participants (56.7%) reported that the price for psychedelics was unchanged, 2.3% reported it was lower, 27.7% reported it was higher. Two third of the participants (68.1%) reported that the quality for psychedelics was unchanged, 12.8% reported it was lower, 5.3% reported it was higher.



Settings and Motives to Use Psychedelics (Micro-Contextual Changes)

A total number of 641 participants (46.6%) reported psychedelic substance use during the pandemic. Most of them (93.3%) stated that they also used psychedelics before the pandemic. There was no change in the top three substances used before/during the pandemic: Most of the participants reported experiences with LSD, followed by psilocybin, and 2-CB (see Table 1). Half of the participants (51.3%) reported no change of their dosage, 20.6% reported it was lower, 20.5% reported a higher dosage.

Settings

Figure 2 displays the settings in which participants reported use of psychedelics before/in the last 4 weeks (during the COVID-19 pandemic). During the last 4 weeks of the pandemic, most participants reported having taken psychedelics (1) alone, at home or outside or (2) together with other people at home. There was a significant decline in all settings that were outside the participants' home (see Figure 2). This included ceremonies and parties but also the use of psychedelics with friends in nature, which had been the most frequently reported setting before the pandemic.

Motives to Use Psychedelics

Figure 3 displays the reasons why participants reported having used psychedelics before/in the last 4 weeks (during the COVID-19 pandemic). The top three reasons why participants chose to use psychedelic substances in the last 4 weeks (during the pandemic) were (1) pleasure (2) self-awareness (3) spiritual or personal development. Those reasons were largely identical

with the top three reasons before the pandemic, except that during the COVID-19 pandemic participants consumed considerably less often out of curiosity. Furthermore, participants less often reported consuming because friends took it or to celebrate and more often out of boredom compared to before the pandemic.

Quality of Psychedelic Experiences

Figure 4 displays 14 common phenomenological aspects of psychedelic experiences reported by participants comparing their experiences before the pandemic vs. in the last 4 weeks (during the COVID-19 pandemic). Approximately one third of the participants did not report changes in their experiences. Among the other participants, both increases and decreases of certain experiences were reported. A significant increase during compared to before the pandemic was observed in the following areas: feelings of love and compassion for myself, $t_{(474)} = 12.23$, $p < 0.001$; feelings of love and compassion for others, $t_{(477)} = 12.08$, $p < 0.001$; deep insights about the world, $t_{(472)} = 11.24$, $p < 0.001$; feelings of connectedness with nature, $t_{(479)} = 9.09$, $p < 0.001$; feelings of solidarity with people around me, $t_{(482)} = 8.08$, $p < 0.001$; ego dissolution, $t_{(415)} = 5.80$, $p < 0.001$; pleasant feelings in the days after ingestion ("Afterglow"), $t_{(460)} = 4.84$, $p < 0.001$; spiritual experiences, $t_{(452)} = 4.62$, $p < 0.001$; visual effects, $t_{(485)} = 3.77$, $p < 0.001$. A significant decrease was observed in near-death experiences, $t_{(346)} = -3.64$, $p < 0.001$.

No significant changes (after Bonferroni correction) were observed in the following areas: feelings of anxiety, $t_{(438)} = -2.72$, $p = 0.007$; feelings of deep despair, $t_{(380)} = -2.88$, $p =$

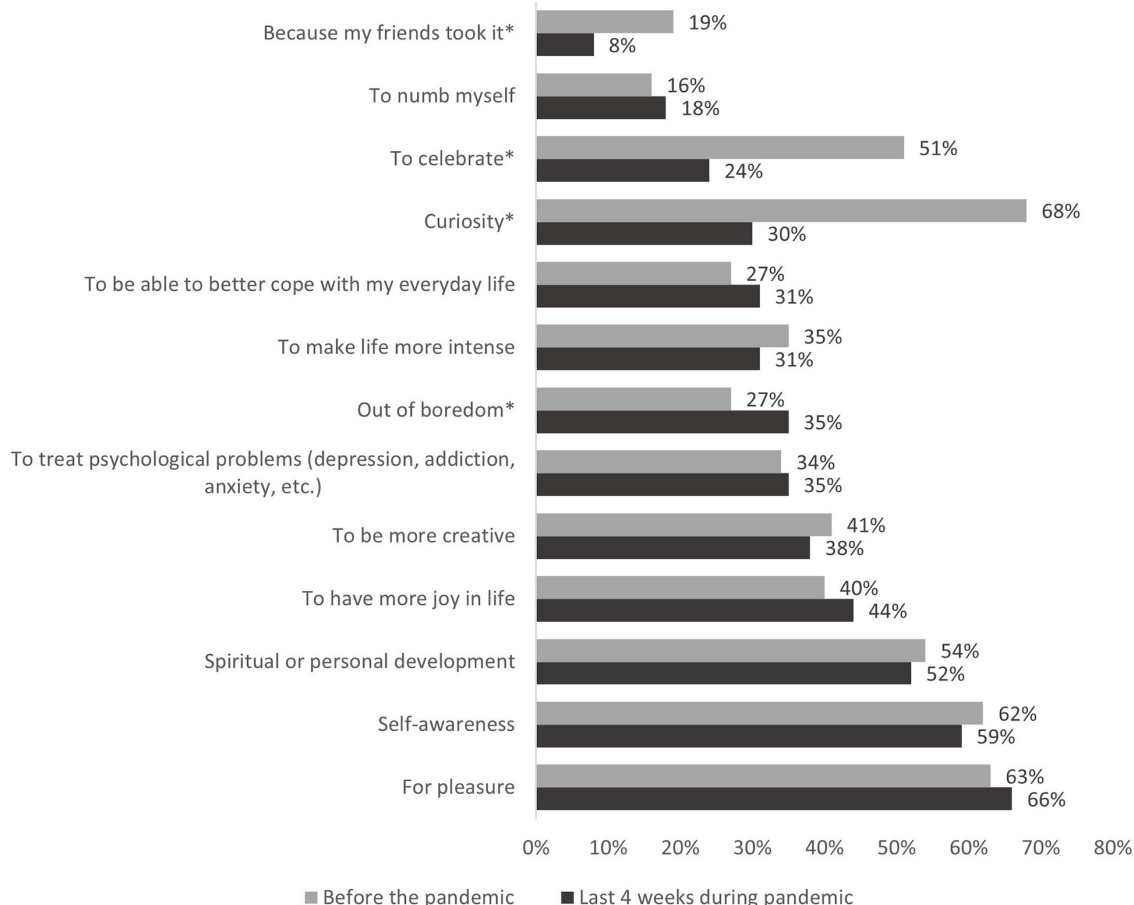


FIGURE 3 | Motives to use psychedelic substances. *Indicates statistically significant difference in the comparison before the pandemic vs. last 4 weeks during the pandemic (McNemar test, $p < 0.05$, Bonferroni-corrected).

0.004; experiences about the end of the world, $t_{(358)} = 1.59$, $p = 0.113$; encounters with entities (God, goddess, demons, machine elves, spirits of the dead, etc.), $t_{(342)} = 0.12$, $p = 0.908$.

There was a positive correlation between increased psychopathological symptoms as measured with items of the SCL-9 and feelings of anxiety, $r_s = 0.26$, $p < 0.001$, and deep despair, $r_s = 0.22$, $p < 0.001$, during psychedelic experiences. Correlations between changes in the quality of psychedelic experiences and restrictions, concerns, or changes in the dosage related to the pandemic situation were very weak and negligible (all $r_s < 0.2$).

We furthermore explored whether positive changes in the quality of psychedelic experiences were associated with positive effects of restrictions reported by the participant (as described in **Figure 1**). Participants that reported that the initial restrictions had any positive effect for them showed a significantly greater change in the quality of psychedelic experiences (in the direction described above) than participants that did not report any positive effect of restrictions. This was true for all abovementioned effects except for feelings of connectedness

with nature, ego dissolution, visual effects, and near death-experiences. Nevertheless, albeit smaller, the effects in the three categories feelings of love and compassion for myself, feelings of love and compassion for others, and deep insights about the world were still significant in the group of participants that did not report positive effects of restrictions.

Regarding the assessment of the usefulness of psychedelics in dealing with different aspects of the pandemic, the following data were observed: 26.8% of participants that used psychedelics in the last 4 weeks during the pandemic did not agree that psychedelics would help them to deal better with the corona crisis, 41.0% agreed slightly or moderately, 25.9% agreed very much or absolutely. Half of the participants (49.6%) did not think that psychedelics would help them to make sense of the corona crisis, 29.8% agreed slightly or moderately, 14.5% agreed very much or absolutely. Furthermore, half of the participants (49.5%) felt that consuming psychedelics did not change their ability to cope with social distancing in the last 4 weeks, while 4.6% reported to cope worse and 39.6% reported to cope better with social distancing by taking psychedelics.

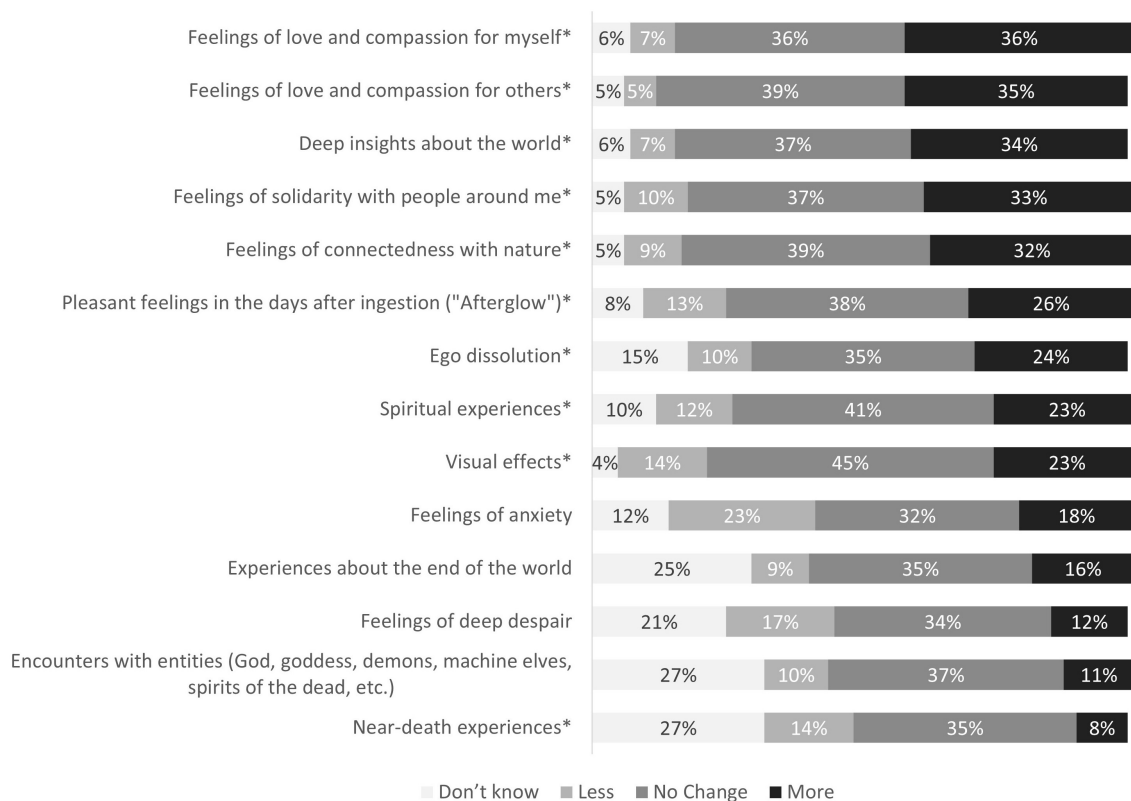


FIGURE 4 | Psychedelic experiences in the last 4 weeks compared to before the COVID-19 pandemic. Numbers indicate percentage of $n = 598$ participants that reported to have used psychedelics during the COVID-19 pandemic and that also had used psychedelics before the pandemic. For each item, percentages not totaling 100% signify missing values. *Indicates statistically significant difference at $p < 0.05$, Bonferroni-corrected.

Comparison of Participants That Used Psychedelics During the Pandemic and Participants That Used Psychedelics Before the Pandemic, but Not During the Pandemic

Participants that used psychedelics in the last 4 weeks during the pandemic (users) and participants that used psychedelics before the pandemic but not in the last 4 weeks (non-users) did not significantly differ in age, gender, education, work situation, household size, or number of children living in the household (see **Table 1**). Also there were no differences in the frequency of quarantine, $\chi^2_{(1)} = 2.77$, $p = 0.096$, cold symptoms, $\chi^2_{(1)} = 0.22$, $p = 0.637$, or whether professional life changed since the beginning of the crisis, $\chi^2_{(5)} = 6.09$, $p = 0.297$. Groups did not differ in whether they felt socially isolated, $U = 227,908$, $p = 0.302$, or concerning how confident they were about coping with the current crisis on their own, $U = 224,133$, $p = 0.130$, or the general frequency with which they reported that the initial restrictions also had positive effects, $\chi^2_{(1)} = 1.39$, $p = 0.238$. Furthermore, there were no differences between the two groups concerning changes of psychopathological symptoms during the pandemic as measured with the SCL-9, $t_{(1339)} = 0.04$, $p = 0.969$.

However, people that did use psychedelics felt significantly less restricted in their lifestyle, $U = 205,314$, $p < 0.001$, less

concerned, $U = 218,818$, $p = 0.014$, and left their home more frequently, $U = 215,044$, $p = 0.002$, than participants that did not use psychedelics during the pandemic. Furthermore, participants that used psychedelics during the pandemic reported a higher frequency of psychedelic substance use before the pandemic when compared to non-users, $U = 185,643$, $p < 0.001$. There was no difference between the groups in the number of other psychoactive substances used in 2019 or 2020, $U = 227,319$, $p = 0.276$.

DISCUSSION

In the present study we explored how the social and cultural macro-contextual changes of the early COVID-19 pandemic affected the setting, motives to use psychedelics, and quality of psychedelic experiences. Our data showed that, during the pandemic, participants used psychedelics significantly less often in settings that were outside their home compared to before the pandemic. Top motives to use psychedelics included pleasure, self-awareness, and spiritual or personal development. Motives were largely comparable before and during the pandemic, but participants consumed less out of curiosity, to celebrate, or because friends took it, and more out of boredom. A significant increase in positively connoted, often pro-social experiences,

e.g., feelings of love, compassion, and connectedness but not in challenging experiences was observed. Two thirds of participants who used psychedelics during the pandemic claimed that psychedelics would have at least slightly helped them to better deal with the corona crisis.

As expected, almost all participants in our sample experienced relevant and serious changes in their socio-cultural environments due to the COVID-19 pandemic. Almost all participants faced some form of measures to contain the spread of the virus, most felt restricted in their lifestyle, isolated, or concerned about the current situation, and reported increased psychopathology. These data are in line with previous reports on the extensive impact of the COVID-19 pandemic in daily life (2) and studies that observed declined mental health outcomes during the pandemic (4–6, 28). Because it was previously suggested that the COVID-19 pandemic could affect the trade business for drugs (29), we also assessed changes in quality and prices of psychedelic substances. In this survey, quality of psychedelics was reported to be largely the same, with few people reporting increases or decreases of quality. One fourth of the subjects reported that the price for psychedelics had increased. Data are in line with observations of the European Monitoring Centre for Drugs and Drug Addiction and Europol that observed that the COVID-19 pandemic temporarily disrupted the drug market resulting in higher prices for some drugs (7).

In accordance with the restrictions of social contacts imposed by COVID-19 measures, most participants reported having used psychedelics during the pandemic alone, at home or outside. There was a steep decline in all settings that were outside the participants' homes and that involved other people (e.g., ceremonies, with friends in nature). Participants also reported that during the pandemic they had taken psychedelics considerably less often at parties and festivals.

The most common motives for using psychedelics during the pandemic were largely identical with the motives for using psychedelics before the pandemic and included pleasure, self-awareness, and spiritual or personal development. Consistent with the pandemic-related changes of the setting, participants reported having consumed less often because friends took it or to celebrate. Furthermore, participants reported having consumed less often out of curiosity and more out of boredom. The increase in substance use out of boredom is a frequent finding during the COVID-19 pandemic and has been described for other substances, like alcohol, cigarettes, and cannabis (30, 31).

To our surprise, and despite macro-contextual changes of a globally present public health-crisis that negatively affected large parts of public and private life, most participants did not report an increase in challenging psychedelic experiences when compared to the time before the pandemic: Feelings of anxiety, feelings of deep despair, and experiences about the end of the world did not significantly differ during compared to before the COVID-19 pandemic. Near death-experiences were even significantly reduced. On the contrary, an increase in feelings of love and compassion for myself, feelings of love and compassion for others, feelings of connectedness with nature, feelings of solidarity with people around me, and deep insights about the world during psychedelic experiences, was reported

by up to one third of participants, along with an increase in ego dissolution, pleasant feelings in the days after ingestion ("afterglow"), spiritual experiences, and visual effects. In the following, we explore some ideas that might explain the findings.

The term psychedelics has long been coined to address the "mind-manifesting" properties of those substances which have been suggested to reveal "hidden" aspects of mind and soul, in order to explore oneself and deepen processes of introspection (32). Accordingly, in times of a global public health crisis, measures of social distancing and profound feelings of disconnectedness, serotonergic psychedelics might have sensitized users to pro-social attitudes and revealed a desire to reconnect and interact with others, while feeling more empathetic toward themselves and others.

Furthermore, it was expected that the pandemic would negatively affect the individual micro-context during substance use. Our data suggest, however, that some macro-contextual aspects of the pandemic may paradoxically have had beneficial effects on individual circumstances of substance use. Although parties and festivals might be described as supportive and positive settings for many users, environmental aspects such as music, lightning, and social interactions might be associated with more unpredictable, overwhelming, and uncontrollable situations. Less controlled settings, in turn, have been identified as a potential risk factor for challenging experiences, as feelings of insecurity or anxiety may quickly escalate (13). Thus, reduced use of psychedelic substances in less controlled settings could have positively modulated the quality of psychedelic experiences. Further evidence for this explanation came from an exploratory *post-hoc* analysis, according to which the observed changes in psychedelic experiences occurred primarily in individuals who reported that the restrictions also brought positive effects (e.g., more free time, or relief from obligations). Thus, more positively connoted changes in psychedelic experiences could possibly be related to the omission of higher-risk consumption sites and/or other beneficial changes in the (micro-) set or setting (e.g., no time pressure, less stress through fewer obligations).

Another reason for heightened positively connoted experiences might be a strong self-selection bias among psychedelic substance users encouraged by the onset of the pandemic. This possibility seems plausible since only half of the participants that had used psychedelic drugs in the year before the pandemic also used psychedelics in the last 4 weeks during the pandemic. As psychedelics are well-known to be context-sensitive (19, 33), certain users might simply have stopped using psychedelics, in order to prevent anticipated "bad trips." Indeed, several differences between users and non-users were observed. For instance, participants that used psychedelics during the pandemic felt less restricted, less concerned, left their home more frequently during the pandemic, and had used psychedelics before the pandemic at a higher frequency than participants that had used psychedelics in the year before the pandemic but not in the last 4 weeks during the pandemic. Thus, the increase in positive experiences in our sample might partially be caused by the abstinence of more restricted and less experienced users that possibly would have been more vulnerable to challenging experiences. Since this survey was cross-sectional, it cannot be

ruled out, however, that the decreased perception of restrictions was not a cause but a consequence of psychedelic substance use.

Intensified experiences could also have been caused by higher doses of psychedelics used during compared to before the pandemic. However, this seems unlikely as not all qualities were equally intensified, and instead a selective pattern of increases and decreases in different experiential qualities was observed. In addition, no significant correlations between the changes in psychedelic experiences and changes in dosages reported by participants were observed.

Taken together, regarding the quality of psychedelic experiences, the observations of the present survey suggest that it may be too simplistic to infer individual micro-contexts from environmental macro-contexts. While the pandemic situation and associated restrictions of lifestyle were present in most participants' lives, it is possible that macro-contextual changes on a global level did not necessarily have a direct negative impact on the individual set and setting during psychedelic substance use. On the contrary, some aspects of the pandemic may paradoxically have positively affected individual contexts of substance use. Therefore, more complex interactions between macro- and micro-contexts must be considered. To our knowledge, there is not yet any model available that describes how different contextual levels interact in their impact on psychedelic experiences, which would be beneficial in predicting individual psychedelic experiences more accurately. The importance of integrating larger-scale environmental aspects in models that predict psychedelic experiences was also suggested in a framework presented by Eisner. She suggested that the concept of "set and setting" should be extended to include another feature called "matrix" and should reflect "the environment surrounding the subject before and after the session, and the larger environment to which the subject returns" [(34), p. 214]. A helpful basis to conceptualize different contextual systems in future research may be derived from existing frameworks, such as the bioecological system theory (35), which emphasizes not only different contextual levels but also provides a conceptualization of possible interactions between these levels.

More than half of the participants that used psychedelics in the last 4 weeks during the pandemic (66.9%) at least slightly agreed that psychedelics would help them to better deal with the corona crisis. This estimate was much higher than for many other substances of the parent-survey, e.g., alcohol (33.9%) and "party drugs" (i.e., amphetamine, methamphetamine, MDMA, GHB/GBL, ketamine and dextromethorphan) (16.4–35.6 %), and slightly below the rating of cannabis (74.4%) (unpublished data). Importantly, these data reflect a subjective evaluation of benefits by the participants. Even though many users considered psychedelics as helpful to deal with the pandemic, no conclusions can be drawn on whether this coping was functional (e.g., supporting a healthy adaption to the pandemic situation in everyday life by promoting problem-focused coping strategies) or dysfunctional (e.g., supporting denial and behavioral or mental disengagement). Traditionally, substance-related coping strategies are often regarded as dysfunctional. However, it has previously been argued that psychedelics could serve as "agents to enhance the perception of meaning" [(36), p. 1], and this idea has

especially been emphasized with regard to psychedelic-assisted therapy for the treatment of existential anxiety and depression in patients suffering from life-threatening illness [(37, 38), for a review see (39)]. In line with this, 44.3% of the participants agreed that psychedelics helped them at least slightly to make sense of the corona crisis. However, most data on beneficial effects of psychedelics originate from highly controlled clinical trials and cannot necessarily be generalized to recreational settings. Two recent papers investigated associations between lifetime psychedelic use and mental health outcomes during the COVID-19 pandemic in anonymous online surveys during the early COVID-19 pandemic (40, 41). Cavanna et al. (40) assessed lifetime use of psychedelics and other psychoactive drugs, as well as measures of personality, affect, well-being, and resilience in participants from Argentina. No associations between lifetime use of psychedelics and impaired mental health were observed. Instead, certain psychedelics were linked to indicators of improved mental health (e.g., higher score of positive affect). Révész et al. (41) assessed associations between lifetime use of psychedelics and psychological distress, peritraumatic stress, social support, and psychopathological symptoms in participants from different countries (mainly Spain, Brazil, and USA). Interestingly, they observed that psychedelic substance users reported less psychological distress during the pandemic than non-users and that effects were more pronounced for regular compared to occasional users. However, because of the correlational design of both studies, no conclusion on causality can be drawn on whether psychedelics serve as a protective factor or whether psychedelics are simply used by more resilient people. Therefore, it cannot be concluded from the current data that the use of psychedelics during the crisis would have a beneficial effect on mental health. Even if most psychedelics exhibit low toxicity and little addictive potential, the uncontrolled use of psychedelics might contribute to the occurrence of mental health problems (13). Findings in this paper should therefore by no means encourage psychedelic substance use. Although many participants reported an increase in positively connoted psychedelic experiences, around 10–20% of the participants reported more challenging or less positive psychedelic experiences during the pandemic. The increase in anxiety and despair during the experience was associated with a general increase in psychopathological symptoms during the pandemic, but not with the level of restrictions reported. This could indicate that the internal processing of changes associated with the pandemic is more relevant for shaping psychedelic experiences than the extent of the objective restrictions. Since this survey was cross-sectional, it cannot be ruled out, however, that increased psychopathological symptoms were not a cause of challenging experiences, but that challenging experiences negatively affected mental well-being of participants, leading to increased levels of psychopathology.

Another aspect of the survey concerned the frequency of substance use. We reported that the median frequency of substance use for the psychedelic substance that participants reported to have used most often was with 0.94 times during the last 4 weeks higher than the estimated frequency of 0.30 times per 4 weeks before the pandemic. However, those numbers should

be interpreted with great caution. The monthly psychedelic use before the pandemic was estimated based on the pre-pandemic median annual consumption. However, psychedelics differ from other substances in that the frequency of use is often irregular and less than once per month and it cannot be assumed that consumption is evenly distributed throughout the year. The comparison of a single month with an annual average can therefore easily be distorted. In order to validly assess whether the COVID-19 pandemic is associated with changes in the frequency of psychedelic use, longer observation periods will be needed.

Limitations

The study has several limitations. Recruitment for anonymous online surveys is always prone to a biased sample selection that is not fully representative of the general population investigated, in this case, users of serotonergic psychedelics. Our sample consisted of relatively young, highly-educated participants that reported many experiences with other psychoactive substances. Results may not be generalizable to other groups of users.

As mentioned above, data collection was cross-sectional. The description of associations between pandemic-related measures, as well as changes in psychedelic experiences is therefore correlational and no conclusion on causality is possible.

Furthermore, pandemic-related restrictions and changes in psychedelic experiences were assessed using pre-set multiple-choice categories. It is possible that these categories did not completely cover all individual experiences perceived as personally significant by the respondent.

The survey period of the Corona Drug Survey coincided in many countries with the beginning or peak of the first pandemic wave, in which public knowledge of the virus as well as its consequences were still very limited. It is possible that results of this early phase cannot be generalized to later stages of the pandemic.

CONCLUSION

We observed that the early phase of the COVID-19 pandemic was associated with changes in the use of serotonergic psychedelics,

including the settings in which people use psychedelics, the motives of usage, and the subjective quality of psychedelic experiences. Surprisingly, those changes were not necessarily adverse in nature, with up to one third of participants reporting an increase in positively connoted psychedelic experiences, including increased prosocial feelings of love, solidarity, and connectedness. Two thirds of participants who used psychedelics during the pandemic claimed that psychedelics would have at least slightly helped them to better deal with the corona crisis. Possible explanations include an interaction of environmental macro- and individual micro-contexts during the pandemic which paradoxically may have positively affected the quality of psychedelic experiences (e.g., by reducing the use in more uncontrolled recreational settings or by encouraging a strong self-selection of substance users due to the expectation of “bad trips”). Increased pro-social feelings under psychedelics might reflect a desire for social interactions in times of social distancing and pandemic-related stress and anxiety.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of the Charité—Universitätsmedizin Berlin.

AUTHOR CONTRIBUTIONS

TM, IM, CM, SG, and RE contributed to conception and design of the study. SR and RM set up the online survey and website. DM, RG, AR, DJ, and MS revised the different language versions of the survey generated by machine translation. RE performed the statistical analysis and wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Couple Therapy With MDMA—Proposed Pathways of Action

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MDMA's first identified potential as a therapeutic catalyst was for couple therapy. Early work in the 1970s and 1980s explored its potential amongst seasoned psychotherapists and their clients. With the completion of the first pilot trial of MDMA-assisted psychotherapy with couples for PTSD, and as the possibility of conducting MDMA-assisted psychotherapy trials expands due to new regulatory frameworks, we have an opportunity to explore and investigate how and why MDMA-assisted couples therapy works. This theoretical paper will explore the neurobiological and neurochemical effects of MDMA in a relational context, the emotional, behavioral, cognitive and somatic effects within a dyadic frame, and how empathy, communication, perception of social connection/support, non-avoidance, openness, attachment/safety, bonding/social intimacy and relationship satisfaction, are all impacted by MDMA, and can be harnessed to facilitate systems-level and interpersonal healing and growth. A model to support MDMA-assisted couple therapy is introduced, and future directions, including implications for intervention development and delivery, will be elucidated.

Keywords: MDMA, couple, therapy, relationship satisfaction, psychedelics

INTRODUCTION

Couple therapy offers the opportunity to heal, grow and change while in relationship. Given that people do not exist in isolation, it creates the context to change in the milieu in which people live their lives. The current paper offers an examination of the reasons for why, and how, a transtheoretical model of MDMA-assisted couple therapy may be an important contribution to couple therapy treatment options. This mini review provides an overview of MDMA, how MDMA functions in an interpersonal context, including its neurochemical, psychological and subjective effects, and how these effects translate into therapeutic outcomes in a transtheoretical approach to MDMA-assisted couple therapy. Potential pathways of action are introduced, and a model to support the enhancement of these treatment outcomes is outlined.

Couple therapy can be utilized for primarily relationally-oriented presenting problems (e.g., relationship distress, difficulties with communication, relationship enhancement, coping with infidelity, abusive interactions, transgressions of trust, life transitions, intimacy, etc.), for relationship enhancement (e.g., to prepare for a life change, such as the birth of a child or marriage), and for focusing on mental health difficulties in one or both partners (e.g., couple treatment for PTSD, depression, OCD, etc.). Findings from dyadic interventions for specific diagnoses demonstrate improvement in both mental health outcomes (OCD, PTSD, depression),

relationship satisfaction and functioning for both partners (Baucom et al., 1998, 2012; Christensen and Heavey, 1999; Benson et al., 2012; Monson et al., 2012; Fischer et al., 2016). Each of these presenting foci can be approached from a variety of therapeutic modalities (e.g., cognitive-behavioral, integrative, emotion-focused, systems-focused, psychodynamic) (e.g., Johnson and Greenberg, 1988; Baucom et al., 1998; Christensen et al., 2020). Common factors among effective couple therapies include objective, shared understanding of the presenting concerns, decreasing emotion-driven dysfunctional behavior, increasing emotion-driven avoided behavior, improving communication and bolstering strengths and gains (Benson et al., 2012). The impact of relational distress has ramifications not only on the relationship, but also each partner's mental health and the functioning of broader family systems (Atkins et al., 2009; Baucom et al., 2012). While couple therapy can reduce relationship distress and increase relationship satisfaction, many couples do not benefit or may not maintain gains over time (Baucom et al., 1998; Christensen et al., 2010). Alternative couple treatment options which can enhance common effective factors are therefore needed.

MDMA

MDMA (3,4-methylenedioxymethamphetamine) is a ring-substituted phenylisopropylamine derivative that increases the release and prevents reuptake of serotonin, norepinephrine, and dopamine (Liechti and Vollenweider, 2001; Farré et al., 2004; Hysek et al., 2011; Bershad et al., 2016). The 5-HT₂ receptor plays a contributing role in its effect (Liechti et al., 2000; van Wel et al., 2011). MDMA elevates serum oxytocin (Wolff et al., 2006; Dumont et al., 2009) and vasopressin (Bershad et al., 2016), as well as cortisol and prolactin (Grob et al., 1996; Mas et al., 1999; Harris et al., 2002). MDMA causes a decrease in cerebral blood flow to the amygdala and hippocampus, an increase in activity in the prefrontal cortex, action in the occipital cortex and insula, and a decrease in functional connectivity between the hippocampus and prefrontal cortex, and an increase between the hippocampus and amygdala (Gamma et al., 2000; Phelps et al., 2001; Carhart-Harris et al., 2014, 2015; Walpole et al., 2017; Feduccia and Mithoefer, 2018).

MDMA-ASSISTED COUPLE THERAPY

MDMA-assisted couple therapy was conducted prior to MDMA being made illegal in the mid-1980s. Greer and Tolbert (1986, 1998) conducted a series of cases of MDMA-assisted psychotherapy, including with couples, that demonstrated improvements in fear of emotional hurt and improved communication and introspection. Reports by Sasha and Ann Shulgin describe MDMA's therapeutic use with couples shortly after it was re-synthesized in the mid-1970s (e.g., Holland, 2001), and that it is an excellent tool for communication and to navigate relational issues. Reports suggest that MDMA had broad use by psychotherapists in non-research settings

(e.g., Passie, 2018). With recent re-initiation of MDMA-assisted therapy research, long term follow-ups of individual MDMA-assisted psychotherapy for posttraumatic stress disorder (PTSD) demonstrate that almost two thirds of participants reported improved relationships with loved ones following treatment (Jerome et al., 2020). One pilot trial has been conducted for MDMA-assisted Cognitive Behavioral Conjoint Therapy (CBCT) for PTSD, wherein both partners participated in the entire protocol, including MDMA-assisted sessions. Findings from the study include improved PTSD scores, relationship satisfaction, posttraumatic growth, and improved social intimacy for the partner with PTSD (Monson et al., 2020; Wagner et al., 2021). These pilot trial results are promising, and suggest the potential for non-diagnostic specific MDMA-assisted couple therapy, given the significant improvements in relationally oriented outcome measures.

MDMA'S PHARMACOLOGICAL EFFECTS AND COUPLES

MDMA's empathogenic qualities have made it a prime candidate as an adjunct to psychotherapy. When considering the couple therapy context, understanding the neurochemical experience related to romantic love illuminates this potentially catalytic combination. The hormones and neurotransmitters most closely associated with the experience of love include oxytocin and vasopressin (linking to attachment and bonding), dopamine and serotonin (causing pleasure and positive mood), and the brain areas most impacted include the amygdala (registering threat, happiness and fear), prefrontal cortex (related to reasoning) and the hippocampus (engagement with thoughts and memories), as well as the caudate nucleus (registering love) and the hypothalamus (registering lust) (e.g., Zeki, 2007; Fisher et al., 2010).

The similarities in these areas of action, and notably the release of oxytocin (which can help facilitate interpersonal trust, attachment, bonding, forming affection) (Kosfeld et al., 2005; Bartz and Hollander, 2006; Domes et al., 2007), notably with its interaction with vasopressin and its context-dependent nature (Carter et al., 2020), and serotonin (increasing positive mood and extraversion, reducing depression and anxiety) (e.g., Hasler et al., 2009; van Wel et al., 2012), demonstrate that similar processes are activated in the neurobiology of love as are with MDMA. Notably, several studies have failed to show a relationship between the social effect of MDMA and oxytocin (e.g., Kuypers et al., 2017), which suggests that the empathogenic effects of MDMA are not unifactorial to the presence of oxytocin. Using the context of an MDMA-assisted psychotherapy session to work with a romantic relationship can therefore allow a potential reactivation or "remembering" of these neurochemical pathways to occur. Additionally, the increase in cortisol and noradrenergic response with MDMA can raise levels of arousal (Mas et al., 1999; Harris et al., 2002; Hysek et al., 2011, 2012a), which may support motivation to engage in therapy and interactions with the partner.

PATHWAYS OF ACTION FOR MDMA-ASSISTED COUPLE THERAPY

Synthesizing the literature on the psychological, subjective and perceived effects of MDMA, the following offers a distillation of pathways in which MDMA may assist couple therapy. Four broad areas of psychological impact (emotion, cognition, behavior, somatic experience) highlight eight cross-therapeutic outcomes for MDMA-assisted couple therapy: (1) empathy, (2) communication, (3) perception of social connection/support, (4) non-avoidance, (5) openness, (6) attachment/safety, (7) bonding/social intimacy, (8) relationship satisfaction (see **Table 1** for synthesis).

Emotions

In experimental contexts of emotion processing, including fMRI, psychophysiological measures and self-report studies, MDMA has been found to facilitate the perception of positive emotional expressions, empathy, and reduce the social pain associated with negative emotional expressions perceived from others and social rejection (Bedi et al., 2009; Hysek et al., 2012b, 2014; Frye et al., 2014). MDMA has been found to improve identification of emotions in others, as well as increase prosocial feelings (Bedi et al., 2010). MDMA has also been found to increase attention to positive emotional cues (Bershad et al., 2019). In therapeutic contexts, MDMA allows for the experiencing of challenging emotions, as well as increased compassion and decreased defensiveness (e.g., Metzner and Adamson, 2001; Stolaroff, 2004; Feduccia and Mithoefer, 2018; Wagner et al., 2019). MDMA has also demonstrated a reduction in anxiety in therapeutic contexts (e.g., Danforth et al., 2018). Evidence demonstrates that MDMA enhances feelings of closeness to others (Borissova et al., 2020), which is particularly useful in couple therapy to allow the individuals to feel connected within the experience, regardless of content being shared. In couple therapy, facilitating the sharing of emotional content leads to improved closeness and satisfaction (e.g., Sanford, 2007; Christensen et al., 2020). MDMA can support this experience. Painful feelings can be seen as useful in the therapeutic process, feelings of love and deep appreciation can emerge, and attenuating the fear response to threat of emotional integrity can help support the full experience of emotion by reducing defensiveness (Metzner and Adamson, 2001; Stolaroff, 2004). MDMA is associated with seeing others as empathetic and caring, beyond the effects of oxytocin release alone (Hysek et al., 2013; Bedi et al., 2014; Kuypers et al., 2014; Wardle and de Wit, 2014). The experience of feeling empathetic toward oneself and others when in an MDMA session allows for an unfettered experience of the emotion and present moment, which outside of this context often gets marred by the presence of old memories, the drive to be right or heard, or distress, pulling the person out of the moment.

Cognitions

The perceived psychological cognitive effects of MDMA include being able to engage with difficult memories, likely due to a reduction in perceived threat and increased interpersonal trust (Kosfeld et al., 2005; Domes et al., 2007), as well as

TABLE 1 | Areas of focus for MDMA-assisted couple therapy outcomes.

Area of focus	How MDMA supports	Proposed therapeutic interventions to facilitate
Empathy	Oxytocin release helps increase interpersonal focus, feelings of interpersonal trust, social affiliation (Kosfeld et al., 2005; Bartz and Hollander, 2006; Domes et al., 2007). MDMA associated with seeing others as empathetic and caring (Hysek et al., 2013; Bedi et al., 2014; Wardle and de Wit, 2014), and increases emotional empathy beyond oxytocin alone (Kuypers et al., 2014)	Centering both peoples' experiences, sharing of feelings
Communication	MDMA associated with greater interpersonal focus in language (Bedi et al., 2014), reduction in reactivity to angry facial expressions and greater reward in happy faces (Bedi et al., 2009)	Present and practice skills of sharing and listening with both negative and positive content
Perception of social connection and support	Reduction in feeling of social pain (Frye et al., 2014), decreased feelings of threat, increased feelings of interpersonal trust (Kosfeld et al., 2005; Domes et al., 2007), increased identification of prosocial feelings (Bedi et al., 2010)	Highlight strength in couples' interactions, remind in integration to reduce likelihood of returning to old patterns after MDMA sessions
Non-avoidance	MDMA assists in fear attenuation, allowing for approach of difficult experiences and memories (Young et al., 2015, 2017; Doss et al., 2018; Feduccia and Mithoefer, 2018; Hake et al., 2019)	Explain why non-avoidance is helpful-while difficult initially, is supportive of growth of relationship to not allow difficulties to expand or root over time
Openness	MDMA can assist in increased openness to experience and decreased neuroticism (Wagner et al., 2017). The ability to engage in interactions may be supported by the release of cortisol, and paired with oxytocin (e.g., Mas et al., 1999; Hysek et al., 2011)	Creating shared intentions, and establishing as a value to bring through the process
Attachment/safety	Decreased feelings of threat, increased feelings of interpersonal trust (Kosfeld et al., 2005; Domes et al., 2007)	Skills to engage in difficult conversations, take breaks and re-engage. Creating a template for future experiences
Bonding/social intimacy	Oxytocin, which MDMA causes to release, supports feelings of social bonding (Bartz and Hollander, 2006). MDMA helps increase cooperation and feelings of trustworthiness (Stewart et al., 2014; Gabay et al., 2019). Increased experience of social intimacy following MDMA-assisted couple therapy (Wagner et al., 2021)	Couple engaging in the whole process together
Relationship satisfaction	Improved relationship satisfaction, decreased distress in MDMA-assisted couple therapy (Monson et al., 2020; Wagner et al., 2021)	Encouraging shared experiences, engagement together in the therapeutic process

having clarity of thought without becoming overwhelmed by the emotions that the thoughts may typically elicit (Wagner et al., 2019). Neuroimaging results demonstrate that negative memories may be perceived as more tolerable following MDMA (Carhart-Harris et al., 2014). Additionally, memories, including those with strong emotional content, can be engaged with differently and fear extinction can occur when engaged in the memory (Young et al., 2015, 2017; Doss et al., 2018; Feduccia and Mithoefer, 2018; Hake et al., 2019). MDMA also increases reported perceptions of trust (Stewart et al., 2014), a salient cognitive process in interpersonal dynamics that can perpetuate significant relational distress. There is evidence that there is a reopening of a critical learning period for social interaction with MDMA in mice, allowing for new learning about social interactions to occur (Nardou et al., 2019). If translatable to humans, this offers an immense opportunity for new learning to occur, which then spans into the next category, behavior.

Behaviors

MDMA has been shown to alter speech, increasing social and sexual words and a willingness to disclose personal information (Baggott et al., 2015), and an increase in interpersonal focus in language (Bedi et al., 2014). MDMA has also been shown to increase cooperation (Gabay et al., 2019). Therapeutically, MDMA can create a reduction in experiential avoidance and engagement in challenging content (emotional and cognitive) without disorientation, including a desire to communicate (Feduccia and Mithoefer, 2018; Wagner et al., 2019). Increased openness to experience, which can facilitate greater engagement and risk-taking in vulnerability in interpersonal relationships, has been shown to increase following MDMA-assisted psychotherapy (Wagner et al., 2017). Reports of increased introspection and improved communication collectively create a behaviorally rich opportunity for relational processing and engagement for the couple (e.g., Metzner and Adamson, 2001; Stolaroff, 2004; Wagner et al., 2019).

Somatic Experiences

The somatic effects of MDMA, specifically linked to psychological processes, can include strong physiological sensations related to past experiences, which are helpful to re-experience in the supportive container of the therapeutic setting (Mithoefer et al., 2014). Somatic effects can be linked to any of the cognitive or emotional content arising, including memories (Wagner et al., 2019). Additionally, soothing or calming somatic effects can occur, which can offer supportive experiences for the couple. Reduced fear response and increased feelings of closeness may help amplify these supportive somatic experiences, and allow for immersion into difficult ones as needed. Results from brain imaging after MDMA demonstrate greater reward from happy facial expressions and less reactivity to angry facial expressions (Bedi et al., 2009), potentially supporting the tolerance of emerging somatic experiences.

A PROPOSED TRANSTHEORETICAL MODEL FOR MDMA-ASSISTED COUPLE THERAPY—THE SET MODEL

The SET Model (Setting, Structure and Safety, Exploration and Experience, Template and Trust) is designed to capture the essential components of MDMA-assisted couple therapy, regardless of theoretical approach and across a range of treatment targets. Principles are derived from effective couple therapy (Benson et al., 2012) and the unique MDMA experience, both from the literature and from the author's experience as an investigator of MDMA-assisted CBCT.

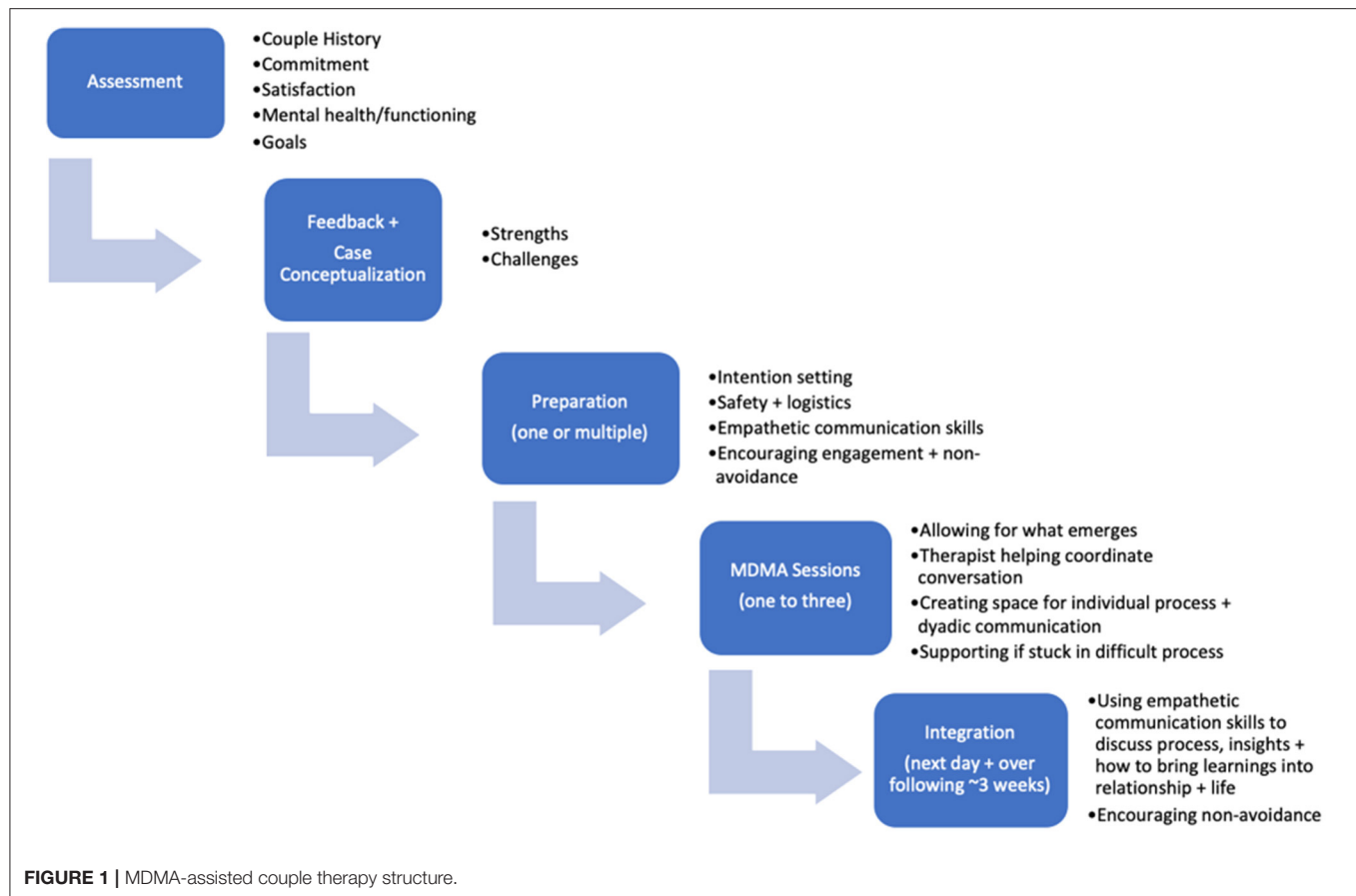
Structure of Therapy

Functionally, it is recommended that practitioners begin with a thorough assessment process to understand the commitment levels and distress of the clients, any co-occurring mental health challenges, the couples' history and to understand their goals for the therapeutic process. Following assessment, feedback and a collaborative case conceptualization with the couple are recommended to understand their particular strengths and challenges. Preparation for the MDMA-assisted sessions would then occur across a series of psychotherapy sessions (ranging from one multi-hour session to several shorter sessions, depending on the needs of the clients). Preparation consists of creating a shared language for the sessions through the learning and practice of empathic communication skills, emphasizing the softening of language to facilitate empathy. Intention setting, and practical preparation for the session should be covered. The MDMA sessions themselves allow for an open experience without agenda, with the therapist(s) serving as facilitator for conversations, and navigating the needs of both individuals to ensure both have the opportunity for deep internal reflection as well as communication together. Integrative sessions allow for processing of the experience in the MDMA sessions, inquiry regarding insights, empathy and shared experiences, and application and exploration of learnings to the couples' stated goals and future. The therapeutic process with MDMA-assisted therapy offers the unique opportunity to create a framework to support an experience that will then be able to serve as a template for future interactions, with MDMA sessions themselves serving as a catalyst. See **Figure 1** for a summary of the therapeutic process.

Principles of Practice

Setting, Structure and Safety

Creating a safe setting (physically and emotionally), as has been well described in psychedelic-assisted therapy literature (e.g., Metzner and Adamson, 2001; Mithoefer et al., 2014), is essential for both people to feel comfortable engaging in deep emotional territory and navigating a non-ordinary state. For couples, this includes discussions of safety related to disagreements (encouraging a process of stopping disagreements before they escalate and returning to conversations when they are more settled), and of no interpersonal violence. This also extends to safety and the structure of approaching the experience together, including the development of shared intentions for the sessions,



and the safety of knowing they will have space to integrate together afterwards. Introducing and practicing communication skills can allow for a shared language and understanding of how to communicate effectively. This structure may allow for a deeper experience in the MDMA session, knowing there is a scaffold to tether to in terms of how to discuss what emerges, which can help mitigate fear, and create safety. Creating the structure that both peoples' experiences are central (that there is no "patient" and that both people are equally participant in the experience) can help mitigate power dynamics and create more opportunity for both people to engage fully.

Exploration and Experience

Fostering an environment of curiosity, openness and non-avoidance (experientially, emotionally and behaviorally to support the relationship and prevent difficulties rooting over time) in preparation before, during the MDMA session, and throughout integration, encourages a full experience of emotions, their expression and communication. Facilitating the process of recapping the insights, shifts, and gains throughout the therapeutic process can help orient the couple to their unfolding experience, and can help solidify their learnings, as there can be a tendency to revert to old patterns in any couple process over time. Encouraging the exploration of difficult conversations and highlighting the shared experience they are having can help

to create the conditions for empathy and bonding, as well as perceptions of social support.

Template and Trust

Through this process, the couple is creating a template for how to communicate effectively, how to debrief together, and how to navigate intense emotional experiences for the future. By establishing a stance of fostering trust and openness to whatever emerges in the therapy process, this can help model the experience for their relationship. Supporting non-avoidance and highlighting strengths in the relationship, as well as their ability to navigate stressors, can help foster trust in themselves and each other.

DISCUSSION

This synthesis of the literature demonstrates the potential usefulness of MDMA as a catalyst to couple therapy, given its neurochemical actions, and emotional, cognitive, behavioral and somatic effects. While preliminary research has been conducted using one model of therapy (CBCT for PTSD) with MDMA (Monson et al., 2020), the SET model proposes a larger, overarching set of principles that can be applied irrespective of therapeutic modality and for different therapeutic targets beyond PTSD. These principles are suggested as common factors

that can enhance and guide the MDMA-assisted couple therapy experience, and future research is needed to test this framework in application.

Additionally, future research can investigate, in both interventional and experimental contexts, the neurochemical and subjective experiences of MDMA in a dyadic context, as the majority of research has been conducted with individuals, not as couples. This synthesis also has implications for treatment development, including the testing of MDMA-assisted couple therapy for the reduction of relationship distress and enhancement of relationship satisfaction. In the recent resurgence of MDMA-assisted therapy research, the majority has been to treat psychiatric disorders, such as PTSD, social anxiety and anxiety related to life-threatening illness (Danforth et al., 2018; Mithoefer et al., 2019; Wolfson et al., 2020). MDMA-assisted couple therapy is a prime opportunity to extend these investigations beyond psychiatric diagnosis, while

targeting outcomes that have broad and important impact on peoples' lives.

Notably, very limited MDMA-assisted couple therapy has been conducted in a research context, and therefore this mini review and proposed model is limited in scope to theorized mechanisms and pathways of action, and is preliminary in nature.

Altogether, this review suggests that the neurobiological and neurochemical effects of MDMA in a relational context, and the emotional, behavioral, cognitive and somatic effects within a dyadic frame guided by the SET model can be harnessed to facilitate meaningful interpersonal healing and growth.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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Psychedelics as Tools for Belief Transmission. Set, Setting, Suggestibility, and Persuasion in the Ritual Use of Hallucinogens

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The use of psychedelics in the collective rituals of numerous indigenous groups suggests that these substances are powerful catalysts of social affiliation, enculturation, and belief transmission. This feature has recently been highlighted as part of the renewed interest in psychedelics in Euro-American societies, and seen as a previously underestimated vector of their therapeutic properties. The property of psychedelics to increase feelings of collective belonging and transmission of specific cultural values or beliefs raise, however, complex ethical questions in the context of the globalization of these substances. In the past decades, this property has been perceived as problematic by anticult movements and public authorities of some European countries, claiming that these substances could be used for “mental manipulation.” Despite the fact that this notion has been widely criticized by the scientific community, alternative perspectives on how psychedelic experience supports enculturation and social affiliation have been yet little explored. Beyond the political issues that underlie it, the re-emergence of the concept of “psychedelic brainwashing” can then be read as the consequence of the fact that the dynamic through which psychedelic experience supports persuasion is still poorly understood. Beyond the unscientific and politically controverted notion of brainwashing, how to think the role of psychedelics in the dynamics of transmission of belief and its ethical stakes? Drawing on data collected in a shamanic center in the Peruvian Amazon, this article addresses this question through an ethnographic case-study. Proposing the state of hypersuggestibility induced by psychedelics as the main factor making the substances powerful tools for belief transmission, I show that it is also paradoxically in its capacity to produce doubt, ambivalence, and reflexivity that psychedelics support enculturation. I argue that, far from the brainwashing model, this dynamic is giving a central place to the agency of the recipient, showing that it is ultimately on the recipient’s efforts to test the object of belief through an experiential verification process that the dynamic of psychedelic enculturation relies on. Finally, I explore the permanence and the conditions of sustainability of the social affiliation emerging from these practices and outline the ethical stakes of these observations.

Keywords: psychedelics, cults and new religious movements, brainwashing, belief, ayahuasca

INTRODUCTION

The use of psychedelics to build or reinforce social connectedness and cohesion has long been observed by anthropologists (Harner, 1973; Furst, 1976; Dobkin de Rios, 1984). Among indigenous groups of the Western Amazon, ayahuasca¹ is for instance mobilized during shamanic initiation or rites of passage to enable participants to have culturally prescribed experiences, such as encounters with culturally postulated supernatural beings (Harner, 1972; Reichel-Dolmatoff, 1972; Kensinger, 1973; Descola, 1996; Délage, 2009). The properties of so-called “hallucinogenic” or “psychedelic” substances² indeed make them strong supports of social affiliation. As they are deeply influenced by cultural background and social interactions, psychedelic experiences are powerful vectors of cultural transmission and consolidation of social groups (Dupuis, 2021).

The use of psychedelics in the initiatic rites of passage (van Gennep, 1960) and the coming-of-age ceremonies of many indigenous groups across the globe³ suggests that these substances are powerful catalysts and facilitators for enculturation and belief transmission. An important function of collective rites lies in their ability to induce a synchronization of affects and behaviors among participants, which has been identified as a powerful catalyst for social affiliation (Hove and Risen, 2009; Reddish et al., 2013; Tarr et al., 2014). Recent study (Kettner et al., 2021) suggests that psychedelics supports the “collective effervescence” (Durkheim, 1912) dynamic generated by rituals, leading to a “fusion of identity” and resulting in a sense of unity within the social group (Swann et al., 2009; Páez et al., 2015) that Victor Turner (1969) called “communitas”⁴. Drawing on cross-cultural data analysis, Grob and Dobkin de Rios (1992) and Dobkin de Rios et al. (2002) noticed that in contrast to Euro-American societies, where drug abuse is an important public health problem, especially among the adolescent population, many indigenous societies use hallucinogens in specific cultural settings – rituals – in order to enculturate youth. These authors suggest that psychedelics are in that context powerful tools in order to inculcate cultural values, beliefs or social norms, and thus to reinforce a sense of cultural identity.

The findings of the comparative ethnographic investigation that I am conducting for about 10 years within various shamanic

centers of Peruvian Amazon (Dupuis, 2016) are congruent with this assumption. My ethnographic observations show indeed that the cultural elements as well as the features of the ritual devices specific to these institutions strongly influence the formal characteristics features of visual and auditory imagery (i.e., “hallucinations,” referred to in this context as “voices” and “visions”) perceived by the participants during psychedelic rituals.

The psychedelic experience is then often experienced by the participants as the concrete and tangible verification of elements of the local cosmological, etiological, or therapeutic knowledge. This knowledge is indeed embodied in the encounters with culturally postulated supernatural entities, occurring in a privileged way through “voices” and “visions.” Analyzing the social learning that underlies the emergence of these culturally prescribed experiences, I have called “socialization of hallucinations” (Dupuis, 2021) the dynamic through which verbal exchanges and social interactions shape the psychedelic experience by directing attention, expectations, and perception.

While observed for a long time by anthropologists, the property of psychedelics to facilitate belief transmission, enculturation and social affiliation has recently been highlighted as part of the renewed interest in psychedelics in Euro-American societies. The ability of these substances to support the emergence of “communitas” has for instance recently been seen as a previously underestimated vector of their therapeutic properties (Kettner et al., 2021). The property of psychedelics to increase feelings of collective belonging needs, however, to be considered carefully, as it raises complex ethical questions in the context of the globalization of these substances (Timmermann et al., 2020).

In the past decades, this property of psychedelics has been perceived as highly problematic by anticult movements and public authorities of some European countries. The emergence of “shamanic tourism” and the success of ritual practices involving the use of hallucinogenic substances have for instance given rise to serious concerns among the French public authorities, who have seen this as a potential source of “cultish driftings.” These concerns were expressed in particular by legal proceedings involving French members of Santo Daime and the “Takiwasi affair,” which led one of the main shamanic centers in the Peruvian Amazon and its French collaborators to be prosecuted by judicial authorities in France and accused of being a “cult group” (Bourgogne, 2011). In the course of this affair, the French public agency responsible for observing and analyzing the phenomenon of so-called “cultish” groups (MIVILUDES)⁵ and some anti-cult associations presented hallucinogens as “powerful drugs” implying “risks of manipulation” (MIVILUDES, 2005). The claim that psychedelics could be used for “mental manipulation,” psychological destabilization, unconscious or not fully consented conversion by cultish groups through so-called

¹The term ayahuasca refers both to a vine (*Banisteriopsis caapi*) and the brew of which it is the main ingredient. This psychotropic and emetic brew is traditionally used in the Western Amazon as part of indigenous and metis shamanic practices and has sparked growing interest among the international public in recent decades as part of the emergence of shamanic tourism and the development of Brazilian religious movements as *Santo Daime* and *União do Vegetal*.

²These substances classically associated with the popular category of “psychedelic” or the medical category of “hallucinogen” produce very similar perceptual and cognitive changes and share a common neurophysiological mode of action, primarily mediated by agonism of serotonin receptors, and the serotonin 2A receptor subtype specifically (Nichols, 2004).

³Among many others, we can mention the examples of the use of iboga in the Bwiti cult in Gabon (Fernandez, 2019), of datura among Chumash of California (Applegate, 1975) and Shangana-Tsonga of Mozambique (Johnston, 1972), of Pituri (*Duboisia hopwoodii*) among Australia Aborigines (Dobkin de Rios and Stachalek, 1999).

⁴Victor Turner (1969) has coined this term to designate an experience of intense togetherness and shared condition that temporarily transcends social distinctions.

⁵MIVILUDES (Mission interministérielle de vigilance et de lutte contre les dérives sectaires – in French – Interministerial Mission of Vigilance and Combat against Sectarian Abuses) is a French government agency created by presidential decree in 2002. It is responsible for observing and analyzing the phenomenon of so-called “cultish” groups, coordinating the governmental response, informing the public of the risks linked to sectarian abuses and facilitating the implementation of actions to assist victims.

“chemical submission” (Pépin and Duffort, 2004) finally led to the prohibition of ayahuasca in France in 2005. By associating psychedelics with the notions of “mental manipulation” and “brainwashing,” this affair has strongly contributed to the social stigmatization of psychedelics and to the legitimization of their prohibition in Europe. Even though the trial was eventually dismissed, this case have indeed had an international impact, influencing public policies in other European countries⁶.

The concept of “brainwashing” was a key element of this case. This notion (also called “mental manipulation,” “mind control” or “coercive persuasion”) was first used by the anticommunist journalist and undercover intelligence agent Hunter (1951) in his book (1951) to describe the techniques through which Chinese Communist Party was supposed to make political opponents and American armed forces prisoners cooperate during the Korean War. In the 1970s, this notion became a popular concept through which was analyzed conversion among emerging religious movements⁷, including those associated with the hippie phenomenon, which were called “cults” by their detractors (Young, 2012). Brainwashing quickly became the central doctrine of American anti-cult movement, which approached emerging religious movements as “cults,” i.e., deviant and dangerous pseudo-religious groups using unethical manipulative techniques to recruit members⁸.

The American psychologist Margaret Thaler Singer was a prominent proponent of the brainwashing theory applied to religious movements and one of the leading theoretician of the anti-cult movement. In numerous mainstream publications (Singer, 1979; Singer and Lalich, 1995/2003), she has defended a theory allegedly inspired by academic research on communist “thought reform” programs (Lifton, 1954, 1961; Schein, 1956). Her conception of brainwashing was adopted from behaviorism (Bitterman, 2006), which was the dominant psychological theory when this concept emerged. In that perspective, brainwashing is thought as a process of intense manipulation based on conditioning techniques considered as able to force people to convert against their wills by altering people’s mental outlook and free will. Even if these conditioning techniques or the underpinnings of their effectiveness have never been precisely described by Singer, this conception has

received an important popular diffusion under the name of “robot theory.” This theory claims that “cultish” brainwashing techniques are able to inhibit the free will in making critical decisions of members, who are then thought of as a kind of automatons devoid of personal autonomy and agency. In that perspective, people actually remains a member of so-called cultish groups against their will, because the group’s control on the member’s mind is total. “Cult” members are thus allegedly not responsible social actors and may be coerced in order to restore their autonomy (Shupe et al., 2004). Despite its lack of scientific support, this approach has played an important role in court situations and has formed the basis of the controversial practice of “deprogramming” used from the 1970s onward by some American anti-cult movements⁹ (Young, 2012).

Since the 1980s, there has been an intense public, scientific and legal debate about the concepts of cult and brainwashing. In opposition to the American anti-cult movement claims, voices raised to point out the unscientific and subjective nature of these concepts and to denounce their use as a rationale for persecuting unpopular new religious movements and for violating the constitutional rights of their members (Wessinger, 2017). After years of debates, an academic consensus has emerged, that brainwashing was pseudoscience. The brainwashing hypothesis as defended by Singer has indeed never been published in scientific journals, and thus has not been available for scholarly evaluation and critique (Anthony, 1990). The claim that so-called “cultish groups” could deprive individuals of their free will in the absence of physical force or threats through “conditioning techniques” had been then discredited by numerous research works, which have shown that “brainwashing” was an inadequate model for understanding the dynamics of conversion in any religious movement (Melton, 1999). Scholars pointed out, among other things, that the brainwashing hypothesis was based on an inappropriate application of the theory of conditioned reflex to social relationships, and on a misunderstanding of academic work on the thought reform programs conducted in Chinese prison camps (Robbins and Anthony, 1980)¹⁰. That consensus was capped in the U. S. Federal Court decision in the case of

⁶The CIAOSN (Center for Information and Advice on Harmful Sectarian Organizations), which is the Belgian equivalent of MIVILUDES, emphasizes for instance in its 2010–2011 report to the Belgian Council of Ministers that the use of ayahuasca “leads to the adherence of the most vulnerable and suggestible subjects, to a rigidification of psychic processes, to an impoverishment and a narrowing of the affective life around this object, ayahuasca” (C.I.A.O.S.N., 2011, p. 21). France continues to play a leading role in the anti-cult movement in Europe and in its coordination, notably through the FECRIS (Fédération Européenne des Centres de Recherche et d’Information sur le Sectarisme) – (in French) European Federation of Centres of Research and Information on Sectarianism. This French non-profit anti-cult association founded in 1994, serves as an umbrella organization for groups which investigate the activities of groups considered cults in Europe.

⁷Such as the Unification Church, the Divine Light Mission, The Way International, the International Society for Krishna Consciousness, and Church of Scientology.

⁸Initially consisting of small and informal groups of distressed family members of individuals joining emerging religious movements, these groups gradually grew into larger organizations operating mainly as non-profit organizations centered on information, education and support of so-called “cult” members and their families. Attempts to create a national confederate organization, however, have always failed because of dissension over local autonomy and funding issues (Shupe et al., 2004).

⁹Deprogramming practices included the abduction and forceful detention of a member of so-called “cult” by parents or anti-cult movement professional deprogrammer, and the subsequent application of pressure for the member to withdraw renounce their religious affiliation (LeMoult, 1978). The methods used in deprogramming have been described by many observers as being just as coercive than the methods the anti-cult movement claims were used by “cults” to indoctrinate their members (Young, 2012).

¹⁰Academic work on thought reform programs has indeed shown that the Chinese Army did not have techniques capable of converting individuals to Communism against their wills (Schein, 1956; Robbins and Anthony, 1980). The techniques used in Chinese prison camps were generally quite ineffective, achieving only short-term and superficial behavioral changes, based on the plausible threat of physical coercion. Most scholars conclude that the few subjects who had been slightly more influenced by Communist indoctrination differed from the great majority of subjects because of personality features that existed prior to the indoctrination process, which predisposed them to respond favorably to totalitarian propaganda (Anthony and Robbins, 1994). Psychologist Robert Lifton, on whose work Singer had based his model, has finally denounced the applicability of his research on military indoctrination techniques to that of religious conversions and so-called “cultish brainwashing” (Shinn, 1993).

U.S. v. Fishman¹¹. It has been then considered that the use of such arguments as a justification of deprogramming and legal action was illegitimate (LeMoult, 1978). Singer has been finally prohibited from testifying as an expert in American courts, due to the lack of scientific validity of her theories¹².

It is nowadays widely accepted by scholars that the brainwashing theory was promulgated by the CIA for the sole purpose of serving as an anti-communist propaganda tool during the Cold War (Anthony, 2008), and that this theory was later reappropriated by the nascent anti-cult movement in the United States, serving as justification for highly controversial measures (e.g., “deprogramming”) against some new religious movements (Robbins and Anthony, 1980). In the United States, as in most countries around the world, concepts such as brainwashing are now considered by the courts to be unnecessary to justify investigations and possible prosecutions of religious groups suspected of breaking the law, including through the use of physical violence and coercion. Even if since the late 1980s the academic community have thus shared an almost unanimous consensus that the brainwashing thesis proposed by Singer and her colleagues was without scientific merit, this thesis has deeply impacted the popular imagination, as shown by its diffusion in many works of fiction, such as *The Manchurian Candidate*¹³. The concept of brainwashing, reformulated as “mental manipulation,” gained new resonance with public authorities in Europe in the 1990s (Richardson and Introvigne, 2004). This can be explained by a number of reasons (Melton, 1999)¹⁴. Perhaps the most important of these is that since the 1990s, violent incidents in Europe by minority religious groups such as the Solar Temple (Lewis, 2006) have come to the attention of the general public and public authorities. Since then, legislators, urged on by proponents of the “mental manipulation” theory and anticult associations, have been asked to create new laws and government agencies aimed at observing minority religious communities and identifying “cultish driftings.” In France, which is distinguished by its deep-rooted secular tradition, this shift was embodied in the early 2000s by the creation of MIVILUDES and the passing of a

new law condemning the “fraudulent abuse of a state of ignorance or weakness” and aiming to repress the practices of “mental manipulation” allegedly used by “sectarian groups”¹⁵. Since then, courts have been asked to bring in rulings based upon testimony of experts in the controverted “brainwashing” perspective.

The prohibition of ayahuasca in France, as the Takiwasi’s legal proceeding – which was one of the first applications of the new law aimed at responding to the concerns of anti-cult associations –, should be thus understood in the light of this contemporary reemergence of brainwashing theory in Europe and its political and legal implications. For the French government, supported by the reports of MIVILUDES (2005) and the positions of anti-cults associations, psychedelics would therefore constitute potential tools of “mental manipulation.” As explained to me during interviews conducted between 2008 and 2013 with members of anti-cult associations and French governmental agencies, psychedelics are in that perspective considered as having the potential to reduce one’s agency and reflexivity and to impair one’s ability to make informed decision, allowing thus a fast and non-consented transmission of specific beliefs, i.e., to allow “brainwashing.”

Despite the fact that the capacity of psychedelics to produce “brainwashing” had already been explored unsuccessfully from the second world war onward¹⁶, these events bring back to the public debate the question of the place of hallucinogens in religious conversion and of their use as a potential tool for “mental manipulation.” If this can make one wonder about the possible emergence of a new witch hunt stigmatizing psychedelic users in Europe, these elements are to be relativized with regard to the worldwide dynamic of growing interest for psychedelics by the scientific and medical community as well as the general public. This point, however, highlights the fact that, despite the criticism that the “brainwashing” model has received, alternative perspectives on how psychedelic experience supports enculturation and social affiliation have been yet little explored. Beyond the political issues that underlie it, the re-emergence of the concept of “psychedelic brainwashing” can then be read as the fact that the dynamic through which psychedelic experience supports persuasion and transmission of beliefs is still poorly understood. These questions and their ethical stakes are, however, bound to become increasingly relevant, as the use of psychedelic substances is rapidly achieving mainstream

¹¹The origins of this federal case lays in a one million dollars fraud scheme Fishman conducted during the eighties. The FBI investigated the possibility of church involvement in the scheme, as 30% of the total amount of the fraud have been spent on Scientology materials and services. Fishman’s attorney used an insanity defense, offering false memory syndrome theorist Richard Ofshe and psychologist Margaret Singer as expert witnesses (Anthony, 2004).

¹²Singer attempted to respond to these criticisms by stating, in the second edition of her book (2003), that brainwashing is involuntary not as “against the person’s will” but in the sense that the subject is unaware that there is an agenda to control or change the person and that this process is happening. However, this definition of brainwashing is so broad that it is difficult to see what distinguishes it from the persuasion procedures observed in numerous social areas (advertising, political campaigns, education, etc.) and, more generally, in any socialization dynamic.

¹³*The Manchurian Candidate* is a novel of Richard Condon published in 1959, in which the soldier Raymond Shaw is brainwashed by communists after being captured during the Korean War. Back to civilian life in the United States, where he becomes an unwitting assassin in an international communist conspiracy to overthrow the United States government. This bestseller has been the subject of two successful film adaptations, in 1962 and 2004.

¹⁴It should also be considered that as the main debates on the concept of brainwashing took place in the 1980s in the United States, most Europeans were not aware of these earlier debates, as the main documents were only available in the English language (Melton, 1999).

¹⁵This law, so-called “About-Picard” law (law n°2001-504 of 12 June 2001, enshrined in article 223-15-2 of the French criminal code) punishes with 3 years imprisonment and a fine of €375,000 “the fraudulent abuse of the state of ignorance or weakness (.) of a person in a state of psychological or physical subjection resulting from the exercise of serious or repeated pressure or techniques likely to impair his or her judgment, to lead (.) that person to an act or abstention which is seriously prejudicial to him or her”.

¹⁶In Germany, military research conducted by the Schutzstaffel (SS) and the Gestapo led to the testing of mescaline in order to improve coercive indoctrination techniques and interrogation tactics. In United States, a similar type of research undertaken by the Office of Strategic Services (OSS), and then continued by the CIA, used LSD for the same purpose. Common goals of these experiments was to create an effective method to convert enemy captives into deployable secrets agents, to train soldiers to remain strong in the face of captivity by enemy forces, or to develop effectual wartime propaganda. The results produced no evidence at all for the success of these researches, and researchers ultimately declared their work a complete failure (Anthony and Robbins, 1994).

status, especially in the context of the emergence of commercial interest for psychedelic therapy (Nichols et al., 2017), the so-called psychedelic science ‘revival’ (Langlitz, 2012), and ritualistic uses in secular and neo-shamanic contexts (Labate and Cavnar, 2014; Labate et al., 2016). Beyond the unscientific and politically controversial notion of brainwashing, how can we think the role of psychedelics in the dynamics of persuasion and transmission of belief?

Based on data collected during an ethnographic fieldwork in Takiwasi, one of the main shamanic center in the Peruvian Amazon, I propose here to explore this question. To do so, I will use an analytical framework rooted in interactionism (Becker, 1963; Goffman, 2002), narrative approaches (Cain, 1991; Seligman, 2005) and cultural phenomenology (Csordas, 1999) dialoguing with anthropology of belief and social psychology. Drawing on a case-study of a young French man participating to Takiwasi’s seminar, I will show that the dynamic of belief transmission is supported by a remarkable property of psychedelics, that of producing a state of *hypersuggestibility*. This property is, however, far from depriving the subject of reflexivity and agentivity as proposed by the brainwashing model. We will indeed see that it is also in its capacity to produce doubt and ambivalence that psychedelics support adherence, cultural transmission and social affiliation. I will show that it is ultimately on the recipient’s efforts to test the object of the belief through an *experiential verification* process that the dynamic of psychedelic belief transmission rely on. The dynamics of belief transmission supported by psychedelics, in that it depends on the efforts of the recipient, is consequently subject to significant inter-individual variations. I finally explore the permanence and the conditions of sustainability of the social affiliation that emerge from this dynamic in order to better seize the ethical stakes of these observations.

MATERIALS AND METHODS

To explore the aforementioned points, I will draw on data collected during an 18-month ethnographic fieldwork divided into three research stays, between 2008 and 2013. By providing thick descriptions of intricate cultural factors and interactional contexts shaping the hallucinogenic experience, the ethnographic method offers valuable insights to answer the questions explored in this article. By allowing for both first-person data collection (through participative observation) and third-person data collection (through interviews and observation of daily interactions), this offer some other major advantages. The cross-referencing of these two types of data offers indeed highly detailed informations about the phenomenological features of the psychedelic experience and makes moreover possible to build robust hypothesis about the interactional dynamics that shape it¹⁷.

¹⁷However, this method will have limitations for so called “hard science” perspective, such as relying on a relatively small number of participants which does not allow for the development of meaningful statistical aggregates, on which, for example, most of the psychology studies are based.

The ethnographic research study was conducted in the San Martín region (Upper-Amazon region of Peru), most of the time in Takiwasi. During the first 4-month stay in 2009, I focused on the treatment of addictions proposed by Takiwasi. I used different methods of data collection, among which the study of daily and ritual interactions through the observation of participants played a central role, along with semi-structured interviews and life stories of about ten drug-dependent patients and the main actors of the institution (ritual specialists and psychologists, etc.). The second 6-month stay was in 2011, during which I attended four “seminars” offered to foreign clients. In each of these seminars there were between 15 and 20 participants. I shared the participants’ daily and ritual activities, as well as the discussion groups. I also conducted individual interviews with around thirty participants, and they shared their life stories with me. The 8-month final visit was in 2013. On this occasion, I attended three more “seminars,” that included a total of 45 participants. I also conducted weekly interviews with two drug-addicted patients who were hospitalized for 6 months and, more occasionally, with other patients. Since then, I have conducted through interviews a long-term follow-up of some Takiwasi’s clients through interviews in Europe and in Latin America.

This research study was also complemented with a comparative study, aimed at becoming more acquainted with the specificities of the institution under study in relation to the shamanic practices of the metis or Lamista people of the region. To this end, I carried out several short field surveys in the San Martín region (San Roque de Cumbaza, Chazuta, etc.), accompanying in their daily and ritual activities metis and indigenous healers offering their services to a local people within their village or to a national and international clientele within shamanic centers.

This ethnographic research study complied with the proceedings related to “informed consent” and was conducted with voluntary participants who were aware of the study objectives and knew that they could leave the investigation if they so desired. In order to protect the anonymity of the informants, all the names of the clients of Takiwasi have been replaced by pseudonyms.

Context of the Study: The “Seminars” of Takiwasi, a Shamanic Center in the Peruvian Amazon

Participation in exotic rituals perceived as “traditional” and invested as therapeutic, religious or personal development practices have been increasingly popular with the Western public since the second half of the twentieth century. Fueled by the craze for the psychedelic brew ayahuasca as well as by the mythified image of the so-called primary forest, an influx of travellers has headed toward the Peruvian Amazon from the 1990s onward (Labate and Cavnar, 2014; Labate et al., 2016). The development of these practices has recently been analyzed by anthropologists as the emergence of a “shamanic,” “ethnomedical,” “mystical,” or “spiritual” tourism (Fotiou, 2010). Many reception centers for this clientele have appeared on the edge of the region’s metropolitan areas. These shamanic centers,

most often based on the partnership between Westerners and Metis or indigenous people, offer an international clientele the opportunity to participate in ritual activities inspired more or less freely by the practices of the Peruvian metis shamanism (*curanderismo*), such as the ritualized use of ayahuasca.

Founded in 1992 by French physician Jacques Mabit as well as Peruvian and Spanish collaborators, the therapeutic community of Takiwasi is both an addiction treatment clinic and one of the most famous places in the region hosting Western travelers to “meet ayahuasca.” The premises are located on the outskirts of the city of Tarapoto, capital of the San Martin region, on a two-hectare plot of land bordered by a green fence and the Shilcayo River. In addition to a central building, which includes administrative and reception areas, an auditorium and a library, there is housing for resident drug addicts, a kitchen, two *malocas*¹⁸ where rituals are held, various workshops (carpentry, baking), a chapel, a laboratory for the production of phytotherapeutic products, a store and a botanical garden where the main medicinal plants used at Takiwasi are grown. The association also owns a 54-hectare plot of forest located a few kilometers away, in the *Cordillera Escalera* nature reserve, where there are 15 isolation huts (*tambos*) used for retreats (*dietas*), as well as a *maloca* inside which ayahuasca rituals are performed. Jacques Mabit is now the main authority in Takiwasi: the French doctor is indeed the last of Takiwasi’s founding members to still hold responsibilities within the institution. Since then, he has been the bearer of ritual authority, and all important decisions are subject to his approval. Apart from the Métis and indigenous healers (*curanderos*) sometimes recruited by the institution, only several people regularly officiate during the rituals. More recently, a priest has joined the team: he provides spiritual direction services as well as a weekly mass in the Takiwasi chapel, and regularly participates in the institution’s ritual practices.

Since its creation, the institution has developed a therapeutic device characterized by the reappropriation of elements of the indigenous pharmacopeia, such as emetic plants or ayahuasca. A team of doctors, psychologists and ritual specialists offers psychological support, medical follow-up and ritualized practices inspired by the Amazonian tradition, combining ritual and discursive elements from the region’s indigenous and metis shamanism, Catholicism and the New Age. These services are proposed in three different modalities: addiction treatment, which involves a 9-month internment, outpatient treatment and “personal development seminars.”

Seminar participants, both men and women, between the ages of 20 and 60, come from the middle and upper classes in the urban areas of French-speaking Europe and Latin America. They most often report a life journey marked by the accumulation and repetition of different registers of misfortune (grief, chronic pain or pathology, accidents, academic or professional difficulties, “loss of meaning”), the resolution of which is presented as the main reason for their coming. The resistance of these difficulties to the treatments offered by medicine and the dominant forms of psychotherapy (psychoanalysis, CBT, etc.)

has most often initiated a process of experimentation with alternative therapies, of which the stay in the Amazon is a step. The coming to Takiwasi also reflects a form of religiosity characteristic of Western modernity (Luhrmann, 1991) based on the accumulation of “spiritual experiences” from various cultural backgrounds as well as on a modular, individual and irregular practice (Hervieu-Léger, 1999).

RESULTS: PSYCHEDELICS AS TOOLS FOR BELIEF TRANSMISSION, AN ETHNOGRAPHIC CASE-STUDY

The Psychedelic Ritual in Takiwasi

Bringing together about fifteen participants for a 2-week period, the personal development seminars offered by Takiwasi include various practices inspired by the metis Peruvian shamanism such as rituals focused on the ingestion of emetic plants and ayahuasca, and a few days retreat in the jungle involving the consumption of other vegetal preparations (*dieta*). Participation in these activities, accompanied by introductory lectures, integration sessions including speech groups and individual interviews, requires compliance with various food (pork, spicy condiments, alcohol), relationship and sexual prohibitions.

The first ayahuasca ritual takes place on Wednesday, the third day of the seminar, after the group’s participation in a purging ritual and several conferences. During these conferences, Jacques Mabit presented the program of the seminar as well as some elements of his etiological theory, including contamination by invisible pathogens of a “spiritual” nature. The experience of ayahuasca is then described as enabling the purification of the participant and his encounter with the “spiritual world” and usually invisible beings. Following an approach inspired by the work of some pioneers of the psychotherapeutic use of psychedelic substances (Grof, 1980), the ayahuasca experience is also presented as a psychological catalyst aimed at facilitating insights, emotional catharsis, childhood regression and understanding the tendencies and dispositions that organize the daily behavior of the participant.

Shortly after nightfall, participants are invited to join the main *maloca*, where about fifteen cushions are placed in a semi-circle. After immersing themselves in a purifying and protective bath of plants, participants take their seats around the ritual specialists. They have reserved places under icons representing Christ, the Virgin and Saint Michael, in front of which are placed their ritual tools (*mesa*). The ritual is frequently preceded by a reminder of the rules, such as body position requirements: participants have to sit, having to keep their back straight, to refrain from lying down and to abstain from sleep in order to “face what arises.” Participants are also invited to refrain from making noise, speaking, singing, interfering with, touching or talking to a neighbor. Ritual specialists usually justify these provisions by the fact that subtle elements are likely to be transmitted between participants through touch or sound. Participants are encouraged to “formulate an intention” before drinking ayahuasca, but not to focus on it during the ritual. In case of difficulty, they are allowed

¹⁸ *Malocas* are traditional Amazonian constructions, oval in shape with a conical roof.

to call upon the officiants. Buckets are available if they feel the need to vomit, while forcing vomiting is not recommended. In case of emergency, it is possible to go to the toilets, located outside the *maloca*, but it will be necessary to report it and wait until a “cleansing” (*sopladas* of perfumes or tobacco) has been carried out by an officiant before returning to the ritual space. These rules will be in place until a ritual specialist turns the light on again, a gesture that marks the end of the ritual.

After these few words, a ritual specialist grabs a censer in which *palo santo*¹⁹ burns, goes around the *maloca*, then stops in front of each participant whom he invites into the smoke presented as purifying and protective. Jacques Mabit then makes a few gestures to materialize the limits of the space occupied by the participants, using holy water and salt, which he spreads behind and between them. These actions, presented to the participants as delimiting a “ritual circle” capable of protecting them from negative interactions, therefore imply compliance with the rules concerning their entry and exit. The master of ceremonies then sings several songs (*icaros*) and blows tobacco smoke (*mapacho*)²⁰ – presented as protective – on his ritual tools, including the bottle containing ayahuasca. Everyone is then invited, one after the other, to come and have a cup of the drink. The light is then turned off. Several songs rise up, recited by the various officiants, while one of them walks by the participants, blowing tobacco smoke on the plexus, fontanel and hands (*soplada*) of each of them. After which come the recitation of an exorcism prayer in French, other songs, as well as a second series of *sopladas*, this time made with the help of *agua florida*²¹. The officiants’ songs, recited in Spanish, Quechua and French, will then follow one another until, 6 to 8 h later, the effects of the drink dissipate.

The Infestation Diagnosis

In Takiwasi, the dynamic of enculturation and belief transmission is most often initiated by a “diagnosis of infestation” formulated by the ritual specialists to the participants during integration sessions. This diagnosis is based on the etiological and therapeutic theory that characterize Takiwasi and distinguish this institution from both the Peruvian *curanderismo* and other shamanic centers of the region. The central element of this theory is the concept of “infestation.” Borrowed from Catholic theology, this concept initially refers to a more minor and common mode of demonic influence than possession, characterized by the presence of a demonic entity abusing the subject by affecting his health, faith or thoughts (du Clos, 2007). In Takiwasi, infestation is thought of as a parasitic relationship with one or more malicious supernatural beings of a demonic nature. This condition, which is also presented as the cause of physical and psychological disorders, is thought of as the consequence of the transgression of taboos (drug use, sexuality, magic practices, spiritualism, etc.), contact

with places or people, or transmission through relations of filiation. Finally, this condition is presented as requiring specific treatment, implying the purification of the patient through the absorption of emetic preparations, ayahuasca as well as practices proposed by the Catholic Church, such as exorcism (Dupuis, 2018a).

This theory, developed by the main actors of the institution over the past 20 years, highlights the increasing use of the Catholic doctrinal body and the ecclesial institution, which has progressively influenced the form and function of the practices proposed by Takiwasi (Dupuis, 2018b). The ayahuasca ritual is now characterized by the use of exorcism prayer, the crucifix, holy water, and the mobilization of the main figures of the Catholic pantheon. If the integration of elements of popular Catholicism is a classic component of the *metis* shamanism of Amazonia (Taussig, 1987; Gow, 1987; Chaumeil, 2003), the central place given here to the motif of demonic possession, the functions of exorcism and evangelization attributed to the use of ayahuasca, as well as the attachment of these practices to the ecclesiastical institution and to Catholic demonology are more original. The evolution of Takiwasi brings now the institution closer to the charismatic, evangelist, and Pentecostal movements which are widely spread in Latin America. In this sense, Takiwasi offers an exemplary case of contemporary cultural recompositions of so-called “shamanic” practices centered on the use of ayahuasca that are currently emerging in the Amazon (Labate and Cavnar, 2014; Labate et al., 2016).

The infestation diagnosis is usually realized during private interviews or speech group integration sessions. The day after the ayahuasca ritual, the participants are in fact invited to meet collectively in the early afternoon to participate in a discussion group called “post ayahuasca.” In the presence of Dr. Mabit and one or more of his assistants, participants are asked to narrate in turn and in front of everyone their experience of the ayahuasca. The ritual specialists then give some comments to the participant. Adrien, a young Frenchman in his early twenties who came to participate in the Takiwasi’s seminar in order to “discover traditional Amazonian medicine” and to “work on oneself,” is subject to a diagnosis of infestation during the first integration session of the seminar. During the speech group, Adrien presents his ritual experience of the day before as difficult to understand and marked by several unpleasant sensations:

“I was super cold at the first part, because my hair was wet. I was blocked, closed, I needed a first contact, a first confidence building. So I contacted the ayahuasca, we started things (.). I was afraid, it was very unpleasant (.). And at one point I thought I was going to suffocate too. I thought I was going to die. I was really, really thirsty.”

He also reports feeling a certain distrust of ritual specialists, expressed in particular in the discomfort he felt when he came into contact with a medal²² given by Jacques Mabit (“Jacques you

¹⁹Barks of a perfumed wood (*Bulnesia sarmientoi*) frequently used in the practices of the Peruvian *curanderismo*. Its use in Takiwasi is to purify and protect the ritual space.

²⁰Brown tobacco of a local variety (*Nicotiana rustica*).

²¹*Agua florida* is a cologne used in the practices of *Métis* shamanism in South America as well as in Central America and the Caribbean as a purification, care and protection tool.

²²Medal given to Adrien by Jacques Mabit shortly before the first ayahuasca ritual. Engraved with the effigy of St. Benedict, the medal of St. Benedict represents the patron saint of monks attacking the devil, holding a crucifix in his right hand and pronouncing a conjuring formula reproduced on the medal. Medals and crosses of St. Benedict were used in Europe from the Middle Ages onward as talismans to protect people, animals, houses and fields from evil influences.

gave me a medal, which I kept for a while. Then at a certain point I became saturated, so I put it down, it weighed me down, it haunted me, I had the impression that it was blocking me”) and which culminates in a vision assimilating the officiant to a demonic figure (“I was afraid of you in fact, because I saw you in a diabolical way at first”).

The account of Adrien’s ritual experience leads Jacques Mabit to diagnose the signs of a “presence” described as “parasitic.” This diagnosis is based on the sensations reported by the participant, presented by the ritual specialist as a symbolic language that should be deciphered. Jacques Mabit begins his comment evoking the sensation of cold felt by Adrien. This sensation is, at first, presented by the ritual specialist not as a normal perception of temperature, but as an element manifesting a daily psychological disposition of the participant, a tendency to “escape in front of fear.” Dr. Mabit then invites Adrien to look for the reason for the fear felt during the previous day’s ritual. The young man mentions his fear of the ritual specialists, to whom he attributed malicious intentions and whom he perceived “in a diabolical way.” This point is interpreted by the officiant as the manifestation of a disposition governing the participant’s daily life consisting of a “fear of being manipulated, programmed without your knowledge, that someone has a hold on you in some way.” Jacques Mabit also indicates that this fear, here “projected” onto the ritual specialists, would in fact find its origin in Adrien’s infantile interactions and kinship relationships. As the young man evokes “a fear of losing spiritual knowledge,” Jacques Mabit invites him to examine the nature of this “knowledge,” suggesting that it is the support of a “hold” of “spiritual connections” serving the intentions of a “manipulative spirit.” The sensation of cold, first interpreted as the manifestation of a psychological disposition, is then presented as a “spiritual cold” signaling a “parasitic presence.”

The presence of a “manipulative spirit” endowed with an intention and an agentivity of its own is thus posited, presented as a parasitic agent pursuing interests antagonistic to those of its host. This entity would manipulate Adrien by influencing his desires, thoughts and emotions without him being aware of it, leading him to confuse his own mental states with those induced by the parasitic entity. The presence of a parasitic entity would result in a loss of discernment of the participant as to the origin and nature of his own states. Thus, Jacques Mabit suggests that the fear reported by Adrien is in fact the fear felt by the entity when it comes into contact with the ritual work, which aims precisely at driving it away.

As we can see, some elements of Adrien’s account are interpreted by the officiant as the signs of the manipulative influence of the parasitic entity, revealing both the presence of the latter and its intention, consisting of opposition to the actions and intentions of ritual specialists. The intense thirst reported by Adrien, like the cold mentioned above, is indeed presented by the ritual specialist not as a normal perception but as a “suggestion” of the parasitic entity aiming at leading Adrien to leave the ritual space. It is thus understood that if the entity aims at expelling him from the ritual space, it is because of the effectiveness of the actions of the ritual specialists which aim at fighting against its presence. The ambivalent relationship reported by Adrien

with the medal is also interpreted by Jacques Mabit as a sign of manipulation by the parasitic entity. Adrien’s ambivalence toward the medal would thus illustrate the participant’s lack of discernment in the face of the intentions of this entity, whose interest here is to keep the artifact away so as not to be discovered and expelled. Despite the discomfort felt, Mabit suggests consequently that Adrien should not abandon the object given by the ritual specialists.

As we can see, the diagnosis of infestation is based on an epistemic asymmetry that endows the ritual specialist with an epistemic authority. In the former sequence, Dr. Mabit has indeed positioned itself as having a capacity to “see” of which Adrien is deprived, and that allows him to identify the presence and nature of an invisible entity with which the young man is in relation without being conscious of it. Where Adrien seems not to have noticed this presence, Mabit claims to have fought against it during the ritual and seems to know it intimately, describing its intentions, its strategies and its weaknesses (“the little beast doesn’t like the medal”). Adrien’s diagnosis thus leads the officiant to deliver to the group of participants the typical reactions – fear, discouragement – that a discovered “parasitic entity” will try to arouse in its host in order to escape the operations of the ritual specialists.

However, Jacques Mabit does not claim to have a full understanding of the events of the previous night. To Adrien, who asks him “of what order” this “parasitic presence” is, he replies that he “does not know.” Dr. Mabit therefore invites the participant to investigate by himself during the next rituals on the nature and origin of this parasitic presence. The ritual specialist does, however, offer some etiological suggestions, such as “deep emotional wounds.” The officiant also suggests that certain practitioners of “energy techniques” that Adrien had frequented in previous years are likely to be “sorcerers,” which he defines as “a magician who uses energies, who works for the forces of evil.” These “sorcerers” are presented here as individuals with malevolent intentions and supernatural powers they derive from their association with demonic beings. Mabit thus poses as a possible origin of the infestation the frequentation of these evil magicians, who would be difficult to identify because of their “seductive” character. The ritual specialist finally mentions “bad and dangerous” techniques such as Reiki. Jacques Mabit ultimately suggests to Adrien, who seems doubtful about the proposed diagnosis, to “observe” during the next ayahuasca ritual in order to “look face-to-face” and verify the proposed diagnosis by himself. Faced with the attacks of the “parasitic presence,” Adrien is finally invited to “hold on” to the ritual specialists and the artifacts that they have given him.

Doubts and Reflexivity: The Dynamic of Belief

The diagnosis of “infestation” formulated by the ritual specialists during integration sessions is far from giving rise to an automatic adherence. During our first interview conducted shortly after the speech group, Adrien seems to be very critical of the diagnosis of infestation proposed by Jacques Mabit which he attributed first of all to a “paranoia” as well as to mercantile intentions:

“The more you believe in demons, the more you attract them. The more you are in protection, the more you attract evil. (.) Finally, it's only suppositions, I don't know, a kind of paranoia (.) I've seen some people, who are specialists, they love demons, they always feel possessed, so they are necessarily possessed! (.) It's also good to say “you're possessed,” it means that there's work to be done, money to be earned!”

In spite of these criticisms, the young man nevertheless evokes during our interview the possibility of being the object of an “infestation,” the existence of which he does not seem to contest. This partial acceptance of the diagnosis seems to be based on the fact that the latter have initiated an investigation into the origin of these “parasitic” entities:

“I have done quite a few rituals, I have worked on a spiritual level on things that I do not master. For example, I had courses with someone I did not know well, advanced courses of healing at the spiritual level. He did some rituals that I didn't practice, but I taught them, and then I practiced them. And there I may have picked up some stuffs. Maybe in the Philippines with the healers, I don't know.”

Adrien thus seems to occupy an ambivalent position, oscillating between doubt and adherence. If at first he seems very critical, we can see that he does not reject the existence of demonic entities or acts of witchcraft. He thus seems to oscillate in an undecidable way about the diagnosis that has been proposed to him, which is revealed by his joke at the beginning of our interview: “Yes, I'm ok to discuss with you a bit. I mean knowing that I am possessed. So what I am saying is a projection of my demons (laughs)!”

If some participants, like Adrien, affirm that they “do not believe” in the proposed diagnosis in the sense of a full and complete adherence, they nevertheless most often show an indeterminacy oscillating between doubt and adherence. Adrien's account illustrates his reluctance to reject firmly the infestation diagnosis proposed by Dr. Mabit. It is quite striking that the object of this ambiguous adherence is designated by Adrien in a vague way (“some stuff”). This approximate evocation recalls the mysterious character of the proposals of the ritual specialists who mobilize signifiers such as “energy,” “energetic body,” “demon,” “parasitic entity” or “sorcerer” whose content never seems to be fully grasped by the participants. Because of this mysteriousness, the diagnosis proposed by the ritual specialists usually provokes an evocative process in the participant, who seeks to clarify its meaning.

The gradual generalization of the use of the categories proper to the local etiological-therapeutic theory is thus far from revealing the adoption of a univocal and complete meaning of this knowledge. The appropriation of the interpretative system is, as we can see, not free of doubts and criticisms. The participants, even when they criticize the proposed diagnosis, seem nevertheless unable to exclude the potentiality of its relevance. Adrien's position thus illustrates that of most of the participants who, far from showing full and definitive adherence to the proposals of the ritual specialists, seem more compelled by their participation in the device to consider, at least temporarily, the possible relevance of these proposals.

Believing, Betting, Committing

As Adrien's reaction at the end of our interview reveals, this strategy is most often concretized by a search for verification of the proposition causing undecidability, in this case the infestation by parasitic entities diagnosed by the ritual specialist:

“I would have seen it, I would have believed him, I may see it, I don't know (.)”

When the young man declares that he “does not believe,” he does not exclude the possibility that the diagnosis is true, but he says that he refuses to accept it without verifying it by “seeing” it, the experiential dimension being the decisive criterion for validating this verification. This search for *experiential verification* is presented by the ritual specialists as likely to be carried out through participation in the next rituals, described as capable of providing proof of their proposals. The ritual specialists thus frequently invite the participants to “verify for themselves in the ayahuasca” the knowledge which they expound during the discursive interactions. This invitation appears to be all the more attractive because the possibility of an experiential verification of the diagnosis is embodied in the figure of the ritual specialist, who presents the origin of his knowledge as strictly empirical.

As illustrated by this testimony from another seminar's participant, the persistence of an illness that has resisted previous therapeutic proposals also invites many participants to adopt this etiological system on a temporary basis. They usually do so in order to test its effectiveness, since they are interested above all in the possible benefits of the cure:

“I don't really know what to think about all this, about these stories of demons, of transgenerational (.) So I don't know, but anyway, I can't stay like that, so, well, I'll play the game and we'll see what the result is. Anyway, I have nothing to lose by trying!”

These calculations of interest often seem to take precedence over the question of the veracity of the proposals of the ritual specialists and lead most of the participants to follow their invitations and recommendations, even though they remain ambivalent about their initial premises. In spite of his doubts and after considering leaving the seminar, Adrien decides to participate in the following rituals in order to benefit from the therapeutic proposals based on the diagnosis of infestation:

“Apparently, the priest, he also saw that I was parasitized. That's why they offer me after the mass, something to free me. Well, we'll do that. (.) I'll do the thing to the end.”

Thus, during the course of the survey, I saw many participants going to the Masses proposed during the seminar, even though they declared themselves to be atheists or were very critical of the proposals of the ritual specialists concerning the “demons.” This behavior, which illustrates in a striking way the paradoxical character of the dynamic of belief, seems to be based on a calculation of interest which is not without evoking a form of “Pascalian wager”:

“Yesterday I went to mass before the ayahuasca session. I am not really religious, at least not Christian, and besides, my family is originally Lutheran! But I don't know, it was cool to be with everybody. And I guess I also thought that if all these stories are

true, it's better to be on the right side. And anyway, it's not going to kill me to go to Mass!"

The Experiential Verification of the Infestation Diagnosis

A few days after the first discussion group, the members of the group go to the plot of forest next to Tarapoto where the *dieta* will take place, a few days retreat in the jungle that will begin the next day. At nightfall, they join the *maloca* to participate in the second ayahuasca ritual. During an interview carried out on the return from the *dieta*, Adrien reports having during this ritual "expelled spirits" that he thinks he had contracted when taking psilocybe mushrooms a few years earlier. He describes this sequence as a "teaching" of ayahuasca and "animal spirits" perceived through visual hallucinations:

"There were spirits that came out. Faces that I had seen in a piece of wood while taking mushrooms [...]. I hadn't noticed that it had actually come in. I was even amused by the faces I saw in the wood. But then it came out (during the ayahuasca ritual) and I realized that it was not good. I saw the same piece of wood with a head in it again, so I saw that I had caught it while taking the mushrooms. I saw it in vision and I threw it up, so I threw up air, I was burping, I was sighing. I also got the information that I shouldn't do anything with the plants (psychotropic ones). And that's the snakes, the ayahuasca and all the animal spirits that passed by, that came in, that taught me that."

The presence of parasitic entities, the discovery of the contaminating nature of certain practices, the encounter with pedagogical and protective entities: on returning from the *dieta*, the sequences reported by the members of the group show a striking adequacy with the belief system exposed by the ritual specialists during the preceding discursive interactions.

During the last interview that he grants me at the end of the seminar, Adrien presents the 2 weeks spent in Takiwasi as an investigation initiated by the partial and mysterious diagnosis of infestation proposed by the ritual specialists during the first speech group. The origin of the infestation is finally attributed by Adrien to the "wild" use of psychotropic substances and to "magical" practices involving the opening of "tunnels" that the participant had never taken care to close. One recognizes here the main features of the local etiological theory: opening of the "energetic body" or the model of parasitism and contamination, which are here imputed to the realization of socio-moral infractions. Although he presents these elements as hypotheses, the young man nevertheless displays his determination not to reproduce the actions that he believes may have caused the infestation. Thus, during our conversation, he avoids reproducing in front of me the gesture that he considers as a potential vector of contamination, which consists in tracing with his fingers a pentacle supposed to "open energy tunnels." At the end of the seminar, the young man presented himself as having finally understood and verified the diagnosis proposed by Jacques Mabit. The mistrust he had shown toward Jacques Mabit, Takiwasi and its ritual practices during our first exchange finally gave way to recognition, to such an extent that he invites me to

"forget" what he had told me during our first interview, which he now interprets as "projections of his demons."

DISCUSSION

The Ambiguities of Psychedelic Enculturation: Doubts, Reflexivity, and Belief

This ethnographic case-study illustrates in an exemplary way the belief transmission dynamic based on psychedelic experience in Takiwasi. As illustrated by Adrien's case, this experience is far from inducing a sudden, linear and automatic conversion. The psychedelic ritual seems rather lead participants to an oscillating indetermination between doubt and adherence, which strongly mobilizes the reflexivity and agentivity of the recipient.

Beside uncertainty, the kind of belief induced by the participation to psychedelic ritual is moreover characterized by the vagueness of the object of belief. The vague and elusive character of the signifiers composing the belief system transmitted by the specialists drapes them with an indeterminacy that allows them to cover varied and flexible – and sometimes even contradictory – interpretations. I could for instance observe during my investigation in Takiwasi a great variety of representations of "demons" among the participants. Some see them as a metaphor for emotional or behavioral complexes, while others show a more complete adherence to the propositions of ritual specialists concerning the existence of invisible entities. As illustrated by the testimony of this Peruvian drug addict patient at the end of treatment in Takiwasi, others still consider this possibility, while considering that it may also be, and at the same time, the product of projective mechanisms:

"The others (patients) talk about demons but I don't think it influenced me much, they didn't really talk to me about it. I must have seen demons eight or nine times in ayahuasca sessions. It started around the second or third month of treatment. Mostly they would watch me, hide and try to intimidate or seduce me. (.) I'm a bit dubious about the accounts of visions from some of the companions. Some of them seem to me to be telling themselves stories or projecting their stuff that they take too seriously. Jeremy has a digestive problem and, for him, it is an entity. I don't believe him, it's probably a bacteria or a parasite. Jeremy sees a lot of entities and demons, I'm more cautious about these things. I know that possession is possible, it exists. But honestly, I don't have the experience or knowledge to discern, to know what is and isn't."

The majority of the participants balance irresolutely between the possibility that there are invisible demonic entities and the possibility that the "demon" is a metaphor for knowing themselves better or for personifying their suffering and misfortune. The signifiers that make up the belief system of the ritual specialists thus constitute plastic terms that are easily appropriated and to which an idiosyncratic and mobile meaning can easily be attributed. The vague and elusive nature of the signifiers composing the etiological knowledge transmitted by the local epistemic authorities is reminiscent of

the “floating signifier” described by Claude Lévi-Strauss (1950). These signifiers designate notions – such as mana, a central concept in Melanesian rites, but whose meaning remains floating or vague – whose function “is to oppose the absence of meaning without having any particular significance in itself” (Lévi-Strauss, 1950). These signifiers thus have the advantage of allowing the experience to be socialized without requiring a strict consensus of the actors on the meaning of the experience. As this seminar participant testifies, their properties will eventually allow people to remain in this state of undecidability without feeling the need to make a definitive decision about the nature of his experience:

“I mean I don’t know, I can’t be sure, really know if they are entities or psychological projections. You never know. Sometimes, during ayahuasca sessions, I see an eagle and I have the impression that it is the spiritual protection of my grandmother, but in fact I don’t know. But still, when I see the demons it is very clear, they are not vague shadows or my imagination, I see them clearly.”

The appropriation of the local belief system supported by the participation to the psychedelic ritual is consequently composed of doubts, criticisms, and allows the maintenance of multiple – and even contradictory – interpretations about the meaning of the object of belief. Adherence to the interpretative framework proposed by the ritual specialists is in this sense reminiscent of the concepts of representational (or reflexive) beliefs proposed by Dan Sperber to describe the relationship of faithful to religious propositions (Sperber, 1982, 1990, 1996)²³. Unlike factual (or intuitive) beliefs, which are more intuitive because they are attached to perceptual anchors that tend to make them unquestionable, the content of representational beliefs is not entirely grasped by those who hold them. Insofar as they are transmitted by authorities, they are nevertheless assumed to be true and preserved by means of “quotation marks.”

Integrating the enigmatic statements of the ritual specialists without fully understanding them, the seminar’s participants thus explore various possible interpretations in order to determine the one that will be the most relevant for them. This field of interpretation is relatively free: if the path is certainly marked out by the propositions of the local epistemic authorities and the normative constraints mentioned above, it remains, however, specific to each person. The participants, even when they criticize or don’t fully understand the local cosmological and etiological theories proposed by ritual specialists, seem nevertheless unable to exclude the potentiality of their relevance. They consequently usually try to verify them by participating in the following rituals.

We understand from Adrien’s account that his reluctance to firmly reject the interpretative system proposed by ritual specialists is based on doubts induced by the psychedelic ritual experience, some aspects of which are very likely to be interpreted as tangible verification of the proposed diagnosis. This dynamic is reminiscent of the negative mode of belief formulated by Severi (2015), who proposes to consider the mental state of belief more as “a dubious not knowing” based

on an “incomplete constellation of clues” rather than a clear and positive adherence to a proposition. This ambiguous adherence characterizes in particular the participants who, as Adrien, present themselves as circumspects or opposed to the possibility of the existence of supernatural entities. The position they display evokes the dynamic proper to bewitchment diagnosis in contemporary French rural populations analyzed by Favret-Saada (1980). Borrowing this model from the ethnologist and psychoanalyst Mannoni (1969), she shows that the subjects of bewitchment diagnoses are caught in a contradictory tension summarized as follows: “*I know well* (that malevolent sorcerers do not exist)... *but still...* (some aspects of my experience seem to accord with the existence of such beings).” In a dynamic evoking this model, Adrien’s psychedelic ritual experience seems to be able to sow doubt, to undermine his certainties, thus leading him to consider the possibility of the relevance of the officiants’ diagnosis, even if it is based on propositions in which the participant affirms that he does not believe.

The specific mode of belief induced by psychedelics reminds in this regard the attitude of belief as described by French anthropologist Hamayon (2006), which “accommodates the expression of doubt (.) (and) the absence of certainty.” In line with this work and based on her ethnographic investigation on a Korean new religious movement, Luca (2013) has emphasized the instability of “belief” by defining it as “the oscillation between being and not being (.) the margin between the two,” which characterizes the position of many participants in the face of the proposals of ritual specialists.

The participation in the ritual induces in this sense a position of undecidability concerning the propositions of the ritual specialists, which evokes the situations of cognitive dissonance described by social psychology (Festinger, 1957; Harmon-Jones and Judson, 1999). In these situations, one simultaneously experiences contradictory elements of knowledge. This position then leads one to try and make these irreconcilable elements of knowledge concur in order to maintain a coherence and to reduce the psychological tension induced by undecidability. The psychedelic ritual appears then as inviting to question and *verify* in a concrete and tangible way the object of belief, and plays in this sense a central role in the participant’s subsequent involvement in ritual practices. As illustrated by Adrien’s journey, the doubts and uncertainty caused by the psychedelic experience are powerful vectors of commitment in the ritual practices. It is consequently paradoxically in their capacity to produce ambivalence and reflexivity that psychedelics support the belief transmission dynamic.

Experiential Verification: The Underpinnings of Psychedelic Enculturation

The sensitive and bodily experience plays here a key role in the verification dynamic caused by the ambivalence experienced by the participation to the first steps of the seminar. Adrien’s case suggests that it is indeed because it is haloed by the evidence of the senses that the psychedelic experience is then leading Adrien to the adherence to the system of belief that surrounds it. The

²³This distinction refers to dual-process models of cognition, contrasting intuitive processes (System 1) that are fast, automatic, and implicit on the one hand, and reflective processes (System 2) that are slow, deliberate, and explicit, on the other (Evans, 2008).

components of the perceptive experience, in that they present for those who experiment them a character of evidence difficult to question, constitute privileged vectors of adherence (Bem, 1970).

The central place given to the sensory experience and embodiment in the dynamics of the conversion and religious transmission, which appears prominently in the case of the hallucinogenic rites, has been observed by the ethnographic works in various cultural areas (Luhmann, 1991, 2012; Csordas and Harwood, 1994; Huang, 2003; Mahmood, 2011; Kopenawa, 2013). Although it is thus not restricted to the religious movements proper to the Western modernity, it constitutes, however, one of the characteristic features of it, particularly salient in the new religious movements of New Age inspiration (Luhmann, 1991). Their settings often surround the ritual practices with discursive sequences explaining the ontological, etiological and therapeutic belief system associated with these practices, while paradoxically underlining the importance of the individual's sensory experience, which is here a decisive normative criterion (Houseman, 2012). The adherence to the belief system exposed during the discursive sequences is then supported by the bodily experience. The latter, charged with sensory and emotional intensity induced by the participation in the ritual practices, is frequently seen as a concrete and tangible verification of the local belief system.

This singular economy of adherence, which I called here *experiential verification*, characterizes a Western religious modernity marked by the growing importance of individual experience and the rejection of a strictly propositional adherence, which until then supported inherited religious identities (Hervieu-Léger, 1999). These observations contrast with the representational conceptions of religious transmission diffused by so-called cognitive anthropology in recent decades (Sperber, 1996; Boyer, 2001; Atran, 2005), which has reduced this dynamic to a set of automatic mental and propositional operations (Severi, 2004). The dynamic of enculturation supported by the psychedelic rituals draws our attention to the aspects neglected by this approach: the social interactions processes, their ecological factors and their experiential underpinnings (Dupuis, 2021).

Psychedelic Rituals as Suggestibility Techniques

A remarkable property of psychedelics seems to play a central role in that experiential verification dynamic: their ability to increase suggestibility. This property, already observed by the first wave of research on these substances (Leary, 1961), has been further emphasized in contemporary research studies (Carhart-Harris et al., 2015; Timmermann et al., 2021). These works claim that, like hypnosis (Lynn et al., 2015), psychedelic substances produce a state of enhanced suggestibility²⁴. Drawing on cross-cultural data analysis, Grob and Dobkin de Rios (1992); Dobkin de Rios and Stachalek (1999), and Dobkin de Rios et al. (2002) have suggested that hallucinogenic substances are used by many indigenous groups to create hypersuggestible states of

consciousness, in order to promote fast-paced socialization for religious or pedagogical purposes, as enculturating adolescents during puberty rituals led by elders.

The example of Adrien's journey at Takiwasi shows that the psychedelic ritual leads to the progressive emergence of experiences whose very content – as well as the interpretation they are subject to – are shaped by the explicit (discourses) and implicit (ritual actions) suggestions of the local epistemic authorities. The state of *hypersuggestibility* induced by psychedelics seems to play a key role here. As we could see, Adrien's psychedelic experience is indeed progressively shaped by social interactions, and in particular by the suggestions of people perceived as epistemic authorities. The interactions with the ritual specialist, by describing part of Adrien's experience of reality as the result of “parasitic” beings influence, is here a driving force. The infestation diagnosis, at first received with circumspection by Adrien, provokes indeed, in a dynamic evoking a form of “epistemic gaslighting”²⁵ (Spear, 2019), a process of (self)-doubt and epistemic destabilization, eventually leading the participant to verify in an embodied fashion the belief system proposed by the ritual authority.

If the ritual experience is initially lived by the participant as a confusing one, the latter is then progressively shaped by the reverberating interplay of the participants' accounts of his experiences and the comments of the ritual specialists, who gradually inscribe it in the local belief system. The “socialization of hallucinations” (Dupuis, 2021) dynamic can be clearly observed here: involvement in ritual and discursive interactions implies an education of attention and an associative learning that progressively shapes the inferences governing the apprehension of the psychedelic experience. The participant learns to spot the signs of culturally postulated entities' presence first in the ritual context, then in his past and daily life. It is this concrete and tangible verification through the psychedelic ritual experience that finally leads Adrien to adhere to the local belief system. I claim consequently that the state of hypersuggestibility induced by psychedelics, by enhancing the susceptibility to the influence of external interpretations of one's experiences, is a driving force in the socialization of hallucinations dynamic, and thus in the dynamics of transmission of beliefs, which, as we have seen, is here conditioned on the experiential verification of the object of belief.

²⁴Suggestibility is understood here in its minimal definition, as a person's propensity to respond positively to suggested communications, i.e., thinking and acting following the suggestions of others (Sidis, 1898).

²⁵Spear (2019) has emphasized the epistemic dimension of what popular psychology refers to as “gaslighting,” i.e., the process through which an agent lead another one to accept that its cognitive faculties, perceptions, judgments, and grasp of its own situation are deficient. This process, occurring in many interpersonal contexts involving trust or authority, has the consequence to build an authoritative relationship, by leading those who are subject to it to internalize a view of themselves that both neutralizes their ability to criticize authority figure and ensures their consent to the perspective proposed by this figure. As Robbins and Anthony (1980) had already observed, the practice of exorcism (which is based in Takiwasi on the diagnosis of infestation) is ironically reminiscent in this respect of the deprogramming practices carried out by the anti-cult movements in the 1970s. The notions of brainwashing and demonic entities are indeed both occult notions that lead to thinking of the individual as unconsciously manipulated by malevolent forces, and that legitimize practices of rehabilitation of behavior perceived as deviant.

CONCLUSION: THE VARIABLE DESTINIES OF PSYCHEDELIC BELIEF TRANSMISSION AND ITS ETHICAL STAKES

Drawing on an ethnographic case-study, I sought in this article to shed light on the vectors through which psychedelics supports persuasion, enculturation and belief transmission dynamics. Proposing to approach psychedelic rituals as *suggestibility techniques*, I claimed that the property of hallucinogens to produce a state of hypersuggestibility strongly supports these dynamics. It seems to be this remarkable property of psychedelic substances that has led the defenders of these practices to extol their “therapeutic” and “transformative” virtues, and their detractors to denounce them as vectors of “mental manipulation.”

Even if the psychedelic ritual strongly increases the suggestibility of participants, the psychedelic experience is far from inducing a sudden conversion and automatic persuasion, but seems rather lead most participants to an oscillating indetermination mobilizing the reflexivity and agentivity of the recipient. As illustrated by Adrien’s case, the psychedelic ritual leads participants to an oscillation between doubt and adherence which is paradoxically a driving force in the belief transmission dynamic. The dynamic of belief transmission relies indeed ultimately on the recipient’s efforts to verify the object of the belief through an *experiential verification* process. As we could see, this verification process relies on the socialization of hallucinations dynamic, which is sustained by the properties of psychedelics to enhance suggestibility.

The belief transmission based on the psychedelic ritual in Takiwasi, although frequently successful, is however, far from being automatic. The adherence aroused by the hallucinogenic experience appears rather as the fact of a progressive learning, carried out in a more or less fast and complete way according to the participants, and which will be moreover never accomplished by many of them. If the cases of “conversion” based on the hallucinogenic experience, exemplified here by Adrien, illustrate a very recurrent pattern in Takiwasi, this case should consequently not hide important inter-individual variations. The testimonies of the participants underline a great diversity in the importance given to the various elements composing the local belief system, which is far from being reduced to the pattern of infestation. In the course of my investigation in Takiwasi, I saw many of them being disappointed by the propositions of local epistemic authorities. As illustrated by the testimonies of participants stating during our interviews that they “will never come back to Takiwasi again,” the local belief system, and in particular the central place given to the motif of demonic possession, arouses in some of them a strong and definitive opposition. These observations highlight the continuing relevance of the proposals of the culture-and-personality school theorists (Kardiner, 1939; Piotrowski, 1946), which have shown that people always socialize on a selective basis: as they react according to various idiosyncratic factors, they participate actively in the dynamics of cultural evolution.

If by producing a community of experience and ensuring the transmission of a belief system, psychedelic rituals appears as powerful potential vectors of affiliation to the social group, the long-term maintenance of membership is also subject to great variability. In following up through interviews some of the seminar participants several years after their trip to the Amazon, I was struck by the great diversity in the credence they gave to the belief system they seemed to have adhered to during their stay at Takiwasi. The specificity of the French context, which is marked by the association of these practices with “sectarian drifting” by the public authorities, plays here a certain role. Back to France, the participants were often seized by doubt: had they had a spiritual and therapeutic experience, or had they been the object of “cult manipulation,” deluded by “hallucinogenic” substances? The long-term follow up of the participants’ journey shows that the fate of membership to what many of participants called “the Takiwasi spiritual family” is then relying on the frequency and maintenance of participation in the practices they experienced in Peru. In order to maintain this membership, participants must continue to participate in practices that are frowned upon in their own country. They have consequently to take the risk of breaking with the dominant representations of their social group of origin, and thus of being subjected to a socially stigmatizing identity: that of a follower of a “cult.” These elements are undoubtedly a driving force in the fact that many of them abandon, after some time, the belief system they adopted during their stay in Peru. Beyond the particular case of Takiwasi, these observations underline, as much as the power of the psychedelic experience in the dynamics of belief transmission, the central role of social interactions and institutions in the maintenance of adherence.

These few points show that although psychedelics strongly support belief transmission by enhancing suggestibility, this dynamic can’t be described adequately with the model of brainwashing, which has recently been associated with the use of psychedelics by some European public authorities and anti-cult associations. This controverted model, drawing on automatist dynamic inspired by behaviorist theories of learning, turns psychedelic users into automatons devoid of reflexivity and agentivity, passive carriers of cultural transmission which leads them mechanically to assent to a belief system. In contrast with this model, we could see here that the belief transmission dynamic is here extremely labile, woven of reflexivity and ambivalence. It seems finally that by denying the subject an agency of its own and by neglecting the active dynamism constitutive of cultural transmission, the brainwashing model prevents understanding belief transmission and religious conversion based on psychedelic experience. This dynamic can be best on psychedelics can be best understood in the light of social influence processes long studied by social psychology (Turner, 1991; Rashotte, 2007), which are here potentiated by the remarkable properties of these substances, as the hypersuggestibility state that they produce.

These observations highlight that despite its common usage in psychology and psychiatry, and the few attempts to apply this notion to anthropological analysis, the concept of suggestibility and its implications in the field of psychedelic studies deserves

to be further explored²⁶. While the ability of psychedelics to increase suggestibility (Leary, 1961; Grob and Dobkin de Rios, 1992; Carhart-Harris et al., 2015; Dupuis, 2021) and the weight of extra-pharmacological factors in the hallucinogenic experience (Hartogsohn, 2016) have been known for a long time, this feature raises indeed ethical concerns about the kind of influence therapists, shamans and other facilitators are having over their clients, even when therapy goes well. In a paper recently written with some colleagues (Timmermann et al., 2020), we argued that the specific features of the psychedelic experiences may act as a *double-edged sword*. While it may drive therapeutic benefits, the ability of psychedelics to induce hypersuggestibility as feelings of reverence and revelation might lead to problematic effects in the absence of ethical guidelines regulating their use, especially considering the blurry distinction between accepted and forced persuasion. In the context of the current globalization of psychedelics and while legal restrictions around these substances are now slowly relaxing in the countries making up the Global North, it now seems essential to think of ethical frameworks regulating the use of psychedelics, beyond the prohibitionist logic held in recent decades. In light of the remarkable properties of psychedelics highlighted in this article and the dynamics of “epistemic gaslighting” that they seem to facilitate, the question that should guide these considerations is not “does psychedelic brainwashing exist?” but rather: to what degree can people be influenced through the use of psychedelics? What are the individual and relational factors that result in

the strongest influence? Does the conditions of persuasion are ethical?²⁷

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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²⁶ A recent model of the brain action of psychedelics inspired by predictive coding, known as REBUS – which proposes that psychedelics render high-level beliefs and assumptions more plastic, and that this process is a driving force underlying their phenomenological effects and potential therapeutic outcomes –, may provide some inspiration for further investigations of the neurobiology of belief change processes under psychedelics and their link to increased suggestibility (Carhart-Harris and Friston, 2019; Timmermann et al., 2021).

²⁷ An important criteria for determining the ethical character of psychedelic persuasion could be: is the subject aware that a process of persuasion and transmission of beliefs is here at work? Has this been clearly explained before participating in the psychedelic ritual and has the subject been able to give informed consent to this process?

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Examining Psychedelic-Induced Changes in Social Functioning and Connectedness in a Naturalistic Online Sample Using the Five-Factor Model of Personality

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The present study examines prospective changes in personality traits relevant to social functioning as well as perceived social connectedness in relation to the naturalistic use of psychedelic compounds in an online volunteer sample. The study also examined the degree to which demographic characteristics, social setting, baseline personality, and acute subjective factors (e.g., emotional breakthrough experiences) influenced trajectories of personality and perceived social connectedness. Participants recruited online completed self-report measures of personality and social connectedness at three timepoints (baseline, 2 weeks post-experience, 4 weeks post-experience). Linear mixed models were used to examine changes in outcomes and the moderation of these outcomes by covariates. The most substantive changes were reductions in the personality domains Neuroticism, and increases in Agreeableness and social connectedness. Notably, reductions in Neuroticism and increases in Agreeableness covaried over time, which may be suggestive of common processes involving emotion regulation. Preliminary evidence was found for a specific effect on a component of Agreeableness involving a critical and quarrelsome interpersonal style. Although moderation by demographic characteristics, social setting, baseline personality, and acute factors generally found limited support, baseline standing on Neuroticism, perspective taking, and social connectedness showed tentative signs of amplifying adaptive effects on each trait, respectively. Our findings hold implications for the potential use of psychedelics for treating interpersonal elements of personality pathology as well as loneliness.

Keywords: psychedelic, personality change, prospective, social functioning, Five-Factor Model

INTRODUCTION

Research on serotonergic psychedelics has accelerated in the last decade (Carhart-Harris and Goodwin, 2017) due to promising demonstrations of psychotherapeutic effects, and relaxed legal restriction on scientific investigation (Nutt et al., 2013). Research in this area has mainly focused on contributions to individual utility, including gains in personal well-being (e.g., Griffiths et al., 2011), personality (e.g., Erritzoe et al., 2018), and remediation of mental health disorders including alcohol misuse (Bogenschutz et al., 2015), major and resistant depression (e.g., Carhart-Harris et al., 2016a, 2021; Davis et al., 2020), and end of life anxiety/depression (e.g., Griffiths et al., 2016). A smaller and growing area of psychedelic research has explored how psychedelic compounds may confer value to both individuals and collectives through such outcomes as enhanced cooperation, trust, and social connectedness within interpersonal systems (referred to here as collective functioning).

Collective functioning can conceivably be enhanced directly through mutual participation in group-format psychedelic experiences (e.g., ayahuasca ceremony, group recreation; e.g., Kettner et al., 2021), and/or indirectly *via* the development of traits in individuals related to social functioning. The present study focuses on the latter path, wherein the link between psychedelic use and collective functioning may be mediated by enhanced social functioning at the individual level. Social functioning is defined as the ability to fulfill important roles within environments of social activity, work, and relationships (Bosc, 2000), but will be used more broadly here to describe personality traits that subserve harmonious relationships including empathic ability, prosociality, low anger reactivity, and moral reasoning. Improved social functioning is assumed to promote positive individual and collective outcomes through augmenting interpersonal trust, social connectedness, relationship longevity, and emotional fulfillment in social interaction. The purpose of this study is to investigate the degree to which naturalistic use of psychedelic compounds results in adaptive changes in personality traits relevant to social functioning and perceived social connectedness. Because personality change effects may depend on other measurable factors, we also examine the degree to which predisposing factors, such as demographic characteristics and baseline personality, and acute subjective factors, such as non-ordinary states of affect and consciousness during psychedelic experience, moderate changes.

A useful framework for our examination lies in the Five-Factor Model (FFM; Costa and McCrae, 1992) of personality, which includes three personality domains that possess empirical support for subserving social functioning. Neuroticism describes a disposition toward negative emotionality and stress reactivity; Extraversion describes a disposition toward positive emotionality, reward sensitivity, and receiving social attention; and Agreeableness describes a prosocial and communal (versus antagonistic) tendency to be considerate of others' needs, desires, and feelings, and is neurocognitively associated with social information processing (e.g., DeYoung, 2010; DeYoung et al., 2010). In the context of relationships, low Extraversion (being withdrawn) and low Agreeableness are associated with peer

rejection (Newcomb et al., 1993), and higher levels of Extraversion are associated with social acceptance and network size, popularity, and dating variety (e.g., Anderson et al., 2001; Paunonen, 2003; Feiler and Kleinbaum, 2015). In the context of romantic relationships, Agreeableness has shown relations with relationship satisfaction (e.g., Cramer and Jowett, 2010; Kimmes et al., 2014). Consistent with this, Neuroticism and low Agreeableness have shown predictive relations with relationship dissatisfaction, conflict, and dissolution (e.g., Karney and Bradbury, 1995; Donnellan et al., 2004; Weiss et al., 2018), outcomes thought to be mediated by a positive feedback loop involving negative emotion and relationship distress (Robins et al., 2002).

In the context of larger groups, Agreeableness and Extraversion has been found to be related to cooperation, and Agreeableness shows evidence of being inversely related to hypercompetition (Ross et al., 2003). Agreeableness may be most relevant to social and collective functioning as it involves higher functioning in empathy, a disposition toward prosociality (or antisociality at its opposite pole), and is associated with relationship stability. Agreeableness bears substantial overlap with affective and cognitive empathy, which, respectively, describe capacities to infer the emotional experience of others and to occupy the mental perspectives of others (e.g., Melchers et al., 2016). Agreeableness was also found to be elevated among young adult moral exemplars (Matsuba and Walker, 2004). At its opposite pole, low Agreeableness (or Antagonism) is thought to reflect the core of personality disorders such as Narcissistic Personality Disorder, Antisocial Personality Disorder, and psychopathy (e.g., Widiger et al., 2012), as well as Antagonistic Externalizing, one of two Externalizing spectra within the Hierarchical Taxonomy of Psychopathology (Kotov et al., 2017), a data-driven and integrative model of psychopathology. Antagonistic Externalizing describes tendencies toward engaging in criminal and antisocial acts involving theft, destruction of property, physical aggression toward others, and violations of rules of conduct (Widiger et al., 2012; Kotov et al., 2017). In sum, Neuroticism, Extraversion, and Agreeableness may be particularly relevant targets of inquiry when examining the effects of psychedelic compounds on social functioning.

There are four sources of empirical evidence that best inform the presence of a link between psychedelic use and enhanced social functioning. These include literature examining the effects of psychedelic compounds on FFM personality, social cognition, social connectedness, and moral behavior. The most relevant evidence to the present study is located in the personality literature. Eleven studies have prospectively examined long-term psychedelic-induced change in personality (e.g., MacLean et al., 2011; Madsen et al., 2020). Of these studies, five have shown evidence of adaptive change in Neuroticism or convergent constructs [e.g., Temperament and Character Inventory Harm Avoidance (characterized by worry)] (e.g., Barbosa et al., 2009; Erritzoe et al., 2018). Two studies have shown evidence of self-reported change in Extraversion (Erritzoe et al., 2018; Weiss et al., 2021), with change notably reflected in facets relevant to social functioning (Warmth/Friendliness, Gregariousness). Lastly, three studies have shown qualified evidence of increased Agreeableness (Carhart-Harris et al., 2016b; Netzband et al.,

2020; Weiss et al., 2021). Although peripherally relevant to our focus on social functioning, seven studies have found evidence for change in Openness (e.g., MacLean et al., 2011; Rocha et al., 2021; Weiss et al., 2021), whereas only one has found evidence of change in Conscientiousness (Barrett et al., 2020). Of note, some studies have found no meaningful evidence of longer-term change in personality (e.g., Schmid and Liechti, 2018; Rocha et al., 2021). In addition, numerous clinical studies, including randomized placebo-controlled trials, have provided support for an antidepressant effect (Andersen et al., 2021). Given that many psychopathological symptoms are increasingly conceptualized as maladaptive variants of basic personality dimensions and share the same structure (Widiger et al., 2012; Kotov et al., 2017), these latter results may be relevant to change in FFM Neuroticism and Extraversion. In sum, long-term psychedelic-induced changes in personality domains relevant to social functioning have been observed, but findings remain somewhat inconsistent. This inconsistency is likely to stem from multiple sources including study variability in sample size, sample type (general population, clinical, healthy), length of follow-up, conditions of administration, and inner experiences during the acute effects of the compounds. One major limitation of the existing literature is that sample size for prospective studies has been low ($N=25$), making it difficult to arrive at precise estimates of change (given high standard error), or to examine moderating factors predictive of change (given insufficient statistical power).

The second source of evidence lies in the area of social cognition. Existing findings are suggestive that psychedelic compounds modulate social cognition for up to a week following use. Specifically, behavioral and neurophysiological findings have shown that 5-HT_{2A} receptor agonists acutely produce attenuated processing of social rejection (based on self-report and dorsal anterior cingulate cortex; Preller et al., 2016) and negative facial expressions (based on self-report and N170, P300 evoked-response-potential; Komter et al., 2012; Dolder et al., 2016), which may be suggestive of downstream emotional resilience in social settings, greater levels of social approach, and lower avoidance. Studies have also been supportive of acute increases in emotional empathy (Dolder et al., 2016; Holze et al., 2021a). More recent research has shown evidence of post-acute changes in amygdala blood oxygen-level dependent response to emotional face stimuli, though the directionality of effects has differed across studies. One study showed reduced amygdala activations lasting at least a week following acute effects, but not longer than 1 month (Barrett et al., 2020). Another, examining patients with treatment-resistant depression, showed increased amygdala activations one day post dosing with psilocybin (Roseman et al., 2018). Collectively, these findings suggest that psychedelic compounds alter social cognition-related neural functioning sub- and post-acutely.

A third source of evidence observes changes in perceived social connectedness during and following psychedelic experience, a phenomenon that may be linked to changes in social cognition just described. In a large cross-sectional examination of festival-goers, Forstmann et al. (2020) showed that psychedelic compounds were unique among substances in producing

increased perceptions of social connectedness with other human beings broadly and with fellow event attendees. However, these effects obtained only for participants who endorsed using psychedelic compounds within the preceding 24 h, but not earlier, suggesting that social connectedness effects may be temporary. Although long-term changes in self-reported interpersonal closeness were found 6 months following the acute effects of psilocybin in one study (Griffiths et al., 2018), these findings remain tentative in view of failure to find a significant difference from the control group. Findings of increased perceived social connectedness are consistent with at least two sources of qualitative data demonstrating an enhanced sense of connectedness to significant others and other human beings, marked by openness to others, sociability, and authentic expression (Belser et al., 2017; Watts et al., 2017). Changes in perceived social connectedness may also be one manifestation of a general sense of connectedness that is described in qualitative reports (Belser et al., 2017) and instantiated in measures of mystical-type experience [i.e., unitive consciousness (or a sense of “oneness” or “unity”)].

A fourth source of evidence involves a small body of literature investigating whether psychedelic compounds promote moral reasoning and prosocial behavior. Findings from this body of literature have however been strongly mixed. Among the supportive findings, there is evidence of a long-term self-reported increase in altruism and positive social effects from three small prospective studies (Dolder et al., 2016; Griffiths et al., 2018; Schmid and Liechti, 2018), the latter of which demonstrated changes over and above a control group. Furthermore, in two large observational samples of criminal offenders, a diagnosis of hallucinogen use disorder was predictive of lower recidivism, violations of supervisory rules in a correctional setting, and future arrests involving intimate partner violence (Hendricks et al., 2014; Walsh et al., 2016). These findings may be suggestive of long-term reductions in Antagonistic Externalizing and Antagonism following psychedelic use. Nevertheless, despite being prospective studies, it is conceivable that other explanations can account for these observations, most notably that participants inclined to use psychedelic compounds already differed from other participants on traits associated with these outcomes before using. These findings stand in contrast to others that fail to support a link between psychedelic use and moral reasoning or behavior.

Although the 5-HT receptor system shows evidence of an involvement in harm aversion (self & other) and deontological (versus utilitarian) moral reasoning (Crockett et al., 2010, 2015), 5-HT_{2A} receptor agonists were not associated with greater aversion to harm others in the only existing examination containing a social moral dilemma task (though sample size was low, $N=33$; Pokorny et al., 2017). Furthermore, when offered the opportunity to express prosocial behavior through the allocation of redeemable lottery tickets and money to strangers, psychedelic users (within the aforementioned festival context) were no more likely to do so than other participants (Forstmann et al., 2020). Psychedelic users in this context also did not differ from others in ascribing moral praiseworthiness to deeds on the basis of the value of the deed's outcome for

others (versus the hedonic value of the deed for the agent). These findings are also consistent with null observer-rated changes in interpersonal perceptiveness, caring, anger expression, and compassion/social concern in a small prospective study (Griffiths et al., 2018). In sum, evidence is mixed with respect to psychedelic-induced improvements in moral reasoning and prosocial behavior. It may also be possible that substantive change occurs selectively in individuals higher in Antagonism (i.e., low Agreeableness).

The present study builds upon these findings through examining change in FFM personality domains relevant to social functioning as well as perceptions of social connectedness in a sample of 148 individuals recruited online. Our naturalistic approach enabled the collection of a larger sample through greater cost-effectiveness relative to laboratory-based studies, and provides an opportunity to gain insight into the effects of psychedelic use in the general population. Understanding how psychedelic experiences unfold outside of a controlled laboratory or shamanic setting—where harm reduction practices may be lacking—is ethically important as decriminalization/legalization policies expand use above and beyond already high prevalence in the West (Krebs and Johansen, 2013a,b; Winstock, 2017). In our study, a web-based survey—embedded within a purpose-built website—was used to measure outcomes and relevant moderators across five timepoints—including (1) 1 week before, (2) within 1 day before, (3) within a few days after, (4) 2 weeks after, and (5) 4 weeks after a psychedelic experience—among which study outcomes were measured 1 week before, 2 weeks after, and 4 weeks after. Using an integrated FFM framework, we also included outcomes conceptually and empirically related to FFM domains (e.g., measures of compassion and affective empathy enrich measurement of FFM Agreeableness). Our first aim was to examine change in personality traits related to social functioning and perceptions of social connectedness, as well as covariance between these sets of outcomes over time. We focused on Neuroticism, Extraversion, and Agreeableness in view of their relevance to social functioning. FFM Openness and Conscientiousness were also examined for comprehensiveness. In line with previous empirical and theoretical work (MacLean et al., 2011; Carhart-Harris et al., 2016b, 2021; Erritzoe et al., 2018; Forstmann et al., 2020; Netzband et al., 2020; Weiss et al., 2021) FFM Extraversion, Openness, Agreeableness, and perceived social connectedness were hypothesized to increase, and FFM Neuroticism was hypothesized to decrease following initial measurement.

Our second aim was to investigate factors that may potentiate or suppress personality change in relation to psychedelic experience. Few studies to date have rigorously examined potential moderators of change (e.g., subjective acute experiences, baseline personality) which may account for inconsistency in the literature and/or provide necessary conditions for change. Specifically, we examined the degree to which differences in FFM domains between timepoints varied as a function of an array of predisposing and acute factors. Predisposing factors relate to individual characteristics as well as psychological states, and spatial, temporal, and social contexts that may influence

the nature of an individual's experience. Acute factors relate to subjective psychological states arising under acute psychedelic effects. In line with previous work (MacLean et al., 2011; Erritzoe et al., 2018; Weiss et al., 2021), mystical-type experience was hypothesized to contribute to a larger difference in FFM Neuroticism, Extraversion, and Openness following 2 weeks and 4 weeks post-experience.

MATERIALS AND METHODS

Study Design

This was a prospective study design using opportunity sampling and web-based data collection. The inclusion criteria were: >18 years old, good comprehension of the English language, and having the intention to take a classic psychedelic drug (psilocybin/magic mushrooms/truffles, LSD/1P-LSD, ayahuasca, DMT/5-MeO-DMT, Salvia divinorum, mescaline, or iboga/ibogaine) in the near future. This approach provided the opportunity to collect a large amount of data in a non-controlled, naturalistic, and observational manner. The study consisted of a total of five surveys completed at different moments. The first survey was completed 1 week before the planned psychedelic experience (Baseline); the second survey was completed 1 day before the experience; the third survey was completed 1 day after the psychedelic experience; and the fourth and fifth surveys were completed 2 and 4 weeks following the experience.

Participants

The following sample sizes were collected for each of the five surveys, respectively, $N=654$, $N=535$, $N=379$, $N=315$, and $N=212$. To better capture substantive effects of psychedelic use, 39 participants were eliminated who reported use of a low dose. An additional seven participants were eliminated who reported use of a substance without sufficiently strong serotonergic 2A receptor affinity [MDMA (4), ketamine (2), ibogaine (1)]. The final sample consisted of 148 volunteer participants who provided data at all timepoints at which dispositional trait-based measures were administered (i.e., 1 week before experience, 2 weeks post experience, 4 weeks post experience). Because a larger number of participants reported on two timepoints versus all three, additional datasets were also used to examine change between baseline and 2 weeks post ($N=249$) and baseline and 3 weeks post ($N=162$). Unless otherwise noted, the $N=148$ sample was used for analyses. Demographic information is provided in **Table 1**. Information regarding the pharmacology of participants' psychedelic experiences is provided in **Table 2**.

Out of the total 741 participants who responded to any timepoint of the study, 576 (78%) dropped out or did not complete the first, fourth, or fifth survey. Because attrition can introduce sample bias and limit generalizability, analyses were conducted examining differences in study outcomes at baseline between the present sample and participants who did not complete the first, fourth, or fifth surveys. Results were indicative of significant differences ($p<0.05$) in one baseline

TABLE 1 | Demographic Information.

Variable	Level	# (% of sample)/ mean $\pm$ SD
Gender	Male	104 (71%)
	Female	43 (29%)
	Other	1 (0%)
Age		31.5 $\pm$ 11.9
Educational level	Left school before age 16 without qualifications	5 (3%)
	Some high school/GCSE level (in UK)	12 (8%)
	High school diploma/A-level education (in UK)	15 (10%)
	Some university (or equivalent)	26 (18%)
	Bachelor's degree (or equivalent)	55 (37%)
	Post-graduate degree (e.g., Masters or Doctorate)	35 (24%)
	Student	42 (28%)
	Unemployed	15 (10%)
	Part-time job	25 (17%)
Employment status	Full-time job	61 (41%)
	Retired	5 (3%)
	United States	33 (22%)
	United Kingdom	34 (23%)
Nationality	Denmark	20 (14%)
	Germany	6 (4%)
	Canada	7 (5%)
	Other (28 in total)	38 (26%)
Psychiatric history	Lifetime diagnosis of psychiatric illness	48 (32%)
	Never diagnosed	100 (68%)
Previous psychedelic use	Never (psychedelic naïve)	13 (9%)
	Once	10 (7%)
	2–5 times	27 (16%)
	6–20 times	28 (17%)
	More than 20 times	30 (18%)

personality item from the brief Ten-Item Personality Inventory (TIPI; Gosling et al., 2003). Completers exhibited lower TIPI Disorganized (i.e., higher Conscientiousness). However, this difference was not present when examining the larger datasets noted above ($N=249$ and $N=262$). Our results were consistent with previous work examining attrition-related sample bias in the present sample (Hübner et al., in press).¹ As a note, the present sample has been used in previous work (Haijen et al., 2018; Roseman et al., 2019).

Participant Recruitment and Dissemination of the Study

A website² called “psychedelicsurvey.com” was created in collaboration with a team of web designers, and a specific domain was created for this specific study, which we called

“global psychedelic survey” given the general nature of the sample and types of psychedelic use we were interested in capturing data on. This website contained all information needed for individuals to be informed about the study design, what was expected from participants and the informed consent. Once the informed consent was read and agreed on, individuals were able to sign up on the website by providing their name, email address and the date on which they expected to have their experience. Online advertisements, including a link to the main website that hosted the survey, were posted and shared on Facebook, Twitter, email newsletters, and online drug forums.^{3,4} Once participants signed up, they were included in an emailing system that was programmed to send out emails and reminders at specific times depending on the anticipated date of the psychedelic experience provided by the participants in the sign up process. Emails contained links to the relevant surveys, which were implemented and hosted by the online service system Survey Gizmo.⁵

Ethical Considerations

The aim of the present study was to sample variables associated with psychedelic drug use, without manipulating or promoting such use. A disclaimer text on the website was included stating: “This survey should not be viewed as advocacy of psychedelic drug use. Its aim is to sample people whose intent to take a psychedelic is already established.” Participants provided their name and email address in the sign up process; however, this information was not saved in the survey responses nor used while handling the data. These data were only used to personalize the emails needed to send out the relevant survey links. When emails were sent out including the survey links, a unique identification code was generated which was included in the survey links as a uniform resource locator. This offered the opportunity to identify and link multiple survey responses of one individual without sampling privacy-sensitive information. Furthermore, Survey Gizmo has features that protect the security of responses, in line with the ethics requirements. The study was approved by Imperial College Research Ethics Committee and the Joint Research Compliance Office at Imperial College London.

Measures

Unless otherwise noted, data for each measure were collected at the first, fourth, and fifth timepoints, and available for 148 participants.

Personality Outcomes

Ten-Item Personality Inventory

The TIPI (Gosling et al., 2003) consists of 10 items, with two items for each FFM domain: “Anxious, easily upset” and “calm, emotionally stable” index Neuroticism; “extraverted, enthusiastic,” and “reserved, quiet” index Extraversion; “critical, quarrelsome,”

¹Hubner, S., Haijen, E., Kaelen, M., Carhart-Harris, R., and Kettner, H. (under review). Turn on, tune in, and drop out: identifying predictors of attrition in observational psychedelic research. *Journal of Medical Internet Research*.

²www.psychedelicsurvey.com

³www.reddit.com/r/LSD

⁴www.reddit.com/r/Psyonaut7

⁵www.surveygizmo.eu

TABLE 2 | Pharmacology of sample's psychedelic experience.

		# (% of participants)
Compound type	LSD/1P-LSD	70 (47%)
	Psilocybin	34 (23%)
	Ayahuasca	17 (11%)
	DMT/5-MeO-DMT	5 (3%)
	Mescaline (Peyote, Huachuma/San Pedro)	6 (4%)
	Other	5 (3%)
Dose	A moderate dose	44 (30%)
	A high dose	63 (43%)
	A very high dose	19 (13%)
	An extremely high dose	11 (7%)
Psilocybin	1–1.99 grams	4
	2–2.99 grams	6
	3–3.99 grams	2
	5–5.5 grams	4
Truffles	1–15 grams	4
	15–29 grams	3
	30–45 grams	3
LSD/1P-LSD	60 µg	1
	100–199 µg	12
	200–299 µg	23
	300–400 µg	10
	800 µg	1

Exact dosage information was not available for the majority of participants; therefore % of participants was not given for these levels; µg = micrograms; % of participants uses $N = 148$ as the denominator.

and “sympathetic, warm” index Agreeableness; “open to new experiences, complex” and “conventional, uncreative” index Openness; “dependable, self-disciplined” and “disorganized, careless” index Conscientiousness. Participants rated each item on a 7-point Likert-scale (1 = Disagree strongly; 7 = Agree strongly). Previous research has demonstrated good test–retest reliability and convergent validity for TIPI domains (Ehrhart et al., 2009). More broadly, FFM traits have shown adequate test–retest reliability across an average interval of 4 weeks ($r_s > 0.77$; Gnambs, 2014), and longitudinal measurement invariance has been supported at the metric and scalar level in large samples (Lucas and Donnellan, 2011; Wortman et al., 2012). Unfortunately, consistent with past research (Gosling et al., 2003), internal consistency for three of five TIPI domains was low ([TIPI OpennessT1: $\alpha = 0.40$]; AgreeablenessT1: $\alpha = 0.37$; ConscientiousnessT1: $\alpha = 0.48$). Because heterogeneity in constructs can substantively obscure clear longitudinal changes and limit interpretation, we assessed TIPI items individually.

Empathic Concern and Perspective Taking

Two subscales from the Interpersonal Reactivity Index (IRI; Davis, 1983) were used to measure empathy and enrich measurement of FFM Agreeableness. IRI Empathic Concern is a 7-item subscale (e.g., “I am often quite touched by things that I see happen”) that measures affective empathy. Given high empirical overlap between IRI Empathic Concern and FFM Agreeableness, IRI Empathic Concern was considered to be reflective of Agreeableness (Mooradian et al., 2011; Melchers et al., 2016). More modern personality models have distinguished between two inter-related but distinct components of

Agreeableness, namely Compassion and Politeness (DeYoung et al., 2007). Although no specific empirical work exists, IRI Empathic Concern is conceptually similar to BFAS Compassion (versus BFAS Politeness) and FFM facets of Tender-Mindedness, Altruism, and Trust (Judge et al., 2013). IRI Perspective Taking is a 7-item subscale (e.g., “I try to look at everybody's side of a disagreement before I make a decision”) that measures cognitive empathy. Given moderate overlap between IRI Perspective Taking and FFM Agreeableness (Mooradian et al., 2011; Melchers et al., 2016) and the relevance of cognitive empathy to the present study, IRI Perspective Taking was also included in analyses, but was not considered directly reflective of Agreeableness. Participants rated each item on a 5-point Likert scale (1 = Does not describe me well; 5 = Describes me very well). Internal consistency (α) for IRI EC and IRI PT ranged from 0.81 to 0.85 across timepoints.

Compassion

The Santa Clara Brief Compassion Scale (SCBCS; Hwang et al., 2008) is a 5-item scale used to measure compassion. Items on the SCBCS were generated from Sprecher and Fehr's (2005) Compassionate Love Scale which assesses altruistic love toward others. Given high empirical overlap between SCBCS and IRI Empathic Concern (Hwang et al., 2008), as well as theoretical and empirical relations between the construct of compassion and FFM Agreeableness (e.g., DeYoung, 2010; Judge et al., 2013), the SCBCS was treated as an index of the component of FFM Agreeableness involving Compassion (versus Politeness; Judge et al., 2013; DeYoung et al., 2007). Participants rated each item on a 7-point Likert-scale (1 = Not at all true of me; 7 = Very true of me). Internal consistency (α) ranged from 0.88. to 0.90 across timepoints.

Tellegen Absorption

The Tellegen Absorption Scale (MODTAS; Tellegen et al., 1991) is used to measure trait absorption. The etymology of absorption is rooted in the search for reliable personality correlates of hypnotizability (de Groh, 1989), but it soon became clear to scholars that absorption also bore high theoretical and empirical overlap with FFM Openness (e.g., Glisky et al., 1991). This work indicated that Absorption strongly overlaps with and therefore presents a good index of certain components of Openness (but not others), including aesthetic appreciation, fantasy, unusual associations, unconventional worldviews, and awareness of inner feelings; Absorption was not observed to overlap with intellectual curiosity, openness to unusual ideas, or liberal values. For brevity, only the 25 scored items were included in this survey. Participants rated each Absorption item on a 5-point Likert-scale (1 = Never, 5 = Very often). Internal consistency (α) ranged from 0.92 to 0.93 across timepoints.

Social Connectedness Outcomes

Social Connectedness

The Social Connectedness Scale (SCS; Lee and Robbins, 1995) is an 8-item scale that measures one's perceived sense of belongingness in relation to others and society (e.g., “Even

around people I know, I do not feel that I really belong”). Participants rated each item on a 6-point Likert scale (1 = Strongly disagree; 6 = Strongly agree). Scores were reverse-scored such that higher scores indicated greater social connectedness. Internal consistency (α) ranged from 0.94 to 0.95 across timepoints.

Relatedness

The Relatedness scale is a graphical scale that measures one's perceived sense of relationship with other human beings. The measure uses a 7-item Likert scale consisting of two circles (“Self,” “Other”) that progressively overlap (see **Supplementary Figure S1**). The scale has been used in previous work (Forstmann et al., 2020) and is a modified version of the “inclusion of others in the self” scale which assesses how strongly people include their romantic partners in their self-construal (Aron et al., 1991). Participants were asked to select the image that best describes their “current relationship with other human beings, in general.”

Moderators

Evaluation of Validity

Suggestibility

The Multidisciplinary Iowa Suggestibility Scale-Short (MISS; Kotov et al., 2004) was used to measure participants' susceptibility to internalize external influences. The MISS is a 21-item self-report scale that uses a 5-point Likert-scale (1 = Not at all; 5 = A lot). Internal consistency (α) was 0.85. Data were collected in the first survey.

Expectancy

Expectancy of favorable change was measured using one original item (“How confident are you that the upcoming psychedelic experience will have a long-lasting positive effect?”). Data were collected in the first survey.

Predisposing Factors

Set and Setting

An original 12-item measure was constructed to assess participants' cognitive and emotional relationship to their psychedelic experience to come. Previous factor-analytic work derived three parsimonious factors: Set (describing openness toward and psychological preparedness for the experience; 7 items; $\alpha=0.75$), Setting (describing positive feelings toward experience companions and planned environment; 3 items; $\alpha=0.74$), and Clear Intentions (describing strong and clear expectations; 2 items; $\alpha=0.46$). Participants rated each item on a visual analogue scale ranging from 0 (Strongly disagree) to 100 (Strongly agree). Data were collected in the second survey, and were available for 145 participants.

Motives

An original 10-item measure was constructed to assess the types of experiences participants sought to consciously create. Previous factor-analytic work derived three parsimonious factors: Spiritual connection (describing motivation for spiritual, religious,

nature-based, or growth-oriented experience; 4 items; $\alpha=0.56$), Recreation (describing motivation for social, fun, explorative experience; 3 items; $\alpha=0.37$), and Emotional (describing motivation for addressing difficult emotions; 3 items; $\alpha=0.48$). Participants rated each item using a 4-point Likert scale (1 = Not at all; 4 = Very much). Data were collected in the first survey.

Baseline Anxiety

A 6-item short version of the Spielberger State-Trait Anxiety Inventory (STAI-SF; Marteau and Bekker, 2020) was used to measure trait anxiety. Participants rated each item on a 4-point Likert scale (1 = Not at all; 4 = Very much). Internal consistency (α) was 0.85. Data were collected in the first survey.

Baseline Depression

The Quick Inventory of Depressive Symptoms-Self-Report-16 (QIDS; Rush et al., 2018) is a 16-item scale that measures severity of depressive symptoms within the preceding 7 days. Participants rated each item on a 4-point Likert scale whose content varies by item. The QIDS consisted of 9 subscales comprising one to four items. For subscales involving multiple items, the maximum score across the items was assigned. The QIDS total score represented the mean of the 9 subscales. Internal consistency (α) across these nine QIDS subscales was 0.81. Data were collected in the first survey.

Acute Factors

The following measures were sent to participants 1 day after they were due to have their psychedelic experience (third survey). Data for these measures were available for 137 participants.

Challenging Experience

The Challenging Experience Questionnaire (CEQ; Barrett et al., 2016) is a 26-item scale that measures unpleasant affective, cognitive, and somatic reactions to psychedelic compounds. Reactions include isolation, grief, physical distress, fear, insanity, paranoia, and death (e.g., “I had the feeling something horrible would happen”). The CEQ is derived from “challenging” items from other psychedelic questionnaires: Hallucinogen Rating Scale (HRS) (Strassman et al., 1994), Altered State of Consciousness questionnaire (Dittrich, 1998), and States of Consciousness Questionnaire (Pahnke et al., 1969; Griffiths et al., 2006). Participants rated each item on a 6-point Likert-scale (1 = None, not at all; 5 = Extreme, more than any other time in my life). Internal consistency (α) was 0.95.

Emotional Breakthrough

The Emotional Breakthrough Inventory (EBI; Roseman et al., 2019) is a 6-item scale that measures productive engagement with emotional problems (e.g., “I felt able to explore challenging emotions and memories”). Participants rated each item on a visual analogue scale ranging from 0 (No, not more than usually) to 100 (Yes, entirely or completely). Internal consistency (α) was 0.93.

Mystical Experience

The Mystical Experience Questionnaire (MEQ; MacLean et al., 2012; Barrett et al., 2015) is a 30-item scale that measures mystical aspects of participants' experiences. The MEQ's items were originally represented on the Pahnke-Richards MEQ (Pahnke, 1969; Richards, 1975). In line with psychometric work (Barrett et al., 2015), four subscales were assessed: Mystical (15-item; e.g., "Experience of the fusion of your personal self into a larger whole"), Positive mood (6-item; e.g., "Sense of awe or awesomeness"), Transcendence of time and space (6-item; e.g., "Loss of your usual sense of space"), and Ineffability (3-item; e.g., "Sense that the experience cannot be described adequately in words"). Participants rated each item on a 6-point Likert scale (1=None, Not at all; 6=Extreme, more than any other time in your life and stronger than 5). Internal consistency (α) ranged from 0.89 (Time Space) to 0.96 (Mystical).

Dosage

One original item was used to measure approximate dosage of participants' use. Participants rated their dose on a 5-point response scale [1=A low dose (equivalent to 50 micrograms LSD); 5=Extremely high dose (equivalent to 300 micrograms LSD)]. Data were collected in survey three.

Analytic Plan Analyses

Four sets of analyses were planned. To reduce Type I error, across analyses, a statistical significance threshold was set at $p < 0.005$ (Benjamin et al., 2018), whereas $p < 0.01$ was set for hypotheses. The first set of analyses examined the degree to which personality and perceived social connectedness outcomes changed in relation to psychedelic experience. Linear mixed models were conducted (equivalent to one-way repeated measures ANOVA) to determine the persisting effects of psychedelic compounds on outcomes, comparing each outcome between each timepoint (baseline, 2 weeks post, and 4 weeks post). The full $N = 148$ dataset was principally used, containing participants who reported on outcomes at all timepoints. However, to maximize sample size and power, additional models were conducted in larger datasets to examine change between baseline and 2 weeks post ($N = 249$) and baseline and 4 weeks post ($N = 162$). Where the significance of results from the larger datasets contradicted results from the smaller ($N = 148$) dataset, results from the larger dataset were presented. The following indices of effect size were used: Unstandardized (B) coefficients indicate mean differences between timepoints. dz indicates effect size change in outcome scores in terms of the standard deviation of within-subject change scores (e.g., $T_2 - T_1$; Lakens, 2013). Cohen's d s (standard Cohen's d ; Cohen, 1988) effect size estimates were calculated using the following equation: $(\text{Mean-score}_{T_2} - \text{Mean-score}_{T_1}) / ((SD_{T_1})^2 + SD_{T_2})^{0.5}$. Marginal R^2 values were used to indicate the degree to which the fixed effect of Time accounted for variance in outcomes.

The second set of analyses used linear mixed models to examine moderating effects on time. Linear mixed effects models were conducted in which we included moderators as fixed covariates

to the base model (including Time). Three sets of moderator variables were examined including validity variables (including biases, expectancy, suggestibility), predisposing factors (including demographic variables, lifetime use of psychedelics, motives, baseline traits), and acute factors. For continuous moderators, unstandardized (B) coefficients were used to indicate the added effect of the moderator to the effect of time at one standard deviation above the mean of the moderator. For dichotomous moderators, unstandardized (B) coefficients were used to indicate the added effect of the moderator to the effect of time at one level of the moderator versus the other. Marginal R^2 values were used to indicate the degree to which fixed effect variables (i.e., Time, moderator) accounted for variance in outcomes.

The third set of analyses used regression to examine covariation between personality and perceived social connectedness outcomes over time. Change scores for each outcome were calculated by subtracting timepoint one (baseline) scores from timepoint three (4 weeks post), and correlations were subsequently calculated between each personality outcome and each social connectedness outcome. The fourth set of analyses calculated zero-order correlations among baseline outcomes (Supplementary Table S1).

Power Analyses

Post hoc power analyses (using "simr" package in R) were conducted to assess power for the first and second sets of analyses. For each set of analyses, effect sizes sufficient to obtain 80% statistical power [α value $p = 0.005$ ($p = 0.01$ for hypotheses), using 100 Monte Carlo simulations] were estimated. Results indicated that the self-report sample was powered (80%) to accurately detect true differences between timepoints exceeding 0.10/0.12 (Tellegen Absorption), 0.12/0.14 (IRI Perspective Taking), 0.12/0.16 (IRI Empathic Concern), 0.13/0.15 (SCBCS Compassion), 0.15/0.19 (TIPI Reserved), 0.17/0.19 (TIPI Extraverted, TIPI Anxious), 0.17/0.21 (TIPI Calm), 0.17/0.24 (TIPI Disorganized), 0.18/0.20 (TIPI Sympathetic), 0.18/0.21 (TIPI Critical), 0.19/0.19 (SCS Social Connectedness), 0.19/0.23 (Relatedness, TIPI Conventional), 0.22/0.25 (TIPI Dependable) and 0.25/0.30 (TIPI Open-minded) standard deviations. The first value reflects power within the $N = 249$ sample (containing baseline and 2 weeks timepoints) and the second value reflects power within the $N = 162$ sample (containing baseline and 4 weeks timepoints). With respect to moderation-based analyses, analyses were powered (80%) to detect true interaction effects of small to medium size (standardized interaction coefficient effect size ranged from 0.13 to 0.30 across domains and moderators).

RESULTS

Examining Change in Personality and Social Connectedness

Results demonstrated that 2 weeks following psychedelic experience, TIPI Anxious ($B = -0.49$, $p < 0.0001$) and TIPI Critical ($B = -0.47$, $p < 0.0001$) were significantly lower; and TIPI Calm ($B = 0.22$, $p = 0.006$), TIPI Extraverted ($B = 0.23$, $p = 0.009$), Social

Connectedness ($B=0.19$, $p=0.008$), and Relatedness ($B=0.27$, $p=0.006$) were significantly higher. Four weeks following psychedelic experience, TIPI Anxious ($B=-0.55$, $p<0.0001$)

and TIPI Critical ($B=-0.56$, $p<0.0001$) remained significantly lower; and Social Connectedness ($B=0.18$, $p=0.008$) remained significantly higher. These results are shown in **Figure 1**, and

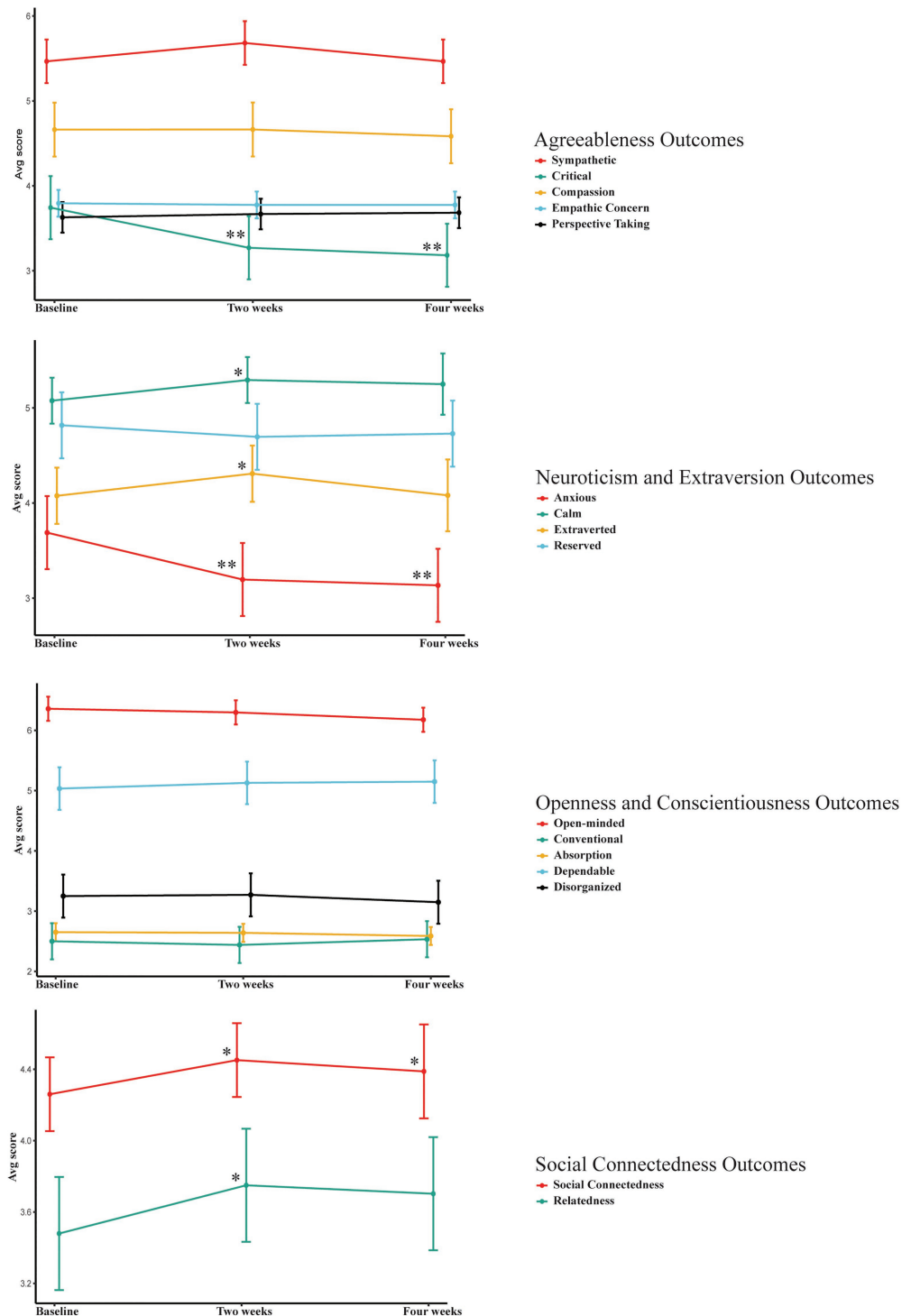


FIGURE 1 | Line plots illustrating change in outcomes. Error bars represent 99% confidence intervals around means for hypothesized outcomes including Agreeableness, Neuroticism, Extraversion, and Social Connectedness; and 99.5% confidence intervals around means for Conscientiousness and Perspective Taking. First and second sets of asterisks denote a significant difference between baseline and 2 weeks and 4 weeks, respectively, following psychedelic experience. * $p<0.01$; ** $p<0.005$.

expanded upon in **Tables 3** where 99% confidence intervals and effect size values (i.e., dz and Cohen's ds) are provided. Full results can be found in **Supplementary Table S2**.

Examining Moderation of Change

To investigate the degree to which change between timepoints depended on predisposing and acute factors, moderation by three sets of variables were examined including validity variables (including biases, expectancy, suggestibility), predisposing factors (including demographic variables, lifetime use of psychedelics, motives, baseline traits), and acute factors. Each of these sets will be examined in turn below. **Tables 4** and **5** are provided to show instances of significant moderation of differences between at minimum two timepoints, and to present change in marginal R^2 after adding interaction terms. Full results of significant moderation-based models are provided in **Supplementary Table S2**.

Validity Variables

With respect to validity variables, three types of variables were examined: biases, expectancies of change, and suggestibility. First, biases involving favorable attitudes toward psychedelic use (e.g., “I have an advanced knowledge about psychedelics”) did not contribute to overreporting of change, as intended in study design, but rather showed evidence of suppressing change in TIPI Calm and Social Connectedness. Specifically, participants endorsing advanced knowledge of psychedelics (Knowledge Bias) and high experience with psychedelic use (Experience Bias) exhibited higher baseline TIPI Calm, and showed no change in TIPI Calm at 2 weeks or 4 weeks, whereas participants denying advanced knowledge and high experience showed a greater increase in TIPI Calm at 2 weeks ($B=0.28$, $B=0.24$, respectively) and 4 weeks ($B=0.29$, $B=0.34$, respectively). For example, a one-standard-deviation decrease in self-reported “high psychedelic experience” was associated with an incremental 0.23 unit increase in TIPI Calm (on 7-point Likert scale) following 2 weeks and an incremental 0.34 unit increase following 4 weeks. Similarly, participants denying advanced knowledge of psychedelics showed a greater increase in Social Connectedness following 2 weeks ($B=0.23$), whereas participants endorsing

advanced knowledge showed no change. That is, a one-standard-deviation decrease in self-reported “advanced knowledge” was associated with an incremental 0.23 unit increase in SCS (on 6-point Likert scale) following 2 weeks.

Predisposing Factors

With respect to predisposing factors, five sets of variables were examined: demographic variables, lifetime psychedelic uses, set and setting, motives, and baseline traits. Lifetime psychedelic uses and baseline traits emerged as significant moderators.

With respect to lifetime psychedelic uses, a one-standard-deviation decrease in lifetime psychedelic uses amplified increases in IRI Perspective Taking by 0.11 and 0.09 units (on 5-point Likert scale) two and 4 weeks following psychedelic experience, respectively. Specifically, participants endorsing average to high frequency of previous psychedelic use showed no change in Perspective Taking, whereas participants endorsing low (~one-standard-deviation below mean) previous psychedelic uses exhibited significant increases in Perspective Taking following two and 4 weeks ($B_{T1-T2}=0.11$, $p=0.002$; $B_{T1-T3}=0.09$, $p=0.005$).

With respect to baseline traits, initial analyses were indicative of moderation by baseline traits in the cases of 14 of 16 outcomes. However, because regression to the mean is likely responsible for many of these trends in adaptive directions (e.g., participants high in baseline anxiety exhibiting amplified decreases in anxiety), subsequent tests were conducted. Effect size estimates were examined while excluding participants with extreme baseline scores most conducive to regression in an adaptive trait direction, namely above the 80th quantile of baseline TIPI Anxious, STAIT Anxiety, QIDS Depression, TIPI Reserved, TIPI Conventional, TIPI Critical, and TIPI Disorganized, and below the 20th quantile of the other outcomes. Next, moderation-based results were inspected using linear mixed models, plots, and pairwise contrasts. An adaptive moderation effect was deemed credible where (a) the interaction term remained statistically significant ($p<0.005$) and in the direction of an adaptive effect; and (b) significant ($p<0.005$) changes in an adaptive direction were present among participants at the maladaptive level of the moderator (e.g., where participants

TABLE 3 | Examining significant main effects of time.

Timepoint comparison	Outcome	B	99% CI	dz	ds
Baseline & 2 weeks post	TIPI Critical	-0.47**	-0.18,-0.77	-0.34	-0.19
Baseline & 4 weeks post	TIPI Critical	-0.56**	-0.26,-0.86	-0.39	-0.23
Baseline & 2 weeks post	TIPI Anxious	-0.49**	-0.20,-0.78	-0.37	-0.19
Baseline & 4 weeks post	TIPI Anxious	-0.55**	-0.27,-0.84	-0.39	-0.22
Baseline & 2 weeks post	TIPI Calm	0.22*	0.01,0.42	0.18	0.10
Baseline & 2 weeks post	TIPI Extraverted	0.23*	0.00,0.46	0.17	0.09
Baseline & 2 weeks post	Social Connectedness Scale	0.19*	0.01,0.37	0.17	0.11
Baseline & 4 weeks post	Social Connectedness Scale	0.18*	0.01,0.36	0.21	0.10
Baseline & 2 weeks post	Relatedness	0.27*	0.02,0.52	0.26	0.15

TIPI, Ten-Item Personality Inventory; CI, Confidence Interval; Unstandardized (B) coefficients indicate mean differences between timepoints. dz indicates effect size change in outcome scores in terms of the standard deviation of within-subject change scores (e.g., $T2-T1$; Lakens, 2013). Cohen's ds (standard Cohen's d ; Cohen, 1988) effect size estimates were calculated using the following equation: $(\text{mean-score } T2 - \text{mean-score } T1) / ((SDT1)^2 + (SDT2)^2)^{0.5}$. * $p<0.01$; ** $p<0.005$.

TABLE 4 | Incremental variance explained by moderators.

Moderator	Neuroticism		Extraversion		Agreeableness		Empathic		Perspective		Santa Clara		Social		Relatedness
	Anxious	Calm	Extra	Reserved	Critical	Sympath	Concern	Taking	Compassion	Connectedness					
Validity															
Pro-use Bias	0.001	0.001	0.012	0.004	0.001	0.013	0.039	0.035	0.036	0.015	0.045	0.058			
Therapy Bias	0.000	0.001	0.018	0.002	0.003	0.025	0.074	0.045	0.090	0.024	0.049	0.002			
Knowledge Bias	0.014	0.022	0.003	0.000	0.001	0.016	0.018	0.049	0.003	0.029	0.026	0.032			
Experienced Bias	0.085	0.067	0.031	0.004	0.000	0.006	0.026	0.061	0.041	0.058	0.061	0.020			
Expectancy	0.079	0.069	0.040	0.012	0.036	0.055	0.072	0.116	0.074	0.000	0.000	0.000			
Suggestibility	0.019	0.013	0.004	0.003	0.033	0.012	0.003	0.003	0.003	0.000	0.000	0.000			
Predisposing Factors															
Age	0.059	0.034	0.004	0.002	0.037	0.006	0.012	0.003	0.002	0.006	0.006	0.005			
Education Level	0.025	0.008	0.011	0.001	0.016	0.007	0.090	0.062	0.059	0.048	0.001	0.001			
Sex	0.018	0.005	0.003	0.004	0.030	0.048	0.036	0.014	0.023	0.014	0.001	0.001			
Psychedelic Naive	0.008	0.000	0.009	0.006	0.002	0.001	0.000	0.009	0.002	0.004	0.003	0.003			
Psychedelic Uses	0.070	0.029	0.034	0.007	0.004	0.003	0.027	0.029	0.029	0.022	0.008	0.008			
Set	0.082	0.071	0.031	0.017	0.002	0.017	0.007	0.005	0.003	0.042	0.007	0.007			
Setting	0.028	0.074	0.015	0.008	0.007	0.015	0.010	0.007	0.018	0.038	0.023	0.023			
Clear intentions	0.006	0.010	0.002	0.004	0.001	0.002	0.033	0.025	0.025	0.024	0.006	0.006			
Spiritual motive	0.036	0.032	0.090	0.039	0.005	0.026	0.085	0.052	0.088	0.019	0.063	0.063			
Recreation Motive	0.011	0.002	0.005	0.003	0.017	0.010	0.014	0.000	0.023	0.002	0.007	0.007			
Emotional Motive	0.056	0.038	0.014	0.021	0.002	0.002	0.001	0.001	0.004	0.023	0.001	0.001			
Respective Baseline Trait	0.677	0.688	0.704	0.684	0.621	0.624	0.829	0.818	0.808	0.640	0.613	0.613			
Baseline STAIT Anxiety	0.382	0.325	0.051	0.004	0.024	0.021	0.005	0.031	0.005	0.145	0.031	0.031			
Baseline QIDS Depression	0.289	0.203	0.054	0.012	0.006	0.014	0.012	0.019	0.005	0.156	0.025	0.025			
Acute Factors															
Challenging Exp	0.034	0.046	0.028	0.023	0.002	0.006	0.003	0.002	0.005	0.022	0.005	0.005			
Emo Breakthrough	0.018	0.004	0.002	0.007	0.007	0.008	0.029	0.021	0.021	0.004	0.011	0.011			
Mystical	0.023	0.026	0.026	0.012	0.003	0.036	0.101	0.140	0.084	0.029	0.048	0.048			
Positive Mood	0.025	0.040	0.031	0.016	0.006	0.020	0.056	0.161	0.048	0.024	0.019	0.019			
Time-space	0.005	0.004	0.009	0.004	0.001	0.020	0.009	0.025	0.007	0.009	0.021	0.021			
Ineffability	0.003	0.008	0.001	0.001	0.022	0.002	0.001	0.007	0.006	0.002	0.004	0.004			
Dosage	0.001	0.022	0.014	0.017	0.001	0.001	0.016	0.011	0.014	0.016	0.021	0.021			

Bolded/italicized marginal R² values are indicative of instances of significant moderation at p < 0.005 threshold. Italicized marginal R² values for Respective Baseline Trait moderators denote a significant interaction term that is significant at p < 0.005 threshold and survived tests of regression to the mean. Marginal R² values indicate the degree to which fixed effect variables (e.g., Time, moderator) account for variance in outcomes. Extra = Extraverted; Sympath = Sympathetic.

TABLE 5 | Incremental variance explained in outcomes related to openness and conscientiousness by moderators.

Moderator	Openness		Tellegen	Conscientiousness	
	Open-minded	Conventional	Absorption	Dependable	Disorganized
Validity					
Pro-use Bias	0.018	0.005	0.005	0.004	0.017
Therapy Bias	0.002	0.005	0.020	0.009	0.006
Knowledge Bias	0.008	0.065	0.026	0.019	0.004
Experienced Bias	0.048	0.023	0.023	0.031	0.008
Expectancy	0.030	0.037	0.086	0.046	0.010
Suggestibility	0.005	0.061	0.018	0.041	0.032
Predisposing Factors					
Age	0.008	0.017	0.000	0.008	0.072
Education Level	0.020	0.027	0.001	0.001	0.008
Sex	0.010	0.023	0.029	0.003	0.008
Psychedelic Naïve	0.005	0.008	0.007	0.000	0.029
Psychedelic Uses	0.028	0.013	0.023	0.008	0.003
Set	0.023	0.014	0.003	0.031	0.003
Setting	0.035	0.042	0.020	0.047	0.041
Clear Intentions	0.003	0.001	0.000	0.007	0.049
Spiritual Motive	0.028	0.045	0.145	0.013	0.000
Recreation Motive	0.005	0.016	0.000	0.004	0.012
Emotional Motive	0.002	0.005	0.006	0.034	0.007
Respective Baseline Trait	0.366	0.596	0.855	0.569	0.654
Baseline STAIT Anxiety	0.028	0.006	0.004	0.066	0.013
Baseline QIDS Depression	0.018	0.008	0.012	0.089	0.058
Acute Factors					
Challenging Exp	0.015	0.012	0.045	0.001	0.005
Emo Breakthrough	0.020	0.059	0.057	0.003	0.007
Mystical	0.008	0.058	0.134	0.011	0.006
Positive Mood	0.002	0.016	0.034	0.010	0.002
Time-space	0.001	0.030	0.065	0.006	0.002
Ineffability	0.002	0.008	0.000	0.004	0.001
Dosage	0.004	0.001	0.009	0.008	0.033

Bolded/italicized marginal R^2 values are indicative of instances of significant moderation at $p < 0.005$ threshold. Italicized marginal R^2 values for Respective Baseline Trait moderators denote a significant interaction term that is significant at $p < 0.005$ threshold and survived tests of regression to the mean. Marginal R^2 values indicate the degree to which fixed effect variables (e.g., Time, moderator) account for variance in outcomes.

one standard deviation above the mean of baseline anxiety showed significant decreases in anxiety). Only moderated change between baseline and 4 weeks post is reported and interpreted. Adaptive moderation effects that survived these tests of regression to the mean were found for TIPI Anxious, TIPI Calm, IRI Perspective Taking, and Relatedness (see **Supplementary Table S1** for detailed results). Using the full dataset, pairwise contrasts were calculated to examine temporal changes in outcomes at different levels of these baseline traits. Participants who presented to the study with high (i.e., ~ one-standard-deviation above mean) baseline TIPI Anxious exhibited statistically significant reductions in these items following 4 weeks ($B_{T1-T3} = -0.75$, $p < 0.0001$). Similarly, participants with low (~one-standard-deviation below mean) baseline TIPI Calm ($B_{T1-T3} = 0.67$, $p < 0.0001$), IRI Perspective Taking ($B_{T1-T3} = 0.21$, $p < 0.0001$), and Relatedness ($B_{T1-T3} = 0.63$, $p < 0.0001$) exhibited significant increases in these items following 2 and 4 weeks. Notably, TIPI Anxious was the only outcome for which adaptive change was also found among participants who exhibited average baseline scores. These results are, however, considered tentative given the likely influence of regression to the mean.

Acute Factors

With respect to acute factors, we examined moderation of temporal change in outcomes by Challenging Experience, Emotional Breakthrough experience, and mystical-type experience including MEQ Mystical, Positive Mood, Space Time, and Ineffability. Dosage was also examined in view of empirical effects on self-reported acute intensity, personal meaning, and spiritual significance (e.g., Griffiths et al., 2011). Only Emotional Breakthrough experience emerged as a significant moderator. Specifically, a one-standard-deviation increase in self-reported Emotional Breakthrough amplified decreases in TIPI Reserved by 0.34 units (on 7-point Likert scale) 4 weeks following psychedelic experience. Results indicated that a significant decrease in TIPI Reserved depended on participants' experience of emotional breakthrough, such that only participants who exhibited a one-standard-deviation increase in Emotional Breakthrough showed a meaningful change (decrease) in TIPI Reserved. Because Emotional Breakthrough did not evince an influence on other personality outcomes including the other Extraversion-based TIPI item, nor did it exhibit an effect on TIPI Reserved between Baseline and 2 weeks post, it is possible

that this effect is the product of Type I error, and as such, should be interpreted with caution.

Examining Covariation Between Outcomes Over Time

Personality and Social Connectedness

To determine whether changes in outcomes covaried over time with other outcomes, we computed change scores between baseline and 4 weeks following psychedelic experience, and calculated the correlations between these change scores (Table 6). The $N=162$ sample was used. Two sets of analyses were conducted. First, we examined the degree to which each personality outcome covaried over time with Social Connectedness and Relatedness. Results indicated that Social Connectedness showed significant covariation over time with TIPI Anxious ($r=-0.23$, $p=0.003$), TIPI Extraverted ($r=0.27$, $p<0.0001$), TIPI Critical ($r=-0.22$, $p=0.004$), and TIPI Disorganized ($r=-0.26$, $p=0.001$). Second, we examined the degree to which personality outcomes covaried over time with each other. In this set, only personality traits that exhibited significant main effect change from previous analyses were examined. Results indicated significant covariation between TIPI Anxious and TIPI Critical ($r=-0.29$, $p<0.0001$) over time.

DISCUSSION

Meaningful prosocial changes were observed across a number of outcomes relevant to social functioning. Overall, participants reported decreases in critical and quarrelsome demeanor and anxiety and mood lability, and increases in perceived social connectedness. Preliminary evidence was additionally found for increases in cognitive empathy, but only among participants initially low in this trait. Adaptive changes in neuroticism and perceived social connectedness also showed signs of being amplified among participants starting with less adaptive initial levels of these traits. We expand upon these findings within

the context of four main questions: (a) Is psychedelic use related to changes in personality traits relevant to social functioning? (b) Is psychedelic use related to change in perceptions of social connectedness? (c) Is change in personality connected to change in perceived social connectedness? and (d) Are there factors that predispose or potentiate change in social functioning-related traits and perceived social connectedness?

Is Psychedelic Use Related to Changes in Personality Traits Relevant to Social Functioning?

Two personality domains with strong relevance to social functioning (neuroticism, agreeableness) displayed substantive, small-sized, changes in the direction of enhanced social functioning. First, agreeableness was measured using four outcomes including TIPI Critical Quarrelsome, TIPI Sympathetic Warm, compassion, and empathic concern. TIPI Critical Quarrelsome was the only outcome to decline substantively between baseline measurement and 2 weeks following psychedelic experience and remain substantively below baseline scores 4 weeks following use. Although limited internal reliability for this single-item outcome qualifies interpretation, this result is suggestive of components of agreeableness that are particularly susceptible to psychedelic change processes. According to the Big Five Aspects model (BFAS; DeYoung et al., 2007), a data-driven model of personality, each FFM domain can be divided into two distinct, but interrelated, components that hold superior parsimony relative to FFM facets, and greater granularity relative to broad FFM domains. For agreeableness, these components represent aspects Compassion (versus Callousness) and Politeness (versus Belligerence). Notably, TIPI Critical Quarrelsome is the only measured outcome that, based on rational analysis, conceptually captures the Politeness aspect of agreeableness, whereas the other agreeableness outcomes capture the Compassion aspect. At its low pole, Politeness, like the TIPI Critical Quarrelsome item, describes an antagonistic and conflict-prone style of interpersonal relating that seeks to express judgment, demonstrate superiority, and gain advantage.

Our results are the first in the literature to suggest a specific decrease in criticism and quarrelsomeness following psychedelic experience. Should psychedelic experience be most targeted to personality functioning in Politeness, it bears noting the clinical and forensic implications of this finding. Politeness, relative to Compassion, bears strongest relations with pathological personality traits most relevant to antagonistic personality disorders (e.g., Narcissistic Personality Disorder, Antisocial Personality Disorder) including attention seeking, grandiosity, manipulateness, deceitfulness, and hostility (e.g., DeYoung et al., 2016). As such, in this data, psychedelic use shows some signs of therapeutic potential for the treatment of personality disorders. Our data appears consistent with three studies that have shown qualified support for prospective increases in agreeableness (Carhart-Harris et al., 2016b; Netzband et al., 2020; Weiss et al., 2021), as well as work showing decreased levels of supervision failure among individuals involved in the

TABLE 6 | Examining covariation over time (baseline—four weeks) between personality and social connectedness outcomes using correlations between change scores.

Δ Personality outcome	Δ Social connectedness	Δ Relatedness
Δ TIPI Anxious	-0.23**	-0.07
Δ TIPI Calm	0.14	0.07
Δ TIPI Extraverted	0.27**	0.12
Δ TIPI Reserved	0.14	0.07
Δ TIPI Critical	-0.22**	-0.02
Δ TIPI Sympathetic	0.22*	0.17'
Δ IRI Empathic Concern	0.03	0.05
Δ IRI Perspective Taking	0.10	0.17'
Δ Santa Clara Compassion	0.14	0.16'
Δ TIPI Open-minded	0.05	0.07
Δ TIPI Conventional	-0.12	-0.02
Δ Tellegen Absorption	0.03	0.17'
Δ TIPI Dependable	-0.06	-0.05
Δ TIPI Disorganized	-0.26**	0.00

$p<0.05$; * $p<0.01$; ** $p<0.005$.

justice system and intimate partner violence in the general population (Hendricks et al., 2014; Thiessen et al., 2018).

No other agreeableness outcomes exhibited meaningful change. One explanation for these results relates to restriction of range in these outcomes versus TIPI Critical Quarrelsome, such that participants in our sample tended to exhibit already above-average standing on TIPI Sympathetic Warm, compassion, and empathic concern, and thus may have possessed less potential for upward change in these traits (see **Supplementary Figure S2** for baseline density plots). Moderation analyses were accordingly conducted to examine whether participants with lower scores on these traits were more likely to exhibit significant upward change. No credible moderation was observed. Power analyses were additionally conducted to evaluate our capacity to form conclusions from these null results, namely that TIPI Sympathetic Warm, compassion, and empathic concern do not meaningfully respond to naturalistic psychedelic use. The results of our power analyses were suggestive that we were adequately powered to detect an interaction effect of small size ($b < 0.20$) for compassion and empathic concern if one was present. As such, our data provide preliminary support for the absence of meaningful longer-term change in compassion and empathic concern in the general population of psychedelic users. Furthermore, our null results with respect to adaptive change in affective empathy (indexed by IRI Empathic Concern) are convergent with previous evidence that explicit emotional empathy (a related construct) does not remain enhanced for longer than 1 week following psychedelic administration (Mason et al., 2019).⁶ It is notable that acute increases in explicit emotional empathy have been observed in three previous studies using the Multifaceted Empathy Test (MET; Dziobek et al., 2008) (Dolder et al., 2016; Pokorny et al., 2017; Mason et al., 2019). This raises the possibility that enhancements in affective empathy and compassion may be time-limited without additional maintenance practices.

Finally, perspective taking, a related construct capturing cognitive empathy (i.e., ability to occupy mental perspectives of others; IRI Perspective Taking), did show some signs of increasing in relation to psychedelic use for a subset of our sample. Although a main effect change in perspective taking was not observed, participants one standard deviation below the mean in baseline perspective taking exhibited substantive change in this trait. Although the measure we used involved subjective self-appraisal, our results provide preliminary evidence that psychedelic use may provide longer-term enhancements to cognitive empathy among individuals with low initial capacity. Of note, however, Mason et al. (2019) did not observe enhanced cognitive empathy 7 days post-psychedelic experience while using the MET cognitive task. We encourage researchers to examine whether a similar subset of individuals with low

standing on cognitive empathy exhibit substantive post-acute enhancements in objective task performance.

Collectively, this pattern of results may be suggestive that psychedelic experience in the general population is more likely to drive adaptive changes in Politeness versus Compassion. On a methodological level, the pattern raises the possibility that mixed findings within the literature may owe in part to imprecise measurement of agreeableness. Future research is accordingly called for that examines psychedelic-induced personality change using granular measurement sufficient to detecting possible differential effects on aspects (or facets) of personality.

Second, perhaps strongest support was found for adaptive change in neuroticism, with data showing small-sized, but substantive decreases in anxiety and mood lability (TIPI Anxious Easily upset) that remained significantly above baseline scores 4 weeks following psychedelic use. Our results are consistent with a number of previous prospective studies showing psychedelic-induced reductions in neuroticism (Barbosa et al., 2009; Fernández et al., 2014; Erritzoe et al., 2018) including one study demonstrating change relative to a control group (Netzband et al., 2020) and a naturalistic study showing change in self- and informant-report data (Weiss et al., 2021). Three randomized and controlled clinical trials (Palhano-Fontes et al., 2019; Davis et al., 2020; Carhart-Harris et al., 2021) also provide support for a psychedelic-induced antidepressant effect, which bears relevance to our present examination of neuroticism in view of common structure between personality and psychopathology (e.g., Widiger et al., 2012; Kotov et al., 2017). Of note, the size of the observed effects are somewhat smaller than medium-sized effects found in other studies (e.g., Erritzoe et al., 2018; Weiss et al., 2021). As such, recreational use outside of therapeutic contexts designed to support introspective inquiry (e.g., psychedelic-assisted therapy, ayahuasca ceremony) may attend smaller effect size changes. Increased emotional stability (TIPI Calm Emotionally stable) was only observed between baseline and 2 weeks, and thus will not be interpreted. Similarly, because changes in TIPI extraversion did not extend to 4 weeks, and its counterpart item, TIPI Reserved, showed no change, this result is not interpreted.

Collectively, our results indicate that psychedelic use may promote personality traits of high relevance to social functioning, namely traits linked to lower reactivity and antagonism in interpersonal communication, relationship stability, and emotion regulation. Results involving decreased neuroticism may be consistent with recent neurocognitive work demonstrating reduced negative affect (and amygdala response) in relation to facial stimuli 1 week following psilocybin use, and decreased trait anxiety and increased positive affect 1 month following psilocybin use (Barrett et al., 2020).

To evaluate the size of these personality change effects relative to alternative interventions, we additionally compared observed effect size changes in TIPI Anxious and TIPI Critical to meta-analyzed effects of psycho- and pharmacotherapeutic intervention. In their large meta-analysis ($k = 199$; $N = \sim 20,000$), Roberts and colleagues (2017) observed that neuroticism declined and agreeableness increased by 0.57 and 0.15 standard deviations, respectively, in relation to 24 week (on average) clinical

⁶As a note, results from the present study are not directly commensurable with Mason et al.' (2019) finding at 7 days as cognitive and affective empathy was measured using a laboratory test (Multifaceted Empathy Test) that elicits empathic ability rather than relying on participants' self-appraisal of empathic ability.

interventions.⁷ When calculated in an equivalent manner in our sample ($N=249$), TIPI Anxious exhibited a lower effect size change, namely a reduction of 0.26 standard deviations; whereas TIPI Critical exhibited a larger effect size change, namely a decrease of 0.27 standard deviations. These results may be suggestive that psychedelic use in the general population does not carry the therapeutic effectiveness for reducing neuroticism that can be found in clinical intervention or in other contexts (e.g., psilocybin-assisted therapy, Erritzoe et al., 2018; ayahuasca ceremony, Weiss et al., 2021), but such use may accompany enhanced effectiveness for enhancing agreeableness (or reducing antagonism). Nevertheless, it is important to bear in mind that Roberts and colleagues' (2017) meta-analysis likely included a small proportion of studies targeting agreeableness specifically, potentially suppressing their observed effect size for agreeableness, and making our effect size estimates appear artifactually favorable.

Although speculative, it may be additionally useful to explore the degree to which the trajectories of change in personality found in this study relate to each other. Covariance of change over time may be diagnostic of common psychedelic-induced processes that underlie multiple traits. To accomplish this goal, we conducted analyses examining correlations of change scores in those traits that exhibited significant change in our study (Table 6). Notably, TIPI Anxious exhibited a medium-sized correlation with TIPI Critical.⁸ Such intraindividual covariation of neuroticism and agreeableness following psychedelic experience may point to lower critical and quarrelsome disposition under psychological conditions of reduced negative emotionality. This relation may also point to common causes involving enhanced emotion regulation ability (e.g., regulation of distress and frustration). Few studies have explored these possibilities in particular. Nevertheless, one previous study showed that men with a history of psychedelic use reported better emotion regulation ability and lower intimate partner violence, and that emotion regulation ability cross-sectionally mediated the relation between psychedelic use and intimate partner violence (Thiessen et al., 2018). Applied to our own work, it is conceivable that reduced neuroticism *via* enhanced emotion regulation accompanies lower stress reactivity and interpersonal aggression, as indexed by our TIPI Critical Quarrelsome item. It will be important for future prospective work to explore how psychedelic use may mechanistically impact BFAS Belligerence (low pole of Politeness) and externalizing behavior, possibly through enhanced emotion regulation, meaning, and fulfillment, and reduced negative emotionality and anger reactivity.

Is Psychedelic Use Related to Change in Perceptions of Social Connectedness?

Our focus on connectedness to other human beings is part of a larger effort to explore the ways in which psychedelic use may engender enhanced connectedness, broadly construed (Carhart-Harris et al., 2018). Such connectedness is thought

to be evident in acute ego dissolution experience by which the coherent self becomes diminutive within awareness and most clearly in acute mystical experiences of oceanic boundlessness and external unity by which one experiences unification with external objects and entities (Barrett et al., 2015). Previous research has shown that psychedelic-induced connectedness also extends to self (Watts et al., 2017), nature (e.g., Forstmann and Sagioglou, 2017; Lyons and Carhart-Harris, 2018) and other human beings (Forstmann et al., 2020). Increases in perceived social connectedness was found using both of our operationalizations: a semantic face-valid measure and a visual measure that asked participants to select the degree of overlap between self and other that best represents their current relationship with other human beings. However, we only interpret changes in SCS Social Connectedness, capturing perceptions of belongingness to the social environment, because changes in Relatedness did not extend to 4 weeks post. Nevertheless, it is important to mention that the present study replicated the findings of Forstmann et al. (2020) using a prospective design and the same measure (i.e., Relatedness in the present study). Our results notably differed in demonstrating that the effect of enhanced connectedness with other human beings persisted for up to 2 weeks (versus 24 h demonstrated in their study).

Our findings may hold important clinical implications. Social disconnectedness is a common feature of internalizing and stress disorders (Karp, 2017; Kintzle et al., 2018), and connectedness is considered a core component of psychological well-being (Lee et al., 2008; Cervinka et al., 2012). Furthermore, social disconnectedness shows concurrent and longitudinal relations with loneliness (Jose and Lim, 2014; Ang, 2016). Accordingly, it will be important for future research to examine perceived social connectedness as a possible psychological mechanism underlying therapeutic psychedelic-induced effects on depression, stress, and loneliness.

Is Change in Personality Connected to Change in Perceived Social Connectedness?

Adaptive change in perceived social connectedness significantly covaried over time with a number of personality outcomes including neuroticism, extraversion, agreeableness, and conscientiousness. The present approach was not able to evaluate the causal directionality of these relations. Therefore, our results provide only preliminary data with regard to the processes underlying adaptive change. It will be important for future work to explore mechanistically how these change processes interact with each other (e.g., through the use of ecological momentary assessment). As one possibility, enhanced perceived social connectedness may lead to expanded in-group identification, lower distrust, reduced neuroticism, and enhanced extraversion, agreeableness, and conscientiousness. Alternatively, reduced neuroticism and enhanced extraversion and agreeableness may be primary and serve to amplify perceptions of social connectedness as individuals deepen their prosocial involvement in the social environment. Given the rapidity with which

⁷Strictly pharmacological interventions produced a change in neuroticism of 0.48 standard deviations.

⁸It bears noting, TIPI Calm did not exhibit a similar pattern.

perceived social connectedness emerged in previous work (Forstmann et al., 2020), the latter explanation may be less likely as changes in social behavior may not have had significant time to unfold. As a further explanation, interindividual overlap between constructs may be suggestive that observations of covariation over time are merely artifacts of the overlapping component changing in both. We consider this possibility while recognizing that interindividual covariation does not *necessarily* imply intraindividual covariation over time (Molenaar, 2004; Fleeson, 2007). Our results indicated that interindividual overlap with perceived social connectedness in the cases of TIPI Critical and Disorganized was small ($|r| < 0.30$), whereas overlap in the cases of TIPI Anxious and Extraverted was more substantial ($|r| > 0.30$). This pattern is tentatively suggestive that intraindividual covariation is more likely to be suggestive of distinct constructs with common processes in the former cases, and common constructs in the latter. As a final comment on our results, only SCS Social Connectedness exhibited covarying relations with personality, suggesting that common processes may underlie change in perceived *social belonging* and personality, but not perceived *relatedness to other human beings* (Relatedness) and personality.⁹

Are There Factors That Predispose or Potentiate Change in Social Functioning-Related Traits and Perceived Social Connectedness?

Four-hundred-thirty-two analyses were conducted to examine the degree to which changes in outcomes were moderated by predisposing and acute factors, with eight significant results emerging (2% of analyses). Although this rate exceeds the Type I error rate expected from setting an alpha level of $p < 0.005$ (i.e., 0.5%), the low number of significant results is suggestive that they should be cautiously interpreted as explorative findings warranting future replication. In general, predisposing and acute factors did not emerge within our general population data. Moreover, our hypotheses of moderated change in neuroticism, extraversion, and openness by mystical experience were not supported. Given that our sample was relatively well-powered to interpret a small interaction effect in most cases, it is important to consider why our null results differ so starkly from other studies that observed greater evidence of moderation (e.g., MacLean et al., 2011; Erritzoe et al., 2018; Weiss et al., 2021). One possibility is that use in the general population—lacking the control and introspective attentional buffers of psychedelic-assisted and ceremonial contexts—includes greater variability in other factors not measured here (e.g., relationship dynamics among participating users) that increase unsystematic variance in change trajectories. Another possibility is that the online volunteer format of survey response impacted the fidelity with which participants rated their experiences, though no evidence exists to this effect. A third possibility is that previous

work has overstated the influence of predisposing and acute factors on psychedelic-induced personality change.

LIMITATIONS

There are a number of limitations that qualify the interpretation of our findings. First, perhaps the larger source of validity concern regards possible differential drop out by participants who did not experience a positive effect of psychedelics. Only 22% of early participants completed all timepoints, and 34% completed baseline and 2 weeks post. As such, the present sample may underreport participant trajectories that would more heavily favor null hypotheses. Future research that reduces such attrition is vital for testing the validity of preliminary findings found in our sample. Second, comparisons of complete and incomplete respondents were suggestive of differences in conscientiousness. As such, attrition-related sample bias could have impacted results pertaining to conscientiousness; in addition, attrition-related sample bias could conceivably extend beyond measured outcomes, and limit generalizability. Third, the naturalistic approach of the present study precluded the use of a control group, raising the potential for significant methodological issues including the influence of placebo, expectancy, and demand effects, especially among those who are advocates for expanded psychedelic use. Third, informant-data was not collected in this study to corroborate results from self-report data. Although self-report data represents a valid source of information, previous work has shown that informant-report data tends to support only a subset of significant personality change results found in self-report data (Weiss et al., 2021). The presence of strong placebo and expectancy effects in this work make informant-data an important source of information. Fourth, our sample was comprised of volunteers, meaning that sample bias may have played a role in excluding individuals for whom enrollment would have required compensation; this property may partially limit generalizability to the broader population. Fifth, our use of TIPI items accompanies low inter-item reliability of personality outcomes, and behooves the importance of future replication, especially in the case of results where only one of two intra-domain TIPI items showed a significant effect (e.g., extraversion). Sixth, our survey study was not able to precisely measure the type and dosage of the substances participants took. Given evidence of dose-dependent effects of psychedelics (e.g., Holze et al., 2021b), this introduces imprecision into our estimates of longer-term change, making our results significantly less generalizable to particular use cases.

CONCLUSION

The present study represented a well-powered examination of how psychedelic use in a naturalistic setting may influence social functioning and connectedness using the framework of FFM personality. Use of psychedelics was associated with substantive decreases in neuroticism and increases in

⁹However, it bears noting that power analyses demonstrated we were limited in detecting true covariation between the latter set of constructs; our sample size provided 80% power to detect a correlation between change scores exceeding 0.28.

agreeableness, both of which are relevant to social functioning *via* links to relationship satisfaction and prosociality. Specific adaptive effects on personality involved changes in anxiety, emotional lability, quarrelsomeness, and enthusiasm. These data add to the robustness of findings involving a psychedelic-induced antidepressant effect and shows evidence of this effect extending to the general population of psychedelic users. Our data also provide preliminary evidence for an intriguing downward effect on a particular aspect of FFM agreeableness, namely BFAS Belligerence (or Politeness at the opposite pole), that involves a conflict-prone style of interpersonal relating. Use of psychedelics was also associated with substantive increases in feelings of belonging to one's social environment. Predisposing and acute factors were generally not associated with change trajectories, though baseline standing on neuroticism, extraversion, perspective taking, and perceived social connectedness showed qualified evidence of amplifying adaptive effects on these traits. Our findings are broadly suggestive of the therapeutic potential of psychedelics for addressing Antagonistic Externalizing and loneliness.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because, but inquiries for responsible use of this data can be made to DE. Requests to access the datasets should be directed to d.erritzoe@imperial.ac.uk

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Imperial College Research Ethics Committee;

Joint Research Compliance Office. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

BW wrote this paper with feedback and editing from DE, RC-H, VN, and LP. All authors read and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpsyg.2021.749788/full#supplementary-material>

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Right-Wing Psychedelia: Case Studies in Cultural Plasticity and Political Pluripotency

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Recent media advocacy for the nascent psychedelic medicine industry has emphasized the potential for psychedelics to improve society, pointing to research studies that have linked psychedelics to increased environmental concern and liberal politics. However, research supporting the hypothesis that psychedelics induce a shift in political beliefs must address the many historical and contemporary cases of psychedelic users who remained authoritarian in their views after taking psychedelics or became radicalized after extensive experience with them. We propose that the common anecdotal accounts of psychedelics precipitating radical shifts in political or religious beliefs result from the contextual factors of set and setting, and have no particular directional basis on the axes of conservatism-liberalism or authoritarianism-egalitarianism. Instead, we argue that any experience which challenges a person's fundamental worldview—including a psychedelic experience—can precipitate shifts in any direction of political belief. We suggest that the historical record supports the concept of psychedelics as “politically pluripotent,” non-specific amplifiers of the political set and setting. Contrary to recent assertions, we show that conservative, hierarchy-based ideologies are able to assimilate psychedelic experiences of interconnection, as expressed by thought leaders like Jordan Peterson, corporadelic actors, and members of several neo-Nazi organizations.

Keywords: psychedelics, authoritarianism, ecofascism, deep ecology, neoreaction, suggestibility, Jordan Peterson, capitalism

INTRODUCTION

The notion that psychedelic experiences can result in individual dispositional change has its roots in their association with the cultural and political upheavals of the late 1960's and 1970's. Because this specific time witnessed an explosion in countercultural fascination with widely available classical psychedelics like LSD, psilocybin, and mescaline, psychedelics have often been conflated with the progressive and radical politics of the moment: sexual revolution, the civil rights movement, and youth radical groups like Students for a Democratic Society or the Yippies. Yet psychedelic usage by modern and premodern culture predates this era, and different contexts did not produce individuals with a more progressive politics. In light of the nascent psychedelic renaissance and burgeoning psychedelic industry, the assumption that psychedelics lead to progressive politics deserves greater scrutiny—particularly given the hype around positive implications for society.

Prosociality and openness have both been shown under experimental conditions to be dramatically affected by psilocybin (MacLean et al., 2011; Griffiths et al., 2018). Among the core personality traits, openness—along with agreeableness—is linked to prosocial behavior (Kline et al., 2017).

Psychological research on political belief and ideology has sought to explain how individuals identify with political movements (e.g., conservatism) or political parties based on relative scoring in Big Five personality traits like openness (Caprara et al., 1999; Best, 2011; Gerber et al., 2011). Nour et al. (2017) investigated liberal-conservative leanings and the libertarian-authoritarian spectrum of drug users, using survey data ($n = 893$) from the recreational use of at least one classical psychedelic. Users of LSD, psilocybin mushrooms, mescaline, or ayahuasca were compared with cocaine and alcohol users as a non-psychedelic control population, finding that those with classical psychedelic experience were more likely to report less authoritarian beliefs than the non-psychedelic using controls. Shortly after, Lyons and Carhart-Harris (2018) addressed authoritarianism as an adjunct to an open-label psilocybin-assisted treatment-resistant depression therapy experiment, but with a much smaller sample size ($n = 14$), concluding that the seven participants who had psilocybin therapy reported lower authoritarian beliefs than before treatment or compared to the non-psilocybin control group. Results from these two studies constitute the only peer-reviewed evidence for the psychedelic experience predicting more liberal and less authoritarian values (see also the recent $n = 1$ observational correspondence by de Wit et al., 2021). Based on the dramatic clinical effects of psychedelics on openness and the putative reduction in authoritarianism, the media have constructed and proliferated an argument—at times, encouraged by researchers—that psychedelic therapy will lead to a more progressive, inclusive society (Gearin and Devenot, 2021). However, there are many historical counterexamples—those whose authoritarian views remained unaffected by psychedelic experience, or those who developed authoritarian views after or even with the assistance of a classic psychedelic—which the authors do not address. We suggest that the historical and cross-cultural records support the concept of psychedelics as “politically pluripotent,” non-specific amplifiers of the political set and setting (Loneragan, 2021).

Authoritarianism is a worldview with deep, cross-cultural roots which exalts obedience to hierarchical power relations above all else. On an individual level, people can display a range of authoritarian behaviors in their interpersonal relationships. Recent work by Zmigrod et al. (2020) has demonstrated that authoritarianism, along with nationalism, patriotism, and social conservatism, are predictable by low strategic information processing (e.g., planning, working memory capacity, and cognitive flexibility)—though each has a distinct cognitive trait signature. According to Arendt (1958):

The authoritarian relation between the one who commands and the one who obeys rests neither on common reason nor on the power of the one who commands; what they have in common is the hierarchy itself, whose rightness and legitimacy both recognize and where both have their predetermined stable place.

So long as hierarchy is held paramount, authoritarianism can take many forms. Typically, a natural law or hierarchy is posited and organized along multiple axes, such as racial identity, nationality, gender, and class (Crenshaw, 1991). Presently, white supremacy, patriarchy, heteronormativity, class, and imperialism constitute the dominant global infrastructure of authoritarianism (hooks, 2000). Elements of authoritarianism are organizing principles in military, penal, business, health, scholastic, and religious institutions (Foucault, 1995) and remain essential features of all political systems exercising state control.

A BRIEF REVIEW OF IDEOLOGICAL CATEGORIZATION AND NOMENCLATURE

In different historic contexts, ideologies have imposed meaning on both self and world, changing the relationship people have toward historically entrenched hierarchies, such as the divine right of kings during the feudal period. Some ideologies naturalize existing hierarchies, while others attempt to deconstruct them and envision alternative ways of distributing power. Many of today's current ideological conflicts can be traced to a basic division between supporters of some form of aristocracy and some form of shared democratic power. Democratic processes of debate, persuasion, individual autonomy, and egalitarianism are antithetical to authoritarianism.

The section following will briefly review a spectrum of the dominant political ideologies, moving from most general to more specific. A glossary of important terms and definitions can be found in Table 1. Historically, liberalism championed the rights of the merchant class and property-owning men, arguing for their exclusive enfranchisement. Liberalism emphasizes the economic liberty of individuals, which makes it the bedrock ideology of capitalism (Losurdo, 2011). Rooted in the philosophy and economic theory of John Locke and Adam Smith, liberalism rose during the Enlightenment as an alternative to hereditary monarchies (McLean and McMillan, 2009). As such, both conservatives and liberals believe in this sort of market-liberalism (O'Brien, 1993). The right wing-left wing divide takes its name from the different sides of French National Assembly of 1789, where supporters of the monarchy were seated on the right and those agitating for revolution on the left (Bobbio, 2016). The left, which opposes private control of the economy, includes socialist parties that have supported revolution and the seizure, socialization, and democratization of the means of production. The right, which supports private control of the economy, includes capitalist parties that center business interests and the private ownership and management of capital. In US politics, the terms left and right are often confused, since members of the Democratic Party are consistently labeled as “left-wing” even though they are technically center-right (Archer, 2007). The “libertarian” designation is also confusing: in US contexts, “libertarian” designates proponents of laissez-faire capitalism, yet this is a result of a historical co-optation of the term long used as a synonym for socialist, as in libertarian socialism (Diemer, 1997; Rothbard, 2007). US libertarianism can be delineated into right

and left presentations, but while left libertarians are synonymous with libertarian socialists and some forms of anarchism, the far more common right libertarianism focuses on reducing government regulations and increasing the power of private industry (van der Vossen, 2019).

Although opposition to government regulation of enterprise has made frequent allies of right libertarians and conservatives, they differ in that conservatives support traditionalism while libertarians seek to reduce government intervention in the personal choices of individuals (e.g., opposition to the drug war), including corporate legal persons (van der Vossen, 2019). While both groups sympathize with free-market ideology, traditional conservatism adds a “concern for moral and communal factors” along with “a greater emphasis on nationalism and the authority of the state” (O’Sullivan, 1993). In *The Reactionary Mind: Conservatism from Edmund Burke to Donald Trump*, Robin (2018) offers a more psychological description, characterizing conservatism as “a meditation on—and theoretical rendition of—the felt experience of having power, seeing it threatened, and trying to win it back.” Adjacent to conservatives is the reactionary phenomenon: reactionaries seek a return to a historical or imagined social order (e.g., Make America Great Again). Whereas conventional conservatives believe in individual freedoms and meritocracy within traditional social relations, reactionary conservatives want the “correct” groups in power with the outgroups subordinate or excluded altogether (Nilsson and Jost, 2020).

Authoritarianism and libertarianism are expressed on both the left and right. Values cannot be neatly sorted into social and economic realms, nor do issues belong to any particular worldview. While there are often strong correlations between political leanings and stances on particular issues (e.g., care for the environment and progressivism), there are frequent enough departures (e.g., conservative love of country and outdoor recreation) that single-issue positions are poor proxies for defining ideologies.

The authoritarian right is populated by a constellation of movements that includes “radical-right, anti-liberal democracy actors to extreme-right, anti-democracy ones” (Forchtner, 2019), as well as ultranationalist, fascist, and neo-Nazi groups (Davies and Lynch, 2002). Right-wing authoritarianism (RWA) reflects “preferences for social conformity over individual autonomy,” whereas social dominance orientation (SDO) emphasizes “preferences for social hierarchies as opposed to egalitarianism” (Cohrs, 2012). Both RWA and SDO are associated with “system justification,” defined as “the tendency to defend and bolster the societal status quo” (Nilsson and Jost, 2020). Conservatism is continuous with ultranationalism, which goes beyond the shared history, language, and traditions associated with conventional nationalism by elevating one’s group identity above all other nations through xenophobic animus (Rydgren, 2018). When a particular ethnicity within a nation is exalted above others within and without the nation, ethnonationalism results (Bonikowski, 2017). Within ethnonationalist worldviews, ethnic minorities are often scapegoated for problems facing the nation—both concrete and fictitious (Forchtner, 2020).

The phenomenon of scapegoating is of particular importance when considering fascism and Nazism (a subtype of fascism).

Fixation about internal enemies is cast in terms of sickness and disease in an organic politic where the nation, its peoples, and borders are conceptualized as a living body, such as in the 1940 Nazi film *Der ewige Jude* (*The Eternal Jew*), where Jews are compared to parasites and rats. Weakness is openly disdained by Nazis and fascists, as reflected in the embrace of social Darwinism and eugenics in both past and present day (Black, 2012). Empathy is affected when problems and people are framed as pathogens, where empathy for an outgroup is seen as analogous to skipping radiation treatment out of empathy for cancer cells. The possibility of increasing empathy for one’s in-group problematizes universal claims about psychedelics increasing empathy for all people in the research literature (Blatchford et al., 2021). In both fascist and Nazi ideologies, out-groups are cast as weakening the nation and robbing the master race of its destiny as the true heir to the Roman Empire. The fascist, anti-materialist mythologizing of past, present, and future rejects intellectualism and intellectuals (Sternhell, 1987)—indeed anything that stands in the way of victory. Fascism can take many forms and vary in degree—hence the term “crypto-fascist,” which refers to those concealing fascist sympathies or “hiding their power level” (ContraPoints, 2017)—but the guiding principle has always been the will to power and domination (or extermination) of out-groups. While fascists will form alliances when convenient, they will easily turn on perceived out-groups that formerly served their interests when conditions allow for it.

POWER TRIPPING

Anyone positing that psychedelics—therapeutically or recreationally applied—result in more liberal or anti-authoritarian views must contend with many contemporary and historical counterexamples (Jacobs, 2020; Johnson and Yaden, 2020; Pace, 2020). There are those who, after one or many psychedelic experiences, held on to pre-existing authoritarian views; and those who developed an affinity for authoritarianism after—or even as a result of—a psychedelic experience. Anthropologist Nicholas Langlitz described his own experience with what he called Rightist Psychodelia:

Today, the classmate who gave me my first LSD trip for my eighteenth birthday does what he can to limit social inclusion of immigrants in Germany. He came to represent the far-right populist party *Alternative für Deutschland* in the parliament of North Rhine-Westphalia. Consciousness expansion and rightist thought have never been mutually exclusive and they are currently reconnecting. (Langlitz, 2020)

In both the experimental and naturalistic studies that claim psychedelics make people more liberal, it is far more likely—and parsimonious—to surmise that environmental factors account for the change toward more progressive views. For example, the inclusion of ayahuasca in Nour et al. (2017) alone skews the survey population to those already so open to novelty as to seek out psychedelic experience in what is most commonly an Indigenous, jungle context. Similar points adhere with the inclusion of mescaline. People predisposed to xenophobia and

TABLE 1 | Glossary.

Term	Definition
Alt-right	Shorthand for “alternative right,” the alt-right is an online rebrand of white nationalism, authoritarianism, patriarchy, and anti-Semitism associated with the politics message board of the website 4chan.
Authoritarianism	A hierarchical belief system that holds obedience to power to be the highest good.
Corporadelic	The term “corporadelic” was coined independently by Dr. Katherine MacLean (a former lead researcher and session guide for psilocybin research at Johns Hopkins University School of Medicine) and Brett Greene (co-founder emeritus of Psymposia) in 2019. Corporadelic refers to individuals and organizations who seek to monetize and privatize psychedelics using pharmaceutical industry strategies, such as generation of strong intellectual property (IP) and use of venture capital funds.
Dark Enlightenment	A twenty-first-century anti-egalitarian, anti-democratic, pro-corporate dictatorship, and authoritarian movement. Associated with NRx.
Deep Ecology	An environmental philosophy founded by Norwegian philosopher Arne Næss and American philosopher George Sessions in the 1970s and 1980s. Deep ecology argues that maladaptive environmental behaviors are symptomatic of Western culture’s anthropocentric and utilitarian attitude toward nature, and that any meaningful behavior change depends on ameliorating this deep-seated sense of separation from nature.
Eco-fascism	An ideology that blames environmental degradation on overpopulation, immigration, globalization, and industrialization, to which it offers totalitarian “solutions” like ethnic cleansing. They believe that finite natural resources and environmental crises like climate change require the conservation and protection of those resources for the enjoyment and use of “white people.”
Ecofeminism	An intersectional philosophy and political movement that links ecological and feminist concerns, based on a critique of the patriarchal domination of society.
Ethnonationalism	An ideology that identifies one’s nation with one’s particular ethnic group while excluding other ethnicities. Ethnonationalists often scapegoat ethnic minorities for perceived problems facing the nation.
Fascism	The ideology of the historical Italian dictator Benito Mussolini and the two political parties he led as well as a modern, transnational ideology combining RWA and ultranationalism. It is characterized by the will to power and by domination (or extermination) of out-groups. Fascism is sometimes used interchangeably with modern forms of Nazism and white supremacy.
Intellectual Dark Web (IDW)	A loose affiliation between authors, academics, podcasters, and vloggers who oppose modern social justice activism, “cancel culture,” and political correctness.
Nazism	The ideology of both the historical National Socialist German Workers Party of the early twentieth century and of contemporary anti-Semitic, white supremacist, misogynistic admirers of Adolf Hitler.
Neoliberalism	Originally a theory of political-economic practices, neoliberalism has become a dominant and hegemonic global ideology that emphasizes individual responsibility and the erosion of the welfare state.
Neo-reaction (NRx)	A reactionary movement associated with the blog Unqualified Reservations. Since NRx expanded to become The Dark Enlightenment, the two terms are interchangeable.
QAnon	A far-right conspiracy movement most associated with the online forum 8chan (now 8kun) and with support for former President Donald Trump.
Race Science	The unscientific use of scientific narratives and vocabulary to justify white supremacist worldviews. It includes eugenics and attempts to reject the single-species designation of <i>Homo sapiens</i> .
Reactionary	A descriptor of persons or movements that seek a return to a real or imagined “golden era.” Reactionaries seek to regain lost power and are quick to act on perceived challenges to existing power structures from which they benefit.
Red Pill	A metaphor from the sci-fi movie <i>The Matrix</i> now commonly used to describe the process of radicalization to right-wing, white supremacist, and misogynistic ideologies. The first usage is attributed to the NRx blog Unqualified Reservations.
Social Dominance Orientation (SDO)	A personality type characterized by preferences for social conformity over individual autonomy and by submissiveness to authority figures.
White Supremacy	The belief that “white people” are a superior race that should dominate society for the purpose of society’s optimal functioning, typically at the expense of racial and ethnic groups deemed “non-white” by adherents.

white supremacy are likely to self-select out of these user populations. However, globalized, source-blind supply chains divorce certain chemicals from their indigenous contexts—darknet and internet-enabled gray market purchases may render psychedelic analog research chemicals or extracted DMT more palatable to authoritarian-leaning users than the DMT and MAOI-containing ayahuasca brew with all of its attendant cultural “baggage” and destination jungle settings.

Prior to the recent wave of studies on psychedelics and liberalism and nature-relatedness (Forstmann and Sagioglou, 2017; Nour et al., 2017; Lyons and Carhart-Harris, 2018; Kettner et al., 2019), Piper (2015) addressed several historical and contemporary examples that demonstrate that intimate knowledge of classical psychedelics have coexisted with far right, authoritarian views since the very beginning of psychedelic exploration by modern Western investigators. For instance,

fascist philosopher, occultist, and author of the introduction of the Italian version of *The Protocols of the Elders of Zion*, Julius Evola, was known to experiment with and write about drugs, and he is an influential figure for the alt-right today. Indeed, the first botanical collection of *Teonanácatl* was facilitated by the Austrian botanist and “ardent Nazi” Blas Paul Reko, who corrected Richard Evans Shultes’ earlier designation of the Aztec sacrament as peyote (Schultes, 1939; Davis, 1996):

Aristocrats, bankers, German right-wing ex-military men, not to mention the CIA and the Nazis: From the 1930s to the 1960s, it is a little acknowledged fact that one of the principal sources of interest in psychedelics, aside from the interest of researchers working on specific therapeutic uses, was people of conservative or right-wing orientation. (Boon, 2002)

The early days of non-therapeutic LSD use was a consciously exclusive and elite—rather than democratic—activity, typified by the private sessions hosted by Dr. Hofmann with Ernst Jünger described in detail in the chapter entitled, “The Radiance of Jünger” in his autobiography, *LSD: My Problem Child*. Most known for his literary works, Jünger was a Wehrmacht officer and censor for the Nazis in occupied France during WWII; he also coined the term “psychonaut” to describe the work of chemist and mescaline explorer Arthur Heffter (Jünger, 1970; Piper, 2015).

Continuing this lineage into the present, neo-Nazis with histories of psychedelic use do not evidence decreased authoritarianism as a result of such experiences. In keeping with the mystical elements of both Nazism and fascism, contemporary fascist beliefs often overlap with or incorporate elements of occult or Satanic practice (Lavin, 2020; Owen, 2020). The Base, an international neo-Nazi group, integrated collective LSD use into a neo-Pagan, male-bonding ritual involving the beheading of a stolen ram (Makuch and Lamoureaux, 2020b). Members of The Base were later arrested on weapons charges and discovered to be attempting to extract DMT (Makuch and Lamoureaux, 2020a). The Base had been under investigation for planning the murder of an antifascist couple and their child. Andrew Thomasberg attended the August 2017 “Unite the Right” rally in Charlottesville, Virginia with the neo-Nazi group Vanguard America. He later became a recruiter for Atomwaffen Division, an occult neo-Nazi organization linked to at least five murders (Weiner, 2020). Thomasberg was arrested for weapons charges and, while in custody, praised the murder of nine black churchgoers by Dylann Roof. In released text messages, Thomasberg stated, “There’s nothing more Aryan [sic] than ethnogenic [sic] drug use,” and described a deep familiarity with LSD, mushrooms, and several other scheduled drugs (Owen, 2019). “Unite the Right” was organized by Jason Kessler, a member of the Proud Boys (Barnes, 2017); although their then-leader, Gavin McInnis, was not in attendance, he applied his extensive drug history (Gollner, 2021) to publicly advise his followers on how to navigate challenging psychedelic experiences in a 2016 episode of his talk show (Flutez, 2016). The Atlantic reported that Andrew Anglin, the Columbus, Ohio native founder of the neo-Nazi website, *The Daily Stormer*, had

extensive experience with classical psychedelics such as LSD and psilocybin as a teenager before his metamorphosis into a fascist propagandist (O’Brien, 2017).

Stormfront is the oldest hate site on the internet, focusing on white nationalism, Holocaust denial, and neo-Nazi organizing. A simple search for “psychedelics” on the Stormfront forum turns up pages of comments—both positive and negative—discussing the science, therapeutic value, and cultural impact of these drugs:

Originally posted by Puddintane:

I wonder what LSD does to racial awareness. People who use it talk about feeling more connected, but how does that translate to racial awareness? Does anyone have any observations about this?

Forum Member: w41n4m01n3n

Join Date: Apr 2017

Location: Embassy of the 4th Reich in Finland

Posts: 8,581

Well I can tell you this much: I have tried LSD several times and it certainly did not make me a liberal idiot. You can go through my posts and see for yourself. There are many studies verifying what most people had already suspected: LSD is not dangerous to one’s physical health. Whether it is damaging to one’s psychological well-being, depends on the person, dose and circumstances. Long-term negative psychological effects are extremely rare. LSD was invented in 1938 by Swiss chemist Albert Hofmann (whom I have met in real life in 2006 on his 100th birthday in Basel, Switzerland), but its psychoactivity wasn’t known until 1943.... But I also think, that we shouldn’t be discussing these matters this much on Stormfront. I don’t think it is the right place for such matters. It could give the wrong message (to youngsters in particular). (Stormfront, 2017)

Psychedelics have a place in the cutting edge of the radical right, both digitally and as literal boots on the ground. Frederick Brennan was inspired to create the free speech absolutist website 8chan while on a psilocybin mushroom trip (McLaughlin, 2019). Long a haven for digital neo-Nazis and other antisocial posters, 8chan has since been disavowed and shut down—chiefly through the efforts of Brennan—after the entrance of mass shooters on the board. Before the shuttering of 8chan and its re-emergence as 8kun, three mass shooters posted their manifestos on 8chan prior to carrying out their murders (Harwell, 2019). The documentary series *Q: Into the Storm* followed Brennan’s crusade against his former business partners, Jim and Ronald Watkins, and makes the case that the father-and-son duo are behind the Q phenomenon (Hoback, 2021). “Q-drops” had their own psychedelic tenor, with the hashtag #followthewhiterabbit being associated with elaborate conspiracy theories about elite child molestation rings and the psychoactive (but, despite popular culture references, not psychedelic) substance adrenochrome. Incitements from President Trump, Alex Jones, and the drip of Q-drops led to the storming of the US capitol building. Prominently included in their ranks was the self-described Q-Shaman (AKA Jake Angeli Chansley, Yellowstone Wolf) and William Watson, both individuals with deep and extensive ties to the psychedelic community (Evans, 2021; Pace, 2021a,b). Beyond multiple and clear intersections of the psychodelia with the cutting edge of right-wing activism, right-wing conspiracy

seems more than able to spring from native psychedelic soil. The name and reputation of Timothy Leary's Castalia Foundation was recently appropriated to praise President Trump and promote Q-reminiscent child exploitation conspiracies, complete with a classic anti-Semitic depiction of Rick Doblin (Castalia Foundation, 2020; Hausfeld, 2021).

Along with hyper-association and boundary dissolution, a core element of the subjective experience of psychedelics is meaning-enhancement (Hartogsohn, 2018). Combined with the influences of set and setting, a psychedelic experience can lead to shifts in worldviews—and even religious and political ideologies—but not in a consistent, directional manner. A more complete model draws from the literature on radicalization where destabilizing experiences—such as the loss of a loved one or subjection to violence or abuse—can induce what is known as a “cognitive opening,” which calls into question an individual's extant worldview, marking the first step on a potential path to extremism (McCauley and Moskalenko, 2017). In such cases, community support for radical belief (i.e., the setting and other extrapharmacological factors) is an important contributing factor. The antifascist investigative journalism outlet *Bellingcat* surveyed online accounts of 75 neo-Nazis on their process of radicalization and found that four cited an LSD experience as foundational to their “red-pilling” to Nazi beliefs (Bellingcat, 2018).

User Europa is a typical example of this trend. He claims his interest in Nazism started in childhood, with his dad watching Hitler documentaries “every day.” Europa carried this interest into adulthood, watching Hitler documentaries and speeches while taking LSD. This convinced him to start “researching” Nazism which, eventually, inspired him to become an activist.

This sensitivity to the “initial rhetorical conditions” (Doyle, 2011) of set and setting is consistent with the measurable impact of suggestibility on psychedelic experiences. In a study of the putative suggestibility-enhancing effects of LSD, for instance, Carhart-Harris and colleagues found that LSD increased the subjective intensity of researcher-suggested sensations that included one's arm becoming heavier, reexperiencing oneself as a child, and drinking especially refreshing water (Carhart-Harris et al., 2015). McGovern et al. (2021, Preprint) explore the implications of this suggestibility for the ways that beliefs interface with psychedelic experience, noting that “[I]f psychedelics change ‘beliefs,’ they do so largely through experimenter suggestion and the pre-existing psychology of the individual.” Dupuis argues that even hallucinatory images are influenced by extrapharmacological factors including “cultural priors and acquired knowledge” (Dupuis, 2021). In the study of Indigenous cultures, anthropologists and other researchers have long asserted that the suggestibility-enhancing attributes of psychedelics are key ingredients in fostering social cohesion and reinforcing group norms.¹ Dobkin de Rios and Rumrill (2008) have linked this phenomenon to the psychological concept

of “bounded rationality,” defined as the human tendency to act based on social influence. They further remarked that when psychedelics are used outside of a normative context, users may develop antinomian ideas (Grob and Dobkin de Rios, 1992; Dobkin de Rios and Rumrill, 2008). Given this link between psychedelics and suggestibility, which had already been noted by the early wave of researchers in the twentieth century, contemporary commentators should be skeptical of claims that psychedelics lead to any specific, essentialized outcomes—including the recent claims about psychedelics increasing environmental concern and liberal politics.

Psychological research has also demonstrated that purported attributes of psychedelic experiences—such as increased feelings of gratitude—are themselves sensitive to the context of set and setting variables. Although gratitude has been referenced to explain the prosocial benefits of psychedelics (Gandy, 2019; Moreton et al., 2020), a recent paper by Tong and colleagues argues that gratitude can facilitate authoritarian obedience under specific context conditions. In their study, participants who were induced to feel gratitude were more likely to obey commands to grind worms in a grinder compared to those without gratitude priming. The authors note that “gratitude could increase susceptibility to social influence, making the grateful person more likely to align with social conventions and directions.... [T]he grateful person is prone to keep in line with social forces, the consequences of which could sometimes be undesirable” (Tong et al., 2020). Similar mediating variables have been highlighted in the literature on mindfulness, which—like gratitude—is conventionally associated with prosocial behaviors and positive emotional adjustment. In a 2021 paper, however, mindfulness induction was shown to decrease prosocial behavior among participants who were primed with self-construals that emphasized independence rather than interdependence, which suggests that prosocial outcomes are the result of specific (set and setting) conditions rather than an inherent quality of mindfulness-based attention (Poulin et al., 2021, Preprint).

DEEP ECOLOGY AND ECO-FASCISM: THE PROBLEM OF HIERARCHY

Recent correlational studies have associated psychedelic use with pro-environmental beliefs and behaviors. On the basis of preliminary evidence linking experiences of “unity and connection with one's environment to empathy-related phenomena and pro-environmental behavior,” Forstmann and Sagioglou (2017) sought to establish whether lifetime psychedelic experience correlated to increased nature relatedness and pro-environmental behavior. The authors focused on 12 “headline” pro-environmental behaviors within four key areas of “everyday” concern: domestic resource consumption, waste behavior, transportation use, and eco-friendly shopping. Based on results from 1487 online survey participants, they found evidence that psychedelic experience correlated with an increased and lasting sense of interconnection with nature. Furthermore, this “ecocentric” identification—wherein nature is conceived of as an “integral” part of one's self-concept—also correlated with higher reports of pro-environmental behaviors. This outcome

¹Group norms famously vary: large-scale ritual human sacrifice of the Nahua Aztecs and Mayans occurred in a context of regular consumption of both mescaline and psilocybin (Carod-Artal, 2015; Jay, 2019). Some members of the Northwestern Amazonian Jivaro-Shuar have used ayahuasca for war-making where the brew is used specifically to prepare the user to fight and improve their killing abilities (Rubenstein, 2012; Gearin and Devenot, 2021).

supports the findings of Nour et al. (2017), who found that lifetime psychedelic use correlated with nature relatedness in addition to liberal political views.

These correlational studies draw on the preexisting psychological literature on “nature relatedness” and the associated Nature Relatedness scale, a psychological tool used to measure “the affective, cognitive, and experiential aspects of individuals’ connection to nature” (Nisbet et al., 2009). To date, there appears to be little overlap between this field and the study of eco-fascism and other right-wing movements wherein nature relatedness plays a prominent ideological role, including “eco-naturalism (the natural world as a blueprint for the social order), eco-organicism (the Volk/people as an ecosystem) and eco-authoritarianism (the need for a strong state to deal with the environmental crises of our time)” (Forchtner, 2019).

In describing their predictions for their study, Forstmann and Sagioglou expected measures of political conservatism to negatively predict both psychedelic usage and pro-environmental behavior, on the basis of two citations in the published literature. In the first paper by Kurzban et al. (2010), conservatives were associated with negative views on “recreational drug use.” In the second paper by Schultz and Stone (1994), right-wing authoritarianism was “highly negatively correlated” with environmental concern, based on a study of reactions to the development of a new power plant and a separate questionnaire about public environmental views more generally. Commenting on the paper by Schultz and Stone, however, J. Christopher Cohrs notes that anti-environmentalism is “not inherent to RWA or SDO” (Cohrs, 2012). In discussing their findings, Schultz and Stone even predict that this negative correlation between authoritarianism and environmental concern is likely to disappear over time. Writing in 1994, they noted that the “established authorities” within local social hierarchies—including public political figures and capitalist developers—overwhelmingly favored economic growth over environmental protectionism, and that authoritarian-minded individuals likely took their cues from these positions. Schultz and Stone argue, however, that this preponderance of progrowth ideology among the ruling elites is unlikely to last, given that climate change and its associated environmental catastrophes will become increasingly difficult to ignore: “If this analysis is correct, as protection of the environment receives more and more attention and support, the new environmental paradigm will become the [new] conventional wisdom.... Thus, we would expect a decline over time in the negative relationship between authoritarianism and environmentalism” (Schultz and Stone, 1994).

Nearly three decades after Shultz and Stone published their initial findings, there are indications that this shift in environmental concern among right-wing authorities is already well underway. The effects of climate change have become increasingly obvious and disruptive since 1994, with observable increases in extreme weather and climate events including wildfires, flooding, droughts, storms, and heatwaves (Ummenhofer and Meeh, 2017). Climate change is projected to increase the intensity, frequency, and duration of extreme weather events in the future, with corresponding increases in vector-borne diseases, food and water insecurity, and property

damage as the century progresses (Pastor-Paz et al., 2020; Rocklöv and Dubrow, 2020; Koren et al., 2021). In light of these trends, environmentalism is expected to become “one of the central political issues of the next decades” across the political spectrum, including amongst the far right (Rueda, 2020).

Historical evidence likewise suggests that the current common association of environmentalism with the values of “progressivism, liberalism, equalitarianism, and respect for democracy” is a matter of historical contingency rather than necessity (Rueda, 2020). As Michael E. Zimmerman points out, many postwar leftists in the mid-twentieth century were “suspicious of environmentalism: they feared that it was somehow linked with racist, reactionary politics, which justified oppressive power arrangements on the basis of their ‘natural’ character” (Zimmermann, 1993).

As Forstmann and Sagioglou (2017) emphasize, social psychological research indicates that the “self-other overlap” characteristic of nature relatedness involves both “an incorporation of the target’s features into the self” and an “ascription of one’s own characteristics to the target.” This two-way process of incorporation and projection is thought to increase the “empathic concern” felt for the target or “other” (in this case, nature), since the “other” is experienced as an extension of the self. This notion represents the theoretical basis for deep ecology, which holds that subjective identification with nature increases the intrinsic motivation to care for the environment.

Founded by Norwegian philosopher Arne Naess and American philosopher George Sessions in the 1970s and 1980s (Devenot, 2016), deep ecology argues that the maladaptive environmental behaviors that fuel climate change are symptomatic of “Western culture’s anthropocentric, dualistic, and utilitarian attitude toward nature” (Zimmermann, 1993). Deep ecologists argue that without addressing this deep-seated sense of separation from nature, environmental “reform” movements that seek to moralize pro-environmental behavior are unlikely to furnish the commitment to meaningful behavior change that will be necessary to avert climate catastrophe. Although the philosophy of deep ecology developed prior to the psychological literature on nature relatedness, psychedelic researchers have cited deep ecology to articulate a theoretical mechanism for the correlation between psychedelic experiences and pro-environmental concern and behaviors (Lawlor, 2008; Luke, 2013). The synergy is especially evident in deep ecology’s emphasis on the importance of non-ordinary states of consciousness for cultivating an ecocentric self-concept, beyond the ordinary sense of separation from nature:

While emphasizing scientific claims about the interrelatedness of all things, deep ecologists insist that intellectual conclusions alone are not sufficient to bring about a basic shift in one’s attitude toward nature. Such a shift requires a change of consciousness, an intuitive sense of identification with all things. Arne Naess [sic] argues that such intuition leads us to reject the idea that we are “in” the environment, as if we were surrounded by something basically different from us. An intuitive sense of wider identification enables us to cultivate “[t]he relational, total-field image.” (Zimmermann, 1993)

Given the relevance of deep ecology for the psychedelic research literature on nature relatedness, it is worth considering how deep ecological constructs can be recuperated for authoritarian purposes based on a hierarchical social order. Historical examples of this recuperation necessarily problematize the commonplace association of nature relatedness with empathy and liberal political values within the psychedelic research literature. As Michael E. Zimmerman has noted, intellectual predecessors of the deep ecology movement include the German philosopher Martin Heidegger along with other supporters of National Socialism and the Nazi party. Like the deep ecologists that came after him, Heidegger diagnosed the need for humanity to transition away “from an anthropocentric, dualistic, and utilitarian understanding of nature” through an “ontological shift” in order to avert ecological crisis (Zimmermann, 1993). Zimmerman notes the compatibility of this perspective with elements of National Socialism, which Robert Pois has characterized as a “religion of nature”:

According to Pois, “[t]he National Socialist call[s] for the establishment of a utopian community, the *Volksgemeinschaft*, rooted in a perceived natural order.... [This ideology emphasizes the] overcoming of alienation, not through some hideous form of class war, but rather through a revolution of consciousness, the result of which would be a new sense of rootedness and belonging.[”]

Jules Evans has likewise pointed to the Nazi professor of botany, Ernst Lehmann, who stated:

We recognize that separating humanity from nature, from the whole of life, leads to humankind's own destruction and to the death of nations. Only through a reintegration of humanity into the whole of nature can our people be made stronger... This striving toward connectedness with the totality of life, with nature itself, a nature into which we are born, this is the deepest meaning and the true essence of National Socialist thought. (Evans, 2020)

The possibility for feelings of interconnection with nature to slip into justifications of hierarchy and social domination has long been a feature of ecofeminist critiques of deep ecology. Although deep ecology and ecofeminism are compatible in principle, ecofeminists have expressed concern that certain interpretations of deep ecology's central tenets risk legitimizing authoritarian forms of social power. Regarding their similarity, ecofeminism shares deep ecology's contention that ecological destruction is symptomatic of a central misapprehension about the nature of the self and its relationship to the environment. Both philosophies attribute this misapprehension to the effects of living under industrial capitalism, wherein “individuals are seen as discrete, atomistic beings, who must be compelled, through the use of reason, to behave in moral ways” (Kheel, 1991). Skeptical of any attempt to improve environmental behavior through abstract, ethical moralizing, both deep ecologists and ecofeminists emphasize the importance of direct experiences of interconnection in order to shift innate levels of environmental concern. As Warwick Fox notes, “Deep ecologists agree...that ‘human beings are more deeply moved by the way they

experience their world than by the claims ethics makes on them” (cited in Kheel, 1991).

In the essay “Ecofeminism and Deep Ecology: Reflections on Identity and Difference,” Marti Kheel explores three case studies involving eco-philosophers who describe an expanded sense of self-identification that encompasses the natural world, as expressed specifically through the act of hunting animals. In each of these instances, Kheel argues, the sense of interconnection allows the hunter to legitimize the hierarchical relationship between self and animal as “natural” and healthy, such that the self's preferences and priorities are projected onto the “other” regardless of the animal's own interests or preferences:

Deep ecologists argue that a widened identification will ensure that one will want to minimize harm to individual beings in that they will be viewed as part of the larger ecological Self. However, it is clear from the above examples of self-realization, that for these men this was not the case.... The mind-set that they reveal is that of a psychological instrumentalism in which the animal is seen, not as a unique, living being, but rather, as a means of achieving a desired [heightened] psychological (or psychobiological) state.... The significance of the reduction of the animal to object status is that the relationship to the animal becomes more important than the animal itself. The feelings of yearning for union, the urge to “outwit”—all these take precedence over the living being that is killed. The animal is swallowed up in the act of merging. Even the death of the animal is considered incidental—a byproduct of the more important desire that finds its expression in the hunt.... When deep ecologists write of expanding the self, ecofeminists must be prepared to examine more deeply the unconscious drives that fuel the self that one seeks to expand.... As we have seen, the danger of an abstract identification with a larger “whole” is that it fails to recognize or respect the existence of independent, living beings.... Ecofeminist philosophy must be wary of a holist philosophy that transcends the realm of individual beings.... Individual beings must not be used in a kind of psychological instrumentalism to help establish a feeling of connection that in reality does not exist. (Kheel, 1991)

Although Kheel's analysis specifically focuses on descriptions of hunting animals by ecophilosophers adjacent to the deep ecology movement, this central dynamic is transferable to any interpersonal scenario where the other is subsumed within a “natural” or “organic” social hierarchy.

As Daniel Rueda documents in his 2020 analysis of the growing threat of neo-ecofascism, this phenomenon is already becoming apparent amongst prominent figures in the alt-right. The alt-right has been defined as “a constellation of right-wing forces...animated by political commitments to white nationalism or ultranationalism, authoritarianism and rejection of democracy, gender traditionalism, hatred of the left and liberalism, and antisemitism” (Taylor, 2020). Although the movement is heterogeneous, it is “united by the belief that...[s]traight white western men are situated at the apex of...civilizational hierarchy,” and that any counter-movements seeking to remedy inequality and oppression—such as feminism or anti-racism—threaten the very foundations of civilization by opposing that natural order (Taylor, 2020). Notably, the alt-right illustrates how this sense of a differential social hierarchy can

still be compatible with a nature connectedness similar to that espoused by deep ecology. Richard Spencer, an avowed neo-Nazi who coined the term “alt-right” in 2008, included an evocation of nature connectedness in his manifesto for the “Unite the Right” rally in Charlottesville, VA: “We are a special part of the natural order, being in it and above it. We have the potential to become nature’s steward or its destroyer. European countries should invest in national parks, wilderness preserves, and wildlife refuges, as well as productive and sustainable farms and ranches. The natural world—and our experience of it—is an end in itself” (Spencer, 2017; Rueda, 2020; Vanderheiden, 2020). In this and similar instances, nature is portrayed as a birthright and constituent element of the social elites, while those lower down the social hierarchy are portrayed as “deviants” who threaten the integrity of the moral and natural order.

The historical evidence of ideological compatibility between interconnection and hierarchy casts doubt on researchers’ claims that psychedelics are inherently destabilizing to existing hierarchies. Roland Griffiths—founding Director of the Johns Hopkins Center on Psychedelic and Consciousness Research—expressed this common perspective in an interview with Michael Pollan: “There is so much authority that comes out of the primary mystical experience that it can be threatening to existing hierarchical structures” (Pollan, 2018). Others have suggested that experiences of interconnection inherently lead to universal increases in care and concern, without hierarchical gradations: “Psychedelic moral enhancement’s goal... is to create individuals better able to engage in interpersonal interactions for altruistic purposes because they have glimpsed the unique value of each part of the interconnected whole of the universe” (Stankey, 2020). Some researchers have even theorized a connection between psychedelic changes to political beliefs and the neurological impact of psychedelics on cognitive hierarchies, as reported in *Vice*: “‘The general take-home message is that the psychedelic state is seemingly the breakdown of hierarchical organization in the brain,’ [Alexander] Lebedev says. In a sense, this breakdown could somehow be mirrored in people’s shift in political beliefs, he suggests. ‘In that way, it’s not completely surprising that we see these changes after such a session’” (Henriques, 2018). In the next section, we will explore the specific example of Jordan Peterson to show how the concepts of interconnection and hierarchy can be intertwined.

LOBSTERS ALL THE WAY DOWN: JORDAN PETERSON ON PSYCHEDELICS

Jordan Peterson bills himself as an individualist, classical liberal, but Peterson has been characterized as an “extreme conservative” thought leader for the “New Right,” and his work—especially his attacks on “intersectional politics and liberal egalitarianism”—carries strong appeal among “Evangelical Christians, paleoconservatives and white supremacists” in particular (Nicholls, 2019). Evidence from both critical (Lewis, 2018) and sympathetic (Finkelstein, 2019) sources document Peterson and the associated Intellectual Dark Web (IDW) community as gateways to the alt-right. The Jungian

psychologist became a conservative icon by railing against an expansion of Canadian human rights legislation Bill C-16, which he characterized as the first step toward compelled speech and totalitarianism. Peterson “found a way to monetize SJWs [Social Justice Warriors]” (Rogan, 2017) by arguing (incorrectly) that the bill would result in the arrest and imprisonment of faculty who refused to use transgendered students’ correct pronouns. Peterson’s dire predictions about the bill never coming to pass did not result in his followers deserting him, which is consistent with the work of Garrett and Bond (2021). In a longitudinal study of viral news stories, the authors demonstrated that US conservatives are more susceptible to political misconceptions, particularly when they benefit the in-group. Peterson abandoned academia to start a career as a conservative thought leader and has spoken on a wide range of topics, from the archetypes of The Lion King to arguing in support of traditional gender roles and sexual conservatism.

However, Peterson’s interactions with the far right have made it clear that he believes in and defends a race-based intelligence hierarchy. While a guest on white supremacist, right-libertarian Stefan Molyneux’s podcast, Peterson specifically appealed to Herrnstein and Murray’s *The Bell Curve* (Herrnstein and Murray, 1994) to support his views:

The IQ literature reveals that which no one would want to be the case, which is that there are profound and virtually irremediable differences in people’s cognitive performance and that those differences have a very solid biological and heritable basis. No one wants to hear that. They don’t want to hear that it’s biological. They don’t want to hear that it’s heritable. They don’t want to hear it’s permanent.... [T]he gender differences in IQ look relatively trivial—but there are differences in ethnicity that don’t look trivial. The Ashkenazi Jews, for example, have on average a 15-point advantage over the rest of the Caucasian population, which is sufficient to account for the radical over-representation in positions of authority and influence and productivity.... We have a really profound problem, then again, that no one’s willing to talk about and that’s the cognitive stratification of society. And of course, that was laid out to some degree in *The Bell Curve* back in the 1990’s. (Perez, 2020)

The Bell Curve is a work of scientific racism that has been thoroughly rebutted by scholars from multiple disciplines (Konner, 2003; Marks, 2010), notably including evolutionary geneticist Stephen Jay Gould, who added two chapters to the second edition of his book, *The Mismeasure of Man* (Gould, 1996) to debunking Herrnstein and Murray’s race science claims. Repeated efforts to push “race realist” narratives have been consistently dismissed as unscientific projects of a white supremacist ideology—and contrary to analysis of both the human genome and human migration patterns. A recent letter to *Philosophical Psychology* by Larsen et al. (2020) is emblematic:

An abundance of evidence about the human evolutionary lineage shows that no human groups were ever phylogenetically distinct in the way that racial realism posits. In other words, the human species never persisted in multiple sufficiently isolated “pure” groups for such a prolonged time that it would, evolutionarily

speaking, make sense to talk about our species being divided into biologically distinct populations. Indeed, migration in and between continents and regions was never a one-way movement, but, rather, an intricate multi-way network of substantial intersections and interactions. Because of this mobility, the genetic variation within the human species is much more complex than presumed or predicted by racial realism.

For Peterson, as for Richard Spencer, the existing social hierarchy of Western civilization must be protected at all costs from the egalitarian “social justice warriors” who seek to upend it. Peterson’s writings naturalize and mythologize (Brooks, 2020) this hierarchy as the bedrock of civilization, which functions to protect humanity from the outlying forces of chaos, madness, and meaninglessness:

The order within the chaos and order of Being is all the more “natural” the longer it has lasted. This is because “nature” is “what selects,” and the longer a feature has existed the more time it has had to be selected—and to shape life. It does not matter whether that feature is physical and biological, or social and cultural. All that matters, from a Darwinian perspective, is permanence—and the dominance hierarchy, however social or cultural it might appear, has been around for some half a billion years. It’s permanent. It’s real. The dominance hierarchy is... a near-eternal aspect of the environment... We were struggling for position before we had skin, or hands, or lungs, or bones... Dominance hierarchies are older than trees. (Peterson, 2018)

Peterson’s thinking provides a philosophical legitimation for social dominance orientation (SDO), defined in terms of an individual’s enduring preference for group-based hierarchies and inequalities. For Peterson, all of humanity is “interconnected” via the “natural” sorting process that shuttles individuals to the appropriate status within this hierarchy, which he grounds biologically in the serotonergic system that we hold in common with lobsters and other lifeforms: “The part of our brain that keeps track of our position in the dominance hierarchy is therefore exceptionally ancient and fundamental. It is a master control system, modulating our perceptions, values, emotions, thoughts and actions.” As he lays out in *12 Rules for Life*, Peterson describes the “dominance hierarchy” as among the “most real” and “ever-present” aspects of society (Peterson, 2018).

Peterson’s interest in the serotonergic basis of hierarchy has recently extended to a fascination with the effects of psychedelics on the serotonergic system, as Peterson laid out in an extended podcast discussion with Johns Hopkins’ Roland Griffiths:

I think your work is of...incalculable import... I actually can’t believe how important this is... I’ve been studying the psychedelic literature for 20 years... in as deep a manner as I can possibly manage, and every time I think I have some grasp on how important it is, I learn something else and I think, “Oh ho! It’s way more important than I thought it was!” It’s—it’s of *crucial* significance. It’s, it’s of central—it’s literally of central significance. [Repeating:] It’s *literally* of central significance. (Peterson, 2021b)

Peterson’s position throughout the conversation could not be more emphatic: in the context of our turbulent modernity,

psychedelics might be a necessary catalyst in revivifying the religious life of civilization and thereby restoring humankind’s rightful orientation toward the cosmos. Far from questioning the inevitability of dominance hierarchies, Peterson easily connects current concepts from the psychedelic research discourse—including the prosocial value of experiencing interconnection—back to his preexisting, hierarchy-based ideology.

According to Peterson’s worldview, serving the “good” requires a hierarchical approach to life’s challenges, such that the most competent and efficient problem-solvers rise to the top and attain positions of authority within society (Peterson, 2021a). From this perspective, intersectional social justice activism threatens the core mechanism whereby suffering is most efficiently ameliorated, since feminists are attempting to dismantle all hierarchies by labeling them as abuses of power. In conversation with Griffiths, Peterson attempts to correct this supposed misidentification of hierarchy with tyrannical power by emphasizing hierarchy’s righteous authority as a form of “reciprocal ethic”:

You hear all these postmodern critiques...of hierarchical structure because of its predication on power; and I think—no, no! *Corrupt* hierarchies are predicated on power. *Functional* hierarchies are predicated...on reciprocity—on *productive* reciprocity.... I was talking to... Jocko Willink, who was the commander of Fallujah... 20 years ago, and he’s a real warrior type, you know? He talked about his Navy Seal training, and he said, “Well, we were taught—it was pounded into us to have the back of the guy next to us.” It wasn’t like every powerful, clambering ape for himself. Not at all! In these intensely competitive hierarchies, which would be—you’d think—as pure a manifestation of the power motive as would be possible, power is not the guiding ethos. He said quite clearly, “No—Your men won’t attend to you unless it’s reciprocal...” They have to know *you have their backs*. (Peterson, 2021b)

Peterson suggests that this sense of hierarchy as a “reciprocal ethic” operates cross-culturally with the functional status of “natural law”:

Hierarchies are organized around an ethical principle [as opposed to brute power] if they’re to be stable and productive across long spans of time. And...that pattern emerges cross-culturally. It’s [based on] reciprocal productivity.... And so, I think you can make a very deep biological case for the...emergent evolution of an ethical sense. And...I think that does speak to people in the voice of their conscience. (Peterson, 2021b)

Peterson theorizes that just as “cocaine hyperstimulates the psychomotor stimulant system,” psychedelics might amplify existing processes in the nervous system—except that, in the case of psychedelics, those processes involve connecting to the dominance hierarchy’s reciprocal ethic: “People come out [of the psychedelic experience]—[and] they’re more prosocial. And so, [do] you think that’s...an exaggeration, or a strengthening, of...our inbuilt, reciprocal ethic?” (Peterson, 2021b).

Unambiguously, Peterson attributes the prosociality induced by psychedelics to grateful acceptance of one’s place within

the dominance hierarchy—a perspective that he situates within Griffiths' discussion of psychedelics and meaning-making:

[Griffiths:] There's a level of meaning-making that comes out of these experiences that end[s] up rewriting the personal narrative that [a] person has about themselves and about their place in the world, and that account[s] for these enduring changes, and the fact that people then become behaviorally much more flexible; because if that narrative structure is changed... the analogy I think of is [that] you're rewriting the underlying operating system. (Peterson, 2021b)

While Griffiths' perspective on meaning-making is a commonplace interpretation of the evidence-based psychedelic research literature, Peterson reinterprets it in a manner that is compatible with his preexisting conservative political assumptions. Peterson communicates these assumptions by responding with an extended analysis of the Biblical story of Cain and Abel, which he interprets as a parable of the "grievance politics" that he associates with social justice activism. In Peterson's telling, Cain represents those who seek to destroy the dominance hierarchy due to resentment over one's subaltern status. Lacking the wisdom of understanding how hierarchy is in everyone's best interest, these types seek to undermine (or, in Cain's case, to kill) the competent achievers of higher status—even at the expense of increasing their own suffering—out of a misplaced sense of rebelling against injustice:

I think of the operating system as [having] a narrative structure... The [narrative psychedelic] rewrite seems to me to be something like the revelation...that things are interconnected, that things are fundamentally good... [which] gives some experiential weight that can be used as a counterposition against that destructive cynicism. And the psychedelic, the mystical experience seems to allow for that transformation. (Peterson, 2021b)

Peterson sees the psychedelic insight as shifting personal identification away from injustice toward the interconnected whole of hierarchy, which justifies experiences of oppression and makes them meaningful. Psychedelics reveal "the *meaningful* interconnectedness" of all people and all things, within which "the entire pattern of connection has some transcendent or ultimate significance that's hidden from us" (Peterson, 2021b).²

²Peterson's embrace of interconnection with hierarchy has deep roots in the "Western" intellectual tradition, which suggests that it was only a matter of time before the popularization of psychedelics united these ideological positions. His ideas are reminiscent of those expressed by Alexander Pope during the English Enlightenment in "An Essay on Man" (1733), which used ideas about the Great Chain of Being (an idea that was newly reinvigorated by the development of the microscope and telescope, which revealed animate worlds beyond the ordinary bounds of human vision) to justify the status quo of hierarchical power relations across society:

See, through this air, this ocean, and this earth,
All matter quick, and bursting into birth.
Above, how high, progressive life may go!
Around, how wide! how deep extend below!
Vast chain of being...
...what no eye can see,

The individual's suffering under hierarchy is sanctified in the name of this transcendent, organic whole—a conceptual framing that Peterson uses to justify the perpetuation of societal inequalities across the categories of class, race, and gender.³

While Peterson attempted to distance himself from the alt-right in the aftermath of the Charlottesville rally, this framework—paired with Peterson's emphatic embrace of psychedelics—is likely to speak to the right-wing authoritarian elements of his audience in the coming years. Peterson's discussion with Griffiths about the psychedelic insight that death is a "reparative mechanism" with a "restorative role," along with his assertion that "if death isn't regulated properly within us, we get cancer," could be warped by those alt-right elements to serve as justifications for weeding out the "undesirable" elements of society. Later in his discussion with Griffiths, Peterson applies this metaphor to society at large:

But...there's this benevolent death that's a reparative mechanism, and when I've allowed my intuitions to extend themselves as far

No glass [telescope] can reach! from infinite to thee,
From thee to nothing!—On superior pow'rs
Were we to press, inferior might on ours:
[...]
Where, one step broken, the great scale's destroy'd:
From nature's chain whatever link you strike,
Tenth or ten thousandth, breaks the chain alike.
[...]
The least confusion but in one...
...the whole must fall.
Let earth unbalanc'd from her orbit fly,
Planets and suns run lawless through the sky;
Let ruling angels from their spheres be hurl'd,
Being on being wreck'd, and world on world;
Heav'n's whole foundations to their centre nod,
And nature tremble to the throne of God.
All this dread order break—for whom? for thee?
Vile worm!—Oh madness, pride, impiety!
[...]
Cease then, nor order imperfection name:
Our proper bliss depends on what we blame.
Know thy own point: This kind, this due degree
Of blindness, weakness, Heav'n bestows on thee.
Submit.— [...]
All nature is but art, unknown to thee;
All chance, direction, which thou canst not see;
All discord, harmony, not understood;
All partial evil, universal good:
[...]
One truth is clear, Whatever is, is right. (Pope, 1891)

Pope implies in "An Essay on Man" that "slavery is not a situation imposed from outside but a moral condition emanating from within" (Richardson, 2003), and that—as with Peterson's Cain—refusal to gratefully accept one's place within an interconnected hierarchy is to threaten the very structure of the cosmos itself.

³From Peterson's perspective, psychedelics thus help to teach a lesson that he earlier described in *12 Rules*: when you aspire to greatness within the hierarchy, "you disturb others, in the depths of their souls, where they understand that their cynicism and immobility are unjustifiable. You play Abel to their Cain. You remind them that...they do not want to lift the world up on to their shoulders, where it belongs" (Peterson, 2018).

as possible, I think, well...that's true of...Being itself...is that, in a manner that we can't comprehend, death plays a restorative role... It's something like the precursor to resurrection, and God only knows where that idea goes. (Peterson, 2021b)

This line of thought connects with a related claim by the adjacent public speaker Jonathan Pageau, a reactionary acolyte of Peterson. Pageau concurs with Peterson's concept of benevolent death as a reparative mechanism and characterizes social justice activists as working to subvert it:

If in traditional societies we see scapegoat mechanisms sacrificing the exception in order to preserve coherence, here it is a desire to sacrifice the entire world for the exception. On a social level, this appears as an upside-down hierarchy, where the strange, the impure, the exceptional, the fluid, the rejected, the sick, and the unknown become a new measure by which society is evaluated. (Pageau, 2021; Thought Slime, 2021)

When “undesirables” become coded as cancer, invasive social measures—including eugenics and genocide—risk becoming justifiable.⁴

RED PILLS FOR SALE: NEOREACTION, RIGHT-WING BILLIONAIRES, AND CORPORADELIC DREAMS

Although Peterson invoked fascist metaphors to opine about psychedelics, members of the far right had already co-opted a colorful drug metaphor to talk about the radicalization process: taking the red pill. Under the pen name Mencius Moldbug, Curtis Yarvin was the first to associate anti-democratic, neofascist politics with the metaphor from the sci-fi film *The Matrix* (Moldbug, 2007). Two years later, in the first chapter of *Unqualified Reservations* (UR), a blog about the neoreactionary (NRx hereafter) movement, Moldbug compared his anti-egalitarian, pro-corporate governance views to red pills—this time in direct comparison to a DMT trip, described in terms that make it clear the author was familiar with the drug's effects (Moldbug, 2009):

There is no such thing as a gentle introduction to UR. It's like talking about a 'mild DMT trip.' If it was mild, it wasn't DMT. UR

⁴Although Jordan Peterson is not advocating for genocide, the logic of coding social undesirables in public health terms informed the “racial hygienics” that justified Nazi policy: “A credo repeatedly articulated by the National Socialists held that what was wrong in Germany could be powerfully and usefully expressed through medical analogy. The ‘body’ of the German people was threatened, and its healer was Hitler. As anti-Semitism was added to social Darwinism and racial hygiene, the so-called Jewish question was rendered a medical problem, ‘the therapy of which was to be realized in places like Auschwitz and Dachau’.... Gradually, the medical profession embraced the belief that to cure individual persons was one thing, but to heal the nation was incomparably more important; thus, most in the profession adopted the ideas of racial hygiene as a massive public health measure. ‘The aim of generating pure Aryans had taken precedence over the most fundamental ethical issues in medicine’...and healing acquired a new, sociopolitical definition that swept aside the vulnerability and suffering of large numbers of individual persons, who, in a sense, lost their humanity and were transmuted into pollutants of the state” (Barondess, 1998).

is a strange blog: its goal is to *cure your brain*. We've all seen *The Matrix*. We know about red pills. Many claim to sell them. You can go, for example, to any bookstore, and ask the guy behind the counter for some Noam Chomsky. What you'll get is blue pills soaked in Red #3.

The red pill idiom has since been adopted by incels, neo-Nazis, members of the Trump first family, and billionaires alike (Swearingen, 2020).

Accelerationist philosopher Nick Land's post-academic writings engaged with Moldbug's NRx aspirations, coloring them sufficiently that the NRx project of balkanizing the world into hyper-capitalist city-states is also known as *The Dark Enlightenment*, after Land's eponymous 2014 essay. During his time at Warwick University, Land co-founded the Cybernetic Culture Research Unit (CCRU), an unofficial project of the philosophy department which orbited around rave culture, post-structuralism, the occult, and technology. Land left academia amid suspicion of providing drugs to students (Whitaker, 2020). Land's vision of acceleration—the idea that capitalist processes should be vastly empowered and hastened in order to bring about dramatic social and political change—evolved to embrace authoritarian, radical right-libertarian ends (Land, 2017), but the philosophy has both right and left (Fisher, 2014) applications. Land's work has been more directly influential on neo-Nazi groups, with altright.org cofounder (with Richard Spencer) Jason Reza Jorjani among them (Goldhill, 2017). Moreover, accelerationism has been appropriated by neo-Nazi circles, inspiring James Mason's *Siege* writings, which have been collected and published by psychedelic-adjacent neo-Nazi musician and journalist Michael Moynihan, whose wife and bandmate, Annabelle Lee, has translated psychedelic works by Albert Hofmann and Christian Rätsch (Piper, 2015). In the 1980's, Mason was in communication with members of the Manson family and today has direct contact with the aforementioned Atomwaffen. Helter-Skelter, Manson's apocalyptic prophecy, was essentially right-wing accelerationism—the murders by the Manson Family were carried out in hope of provoking a race war (Lexington County Chronicle, 2020).⁵

Although Silicon Valley's interest in disruption differs from the overt violence of mass racial attack, the frequent result of market-based disruption is catastrophic upheaval for the marginalized communities. Corporadelic actors are currently folding psychedelics into a corporate ethos predicated on novelty and cognitive labor: from microdosing coders to ayahuasca business coaches, psychedelics are seen as shortcuts to divergent market insight in a globalized, neoliberal marketplace. Following atai Life Sciences' successful IPO, founder and Chairman Christian Angermayer said on CNBC's *Squawk Box*: “The world we're building is a bad place for our brain, so mental health issues will go up. But I do think we have some real shots in our portfolio to end the mental health crisis” (Costa and Shead, 2021). Yet despite publicly discussing his experience with

⁵Matthew Johnson cites Manson's manipulative influence over his psychedelized subordinates as an extreme example of the dangers of imposing one's beliefs on others in a psychedelic setting (Johnson, 2021).

psilocybin and his desire to improve the world, he also directly supports authoritarianism in his advertised resume: Angermayer is on the presidential advisory board of Rwandan head of state Paul Kagame, known internationally for human rights abuses and domestic political repression (Human Rights Watch, 2020; Angermayer, 2021). One of the defining features of authoritarian regimes is unchecked human rights abuses. Since the violence that we do to each other tends to cause the most severe cases of PTSD—more so than natural disasters such as hurricanes or tsunamis—it is unlikely that Angermayer's efforts to spread psilocybin therapy will be an adequate substitute for widespread social change (Kessler et al., 2017). Since billionaires are invested in preserving the status quo of massive wealth inequality, their enthusiasm for psychedelics suggests that this class of drugs is not inherently a solution for ameliorating the extensive harms caused by social inequality.⁶ As described by Tim Ferris, a multi-millionaire psychedelics donor and coach for attaining “expert status...in less than four weeks” (Day, 2018): “The billionaires I know, almost without exception, use hallucinogens on a regular basis” (Fink, 2015). Both Steve Jobs and Bill Gates have admitted to LSD use (Playboy, 1994). Minecraft inventor and billionaire Markus “Notch” Persson is a vocal opponent of feminism, gay pride, and trans acceptance while simultaneously supportive of QAnon and self-experimentation with LSD (Notch, 2017). Tech billionaire Peter Thiel has also invested \$12 million in atai Life Sciences and was an early investor in COMPASS Pathways, a company plagued with accusations of seeking to monopolize and patent every conceivable application for psychedelics, including elements of prior art (Hausfeld and Nickles, 2021; Love, 2021; McDaniel, 2021).

Thiel has not definitively acknowledged psychedelic use, but his investment conveys interest, and his politics are decidedly authoritarian: he has stated his ideal business strategy is the formation of a monopoly (Thiel, 2014). Thiel's Stanford peer wrote an essay detailing his allegedly unapologetic support for South African apartheid: “He said, with no facial affect, that apartheid was a sound economic system working efficiently, and moral issues were irrelevant” (Lythcott-Haims, 2016). He has also been a vocal and monetary supporter of President Trump and Senator Ted Cruz. Thiel co-founded the surveillance capitalism firm Palantir, which aggregates personal data about private citizens and makes a high-resolution profile easily available to corporate clients (e.g., hedge funds), government agencies like the US Immigration and Customs Enforcement (ICE), police, and militaries. Palantir's billionaire co-founder and CEO Alex Karp has acknowledged that their technology is sometimes

used in targeted assassinations (HBO, 2020). Around the same time that Moldbug, described as “[t]he supreme Sith Lord of the neoreactionaries” (Land, 2013), compared his NRx blog to a potent tryptamine, Thiel wrote a disquieting piece for CATO Unbound (a right-wing libertarian think tank funded by billionaire brothers Charles and David Koch). In addition to lamenting women's suffrage and hinting at his own recreational drug use—he opened the piece with: “I no longer believe that freedom and democracy are compatible” (Thiel, 2009). At the end of the essay, Thiel explicitly recommends Moldbug's UR as suggested reading. Moldbug and Thiel share more than corporate monarchist ideology: in 2011 Thiel's Founders Fund provided \$100,000 in start-up capital for Moldbug's software company Tlon, where his official title was “benevolent dictator for life” (Pein, 2014; Tait, 2019). Undoubtedly, the kind of corporate feudalism advocated by Thiel and Moldbug is an updated form of digitally-empowered fascism (Smith and Burrows, 2021).

The merger between fascism and big data is nowhere better exemplified than with Cambridge Analytica (CA), the artificial intelligence (AI) company co-founded by billionaire Robert Mercer and former Trump strategist Steve Bannon (Mayer, 2017; Cadwalladr, 2018). Highly targeted voter data scraped from social media sites including Facebook allowed CA to focus on, for example, Catholics who regularly attend mass and voted in the previous election. Such granularity has been credited with swaying results rightward in both Brexit and the 2016 US presidential vote. Both the Mercer Family and Bannon have been the subject of targeted lobbying by psychedelic reformers at the Multidisciplinary Association for Psychedelic Studies (MAPS), enacted directly by former MDMA PTSD therapy recipient and MAPS employee (MAPS, 2018), self-described “conservative whisperer,” Sgt. (R) Jonathan Lubecky (Lubecky, personal communication). MAPS has stated that Lubecky's lobbying work included arranging for placement of a favorable story about MAPS' clinical trials with veterans in the white nationalist mouthpiece, Breitbart News (Bernstein, 2017; Kessler, 2017; Nickles, 2020), which is co-owned by Robert Mercer's daughter, Rebekah Mercer (Church, 2017). Rebekah Mercer is reportedly highly active in the editorial process at Breitbart, to the extent of reading every story and “call[ing] when there are grammatical errors or typos.” Rebekah Mercer has since committed to donating \$1 million to research on MDMA therapy for veterans with PTSD. According to social media posts by Lubecky and Rick Doblin's description of Lubecky's work,⁷ his contact with the American political right wing is far-ranging

⁶Commentators and psychedelics researchers have a tendency to ignore the structural realities and incentives of capitalism while arguing that psychedelic experiences of interconnection will inspire billionaires to act for the betterment of society. This perspective parallels arguments for sending billionaires to space, in order to facilitate an “overview effect” that inspires social change. Amazon Executive Chairman Jeff Bezos suggested that his trip into low Earth orbit increased his concern for Earth's “fragile” ecosystem; however, the solutions he has offered thus far are still predicated on the market logic of infinite growth with extractive industries. Rather than questioning whether feelings of interconnection are sufficient for systemic social change, Johns Hopkins psychedelics researcher David Yaden speculated that Bezos might not have achieved the overview effect with just 10 minutes in low orbit (Woodward, 2021).

⁷As Doblin stated on The Tim Ferriss Show: “And after our treatment, he was able to go back to work and he was actually the liaison to the veterans for Senator Rand Paul for his 2016 presidential nomination campaign for the Republican nomination. And so when I met Jon, he was doing much better, but he also had political connections. And so I felt that that's really what we need to broaden the support for what we're doing to have a veteran who's got connections with a lot of Republicans who is willing to speak about the benefits of MDMA. And so actually Jon has met with Vice President Pence, with Stephen Miller, with all sorts of Republicans that he was able to speak with and have, in a way, the first impressions that they get about MDMA and the potential of MDMA to help prevent suicides among veterans, to help veterans come back and lead more healthy lives. They would hear about it from Jon. So now he's working as a consultant for MAPS to try to broaden our political support.”

and includes figures such as former President Donald Trump, former Vice President Mike Pence, Rudy Gulliani and Alex Jones (Ferriss, 2020; Nickles, 2020). A year prior to her donation to MAPS, Rebekah Mercer founded Parler (Benveniste and Yurieff, 2020), a social media platform used by many of those who stormed the United States Capitol Building (Cameron and Mehrorta, 2021).

ADDRESSING THE TROJAN HORSE IN THE ROOM

The argument for psychedelic medicalization is made in dollars and cents—MDMA for PTSD is projected to be more cost-effective (Marseille et al., 2020) and profitable than standard treatments. When articulating a broader vision beyond legalizing psychedelic therapy, psychedelic advocates frequently describe a strategy consistent with a Trojan horse theory of change: broader psychedelic use will catalyze geopolitical reconciliation and become the chemical feedstock of world peace. Most recently, MAPS Executive Director Rick Doblin advanced the hypothesis that the mystical experience could be used as “a tool of political reconciliation.” In an interview with spiritual leader and former Democratic Presidential candidate Marianne Williamson (The Marianne Williamson Podcast, 2021), Doblin argued that “humanity is in a race between consciousness and catastrophe.” To wit, the consciousness to which Doblin refers is that of religious fundamentalists. Doblin asserts that the psychedelic experience is the true religion, hoisting a banner under which a global Pax Psychodelia can be negotiated:

I would say that the key challenge I see going forward with the psychedelic renaissance, and also with [the] survival of humanity, is that we have to really help fundamentalists of all the different religions move to a more mystical orientation, and I think that is our challenge. And psychedelics can help that, to see that... what people take literally are metaphors and are symbols; and when you concretize them and... make them literal. And then you are fearful [that] people are infidels, or they don't believe it. So, I think back to America now where we got the Christian fundamentalists... as a major force: how do we help them see that there is a deeper spirituality, that they can have a richer life by surrendering some—And it's not just Christian fundamentalists, it's Orthodox Jews who are crazy in their own way too. And... orthodox Muslims [also].” (The Marianne Williamson Podcast, 2021)

Indeed, Doblin has been making similar claims for most of his career, having once proposed a project entitled “Shaping a Global Spirituality While Living in the Nuclear Age” (Klein, 1985) to the United Nations, which articulated such a vision. Doblin is far from the only psychedelic advocate making sweeping claims about the power of psychedelics to potentiate systemic change, rather than being assimilated and put to use by the current political and economic order (e.g., Peck, 2020).

But if Doblin's gambit is that ingestion of psychedelics by evangelical Christians will help them find “a deeper spirituality,” the case of close Trump ally and “active member” of the First Baptist Church Matt Gaetz (R-FL) is a stubborn datapoint

(Kaylor and Underwood, 2021). Although Gaetz co-sponsored an (unsuccessful) amendment to remove a bill rider that inhibited therapeutic research into Schedule I controlled substances such as psilocybin, MDMA and marijuana (Jaeger, 2019), it is now plain that the Representative's interest in psychedelics was not solely legislative. Evidence has since surfaced that he allegedly used MDMA himself during encounters with sex workers (Bort, 2021). Famously, Gaetz supported drug-testing welfare recipients (Vlamiš, 2021), demonstrating that conservatives may support psychedelics for medical or recreational purposes, but they will likely continue to defend wealth-based hierarchy.

PSYCHEDELIC CULTURES OF AUTHORITARIANISM AND VIOLENCE

Even if the policy goals of psychedelic reformers come to fruition, they will still have to reckon with the authoritarianism and violence that have haunted psychedelic-assisted therapy since its inception. In Torsten Passie's history of MDMA, he cites Deborah Harlow's account of how the male-female therapeutic dyad arose as a safeguard against therapists sexually manipulating their drugged clients (2018). Despite these historical roots, subsequent scientific accounts of the dyad have emphasized its psychoanalytic rationale (e.g., providing a mother and father figure to facilitate developmental transference) while omitting warnings about the danger of therapist abuse: “With a male-female dual-therapist model, the therapists hold different transference roles during the session and are often secure attachment figures available to the patient for contact and bonding” (Penn et al., 2018).

This rebranding of the therapeutic dyad does little to institute meaningful safeguards for the exaggerated power imbalance inherent in psychedelic therapy. The case of the psychedelic researcher who facilitated a MAPS MDMA PTSD Phase II therapeutic trial, Richard Yensen, is illustrative. Yensen was chaperoned by his wife and dyad counterpart Dr. Donna Dryer in recorded sessions with patient Meaghan Buisson. Nevertheless, Yensen used his authority to initiate a multi-year sexual relationship with Buisson that was counter-therapeutic and predatory (Goldhill, 2020; Lindsay, 2021).

A recent *Mad in America* article, “Breaking the Silence Around Psychedelic Therapy Abuse,” details many examples of authoritarian mistreatment and assault by influential practitioners—some of whom remain influential and promoted in the field (Hall, 2021). Citing Salvador Roquet, an early psychedelic therapist, Hall points to a lineage of practice wherein authoritarian methods are encouraged through formal, underground training. Assault has been a problem in other environments where vulnerable, psychedelized people are supervised by unscrupulous authority figures, as in the therapy-adjacent shamanic and neoshamanic contexts described by Ross (2018). Ross' subsequent research has demonstrated how dominant approaches to sexual abuse in psychedelic contexts rely on neoliberal narratives about individual responsibility. These narratives avoid the systemic nature of power imbalances magnified by vulnerability and suggestibility (Ross, 2020).

Within hierarchical organizations, these dynamics have been weaponized by powerful, charismatic figures for the purposes of influencing group behavior. Among new religious movements, a still-living founder's perceived omniscience, esoteric knowledge, or prophetic ability can promote an extremist worldview of "absolute righteousness" where "killing becomes healing" (Strozier, 2010). For example, psychedelics played a role in both the Aum Shinrikyo and Rajneesh cults, which committed terrorist acts against unsuspecting civilians using chemical and biological weapons (LeHardy, 1997). Members of both groups were intimately involved with psychedelic manufacture and use. Aum Shinrikyo began as a small yoga school in the mid-1980s, attracting New Age spiritual seekers with teachings directed toward "enlightenment" and "awakening" (Maekawa, 2001). Many top leaders in Aum Shinrikyo admitted to using LSD in ritual practices "to stimulate spiritual activity," and psychedelics were also administered to Aum's recruits as part of the conditioning and indoctrination process (Kogo, 2002; Thornton, 2017). In 1995, members of Aum Shinrikyo intentionally released the chemical nerve agent sarin in the Tokyo subway, killing 14 people and injuring 5,500. The same Aum scientist who produced its sarin gas was also responsible for producing "research quantities" of LSD for the cult (Danzig et al., 2012; Thornton, 2017).

Cult violence in the New Age was prefigured by the Rajneesh movement in the decade prior. The sanyassins, as its followers were called, frequently had experience with LSD before joining the group as there was significant overlap between psychedelic culture and the movement's spiritual ideals (Palmer and Sharma, 1993). Many sanyassins were apprehended internationally on drug trafficking charges. According to its own members, Rajneesh activities were at least partly funded by drug smuggling, and drug trafficking was a major source of income for the movement (McCormick, 1987). At least one follower was directly involved with LSD manufacture: prolific LSD chemist Nick Sand lived and worked in several sanyassin ashrams, first moving to Pune, India to be closer to Bhagwan Rajneesh. Sand bought a house near the ashram, where he built a lab and manufactured "massive" quantities of LSD. Sand also claimed that he helped Rajneesh get a passport to move to Oregon (Scully, 2017). It was in Oregon where the inner authoritarianism of the group bled out into the wider world, when sanyassins attempted to influence a local election by driving down voter turnout with a bioterror attack on a salad bar.

CONCLUSIONS

Experiments or studies that have sought to explore whether psychedelics have a consistent impact on political ideology and psychedelic use have thus far failed to rule out lurking variables in participant set and setting. Researchers should be careful to avoid conflating single-issue beliefs with specific ideologies, since particular values (e.g., environmentalism) are represented across different political perspectives and shift over time. We discourage the use of underpowered studies to make broad claims, especially given the risk of exaggeration and distortion in the media, which can further influence patient expectation and researcher bias (Carhart-Harris et al., 2018). Because of the sensitivity of study

participants to suggestion under the influence of psychedelics, it is crucial that researchers publish the manuals used in psychedelic therapy and describe any significant variation within the study of the therapeutic environment (e.g., the presence or absence of religious imagery) (Lattin, 2021). Since public relations campaigns, intake procedures, questionnaires, and preparatory sessions can all prime and influence participant expectations, which can in turn affect a study's measured outcomes, we recommend the development of new standards for reporting on psychedelic clinical trials that include open publication of these materials (Petranker et al., 2020; Muthukumaraswamy et al., 2021).

Assertions that psychedelics induce a shift in political beliefs will have to address the many historical and contemporary cases of psychedelic users who remained authoritarian in their views after taking a wide variety of psychedelics or became radicalized after extensive experience with them. We propose that anecdotal accounts of psychedelics precipitating radical shifts in political or religious beliefs are common but result from factors relating to the set and setting and have no inherent directional basis on the axes of conservatism-liberalism or authoritarianism-egalitarianism. Instead, we draw from critical perspectives in the humanities and social sciences to argue that any experience which challenges a person's fundamental worldview—including psychedelic experience—can precipitate shifts in political belief.

Whether on grounds of supporting the troops or following doctors' orders, psychedelics—properly contextualized—are palatable to conservatives. In fact, themes of psychedelic authoritarianism within the context of medicalization go beyond the PR campaigns of organizations such as MAPS. Such authoritarian tendencies have appeared in clinical trials, underground contexts, and instances of state-sanctioned psychedelic torture (Nickles, in press). Additionally, several modern conservative cultural icons are on record as supportive of psychedelic medicalization. During a conversation on *The Rubin Report*—an IDW-affiliated interview show—Jordan Peterson, conservative ideologue Ben Shapiro, and host Dave Rubin discussed the spiritual and medical benefits of psilocybin and MDMA. Peterson admits to experience with psilocybin (The Duncan Trussell Family Hour, 2017) and Rubin confirms experience with both. While pressing the uninitiated Shapiro about the merit of these drugs, Shapiro concedes that he would be supportive of their use, but only if under the care of a physician:

I think the answer is that it depends on, you know, the level of expertise of the person using it is what I would suggest, you know, the idea—like, I'm not against prescription medication, so if you're talking about, you know, an actual program that's going to better somebody's life that's one thing, but if it's somebody who's just 'I want to have a religious experience, let me pop some LSD' then—there's some serious downsides to drugs. (The Rubin Report, 2018)

To Shapiro, the authority of a medical provider would be enough to overcome his personal reticence about currently illegal psychedelic substances. For Peterson and Rubin, there is no evidence that their psychedelic experiences present a barrier to

their activities—not only as conservatives, but as elite thought leaders of the conservative cultural project.

As institutional support for psychedelic therapy grows, hierarchy-conscious conservatives are likely to shift their opinions about the acceptability of taking psychedelics themselves. Within the field of psychedelic studies, the non-specific nature of the interface between psychedelics and ideology is a positive opportunity for interdisciplinary scholarship on the cultural plasticity and suggestibility inherent to psychedelic experiences:

As the project of mainstreaming the uses of psychedelic drugs is proving surprisingly successful, these substances also enter into forms of life that are very different from the ones that have fostered the revival [of institutional psychedelic research]. While liberal and left-leaning anthropologists might find this pluralism...disturbing..., it's a boon to the anthropology of psychedelics. Studied ethnographically, rightist psychedelia might teach us a great deal about the cultural plasticity of the relationship between human beings and these wondrous molecules. (Langlitz, 2020)

The fact that members of reactionary and right-wing authoritarian political movements make their own uses of psychedelics is an opportunity to broaden theoretical claims about psychedelic mechanisms, which can help researchers to avoid making uncritical and simplistic generalizations based on the limited data of existing studies. This is critical to acknowledge as simplistic narratives about the social benefits of psychedelics are being trumpeted by profit-motivated actors. As corporate speculation on psychedelic medicine booms, commentators have seized on the potential for psychedelics to disrupt a mental health industry valued at \$100 billion (Yakowicz, 2021). Although much of this discourse focuses on individualistic therapeutic effects, a recurring theme is the notion that psychedelics can solve complex social problems by making people more politically liberal (Adams, 2020).

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While the notion of individual solutions for systemic problems has been widely critiqued across academic disciplines, we believe that the common narratives regarding the effects of psychedelics on political orientation present persistent blind spots within the psychedelic literature. It is imperative to address these blind spots to advance coherent, interdisciplinary socio-political frameworks for analyzing and engaging with the experiential realities and potential implications of psychedelic drug use.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

BP and ND contributed to the research conception, drafting of the article, critical revision of the draft, and final approval of the manuscript. Both authors contributed to the article and approved the submitted version.

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An Encounter With the Other: A Thematic and Content Analysis of DMT Experiences From a Naturalistic Field Study

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Introduction: *N,N*-dimethyltryptamine (DMT) is an endogenous serotonergic psychedelic capable of producing radical shifts in conscious experience. Increasing trends in its use, as well as new trials administering DMT to patients, indicate the growing importance of a thorough elucidation of the qualitative content, over and above structure, which the drug occasions. This is particularly in light of the hyper-real, otherworldly, and often ontologically challenging yet potentially transformative, nature of the experience, not least encounters with apparently non-self social agents. Laboratory studies have been limited by clinical setting and lacking qualitative analyses of experiential content, while online surveys' limitations lie in retrospective design, uncontrolled use, and both of which not guaranteeing 'breakthrough' experiences, i.e., producing very strong psychoactive effects.

Methods: We report on the first naturalistic field study of DMT use including its qualitative analysis. Screened, healthy, anonymised and experienced DMT users were observed during their non-clinical use of the drug at home (40–75 mg inhaled). In-depth semi-structured interviews (inspired by the micro-phenomenological technique) were employed immediately after their experience. This paper reports on the thematic analysis of one major domain of the breakthrough experiences elicited, the 'other'. Thirty-six post-DMT experience interviews with mostly Caucasian (83%) males (eight female) of average 37 years were predominantly inductively coded.

Results: Invariably, profound and highly intense experiences occurred. The first overarching category comprised the encounter with other 'beings' (94% of reports), encompassing super-ordinate themes including the entities' role, appearance, demeanour, communication and interaction; while the second overarching category comprised experiences of emerging into other 'worlds' (100% of reports), encompassing super-ordinate themes of the scene, the contents and quality of the immersive spaces. Many further mid-level themes and subthemes also illuminate the rich content of the DMT experience.

Discussion: The present study provides a systematic and in-depth analysis of the nuanced content of the otherworldly encounter within the breakthrough DMT experience, as well as elaborating on the resonances both with previous DMT studies focusing on

entity encounters and other types of extraordinary experiences entailing such encounters. These include the alien abduction, folkloric, shamanic and near-death experience. Putative neural mechanisms of these features of the DMT experience and its promise as a psychotherapeutic agent are discussed in light of such findings.

Keywords: dimethyltryptamine, thematic analysis, naturalistic, field study, social, psychedelic

INTRODUCTION

DMT: ‘The Spirit Molecule’

N,N-dimethyltryptamine (DMT) is an indole alkaloid and potent serotonergic psychedelic, acting on the 5HT-2A receptor, which is virtually ubiquitous in nature (McKenna, 2018) and endogenous to humans. Reviews of its detection in the urine, cerebrospinal fluid and blood of human beings points to a maximum possible endogenous concentration of 55 ng/ml (Barker et al., 2012). Dean et al. (2019) have evidenced the presence of indole-ethylamine-methyltransferase (INMT), a key requisite enzyme for DMT synthesis, in the human cerebral frontal cortex and pineal gland.

DMT is one of the major active constituent in the Amerindian shamanic decoction, ayahuasca (‘vine of the dead’), typically blending the DMT-concentrated *Psychotria viridis* and *Banisteriopsis caapi* that contains the beta-carbolines rendering DMT orally active. DMT ingestion amongst humans has a potentially ancient history; it was identified, alongside harmine (one of the other ayahuasca beta-carbolines), in a ritual bundle from the Bolivian Andes dated to at least 1,000 CE (Miller et al., 2019). Use of DMT (and similar compounds; 5MeO-DMT and 5MeO-DIPT) in contemporary society, at least in the United States general population, is relatively rare at 0.7% (Palamar and Le, 2018). Research slightly prior to this finding suggest that its use may be increasing, as a larger proportion (24%) of DMT users were identified as new users compared with other psychedelics (Winstock et al., 2014). With its physiological role yet to be clarified (Rodrigues et al., 2019), given its profound psychoactivity as well as proclivity to engender subjective experiences of sensed presence, or interactions with other-than-self social agents, it has been suggested that DMT models or may be implicated in a host of altered states ranging from dreaming or psychosis (Dean, 2018), to spontaneous transpersonal experiences such as alien abduction experiences (Luke, 2012) – or near-death experiences (NDEs; Strassman, 2001; Timmermann et al., 2018), DMT’s precise qualitative relationship with which will be the dedicated subject of a subsequent paper.

Not many studies have been dedicated to systematic qualitative analyses of the psychedelic experience more generally (e.g., ayahuasca: Kjellgren et al., 2009; Wolff et al., 2019; psilocybin: Turton et al., 2014; ibogaine: Schenberg et al., 2017b; see below re: DMT), while some have explored the subjective mediation of psychedelic therapy (e.g., ayahuasca: Loizaga-Velder and Verres, 2014; Dos Santos et al., 2018; psilocybin: Belser et al., 2017; Watts et al., 2017; ibogaine: Schenberg, et al., 2017a; LSD: Gasser et al., 2015). Beginning with a surveying of DMT use in modern and indigenous Australia (Tramacchi, 2006),

there has been a recent surge in interest in the phenomenology of DMT, including its cultural history, and the gnostic insight and essential liminality that is defining of the experience (St John, 2015, 2018; John, 2018). The remarkable consistency in many of its motifs has been noted (Gallimore and Luke, 2015) including the nature of the encounters with entities, which is itself a subtopic of significant attention, with direct implications for mechanisms of social cognition, and possibly for ontology (Luke, 2008, 2011; Luke and Spowers, 2018).

Varieties of DMT Experience

In April 1956, Stephen Szara self-administered DMT intramuscularly (I.M.) – representing the very first human experience with pure DMT – and at 1 mg/kg reported sensations such as ‘brilliantly coloured oriental motifs and wonderful scenes altering rapidly’ (Szára, 2014). The study of Sai-Halasz et al. (1958) constitutes the very first research study in human participants, and used 0.7–1 mg/kg I.M. DMT in 30 healthy individuals. The report divided the experience into coarse and pathological categories, as symptomatic of such early DMT studies, including with patient populations (Boszormenyi and Szara, 1958; Turner and Merlis, 1959) – saliently however, incorporating ‘anxiety’ qualified with the statement, ‘when the world changes so suddenly and intensely that the subject loses his solid environment’ (Sai-Halasz et al., 1958, p. 9). Strassman (2001), in one of the first landmark psychedelic studies post-prohibition, documented the experiences of 60 participants undergoing over 400 DMT doses, which resulted in at least half of the *high-dose* (21–28 mg/kg, I.V.) participants reporting otherworldly adventures with other beings (Luke, 2013) – a closer content analysis of which will be the focus of a subsequent paper.

Constituting the only other thematic analysis of the DMT experience, Cott and Rock (2008) coded 19 narrative reports from an online survey, with a sample of mean age 23 (*SD* = 6), 95% male, and time since last DMT usage ranging from 2 days (11%) to 2 years (5%). Twenty percent were previously DMT-naïve (5% having used DMT >100 times). Nine very generic themes were identified, as follows – *Hallucinations*: which were visual, bodily, or auditory; *Veridical hallucinations*: entailing transportation to another world and supplanting of ordinary experience by ‘DMT hyperspace’, persistently considered to be true or real, and contact with sentient beings attributed ‘exosomatic ontological status’; *Affective distortion*; *Distortion in time, space and self*; *Spirituality*: denoting descriptions of beauty, love, religious experiences, or insights into self or the nature of the universe; *Familiarity*: denoting a sense of having been in the DMT space before (or even always residing there); *Lucidity*; *Ineffability*; and *Extreme intensity*.

Most recently, Timmermann et al. (2019), in the latest laboratory research with DMT, have provided a unique, valuable neurophenomenological study of the DMT experience, in which they illustrate intimate correlations between the phenomenological structure of first-person reports, specifically the 'visual', 'bodily' and 'metacognitive/emotional' domains they identified, and real-time neurophysiological measures. Lyke (2019) has conducted a content analysis of entity descriptions specifically, across 149 online published DMT trip-reports (90% male, mean age 25 years) from 2009 to 2019, which entailed 180 entity encounters in total. Comprehensively, Davis et al., 2020b undertook an international survey encompassing 2,561 respondents reporting 'encounter' experiences after a 'breakthrough' dose of inhaled DMT (that is, 'one that produced very strong psychoactive effects'). Seventy-seven percent of the sample were male, slightly lower than the prior studies, though 85% were Caucasian/white, 64% living in the United States, and an average age of 32 ($SD=9$). Respondents had used DMT an average of 14.5 times, and 67% reported that their most memorable entity encounter, about which they are answering the survey, was their first encounter.

Other schematisations include Meyer (1992), which incorporated a 'hyperspace' populated with intelligent, communicative entities in 66.5% of 340 online trip-reports (also see Strassman et al., 2008). Lastly, Shanon (2002) anthropological charting of the phenomenology of ayahuasca (whose principal component is DMT) culminates in the transportation 'to another realm of existence, one which he or she feels to be very real', where also taxonomised are the 'supernatural beings' observable in the ayahuasca world. Specific cross-referencing between the results of these particular studies and the current analysis' themes is given thorough attention in the discussion section below.

Rationale for the Current Study

The thematic analysis by Cott and Rock (2008) and the encounter survey of Davis et al., 2020b are significantly limited in the following ways: under-representation of the general population, respondents' self-selection – but primarily, small sample size (only the former case), relying on, sometimes triaged, narratives (instead of interview) or fixed-answers, retrospective reports resulting in potential memory bias (deterioration or elaboration), phenomenological (versus qualitative) analyses, inability of monitoring or regulation of not only dosage but set and setting and potential contamination of the experience by use of other substances. The present naturalistic field study of DMT use aimed to address almost all of these limitations, by performing a large-sample, thematic analysis (including content analysis) of a discrete dataset of breakthrough DMT experiences with convenience sampled participants, extracting rich content by *in situ* semi-structured interviews (SSI) immediately post-experience. Also, contrasting with prior laboratory studies, Strassman (2001) reports were based on unsystematic bedside notes after doses (albeit with a large sample size) ranging from 7 to 28 mg I.V. DMT, and Timmermann et al. (2018) purely psychometric analyses ($n=13$) resulted from 7 to 20 mg I.V. DMT with only a subset receiving high-dose – whereas

this study aimed to analyse only high-dose breakthrough experiences. While the SSI's of this study are consistent with methods in qualitative psychology, it also aimed to employ the 'bracketing' technique (a central function of micro-phenomenological interviewing; Petitmengin, 2006, 2017; Timmermann et al., 2019). This allows for a provision of inductive pre-reflexivity, that is, encouraging participants to avoid judgements of experiences into predefined cultural categories (such as 'alien', regarding DMT, which may otherwise lead to propagation of such memes) or confabulating by biased recourse to one's conceptual repertoire, and to instead attentively describe the constitutive features in one's own words.

The aim of the present paper is to achieve, *via* the above improvements, a finer and more naturalistic resolution, and thus greater understanding, of the DMT experience. Especially, the nuances of the qualitative content of the experience, over and above the more gross phenomenological structure (such as Timmermann et al., 2019; see Varela and Shear, 1999; Petitmengin, 2006, for this valuable distinction, e.g., the former being of a variable nature and the latter relating to more invariant processes). This is crucial given its increasing use amongst the population, and more importantly owing to the scheduling of the first clinical trials to administer this intense and fast-acting psychedelic to depressed patients (Steiner et al., 2020; D'Souza, 2021) as well as healthy participants (Liechti and Ley, 2020; Scheidegger, 2021). The paper's particular focus lies in the 'otherly' phenomena evoked by DMT, of immersion into different environments which, crucially, gives way to engaging with non-self entities. This is later discussed in terms of similarity with other exceptional experiences, including possibly shared neurobiological mechanisms, all of which may have implications for therapy. While the psychedelic mystical experience has garnered most attraction as predicting clinical outcome (Haijen et al., 2018; Roseman et al., 2018), the profundity of the entity encounter itself has recently gained attention as to its therapeutic potential (Davis et al., 2020b; Lutkajtis, 2020). Other themes, spanning the particular experiences associated with the 'self' (vs. other) such as psychological and emotional effects, including experient's personal and ontological interpretation and impact, i.e., phenomenological features especially pertinent to DMT's therapeutic capacity, will be delineated in a subsequent paper.

MATERIALS AND METHODS

Participants and Recruitment

Most volunteers were convenience sampled *via* online (social media) advertisement, with many sampled *via* snowballing. All prospective participants were subject to stringent inclusion–exclusion criteria. All recruited participants were experienced DMT users, with inclusion criteria entailing having taken DMT on three occasions, or at least significant other DMT analogous experiences such as ayahuasca or 4-AcO-DMT, with at least one 'breakthrough' experience (typically highly intense and perceptually immersive or remodelling; see Table 1). Participants were also required to provide their own DMT supply, exclusively

TABLE 1 | Participant demographics and DMT experience: average age, 37.4 (range: 23–58), eight female, 83% caucasian; AYA, ayahuasca; N/A, unprovided (free to withhold information due to illicit activity admission).

Participant number	Pseudonym	Age (range)	Sex	Nationality	First time DMT used	Last time DMT used	Overall times DMT used	% break-through DMT experiences (%)
1	MP	45–49	M	White British	2011	11/2016	20	33
2	TM (three doses)	30–34	M	White Romanian	2015	11/2016	5–6	100
3	BB	35–39	M	White British	2013	02/2018	15–20	25
5	JM	35–39	M	White British (Scottish)	2015	03/2017	12	66
6	RV	40–44	M	White British	2015	08/2018	1 (+4 AYA)	75
7	TC	25–29	M	White German	2014	06/2018	10–15	100
8	HV	35–39	F	Black British (Ghanaian-Egyptian descent)	2016	02/2018	80	<100
10	GR	25–29	M	White Romanian	2015	2015	2 (+4-ACO-DMT)	Once
11	SP (two doses)	35–39	M	White British	2003	06/2017	10–15	>50
12	RH (three doses)	55–59	M	Asian British (Indian descent)	2013	08/2018	Hundreds	75
14	AZ	25–29	M	Israeli	2013	02/2018	7	>40
15	ZD	30–34	F	White British	2017	03/2018	20	90
16	RS	25–29	M	Black British (African descent)	2016	05/2018	40	50
17	LR	25–29	M	Chinese-Italian (Dual)	2010	2011	25	40
23	AF	40–44	F	White Italian	2018	05/2019	2 (+8 AYA, 10 changa)	>75
24	LG	30–34	M	Mixed British (Sri Lankan-German descent)	2011	07/2019	20	20
25	AN	25–29	F	White British	2018	07/2019	7	>40
26	EM	20–24	F	White Romanian	2017	05/2019	10	90
27	AB	35–39	M	White British	N/A	N/A	10	100
30	SH	30–34	F	White British	2007	2008	6	50
32	OR (two doses)	25–29	M	Brazilian	2012	2018	3 (+Hundreds AYA)	Once
34	FF	45–49	M	White British	N/A	N/A	10	80
35	JB	40–44	M	White British	N/A	N/A	8	75
36	BW	45–49	M	White British	2000	07/2019	3 (+4 changa)	Once
40	JA	35–39	M	White British	2014	10/2019	70	>70
41	AV	45–49	F	Brazilian	2003	06/2019	20	100
42	MS	55–59	F	Mixed British (Iraqi-Italian descent)	2013	2017	5	100
43	DD	40–44	M	White British	N/A	N/A	Over hundred	>40
44	DS	45–49	M	White British	N/A	N/A	Hundred	50
47	ST	35–39	M	Nigerian	N/A	N/A	3	66

of the form *N-N-dimethyltryptamine* (N-N-DMT; hereafter, referred to as DMT), and to live within the Greater London, Sussex or Kent area of the United Kingdom. Participants were selected in accordance with Johnson et al. (2008) volunteer safety guidelines for hallucinogen research, with exclusion criteria entailing prior psychedelic experiences which were difficult, i.e., putting self or others at risk, or leaving lasting psychological harm to self. The Structured Clinical Interview for DSM-IV Axis-I Disorders – Clinical Trials version (SCID-CT; First et al., 2007) was utilised by a trained SCID administrator as a screening tool, also excluding those with a current or past history of meeting DSM-IV criteria for schizophrenia or other psychotic disorders, or bipolar I or II disorder, as well as individuals with a first-degree relative with these disorders. Also excluded were those with lifetime presence of any major depressive or manic episode, substance abuse or dependence within the last 5 years, and any other current psychiatric diagnosis. Sixty-four prospective participants were screened, where 39 were finally included, resulting in 47 DMT sessions in the parent field study. Thirty-six sessions were the basis of the present thematic analysis, after removal of interviews not meeting several criteria, such as minimum use of 40mg DMT (see **Figure 1** for details).

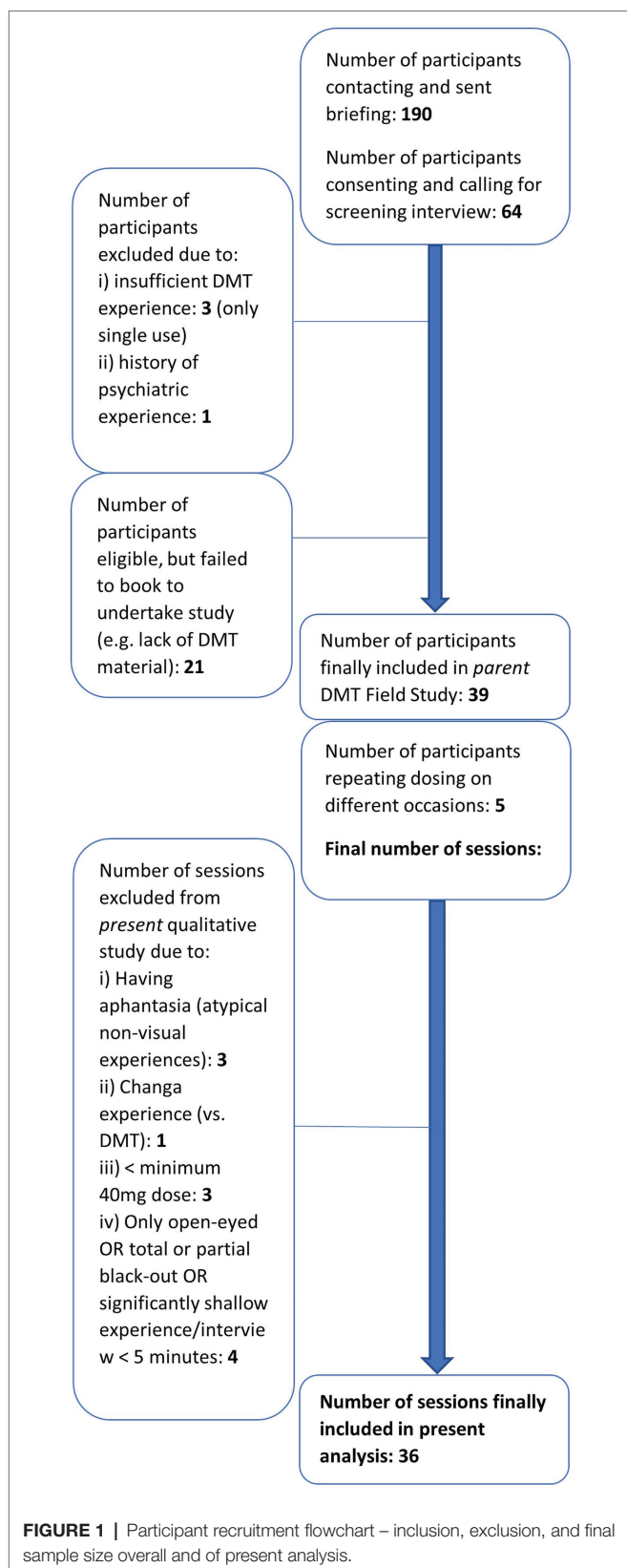
Measures and Materials

The DMT material was weighed using 0.001g microscales to monitor dosage. Given their experienced nature, 'breakthrough' doses were invariably desired by participants leading to a minimum dose of 40mg (max. 75), and mean of 54.5mg (*SD* 9.8; a crude approximate equivalent of at least 18mg I.V.* to loss by exhalation, bioavailability and pyrolysis), inhaled *via* participants' own smoking paraphernalia (almost always glass pipe. RH: Vape pen; DS and DD: 'Dab rig').

A detailed semi-structured interview was employed to explore the resultant DMT experience (see **Supplementary Material 5**). After recounting the experience as entirely and chronologically as possible, interview probes for elaboration spanned domains including entity encounters and visionary environments, as well as sensorial, bodily, emotional and cognitive experiences, corresponding (except the former two) to some of the major categories of the Hallucinogen Rating Scale (HRS), which was employed in the original studies of DMT administration (Strassman et al., 1994).

Procedure and Anonymity

The field study and present analysis was approved by University of Greenwich Research Ethics Committee (Ref. 17.3.5.15). Given



the class-A legal classification of DMT as a controlled substance, strict anonymity of all participants was held throughout.

After reading of the online briefing, participants were given the option to consent (repeated again upon screening call and study day) and followed a link to book a timeslot to call a provided phone-number for the SCID-CT screening interview and were advised to block their caller ID. During the call they were asked to provide their chosen pseudonym by which they were to be called for the study's duration. If they were eligible after screening, a mutual available time between subject and researcher was agreed to book when they plan to take the DMT, while establishing a meeting place from which to lead experimenters to their home or other suggested location agreed by researchers, to serve as the setting for the experience and study. In this way, no personal, identifiable information from the participant such as name, phone number or address was shared or recorded, and all reporting of data was anonymised. Naturalistic field research with psychoactive substances has previously been successful with ayahuasca and with neural and psychometric measures of DMT (Kuypers et al., 2016; Pallavicini et al., 2020).

Intensity ratings were asked of each participant (who stated their willingness to be asked) at 1 min time-intervals during their DMT experience, on a scale of 1–10 (1 = baseline; 10 = most intense experience ever experienced). The SSI was conducted immediately after the subsiding of the DMT experience, as indicated by participants' indication of intensity being 1/10, and most often lasted at least 30 min (approximate range 12–75 min).

Analyses

Interviews were audio-recorded by the researchers and deleted once uploaded to a secure cloud-storage system. All 45 (of 47, as two resulted in no experience) interviews were transcribed *verbatim*, including each of the 36 interviews reported herein. These were then coded with software package *NVivo* v. 12 (Windows).

The interviews were subjected to thematic analysis using a hybrid deductive-inductive process, wherein many of the eventual highest-order, overarching *categories* were based on, but not identical to, most of the major categories dividing the HRS (including 'perception', 'somaesthesia', 'affect', 'cognition'; Strassman et al., 1994). After this point, all analyses and coding efforts were in accordance with the guidelines as provided by Braun and Clarke (2006), as well as being purely inductive in nature with codes and latter themes elicited by the interview data only. Importantly for the present paper focusing on only a subsection of wider analyses (the 'Other'), this deductive aspect is not applicable here given the two overarching categories (elaborated in Results below) not being included in the HRS, and as such all analyses herein are inductively developed.

The extensively iterative thematising process predominantly comprised thorough re-reading of the narratives, the noting of preliminary concepts as initial codes which were then clustered according to thematic similarity into provisional but usually highly specific lowest-order *subthemes*. Such subthemes were then subsumed under the pre-determined overarching categories, and the process was repeated for each of the 36 interviews. The process of reviewing these many subtle themes,

collated within the few broad categories, only until all interviews were coded allowed for more resolved identification of distinct or comparable concepts across the entire scope of interviews. This then led to construction of *super-ordinate* and even finer *mid-level themes*, both subsumed by the overarching categories but subsuming the lowest subthemes. Further refining processes included merging of redundant themes captured by other themes, or expansion of themes covering disparate concepts. Final naming of the themes, especially super-ordinate and mid-level, was decided upon once all subthemes were finalised to ensure a thorough capturing of total explored content.

When using the software *Nvivo*, the number of interviews (as separate documents) ascribed to each given code is automatically calculated. The frequency across the whole dataset with which each theme occurs is thus recorded, and this both serves to provide a content analysis, as well as highlighting the repeated nature of many highly specific themes across reports. Finally, during the write-up, an idiographic emphasis was assumed by reporting many participants' accounts to extensive degrees, to illuminate the details of individual subthemes' content over and above the superficial, summated, and thus nomothetic, overarching categories.

RESULTS

The following table (Table 2) presents all levels of themes to be described in the present paper's qualitative analysis of the DMT experience – the two overarching categories comprising 'Other beings', and 'Other worlds'. This is except all final subthemes, which are listed in **Supplementary Table 3** in the Supplementary Material, where extra clarificatory notes for many of the themes can be found. Also available in the SM is a graphical representation of the themes (**Supplementary Material 4**). Both in the tables and the ensuing descriptions of themes, **bold** signifies super-ordinate themes (e.g., **Role of the beings**); *Italics* signify mid-level themes (e.g., Beings as *Showing*). In the descriptions of themes only, final subthemes (e.g., Beings as 'Presenter') are flanked by 'apostrophes' (and number of participant interviews in which final subthemes are present, out of total interviews, are shown in parentheses).

Encountering Other Beings

Thirty-four of thirty-six experiences (94%) incorporated an encounter of some nature with sentient entities that were experienced as beyond the self. These were highly complex dimensions to the DMT experiences, all of which involving characteristics such as a definable disposition, mode of interaction and most (29, 81%) with individualised visual form. However, some participants did describe sensed presences. This may have been either discreet *Presences* with no imagery, as six participants conveyed, for instance JM reporting 'other vague hints at characters...more areas which had personality'. Or as how five participants articulated, where the presence in fact felt more like an *Omnipresence*, for example, SH invoking her understanding of tantric philosophy, 'the Shiva principle is the kind of indivisible consciousness that is everything, that is also the manifest

TABLE 2 | Thematic analysis of the DMT experience: an encounter with the other; tabularisation of categories, super-ordinate and mid-level themes explored in the present article – see **Supplementary Table 3** for list of all subthemes.

An encounter with the other	No. interviews/36 (%)
Encountering other beings	
<i>Transformation of persons present</i>	7 (19)
<i>DMT personification</i>	5 (14)
Sensed presence	
<i>Presences (No imagery)</i>	6 (17)
<i>Omnipresence</i>	5 (14)
Role and function: entities fulfilling elaborate, inter-relational purposes	
<i>Helping or nurturing</i>	19 (53)
<i>Showing or communing</i>	17 (47)
<i>Manipulating or controlling</i>	6 (17)
Appearance and features: a myriad of entities manifesting	
<i>Human</i>	6 (17)
<i>Other animals</i>	4 (11)
<i>Otherly creatures – non-human/non-animal</i>	26 (72)
<i>Sentient structures</i>	9 (25)
<i>Specific features</i>	9 (25)
<i>Visual quality</i>	19 (53)
Demeanour and nature: entities as magnificent, mischievous or menacing	
<i>Charming and inviting</i>	20 (56)
<i>Other dispositions</i>	12 (33)
<i>Mischievous or jestful</i>	5 (14)
<i>Fearsome or menacing</i>	3 (8)
<i>Nature</i>	17 (47)
<i>Expectation of subject</i>	6 (17)
<i>Gender</i>	17 (47)
Communication and messages: entities as instruments of personal and universal insight	
<i>Communication mode</i>	14 (39)
<i>Messages received</i>	12 (33)
Interaction and behaviour: entities as interfacing or independent	
<i>Active involvement</i>	10 (28)
<i>Passive activity</i>	19 (53)
Exploring other worlds	
<i>Breaking through the veil</i>	8 (22)
<i>Emergence into novel reality</i>	21 (58)
<i>Navigation through space</i>	11 (31)
The scene: from natural to artificial worlds	
<i>Human worlds</i>	6 (17)
<i>Natural worlds</i>	10 (28)
<i>Artificial worlds</i>	6 (17)
<i>Children's worlds</i>	3 (8)
<i>Nebulous worlds</i>	13 (36)
The contents: from organic-mechanic to abstract objects	
<i>Organic objects</i>	16 (44)
<i>Technological objects</i>	8 (22)
<i>Infantile objects</i>	3 (8)
<i>Geometric objects</i>	16 (44)
<i>Symbolic objects</i>	6 (17)
<i>Miscellaneous objects</i>	14 (39)
The quality: a mixture of textures and transformations	
<i>Transforming or exploding</i>	7 (19)
<i>Synthetic textures</i>	15 (42)
<i>Generic textures</i>	11 (31)

universe that's Shakti – so it kind of felt like that'. It is noteworthy that 4/5 of these last participants were of the total 7 who at no point reported a more defined encounter accompanied by a visual form and behaviour. Additionally, five participants had a tendency to refer to *Personification of the DMT* itself, such as 'the DMT was showing me around... it felt very feminine...pulling me into these vortices' (SH). Finally, three

participants also experienced the *Transforming of those present* in the room in different ways, for example ‘you just melded in with this bright light and you became this angelic shaman kind of guy’ (LR).

Role and Function: Entities Fulfilling Elaborate, Inter-relational Purposes

Each case of interfacing with these beings was also classified in terms of a specific role the majority of them played, reflecting their function and purpose while actively engaging with the experient: *Showing or Communing*, *Helping or Nurturing*, and *Manipulating and Controlling*. TM (Trip 2) reported a particular encounter illustrative of the first role *Showing or Communing*, reported by 17 individuals and mainly comprising of beings acting as a ‘presenter’ (10; hereafter all numbers in parentheses are the number of participants out of 36 reporting this feature) usually of intriguing objects, and ‘focuser’ (5) of their attention upon them:

“A lot of very strange clowns...mechanical entities. Very cartoonistic. And again trying to show me something... It was like a toy ...continuously moving and changing shapes and colors... [they would] push them in my face... and I could see every single detail”

TM continues to encompass the *Helping or Nurturing* function, the most often reported, by 19, i.e., over half the participants, entailing the most benign aspects such as serving as an ebullient ‘playmate’ (5) or reassuring ‘soother’ (5):

“Floating, jumping around, very happy to show me those things, [and] that I’m there, but again I could not play with them, that game that they asked me to do...I’m paying attention to them...this entity was asking me to look at his toy, then another ask[ed] me ‘No, look at my toy, play with me!’... Very childish in what they were doing... Yeah, those entities calmed me down...their message somehow...gave me [the] impression that ‘everything’s ok, I’m in [a] good place, I do not need to worry, I’m too scared for nothing, and let us play with these toys!’”

The role of *Manipulating and Controlling*, in the minority at six reports, was very clearly conveyed by DD’s encounter with a Faerie-like entity who embodied the multifaceted ‘trickster’ archetype (Jung, 1969) (3) – that is, integrating other themes, i.e., the demeanours of being mischievous and childish, as well as the activities of laughing and tempting – who was also an ‘orchestrator’ (2) of the DMT-space:

“A female face which was tempting me, which I’m kind of familiar with... Then, everything slipped, everything stripped away. As I was tempted in, lured in... and there was like a ‘Hehehe’, there was a mischievousness to it. She was definitely giggling, as if to say, ‘This fucking stupid idiot here he comes again I’m gonna show him, Bang!’... She’s beckoning with a sort of finger like this,

going ‘come in, come in’, and I thought OK, I’m mesmerised, so I follow her in... This female entity is fucking all-powerful but at the same time very mischievous and jokey and infantile... So she’s like, ‘I’m the master and orchestrator of this whole situation, but I like having a laugh at the same time’... In that space it’s almost like she came to get me, kind of knew I was coming – ‘Come, come, come, giggle giggle, laugh, look at that, now you are here, now I just sit back and watch you!’”

He reveals at the end, perhaps paradoxically (apt to trickster territory, given the ambivalence and boundary-breaking of the archetype) a protective ‘guardian’ (4) manifestation of the *Helping* role as well:

“She wasn’t a god-like deity...she was like a child God!... Sometimes very nurturing and maternal, very protective if she feels like I’m getting into bad, deep water”

Appearance and Features: A Myriad of Entities Manifesting

The ways in which participants articulated the overall appearance of their perceived entities, and the defining features and aesthetic thereof, yielded the greatest number of subthemes – 48 in total, all of which listed, alongside all other mid-level and subthemes, in **Supplementary Table 3**.

Human beings were seen only in six cases, and only in two of these were they persons known to the subject – and of interest, both of whom were deceased. The great majority, 26 reports, composed of forms attributable in some way to some *Otherly Creature*, that is of a non-human and non-animal nature. These infrequently consisted of more simplistic ‘silhouettes or featureless’ figures (5) – but ‘humanoid’ was the most common (9) generic shape to these creatures, mirroring their human experiencers, albeit with the vast array of inhuman manifestations. We have already met TM’s (Trip 2) cartoonistic mechanical clowns, with three other ‘jester’ or harlequin-like entities also encountered, while some other entities assumed ‘insectoid proportions’ (4), such as one ‘multidimensional moth-like structure’ (MP).

However, TM’s first DMT experience perfectly portrays a very colourful number of the elements of the *Otherly Creature* variation, specifically fusing ‘octopoid’ (4) and ‘serpentine’ (3) features while incorporating elements of elongation, popularly associated with the ‘Grey- or Mantis-like’ aliens (2):

“If I need to compare with something on this planet... they are like octopus, from...another planet. They had many similarities, like that long head...the scalp here was big... It’s far from octopus, but that’s the closest... Long heads and faces... They did not have the nose I think...they had a flat face somehow, maybe they had some holes under that mask... and their eyes were much bigger than normal... Yeah, I wasn’t scared, it was like alien eye, [a] big one. No it was like an animal, lamb... feeling only kindness... Very long hands...”

I could see very strange hair...very similar to very thin and long snakes, kind of snakes...long and moving by itself”

Sentient structures were observed in nine cases, objects normally considered inanimate were animated. The entoptic displays were sometimes considered ‘sentient geometries’ (3), described as ‘hyperdimensional...dancing lattices’ and ‘unbelievable hyperintelligent geometry’, while ‘boxes’ (1) topped with ‘transparent interlocking mobius strips going round and round’, and ‘computer symbols’ (2) at the onset of the trip’s ‘start screen’ were additionally experienced.

The *Visual quality*, that is the texture with which these presences were furnished was also very diverse. ‘Self-transforming’ (as per ‘machine elves’, McKenna, 1993), a tendency to morph in a dynamic state of flux, was the most oft-reported, alongside being ‘geometric’ in aesthetic (8). Sometimes the geometric backlight of the DMT space itself informed the entities’ forms as if emerging from it. Of the four insectoid encounters, two were explicitly described as such; MP’s moth was ‘made of the same geometry...but wire-frame’, which was also ‘hyperdimensional’ (3), and ST’s grasshopper-like familial beings were described as ‘if light was coming from behind the curtain, how you would see silhouettes... The flower of life overlaid over everything...I could see an entity coalescing’.

The experient EM conveys the ‘self-transforming’ (8) nature of her ‘construction with a mind of its own...moving around, everything was changing inside’, closely echoing RH’s (Trip 1) living structure, a ‘honeycombed...massive building...evolving and changing’. However, EM also qualifies hers by stating ‘it was like this massive machine that keeps everything together’, referring to a further quality of being ‘mechanical’ (3) – and while not articulated as a sentient edifice, JM’s writhing environment has resounding parallels: ‘lots of wheels, cog-like representations, things spinning in multiple layers... They would all speed up as part of a larger geometry...mechanical movement... fluid, like a wind you could see’ – whose self-transforming machine world was, incidentally, inhabited by entities of an ‘elf’-like mischievousness.

FF’s following encounter mimics EM and JM’s above, in being apparently contained within the fluctuating ‘innards of a machine’ (see *Artificial worlds*, **Scene**), but the populace therein had a peculiarly simultaneous ‘organic-mechanic’ (1) aspect to them:

“There is a recurring image of like a space invader figure, sort of like an icon... It was definitely...maybe your blood flowing through your system... These things... were the workings of something!... [They] were following along these sort of trackways which were doing something, part of a bigger, maybe it was keeping me or keeping something alive...like seeing the workings of possibly myself or the human form, being inside seeing it maybe from a microscopic perspective. But it was much more mechanical and sort of alien... definitely more spacey...”

Interviewer: And that tiny scale might blur the boundaries of what looks organic or mechanical?

Yeah absolutely!... there’s definitely life in there, or some sort of sense of being... It was almost like a ‘marble run’...like roller coasters, loads of these track ways where these things were moving along them”

Demeanour and Nature: Entities as Magnificent, Mischievous or Menacing

As many of the excerpts already provided will attest to, the great majority of the entities with whom participants connected came in peace – their disposition cultivated a positive encounter, and sometimes overwhelmingly so. Over half of cases, 20, involved *Charming and Inviting* beings; most participants used terms like ‘benevolent’ (10) – sometimes associated with healing the participant (see *Helping*, **Role**) – almost equally conveying them as ‘benign’ (9), denoting their friendliness while not quite as profoundly loving. A diversity of 12 *Other dispositions* involved beings who were intensely ‘curious’ (4), itself notably always co-extant with the former two temperaments. For example, these participants describe entities with both such qualities:

“There was...a sense of being healed, a sense of [the observers] working on my physical and psychic body, eliminating toxins. Very benevolent, some curiosity from their perspective... They were curious to understand what I am, what I’m seeking... All very benevolent, looking out for me” (MP)

The next most commonly appraised demeanour, by five participants, was *Mischievous or Jestsful*. However, as the inherent light-heartedness of the terms suggests, this does not preclude a warmer and playful character. This includes DD’s described above, and SH’s ‘fun and light’ was underscored by ‘an edge’ where there was ‘something about the presence that always feels slightly mischievous... Like it could take you somewhere really dark if it wanted to’, and while JM describes that ‘there were hints that it could get dark’ he caveats this with that ‘everyone was in a good mood, for whatever reason! It was quite jovial.’

The only three encounters which had particularly challenging episodes (8% of total), labelled under *Fearsome or Menacing*, included two transient stages from RH. His third and last experience involved an emergence from ‘terrifying blanket’ patterns of hundreds of closing-in ‘hooded dark creatures, forbidding, quite forbidding, scaring me a bit’. Which was an apt judgement, given their eventually “saying something like, ‘Do not go there! Are you sure?’...like a test or something. ‘You sure, you sure? You can still get out of this!’”. It remains ambiguous as to whether they were displaying a more protective role to RH, or as part of some trickster-ish agenda (implied by the ‘test’ remark), akin to DD.

Often, as per the broader *Nature* of these entities, participants described themselves as ‘one with, or one of the beings’ (10) – one stating ‘the entities were my friends, I felt they were like my sisters, they were telling me that I’m like them’ (AF). RH’s third journey entailed an extensively tendrilled

ever-evolving green-ish being of immense proportions (as did his second):

“Tough thing was that we knew each other so well, and I felt like I was one of them or something like that... I was much more connected to the body of it, the body and I were really close, like in an embrace of some sort, really close... I felt way more, much more like them than human.” (RH, Trip 3)

This refers to the same encounter in which he described such unity with the entities that they spoke and lived through him (see ‘possessing’, **Interaction, Supplementary Material 1**). Intimately dovetailed with this is that virtually all these reports of kinship also refer to a ‘familiarity’ (10) inherent in their relationship (that is, they are not familiar purely due to seeing them in prior DMT states), and two again describe the beings in a familial fashion as ‘seeming like a family [who] appeared around me for my lesson’ (ST):

“We were doing something that we have done before... We know each other. We are these things or something... They absolutely love us... Just wonderful, delighted, at home! It’s home” (RH, Trip 3)

‘Hyper-intelligence’ (7) was ascribed to the entities in several cases. RH (Trip 1) describes what he could only articulate as animal-like with circular pods on their heads:

“Yeah, hugely advanced...the difference in form, compared to this planet, that they were in just made me think this has to be a form of advanced [life]”

Communication and Messages: Entities as Instruments of Personal and Universal Insight

This super-ordinate theme encompasses explicit exchange of some form of understanding between the entities and the experient, evidenced by the majority of the beings. The *Mode of communication* was sometimes with the use of ‘dance or gesture’ (3), but for the most-part was purely ‘intuitive or telepathic’ (11), as RH (Trip 2) clearly conveys saying:

“I do not think it’s the ‘I’ that I think with that’s doing this at all, it’s something else. Because I often notice that I’m already communicating – I’m aware now, I’m effortlessly communicating with this entity... It’s not language, it’s just a knowing, just a complete knowing. I tried to tell them what I was doing at one point in English, but it’s just pointless!”

Listed in **Supplementary Table 2**, under *Messages received* are only the communications expressly verbalised by the participants and are by no means an exhaustive collection of all the subtle messages conveyed to each. These overt communications would be heavily associated with the aforementioned ‘teaching’ and ‘healing’ **Roles**; imparting to the subject of interpersonal guidance around ‘love for others

and the self’ (5), entreaties for the person to ‘let go’ of suffering (3), ‘warnings’ (2) such as that ambivalently issued to RH, and another explaining ‘insights into the nature of the universe’ (1). The following, independent subtheme has been derived from this latter subtheme of universal insight:

The subtheme of ‘the Cosmic Game’ represents a constellation of profound communications expressed independently by five participants. Three of these had remarkably comparable messages; that the universe is a vast interconnected playground for beings to simply enjoy. AF is reproduced here, yet both her and SH were interfacing with a playful, flirtatious, feminine creature, functioning as both guide and teacher of such universal insight:

“Oh God, very very sensual. And this, like ‘it’s a game, it’s all a game’. They were playing with me, and they were like ‘come and play’. It was all a game, it was very very playful. Just enjoy... It’s like I’ve known them before, they were like ‘Yeah you know the game’, this is the relation. I know the game... They were showing me things. The main thing was this geometrical figure that kept changing shapes and colour. And they were...saying ‘Look what we can do, look what *you* can do!’ Very interacting, very interacting... These sensual females, they were like ‘Ok you wanna do this, Ok we are ready, whatever you want to do, we are ready’... They were telling me that I’m like them and I have to enjoy the pleasure of this existence, and life is fun, and it is all about playing and enjoy life and all that life has to offer... It was very liberating, and just like, let it out...just be... I had that sensation of just existing... I just opened myself...even the crying was like Yeahhh, crying, just Ahh, let it go!... It was showing me the things that exist. This exists and this exists, and they all had a pattern, they all looked like each other... They exist...in everything. We all exist in the same way. So there’s no separation of things... Everything already exists and is it out there”

A further super-ordinate theme, **Interaction and Behaviour**, encompassing its respective themes and descriptions, namely *Active Involvement*, 28%, and *Passive Activity*, 53%, has also been analysed (see **Table 2; Supplementary Material 3**). Owing to its close comparability to, and thus further refining of, the above theme covering the roles and functions of the entities; however, it has been inserted into the supplementary material (see **Supplementary Material 1**).

Exploring Other Worlds

One hundred per cent did describe the concept of arriving at a qualitatively different space of consciousness or reality, characteristic of the so-called breakthrough DMT experience, and the major content of which is elucidated below. Smaller proportions variously reported more minor themes of *Breaking through the veil*, 22%, discovering their *Emergence into a novel reality*, 58%, and a *Navigation through the space* in which they now found themselves, 31% (see **Table 2; Supplementary Material 3**). For an elaboration of these, see the Supplementary Material (**Supplementary Material 2**).

The Scene: From Natural to Artificial Worlds

Entering into entirely different domains appears ubiquitous with these experiences, where the nature of this new world-environment took on myriad forms for participants: Weird worlds, yet betraying a familiarity, since within their transformed nature they may uncannily echo worldly experience (Shushan, 2018). *Natural worlds* recurred in 10 cases, where those pertaining to a 'space-like environment' (6) was most prominent. AZ saw himself 'enveloped by a mystical black colour of the universe, inside of which there were an infinite number of geometric figures', and SH, alongside the emergence of similar shapes, relates:

"I pulled back and it changed into a blackness, kind of like pyramids, quite angular shapes, but like black with almost like stars or something, there was some white or gold bits in there... these dots that could almost be stars, which felt tied up in the astrology in the Egyptian ancient wisdom"

Natural landscapes (4) which may be recognisably earthly, albeit a divinised mirror-image, included RH (Trip 1) and EM which shared an environ of living mercurial structures, and were again paralleled in their visions of gardens of biblical proportions:

"The beauty...is just so intense... I do not know what 5D looks like, but it was like that or more... A garden of extraordinary beauty, that [the animal-entities] were coming out of" (RH)

"Actually, it had gardens as well, because I was remembering there, like Oh you can definitely go to the garden and see some other stuff, it has rivers and everything. It was just like one of those palaces from ancient Babylonian gardens or something, it was beautiful, and every single bit of the wall – you know like mosques have all these patterns and all these beautiful glass like stuff inside, that everywhere, on every single little bit" (EM)

Artificial worlds comprised of six cases of vision-scapes possessing a particularly unnatural flavour, but most simultaneously expressed using natural imagery. This was observed before with FF's icon-like creatures, which he again describes here as within a 'mechanism' of some description (2):

"Like conveyer belts, but within conveyer belts, they were everywhere... there was definitely a sort of sense of almost mechanical conveyor belts of psychedelic energy... Very sci-fi... how the space invaders moved across the screen, in very basic computer graphics... But beautiful, it felt like the natural order of things... There was a purpose to it! Yeah, they were up to something... Like this whole thing was like the innards of a machine... but maybe your blood flowing through your system"

Visited by three participants were *Children's worlds*. TM says of his second experience that he was clowning around

in a 'playroom' (2), with 'toys and entities and kids, someone just threw me there and said play with these entities'. The first words of GR's interview, who was greeted by a sticker-like cut-out clown, were:

"It was literally like...everything was like completely shifted into another way of interpreting reality... into like, a circus sort of!... It was very 'circusy', because of the hilarity of it all!"

After asking what it was about the hilarious quality that transposed into a 'circus' (1), he replies, echoing his moving through the space *via* its own hysterically impossible 'folding':

"Because reality was just shifting – like you know those books, when you take one page and then they create like a thingy, a 3D object... Like that experience of a universe folding and unfolding, like that. It was just hilarious"

Interviewer: Like the hilarity of the cosmos being distilled into a children's playful pop-up book that you were being shown through?

"Yeah, exactly! Exactly!"

Thirteen individuals expounded on, at least segments of their experience, being not so much well-defined worlds as much as a *Nebulous worlds*. One experient, OR (Trip 2), speculated he was witness to the etheric 'fabric' of the world around us:

"There was a time where I see like, atoms and scales and the matrix, like buzzing *Chh, chh, chh*... this was like you know, what's the word, an ether...and it could just transpass [*sic*] me and everything... The fabric, like the fabric of what is this we see ...this [gestures to room around him] is a manifestation, *not* an emanation... everything's just wave or formless, and this [gestures again] is more dense you know, frozen part of all of this"

Various articulations of finding oneself amongst 'gridwork' (9) were most common here, alternately described as 'not quite a honeycomb... lattice-work' or 'loads of intricate crisscrossing, like an amazing beautiful little spiderweb'. In both SH and GR's very resonant experiences, there appeared a vast, devoid expanse, but one rich with potential in which objects were seen to materialise. GR's lattice-like space represented a kind of cosmic template (2):

"I just did not exist anymore, it was just like raw data outside of me existing... In an infinite universe of raw information... [Like an] empty blueprint of the universe... Like this [points to mathematical paper] literally... it was a simple grid on horizontal, then a chalice there, but this was like one image out of a million [objects]... [It] was basically deeply knitted...like a fabric... So imagine this [sweater], but...with really big strings, but as if you'd make a huge cube out of it which was infinite"

The Contents: From Organic-Mechanic to Abstract Objects

As is the prolific nature of the content-full DMT journey, these other worlds are densely populated with a litany of articles and artefacts. *Organic objects* seemed to be the prevalent-most, aligned with the natural scenery (above) as being amongst the commonest, surveyed by 16 journeyers. For instance, ‘plants and flowers’ (10) stemmed from such simple images ‘of a tree, big kind of oak tree with a swing in it, and then loads of birds singing’ (JA), extending to more complex arrangements as AF’s floral, fractal encounter (much like BW):

“Some vase of flowers... And from inside there was this geometric shape, but they looked like flowers, like sacred geometry – and what it was really, was... a male entity in front of me... showing me a flow of energy, shapes, colours – flowers coming out his solar plexus... Everything he was throwing out of his body was related to one another and linked by shape and meaning”

Imagery of a ‘cellular or sub-cellular’ nature was also recounted (4), where two such experiencers expressly noted DNA. EM upon entering her ‘impossible... cube but hexagonal’ (‘hyperdimensional structures’, below) was privy to ‘a cell or something... and loads of organelles... So it’s like a 3D hexagon, with an interior made out of cell-like structures, like DNA strands’. TM, during his third time, upon being swallowed by a child, couched his double helix in the following terms, very analogous to the ‘organic-mechanic’ aesthetic reported by FF which he posited as a view inside biological machinery:

“I saw very strange DNA, but wasn’t DNA that I know, it was made by... It was like a chain, and in the middle they had... definitely a sphere with, they were not symbols, it was made of something, seems mechanical... I remember very well a sign... It was intense red these things, and all of these were functioning somehow, like a mechanism, not a biological one, more mechanic... And everything with a note of cartoony. I wasn’t sure if I was seeing inside a biological being of someone”

Descending ever further in scale, the ‘molecular or subatomic’ (3) revolves around ‘seeing all these different molecules... just everywhere were just collections of molecules and geometry’ (JA), or in RH’s case (Trip 3), initially speaking of a building, ‘like the girders inside, the structure inside something’, yet qualifying that it ‘looks like in chemistry, the shapes of atoms’. The elaborate-most exposition of this idea comes from part of ST’s depiction of his hyperactive hypercube (see *Geometric objects*) – also verging on interpretations of a metaphysical ilk (*Meta-narratives*, as discussed in the subsequent paper of DMT’s effect on the self):

“When I stepped into it, it seemed like [the hypercube] was a fundamental thing in reality, almost like [the entities] took the smallest thing on the Planck scale for example... to maybe represent the scale, then you blew

it up to show you that this is the way things are on the tiniest layer... This is what builds up everything!... It’s like a computer screen or a newspaper, where they have a big image and then they have a close-up. Like a microscopic image of this whole thing and here’s what’s going on there...

It seemed the Borg thing [i.e., the hypercube] came in 3-dimensional space... everything else was shimmering... because it was in more high detail... I can actually see the finest definitions of this... It seems like I’m looking at this and I can actually see it inside-out almost, I can see the whole thing, like on a molecular level”

ST had also referred to his tessellating tesseract, in its rapidly rotating configurations, as like the ‘Autobots’ (of the *Transformers* franchise), thus representing one of eight instances of *Technological objects* appearing. A sense of ‘mechanics’ and curious ‘devices’ were sometimes evident (4). Both AN and JM turn to cog-like imagery, the former describing her pressing up to her DMT partner’s back as ‘a fusion of the spines and all the energy around them, like turning into one another, like cogs, like kind of twisting in... that central column entwining’

Lastly, ‘satellites and spaceships’ (2) were volunteered, where comparably to ST’s hypercube framed as that from ‘The Borg’ (of *Star Trek*) – so in precisely the same way does BB paint his hypercubic craft as:

“you know, the Borg, and their cubes... it’s a big spaceship and it’s a cube, obviously not grim and grizzly like that. But a big cube that has a lot of detail within it, almost with little cutaways, and each cutaway is its own 3D space – and the whole thing, this 3D shape rotates, sort of spins, not slowly, almost as if some really cheesy American documentary is trying to make everything look razzmatazz and sort of sex it up, like *dumdahdahdumm!* Everything’s moving, almost as if it’s trying to catch your attention”

Such ‘hyperdimensional structures’ (6) recurred with noteworthy frequency, subsumed under *Geometric objects* presented to 16 experiencers, where five of the six such hyperstructures being cubes of multidimensional proportions. Here, DD fleshes out his feminine-faerie as puppeteering him through:

“a cube... the multiple dimension aspect of it was that she- it started off like 2D then it sort of slipped into this cuboid which then fractalated...

Interviewer: ...a cuboid, but more than 3D?

Oh mate, you fucking- absolutely!... as this cube sort of splintered off, and I was able to sort of look around the other facets of this cube if that makes sense... it was weird- it’s such an understatement innit [*sic*]. So as this cube- she’s lured me, and the cube is fucking sort of disintegrating in multiple dimensions at the same time... but that scene [of the woman and child] was the mirror in one of these shards of this cube that had just splintered...

The female entity that I'm quite familiar with, she then came back in this sort of multi-fucking-splintered multi-dimensional thing, and was giggling... the 2D square then broke into this sort of hyperdimensional cuboid fucking thing that just then exploded, and I sort of kind of went into it... then it just went fucking- accelerated into super crystalline- I remember looking at it and appreciating how unbelievably fucking impossible those lines are and that situation"

Virtually the only other geometric object, dissociable from the perhaps pervasive geometric patterns in DMT, appeared to be 'spherical shapes' (7). For example, TM's (Trip 3) earlier organic-mechanic DNA mingled with a sphere, and others express similar impressions that 'there were definitely balls there as well...like spinning balls amongst it' (DD).

Symbolic objects occurring in six total cases were signalled perhaps most vividly by TM's experiences, especially his second immersion. For instance, in terms of 'symbols or signs' (5), many such signs to him represented medicine, alongside a 'kind of cross or something in the middle, then borders like an arms crest' (TM 2). This echoes his first trip where 'around that pill were floating four or five symbols' (a shuriken-like cross, large tree and swirls).

Similarly, 'ancient language or hieroglyphics' (3) were repeatedly observed, from 'very, very Aztec...patterns' (RS), to TM's (Trip 2) toys endowed by his clowns which:

"appeared like, Egyptian, maybe not, but hieroglyphical writings, that was a kind of paper, but it was floating like a papyrus but... Some of them were pictographic, some of them were hieroglyphical writings near [the toys]... Some of the toys looks like a Greek vase...I saw Greek motifs on some"

Again, TM's (Trip 2) experiences continued in highly symbolic form, reporting the classic digital 'raining code' from *The Matrix* trilogy, as had one other journeyer – which was, for TM, manifested alongside a trinity of black holes ('space', *Natural worlds*):

"I saw codes, a lot of codes, walls infinite with codes. At one point, very fast, to form three black holes in those codes that were flowing all over. It was like The Matrix code, it was even green. Very, 'MS DOS' code... alien language, I could not recognise those... crawling down and up, and some of them were attracted toward those black holes

Interviewer: So they were bending in space toward the black holes?

Yeah, yeah, yeah! And after that I could see...other kinds of codes, different language...and this one was somehow more complex, and it came like a typhoon over me... So all my visual spectrum was codes, and they were green, and it was a black space. Bright green, neon green"

Apart from the aforementioned nursery and children's book scenery, TM (Trip 2) is most representative of the three case's

Infantile objects. He here tries to comprehend his gifted toys, the gyrating gadgets which:

"were somehow alive, continuously moving and changing shapes, and colours... Some of them had fluffy texture, some of them were mechanic. Some of them some strange, very strange material I cannot define... at the second look, it changed very radically the form, it was something undefined, because morphing continuously...

these bubbles transformed into the toys – they were very coloured, the colour became cartoonish somehow. They were starting- it was a screen-saver of Windows 98 with these kind of orbs changing shapes...from bubbles into the toys"

At least 14 experients offered up myriad *Miscellaneous objects*, perhaps more arbitrarily positioned amongst the vision. However, additionally to the snake-haired experimenters of TM (Trip 1; and several other snakey entities) – who also added that 'snakes I think they were one...or two of the symbols' – many other kernels of imagery had decidedly 'serpentine or cyclical' spins to them (7). Again, in his second session, TM rounds off his description of his intricate symbol-adorned toys, redolent of the medical insignia of the serpent-entwined staff, by saying:

"you know, the Chinese carnival, those kind of motifs, they were very similar... Some of them were boxes made by kind of dragons that were moving in that form...for example, the dragons had the crest and everything, red, blue, green, very colourful... This sign morphed from that dragon, Chinese dragon...because at first that dragon was moving on that toy like a snake, and protecting that toy, and the end of the tail it had a sign... for me it looked like a medical thing"

The Quality: A Mixture of Textures and Transformations

Pertaining to the kind of visual texture to the general world-space and its constituents – at least three of the five tesseract-structures were explicitly qualified as *Transforming or exploding*, including BB's 'rotating' or 'spinning', and DD's impossibly 'fractallating [*sic*]' or 'splitting' cubes. These transforming configurations have also been visited in four other instances, like during TM's (Trip 2) clockwork-clowns' shifting gifts.

Fifteen participants noted aspects aligning more with the environment's *Synthetic textures*. Perhaps more *semi-synthetic*, most evoked was the (by now familiar) peculiar hybrid-aesthetic of 'organic-mechanic' (5), such as with TM's (Trip 3) DNA-complex he 'was looking to see if it was molecular or mechanical – and it was a mix, definitely!'. Again though, much of this *synthetic* quality in general pivots around the hypercube phenomenon – where both BB and ST analogised theirs as like that of 'the Borg', which is a contraction of 'Cyborg' (and in turn, of cybernetic organism). BB elaborates:

"There was a woody quality to it. Bark-like. It's never pure geometry. If you have got [at] one end of the

spectrum, artificially, a 1990s fractal poster, to a tree and its fractal patterns – it's sort of somewhere in the middle”

Equally as many individuals reported a ‘cartoony’ or sometimes ‘animated’ quality to things (5). Resonating again with BB's high-dimensional cube – also depicted as ‘razzamatazz’ (1) – ST relates that ‘it's the Borg in cartoon... Imagine a *Rick and Morty* version of it. With every single component of it moving about and in different colours’, thus evoking another animated, space- and interdimensional-themed TV show. Finally, scenic finishes such as MP's ‘super holographic, very digital looking’ (3) world occasionally arose, which was also inhabited by a hypercube. Although this evinces artificial feelings much akin to BB's or ST's CGI-like, technological cubes – ST considered his as part of the substructure of reality, and MP in fact also qualifies his as ‘hyper-real’.

DISCUSSION

The present analysis from high-dose (>40 mg) smoked DMT in naturalistic settings yielded all 100% of the 36 experiences to include either contacting representations of another being, or emerging in a different environment (virtually always co-occurring), of some nature. The experiences of ‘breaking through’ to other immersive worlds, that are hyper-vivid, intricate and impossible, as well as interacting with other beings, apparently sentient, independent and familiar, have been retold from the original and revitalising human experiments with DMT, to the only other modest thematic analysis and very recent online studies of the encounter discussed below. Such experiences have been thoroughly reconfirmed by the present analysis. Indeed, the frequent overlap of, often specific and nuanced, content between participants in the present study is testament also to the interesting internal consistency of the DMT experience.

Parallels With Major Studies of the DMT Experience

Shanon (2002) categorisations, though pertaining to ayahuasca, also very closely reappeared in the present analysis, such as ‘soul-flight’ through the other realms, which may similarly be of natural or heavenly landscapes; ancient or magical cities; seeing Earth, outer-space voyages; amusement parks and circuses; mythological imagery, scripts and symbols, mathematical formulae, and biological evolution. As per the native populace of these realities, while animals were comparatively uncommon in this analysis, snakes, and serpentine beings and imagery, were also the commonest animal-motifs met. Saliently too, all the (albeit few) known human beings met were deceased – DMT echoing ayahuasca as ‘the spirit molecule’. While shamanic-like spirit transformations were not directly reported, several participants did describe feeling ‘one’ with the beings encountered, and one transformed into plant-life (where two participants reported human-animal hybrids). Other strata of Shannon's phylogeny were again mirrored, including mythological-types such as other animal-hybrid beings or faerie-natured entities, ET or alien-types (like serpents, octopoids

or insectoids, grey-like beings or Navis); beings divinely angelic in character and function; though entities of ‘demonic’ dispositions were barely encountered, where one subject reported a succubus-like figure and another a multi-eyed entity congruent with many religious depictions of beings of death, also elsewhere reported with DMT (Luke, 2008). Specific deities of particular religions or mythologies were *never* explicitly identified in this analysis – though overlapping qualities were certainly discussed (such as *Shakti*) – perhaps related to the bracketing (inherent to micro-phenomenology; Petitmengin, 2006, 2017), similarly encouraged in the semi-structured interview (see Materials and Methods).

The content analysis of discarnate DMT beings by Lyke (2019) – subtitled ‘Not everyone gets machine elves’ – elicited highly similar findings to the present paper's results. She identified that 75% of reports included at least one form of entity where 37% described more than one, though the present study in fact found 19% to have at least one and 75% with more than one. When using only her specified lists for comparison, comparing Lyke first and the present analysis following, entities were highly significantly more likely to be female in Lyke versus twice as common in the present sample, and poorly defined/featureless (29 vs. 22%), as well as humanoid beings (22 vs. 25%) the commonest in both. Though more difficult to make direct correspondences, due to the splitting into nuanced and various subthemes in the present thematic scheme, Lyke listed divine (10%) followed by alien beings (8%) as the next most common, where those entities with obvious physical or behavioural attributes of an angelic or alien nature would also approximately follow next here (however the latter, e.g., Octopoid, Grey/Mantis etc., more prominent than the former, e.g., Benevolent, Beautiful – though, the categorical alien-angel distinction likely lies only in *appearance*). Lyke's categories then follow with elves/faeries (7%), animals (6%), then mechanical and geometric objects (6%), where similarly, all such entity types were found in this analysis – albeit reversed in frequency in the present (i.e., 3, 11, 8–22%), though here with elfish creatures defined only by appearance versus nature (e.g., Mischievous, Childish). Identically, voices (4 vs. 3%) and faces (4 vs. 6%) alone were the least most likely type.

Lyke and the present analysis again closely converge in relation to interactions with the encountered beings. All of her thematic labels were evident in the present framework (except for ‘questioning’, 3%) and the prevalent-most theme being ‘showing, teaching or guiding’ (25%) – equivalent to the roles of ‘presenter’ (28%), ‘teacher’ (25%), and ‘guide’ (14%) in this analysis. Similar order of prevalences included Lyke's ‘love’ as the 3rd most common (9%), with ‘benevolence’ being the commonest demeanour in this analysis (28%); ‘observation’ was the 5th most common (7%), with ‘watching’ being the commonest interaction here (25%); middling themes included ‘excitement’ (9%), ‘reassurance’ (8%), or ‘play’ (4%), which may correspond to similarly middling ‘jovial’ nature (11%), and ‘soother’ (14%) and ‘playmate’ (14%) roles here. ‘Power/control’ (3%) and ‘sexuality’ (3%) may correspond to the comparably minor ‘orchestrator’ role (6%) and ‘sensual’ demeanour (3%)

here. Particular discrepancies however include Lyke's 'hostility' as being the 2nd commonest (10%), while the equivalent 'menacing' beings (8%) in the present study were certainly the *least* frequent – most likely a function of our participants' being accustomed to DMT and in a quasi-controlled space amongst quiet researchers (suggesting, even at breakthrough levels, DMT's sensitivity to 'set and setting'). 'Reminding' was Lyke's least common (2%), whereas, though nebulous, virtually *all* themes within 'communication' herein, of insights into relationships and the universe (3–14%), often had an essence of reminding inherent, and indeed familiarity with the entities was the commonest 'nature' herein also (28%). While Lyke reports no interaction (10%) as joint-second commonest, the vast majority of encounters here exhibited some role or interaction (14% minor/no engagement).

Parallels between this study's results and those of Davis et al., 2020b DMT entity survey include many of the same parallels with Lyke (2019). Though, one important difference between the present analysis and Davis et al. is that the latter employed mostly fixed, pre-categorised responses, meaning fewer and pre-conceived options versus the free vocabulary of this study's participants. Davis et al. most frequent selections included 'guide' (43%), 'alien' (39%), spirit (39%) or 'helper' (34%), where in the current analysis the Helping roles (53%) incorporating 'guide' (14%), as well as alien appearances (e.g., Octopoid to Grey-like, 6–11%) were certainly amongst commonest – though 'indigenous' or 'succubus'-like spirits were among the least reported (3–6%). Davis et al. next most frequent included 'angel' (16%), 'elf' or 'faerie' (14, 8%), or 'religious personage' (11%), where again, angelic-resembling beings would also approximately be some of the next commonest types here (e.g., Benevolence, 28%) – though elf- or faerie-looking beings were of the *least* common (3%), and specific deities were not explicitly identified. Then decreasingly prevalent were 'clown' (6%) or 'demon' (6%), where 'menacing' beings were certainly the utmost least major demeanours herein (8%) – though, clown-like characters were actually one of the dominant (11%). 'Plant-' (10%) and 'chemical-spirits' (8%) were reported in Davis et al., where though highlighting shamanic-type motifs as found in our study (which Lyke had not), these particular descriptors were lacking here, as were 'animal-spirits' (7%; except animals, 11%, and therianthrope-types, 6% here). To be discussed further in a subsequent paper relating the present analysis to near-death experiences – pertinently, both Davis et al. (1–2%) and this study found the deceased to be amongst the very least reported.

With regards to participants' interpretations of entities' natures, the majority of Davis et al., 2020b respondents endorsed 'benevolent' (78%) and 'sacred' (70%), where again 'benevolent' (28%) was the commonest nature in this study; 'all-knowing' (38%) was one of the next most selected, and 'hyper-intelligent' (19%) also being amongst the commonest natures here; and similarly 'malicious' was the least common (11%; contrary to Lyke), as it was here (8%). Familiarity was 'slight' for Davis et al., whereas over a *quarter* described the entities' familiarity in this study – though notably about two thirds of the Davis et al. sample referred to their first encounter, versus the usually

multiple past encounters in the present study (though again, almost all entities herein were novel, thus familiar for other reasons). Davis et al. also included having agency (54%), positively judgmental (52%), eternal (42%), and petitionable (23%), not directly coded here. 'Distrust' of the entity was reported by Davis et al. (10%), which may well align with the trickster-like beings of the present study (11%), those mischievous characters evoking ambivalence.

Davis et al., 2020b communications ('Message, task, purpose, insight' and 'predictions') transmitted to 69% of respondents were also similar to the present analysis's 'communications' theme; 39% of participants articulated messages though many more qualifying for communication. Namely, Davis et al. 'personal insight' (22%), 'love' (16%), 'reassurance' (10%), 'interconnectedness' (7%), 'death' (7%), 'knowledge' (6%), 'afterlife' (2%) – also, crudely, matching in terms of decreasing prevalence – correspond to this study's messages of 'insight into world' incorporating 'cosmic game' (14%), 'love for self/others' (14%), and 'letting go' (8%), as well as the roles of teaching (25%; and content of said lessons) and soothing (14%), and benevolent demeanours (28%). Specific 'tasks or purposes', as well as almost all 'predictions' about the personal or global future however, were decidedly *absent* herein. The vastly telepathic, then visual mode of communication, was also shared in Davis et al. (74, 40%) and here (36, 6–8%) – though verbal (26%) and tactile (17%) were not present here. The encounter is finally reported as 'hyperreal' by the majority (81%), including causing significant ontological reorientations (80%) – as also identified in this study (mainly former; though reported in the subsequent paper on effects on the self).

Echoes With Other Extraordinary Human Experiences

While *all* participants volunteered many basic features considered endemic to the near-death experience syndrome, as similarly found with a recent psychometric study comparing items of the NDE scale (Greyson, 1983) between near-death and DMT experiences (Timmermann et al., 2018), the similarity remained superficial in the present qualitative analysis of DMT content. To briefly short-list the generic near-death themes coded in the remainder of the wider DMT analysis (not expressly reported here) which may correspond to the most frequent structural features across NDEs (Charland-Verville et al., 2014), these included – deep positive mood, bodily dissociation, bright light(s), deceased loved ones (albeit comparatively low), explicitly god-like beings or light-beings, and time transcendence. Also coded and aligning to traditional NDE-themes were tunnel-like structures, translocation elsewhere and a sense of dying.

Possibly the most comparable experience to the present DMT report in content and not only structure is that of alien abduction. Many such as Mack (1994, 2000) have thoroughly documented this phenomenon, where Hancock (2005) has already found considerable overlap between them and ayahuasca and other shamanic experiences (and faerie folklore), and Strassman (2001) emphasises the alien abduction-DMT

resonance. Here, very many themes are evocative of abduction, such as the entity roles of ‘presenter’, ‘orchestrator’, and especially ‘experimenter’, and the appearances of ‘insectoid’ and ‘serpentine’ beings, and particularly the ‘grey- or mantis’-like beings who although not reported in Davis et al., 2020b seemed present in two participants’ experiences here (admittedly, without the short stature or grey colour as per the former). An ‘intelligent’, ‘powerful’ and often ‘familiar’ nature; mostly ‘telepathic’ and ‘visual’ mode of communication, propensity of simple observation, and notably often ‘curious’, sometimes ‘urging’ demeanour were also highly reminiscent of abduction lore. The two experiences in this study, explored variously above but revealed further in a subsequent paper, incorporating such themes and most resembling the phenomenon, would be TM (Trip 1) and MP. Despite suggestions of the laboratory environs of Strassman (2001) producing the abduction-esque scenarios (Luke, 2017; at least regarding medical-type procedures), this naturalistic study still yielded resonant themes in at least these two (albeit expectation may be a factor).

In a similar vein, parallels between faerie folklore (of the British Isles) and DMT experiences have been explored (Rushton, 2016, 2020), and compellingly demonstrated with ayahuasca (and other shamanic) experiences (Hancock, 2005). Those themes in the present study which are redolent of the ‘little folk’ have already been touched on above (in the reports of TM, DD and JM), also encompassing such appearances as ‘faerie’- or indeed, more commonly, ‘clown’-like; demeanours of ‘playful’, ‘childish’, ‘laughing’ or ‘bounding’ around, and not least ‘dancing’ entities (akin to the quintessential ‘fairy dance’ in the lore). The faerie phenomenon itself, however, has been cogently argued to be a progenitor of the contemporarily stylised alien abduction experience (Vallee, 1969; c.f. Hancock, 2005), where both converge, for example, on a spiriting away by little humanoids (often with large black eyes) leading to experiences of subjugation, learning, or (not evident here) breeding. More precisely, for the purposes of the present DMT comparison, faeries/aliens have also been depicted as being ‘trickster’-like, with ‘mischievous’ or deceptive inclinations – and as ‘hyperdimensional’, with such origins in hyperspace indeed speculated by others (Evans-Wentz, 1911; Jacques Vallee, 1993) – as have the DMT entities herein. Perhaps an exemplar of this elf-alien-DMT entity triad would be DD, with his childish (but powerful), faerie-faced, hyperdimensional trickster luring him through a tunnel and focusing his attention on screen-like shards. Importantly, a further prong to this trinity may be the spirits of the dead, taking us closer to the near-death experience. While the ‘spirit’ molecule’s evocation of the dead was minorly revealed in the current report, faerie folk were considered entangled with spirits of the dead (Evans-Wentz, 1911) and the materialisation of the deceased may be more common than appreciated around alien abduction (Streiber, 2022).

Shamanic flights to, and animistic encounters within, other worlds has also been shown to have substantial consistency, not only with ayahuasca, but with DMT experiences (Winkelman, 2018). Briefly, some themes elicited in the current study and such shamanic experiences include entities enacting ‘healing’,

‘teaching’ and ‘possessing’ functions and actions, who may be in the form of spirits; the observing of realms composed of ‘lattice’-patterns or other geometry, viewing inside the body, and molecular structures like ‘DNA’ or ‘serpentine’ imagery (e.g., Narby, 1998). Deep qualitative resonances between shamans’ journeys and both faerie and modern abduction lore have also been evidenced (Ring, 1992; Hancock, 2005), in turn resonating with DMT reports herein. These entail the ‘soul flight’, communications intended for ‘insight’ into the nature of the world or relationships in it, such as the spirit realm or interdependence; as well as ‘therianthrope’ beings, or even the few cases of sweets in cellophane (RH; as offered by those in the ‘spirit world’), a ladder toward light (AN), and a bible-like book (HV). The participants RV, JA and HV are mostly comprised of such shamanic elements – the latter two being the only participants who actively engaged with DMT in a ritualistic context.

Potential Neural Mechanisms

Of course, such echoing between DMT, near-death, abduction and shamanic phenomena could indicate a role for the endogenous psychedelic in each (qualitative evaluation of this regarding NDEs will come from a subsequent analysis). Alternatively, similarities may be owing to converging downstream mechanisms, such as default-mode network (DMN) disintegration (e.g., Winkelman, 2017), considered the gross neural correlate of psychedelic action by 5HT-2A agonism. For example, *salvia divinorum*, a Mexican shamanic herb and atypical psychedelic generative of disconnection of consciousness to immersive spaces, though stimulating the kappa-opioid receptor it similarly reduces static functional connectivity in the DMN (Doss et al., 2020). Neurophysiologically, such radical perceptual restructuring and ‘world building’ may be owing to collapse of alpha-beta wave, and dominance of delta-theta wave (Timmermann et al., 2019; Pallavicini et al., 2020) and forward travelling wave activity across the cortex (Alamia et al., 2020; Gallimore, 2020), evidenced at least by DMT.

In terms of the entity encounters analysed herein, and characteristic of many of these other altered states, Winkelman (2018) elaborates that the relinquishing of cortical control by structures like the DMN over hierarchically lower brain systems may release innate neural modules, key of which may be a ‘hyperactive agency detection device’ (HADD; linked to the faculty of mentalising), evolutionarily conserved to identify probable social agencies, and especially human-like agents in humans. This is also congruent with the anthropomorphic natures and behaviours to the present studies’ entities, including the most-endorsed ‘humanoid’ appearance. Timmermann (2019) has presented preliminary results from functional magnetic resonance imaging (fMRI) of the DMT state showing decreased connectivity in several intrinsic networks, including the DMN (consistent with previous psychedelic imaging data), as well as electroencephalographic (EEG) results suggesting inhibited alpha and elevated theta power, the latter across the temporal lobe (also exhibited by many dream-like states, Harris, 2007). Such data also appear consistent with recent findings of baseline

temporal (and frontal) theta oscillations inversely correlating with mystical experiences of unity and transcendence (Tagliazucchi et al., 2021), where presumably such a non-dual subjective state may preclude the dualistic encounter with a non-self 'other'.

As per Timmerman et al.'s fMRI findings, similar DMN disorganisation is concurrent with alpha power attenuation over the posterior cingulate cortex, a key node of the network, under psilocybin (also correlated to 'ego disintegration'), where higher cortical alpha is otherwise thought to carry forward predictions (Muthukumaraswamy et al., 2013; Carhart-Harris et al., 2014). There is also evidence pointing to such predictive processing operating when exposed to biological motion and traits, thus applying to theory of mind (ToM; inferring about the internal state of another; Koster-Hale and Saxe, 2013). In this way, theory of mind may be disrupted by DMT with the brain struggling to make the best prediction resulting in inappropriate interpretations of social agency. Regarding the above temporal EEG findings under DMT, it is likely that the release of the top-down constraining by the PCC (and DMN generally) of the medial temporal lobe (mTL) disinhibits the inherent driving activity of the latter over the former, with such freed intrinsic activity giving way to the psychedelic 'primary state' (Carhart-Harris et al., 2014) which may include as part of it ToM processes. For instance, mTL epilepsy patients show significant impairments in ToM (versus other epilepsy and schizophrenia subgroups; Broicher et al., 2012; Okruszek et al., 2017). Additionally, both the superior temporal sulcus and temporo-parietal junction are considered part of the 'mentalising network' (Aichhorn et al., 2009), where the latter as well as the medial prefrontal cortex (possibly unique to the human brain) are activated during social inference (Frith and Frith, 2000) – which, as such, may be similarly implicated under DMT.

Despite the above putative mechanisms, it still presents a challenge to account for the entity experience, especially given their manifestly baroque and highly profound (and reportedly 'hyper-real') nature evident by the present study. Generally, the novel statistical associations of the disparate, normally non-correlated, neural networks afforded by the intrinsic network disintegration and concurrent global network desegregation under DMT (and psychedelics generally, e.g., Carhart-Harris et al., 2016), may integrate into it the activated substrates of theory of mind in a broader synthesis, where such ToM activity may now 'drive' other neural systems such as the occipital and association areas, and the resulting subjective visual and social content is simultaneously available to conscious experience. This is also echoed by the 'phantasy' mode of consciousness, serving to construct a storyline-like narrative embellished from the data presented to awareness (Horváth et al., 2018; Winkelman, 2018). That entities may be an end-stage result of the integration of the brain's disturbed capacity to accurately predict patterns in ambiguous stimuli and an aberrant agency detection, alongside the complex visual, often kinetic, fractal-geometric, imagery presented under DMT, may be consistent with the 8 participants herein reporting the beings to have a geometric flare to them. This

said, this appears to be more the exception than the rule out of the 36 interviews analysed.

Consistent with Laughlin (2000) model of the Jungian archetypes as being encoded into evolutionarily conserved 'neurognostic structures' in the brain, Stephan Szara, the discoverer of DMT as a hallucinogen, himself recommends looking for the origins of these entities 'right in the brain', yet 'deeper than conscious memories', further elaborating that such archetypes may be:

"...stored in neuronal connectivity patterns early in development. What DMT might do... [is] let the Default Mode Network release the stored images and symbols into the perceptual system" (Gallimore and Luke, 2015 p. 11; Szára, 2014).

Therapeutic Potential

The fact that the DMT experience is clearly evocative of all the above classifications of experiences also has central implications for its therapeutic potential. For instance, the near-death and abduction (or UFO) experiences are shown to increase ecological connection, spiritual worldviews (Ring, 1992; Groth-Marnat and Summers, 1998; Mack, 2000) and decrease death anxiety (Greyson, 1992; Mack, 2000; Bianco, 2017), while NDEs also foster connection to oneself and others (Groth-Marnat and Summers, 1998; Van Lommel, 2002) – all of which have been shown or proposed to mediate enhanced wellbeing in psychedelic settings (Watts et al., 2017; Kettner et al., 2019; Davis et al., 2020a; Moreton et al., 2020). Additionally, as supported by Davis et al., 2020b, the interpersonal and transpersonal insights received during DMT entity communication in this study suggests therapeutic capacity, in light of various studies indicating psychotherapeutic effectivity being attributable to psychedelically-inspired psychological insight (e.g., Gasser et al., 2015; Belser et al., 2017; Watts et al., 2017). Similarly, ontological implications of encounters with seemingly other-worldly beings who are hyper-intelligent, familiar and sometimes omnipresent, may be associated with elevations in psychological flexibility, which have in turn been evidenced or suggested as a therapeutic mechanism of the psychedelic experience (Davis et al., 2020a; Watts and Luoma, 2020).

All this said, although the vast majority of the encounters amongst seasoned DMT users herein were extremely positive, for less prepared and more vulnerable naïve and/or patient populations these same psychological ramifications related to ontology and the sheer intensity could well be challenging and yield adverse effects. Similarly, the precise relevance of the present study's resultant experiences, using such experienced users in their habitual settings, thus with likely differing subjective content, for any therapeutic application of DMT with naïve populations may be undermined. Even so, there is extensive anecdotal evidence of the same specific themes recurring even amongst first-time DMT users (Luke, 2017), the unique richness of the content elaborated in the present study should still be of significant guidance to any party involved in DMT's therapeutic research or use – and while experiences herein may be less challenging

due to home environments, the presence of guides or therapists in therapeutic contexts should also be beneficial.

Distinguishing Features of DMT

It seems that there is virtually no single experiential feature of the above thematised DMT experience which cannot be found in either the alien abduction, faerie lore or shamanic, especially ayahuasca, experience. However, there may be a select few which may be more unique to the DMT trip itself (possibly with ayahuasca, given DMT as, arguably, the major constituent). For instance, beings here described as clowns or clown-like (though perhaps finding their analogue in the faerie folk), or otherworldly environs as playpens or circuses – for instance, both articulated by GR; as well as entities with a decidedly mechanical or indeed an organic-mechanic quality to them (though UFOs also, for instance, have actually been described as having biological (Kripal, 2022) or animal-spirit dimensions (Luna, 2022)), or realms expressed as the inside of a ‘mechanism’ – again both expressed by FF. The repeated phenomenon of the hyperactive hyperdimensional cube (DD, ST, AF, BB, MP) may also be considered a preferred trope of DMT, as well as the raining code iconic of The Matrix (TM Trip 2, HV); as might the ‘razzamataz’/garish, retro game or even holographic-digital style. In short, prototypically infantile, synthetic or, unsurprisingly, psychedelic imagery. The current report’s cellular-molecular or skull-skeletal imagery are not typical of faerie or abduction literature, though may well be found in certain shamanic contexts (including ayahuasca).

Limitations

While there have been a number of improvements by the current study on previous studies in their analysis of the DMT experience, not least its focus on content, prospective nature and in-depth semi-structured interviews, various limitations are still present. For instance, similarly to, though improving on Lyke (2019) and Cott and Rock (2008), over three quarters of participants were male, and roughly equalling Davis et al., 2020b slightly over 80% were Caucasian, thus decreasing generalisability to the general population. However, Caucasian males are the main DMT using demographic (Palamar and Le, 2018). The present report also involves an improved age-range (23–58 years). Additionally, the present sample were affected by a degree of self-selection, imposing certain selection bias, given participants’ likely volunteering due to typically experiencing more elaborate, meaningful, and even positive DMT trips. A stringent screening procedure was also employed, involving the inclusion criterium of at least one breakthrough DMT experience as well as other DMT or analogue experiences, meaning that participants were not naïve, usually having vary many past trips (see Table 1). This is a salient point, given the present study’s focus on experiential content, and content’s sensitivity to psychological history (Hartogsohn, 2016). More novice users may well have reported qualitatively different experiences, for example as suggested by Davis et al., 2020b finding that

most respondents reported their *first* entity encounter as their most memorable. Such a narrowed sample is tantamount to the recruitment of a specific ‘subculture’, characterised by exposure to and interest in certain media, both fictitious and that regarding DMT research and ‘lore’ – which may well prime participants’ ‘sets’ and expectations. At least one way this may have contributed to the resultant phenomenology is the comparatively high rate of entity encounters in the present study (94%), contrasted to Strassman (2001) finding approximately half of the *high* dose participants reporting this main feature (Luke, 2013), only very few of whom had previously taken DMT. How this may have affected the content itself is very difficult to untangle, even if comparing against a hypothetical (and improbable) study amongst entirely psychedelic-naïve individuals. This said, a key boon of using such ‘psychonauts’ is their deeper acquaintance with the DMT-space and lack of ontological shock expected of first-time users. This was not only a matter of ethics in avoiding unpredictable and possibly alarming reactions, but would have allowed a calmer, attentive and exploratory stance during the experience, thus returning having extracted, and able to articulate, more of its phenomenological essence. In a similar vein, the majority of the sample’s nationalities being British (with some different ethnic descent), and most of these White British (see Table 1), may also have shaped the content of the experiences presented here. While a comparative analysis of the content differences between nationalities (or ethnicities) is beyond the scope of this study, future research would be of interest to illuminate this contextual sensitivity of DMT experience.

Finally, as to the relative control of the present study – the substance used was not tested for its genuinely constituting *LG-DMT*, nor for purity, and was always of plant-extract as opposed to laboratory-grade synthesis as used in the only two laboratory studies to date (Strassman, 2001; Timmermann et al., 2018). In spite of this, doubt can be minimised given that participants were seasoned DMT users intending breakthrough experiences attesting to the quality of the sample, as well as the researchers’ understanding of the appearance of the substance, and not least the resultant phenomenology of participant experiences being highly concordant with other lab. Studies’ reported DMT experiences – as emphasised in the above discussion. Additionally, the setting for each participant was not a closely controlled laboratory environment, and as such the different physical contexts between participants may well have influenced the resultant experience (Hartogsohn, 2016). This said, the naturalistic nature of the study meant participants undergoing the DMT experiences in their regular environment (own homes or gardens) with only researchers present, thus introducing a level of standardisation. Also, the uniquely stimulating setting of lab. Environments, though more homogenised, equally present a host of experiential primes which may have limited such studies (Luke, 2017). In this way, this degree of regulation of substance and setting, made possible by the present field study, was markedly improved compared to other major DMT studies using only online surveys or forums (Cott and Rock, 2008; Lyke, 2019; Davis et al., 2020b).

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Greenwich Research Ethics Committee (Ref. 17.3.5.15). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

PM and DL: conceptualization, data curation, and funding acquisition. PM, DL, and OR: methodology and review and editing. PM: formal analysis and writing original draft. DL and OR: supervision. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpsyg.2021.720717/full#supplementary-material>

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Evaluating the Potential Use of Serotonergic Psychedelics in Autism Spectrum Disorder

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Recent clinical and preclinical evidence points towards empathogenic and prosocial effects elicited by psychedelic compounds, notably the serotonin 5-HT_{2A} agonists lysergic acid diethylamide (LSD), psilocybin, N,N-Dimethyltryptamine (DMT), and their derivatives. These findings suggest a therapeutic potential of psychedelic compounds for some of the behavioural traits associated with autism spectrum disorder (ASD), a neurodevelopmental condition characterized by atypical social behaviour. In this review, we highlight evidence suggesting that psychedelics may potentially ameliorate some of the behavioural atypicalities of ASD, including reduced social behaviour and highly co-occurring anxiety and depression. Next, we discuss dysregulated neurobiological systems in ASD and how they may underlie or potentially limit the therapeutic effects of psychedelics. These phenomena include: 1) synaptic function, 2) serotonergic signaling, 3) prefrontal cortex activity, and 4) thalamocortical signaling. Lastly, we discuss clinical studies from the 1960s and 70s that assessed the use of psychedelics in the treatment of children with ASD. We highlight the positive behavioural outcomes of these studies, including enhanced mood and social behaviour, as well as the adverse effects of these trials, including increases in aggressive behaviour and dissociative and psychotic states. Despite preliminary evidence, further studies are needed to determine whether the benefits of psychedelic treatment in ASD outweigh the risks associated with the use of these compounds in this population, and if the 5-HT_{2A} receptor may represent a target for social-behavioural disorders.

Keywords: autism, psychedelics, behaviour, neurobiology, LSD

INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental condition affecting 1–2% of the global population (Chiarotti and Venerosi, 2020). ASD is often diagnosed in childhood, with individuals displaying characteristic atypicalities in social communication and interaction, as well as repetitive patterns of behaviour and restricted interests (American Psychiatric Association, 2013). These features are highly heterogeneous in ASD and are often accompanied with co-occurring diagnoses of depression and anxiety (Rai et al., 2018; Hollocks et al., 2019). At present, there is a lack of selective medications targeting the major phenotypes of ASD: impaired social behaviour and communication.

Psychedelics are currently experiencing a resurgence of scientific investigation, following in the footsteps of pioneering mid-twentieth century research. Although the term “psychedelic” encompasses a variety of compounds, the present review focuses on the serotonergic, or

“classical,” psychedelics, which produce their hallucinogenic effects via the serotonin 5-HT_{2A} receptor (De Gregorio et al., 2016a; Holze et al., 2021b; Inserra et al., 2021a). These include lysergic acid diethylamide (LSD), psilocybin, N,N-dimethyltryptamine (DMT), and their derivatives (which will be hereafter referred to as “psychedelics”). Other non-serotonergic psychedelics, such as the empathogen 3,4-Methylenedioxymethamphetamine (MDMA), have also been shown to increase social behaviour and empathy (Bedi et al., 2010; Hysek et al., 2014; Heifets and Malenka, 2016), and to reduce social anxiety in individuals with ASD (Danforth et al., 2018). However, due to MDMA’s vastly different pharmacological properties from serotonergic psychedelics, it will not be discussed in the present review.

Recent clinical and preclinical research demonstrates that psychedelics may hold therapeutic value in the treatment of some of ASD’s core features. Despite the emergence of compelling research, early clinical trials carried out in the 1960s and 70s revealed a variety of side effects after psychedelics were administered experimentally to children with ASD. Thus, the risks associated with the use of these compounds must be carefully examined when considering their potential use in neuroatypical individuals.

CORE BEHAVIOURAL ATYPICALITIES AND CO-OCCURRING CONDITIONS

ASD diagnoses are contingent on atypicalities in social behaviour. Clinical manifestations include a preference for non-social stimuli (Gale et al., 2019), aberrant non-verbal social behaviours (Osterling et al., 2002), and decreased attention to social stimuli (Sasson and Touchstone, 2014). Despite this diagnostic criterion, no selective treatments for ASD target these core traits. Instead, antipsychotics, antidepressants, mood stabilizers, and stimulants are used to target ASD-associated features, such as irritability, anxiety, and depression (DeFilippis and Wagner, 2016).

It is increasingly apparent that psychedelics enhance social behaviour and elicit empathogenic effects in healthy individuals (see **Table 1** for a summarized list of recent clinical trials assessing the use of psychedelics in individuals without ASD). For instance, two psilocybin therapy sessions increased extraversion and openness for up to 3 months in individuals with treatment-resistant depression (Erritzoe et al., 2018). Similarly, a single administration of LSD enhanced sociability and the desire to be with others, while also increasing feelings of trust, closeness, and empathy (Dolder et al., 2016). Another recent study demonstrated that LSD acutely increases emotional empathy and blood levels of oxytocin, a neuropeptide implicated in social behaviour (Churchland and Winkelman, 2012; Holze et al., 2021a). These results have also been corroborated by preclinical evidence, which demonstrate that both acute (Vesuna et al., 2020) and repeated LSD (De Gregorio et al., 2021) enhanced social behaviour in mice.

ASD is often accompanied by depression, generalized anxiety, and social anxiety in particular (Spain et al., 2018; Hollocks et al.,

2019; Kirsch et al., 2020). These co-occurring diagnoses may also be potential targets of psychedelics. For instance, LSD (Gasser et al., 2014) and psilocybin (Griffiths et al., 2016) have been shown to reduce symptoms of anxiety and depression in patients with life-threatening conditions. Importantly, the anxiolytic effect produced by LSD was appreciable after only two psychedelic-assisted therapy sessions and lasted for up to 12 months without any serious adverse effects; while the attenuative effects of psilocybin occurred after only one dose and were still present 6-months post-administration. Likewise, psilocybin has been shown to reduce depressive symptoms in those with treatment-resistant depression for up to 6 months (Carhart-Harris et al., 2018; Davis et al., 2021). The antidepressant and anxiolytic properties of DMT and ayahuasca have been observed similarly both clinically (Osório Fde et al., 2015; Palhano-Fontes et al., 2019) and pre-clinically (Cameron et al., 2019). It cannot be ruled out that the prosocial effects of psychedelics may reflect their anxiolytic effects, notably with regard to social anxiety.

Further, a recent double-blind randomized trial found that the antidepressant effects of psilocybin were not significantly different than those of the selective serotonin reuptake inhibitor (SSRI) escitalopram (Carhart-Harris et al., 2021). This result, in addition to the lack of a placebo-controlled group, limits support for the efficacy of psilocybin and highlights the importance of assessing whether or not the relative benefits of psychedelics (compared to established medications) warrant their potential side effects.

Despite ongoing research, there is still a lack of systematic, double-blind, placebo-controlled clinical trials assessing the specific therapeutic and adverse effects of psychedelics in neurotypical individuals and in those with ASD. Thus, further research is needed to identify an optimal dose that both minimizes the risk of adverse effects, and importantly, to elucidate whether or not the therapeutic effects of psychedelics observed in neurotypical individuals can be clinically observed in those with ASD. Further research is also needed to better understand how the effects and mechanisms of action associated with psychedelics differ when administered acutely or chronically, and to what extent such interventions provide therapeutic effects for people with ASD.

NEUROBIOLOGY

Due to the heterogeneity of ASD, the neurobiological underpinnings of its behavioural phenotypes remain difficult to characterize. ASD is diagnosed according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, including individuals with genetic and non-genetic etiologies across the spectrum. This presents an inherent challenge in hypothesizing how individuals with ASD might respond to psychedelic administration, given that ASD diagnoses cover a large spectrum of neurobiological and genetic profiles.

It is important to note that due to the lack of recent studies assessing the use of psychedelics in ASD, the following discussion reflects neurobiological processes that represent potential targets

of psychedelics in ASD, not phenomena which have been proven to be associated with their effects in this population.

Synaptic Function

Many genes associated with ASD play integral roles in synaptic function (Guang et al., 2018), suggesting a critical involvement of synaptic dysfunction in ASD pathogenesis. Mutations in the SH3 and Multiple Ankyrin Repeat Domains (*SHANK3*) gene—encoding a synaptic scaffolding protein—can cause ASD (Durand et al., 2007). In a transgenic mouse model, this mutation produced a lengthening of dendritic spines and long-term potentiation deficits in the hippocampus (Wang et al., 2011). Mutations in the Contactin-Associated Protein-Like 2 (*CNTNAP2*) gene can also result in ASD (Penagarikano and Geschwind, 2012). *CNTNAP2* encodes a synaptic cell-adhesion protein, and its deletion leads to altered dendritic arborization, spine development, and global synaptic transmission in mice (Anderson et al., 2012; Lazaro et al., 2019). Hyper-methylation of the Fragile X Mental Retardation 1 (*FMR1*) gene—which encodes an important regulatory protein for dendritic mRNA—is an epigenetic modification that can cause ASD (Bassell and Warren, 2008). *FMR1* knockout rats display decreased hippocampal long-term potentiation and long-term depression, in addition to impaired α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor-mediated synaptic strength (Tian et al., 2017). Recently, ASD-induced synaptic impairments have also been identified in human-derived samples. Induced pluripotent stem cell-derived neurons from individuals with ASD exhibited reduced miniature excitatory post-synaptic current frequency and impaired N-Methyl-D-aspartic acid (NMDA) receptor function (Ross et al., 2020).

Given that alterations in synaptic properties are consistently found in different mouse models of ASD and recently in humans, the ability of psychedelics to modulate synaptic events might play an important role in their potential therapeutic effects in ASD. Recently, a single administration of psilocybin in mice was shown to produce AMPA receptor-mediated synaptic strengthening in hippocampal brain slices (Hesselgrave et al., 2021); an effect which may normalize the synaptic dysfunction of *FMR1* knockout rats (Tian et al., 2017). Additionally, LSD and DMT were shown to promote structural and functional neural plasticity in rodent neuronal cultures and in *Drosophila* larvae (Ly et al., 2018). This study demonstrated that the increased dendritic arbor complexity, dendritic spine growth, and synapse formation caused by psychedelics were mediated by the mammalian target of rapamycin (mTOR)- and 5-HT_{2A}-signaling. Accordingly, our study revealed that LSD requires intact mTOR signaling in excitatory neurons and intact 5-HT_{2A} neurotransmission in the mPFC to enhance social behaviour (De Gregorio et al., 2021). Given that mTOR (Hoeffler and Klann, 2010; Li et al., 2010) and the 5-HT_{2A} receptor (Barre et al., 2016; Berthouet et al., 2019) play important roles in mediating neuroplastic events, LSD's ability to increase social behaviour might be contingent on its ability to modulate neuroplasticity.

Despite the pronounced neurotrophic effects of psychedelics, the dysregulation of mTOR and 5-HT_{2A} signaling in individuals

with ASD may be a limiting factor for the therapeutic action of psychedelics on synaptic structure and function. For instance, hyperactive mTOR signaling was found in T cells isolated from children with ASD (Onore et al., 2017) and in post-mortem ASD brain samples (Tang et al., 2014). Positron emission tomography (PET) imaging studies have also revealed that individuals with ASD have reduced 5-HT_{2A}-binding affinity in various brain regions compared to neurotypical individuals, suggesting a reduced expression of this receptor (Murphy et al., 2006; Oblak et al., 2013; Brandenburg and Blatt, 2019). In agreement, a significant overrepresentation of the G allele in the -1438 A/G polymorphism in the 5-HT_{2A} gene was found in individuals with ASD (Hranilovic et al., 2010) and this has been associated with decreased receptor expression (Parsons et al., 2004; Myers et al., 2007). Given that mTOR and 5-HT_{2A} mediate psychedelics' synaptic effects, their dysregulation in ASD might limit or alter the therapeutic effects in these populations.

Serotonin Signaling

Serotonin (5-HT) is a neurotransmitter and hormone implicated in a variety of physiological phenomena and psychiatric conditions including neuronal development (Brummelte et al., 2017), synaptic plasticity (Kirkwood, 2000), depression (Cowen and Browning, 2015), and ASD (Chugani, 2002). Several lines of evidence suggest a dysregulation of the serotonergic system in ASD. Elevated blood serotonin levels was identified as one of the first putative biomarkers of ASD (Schain and Freedman, 1961), a finding that has been corroborated using meta-analysis, revealing that 28.3% of individuals with ASD have elevated 5-HT levels (Gabriele et al., 2014). Differences in 5-HT production have also been found in the brains of individuals with ASD. For instance, the development of brain serotonin synthesis capacity during childhood is robustly different in children with ASD (Chugani et al., 1999). Human studies generally point to lower levels of brain serotonin in ASD (Adamsen et al., 2014; D'Eufemia et al., 1995; McDougle et al., 1996; Nakamura et al., 2010). However, these studies have used proxy markers of serotonin levels such as PET binding of serotonin transporters and receptors, and cerebrospinal fluid serotonin metabolites. Thus, more direct studies are needed before low brain serotonin can be characterized as a biomarker of ASD. However, in support of this hypothesis are preclinical studies demonstrating that the depletion of brain serotonin in neonatal mice produces ASD-like behaviours such as altered social and stereotypical behaviours and increased anxiety (Boylan et al., 2007; Hohmann et al., 2007).

Interestingly, the 5-HT_{1A} and 5-HT_{2A} receptors may be key mediators of the role that serotonin signaling plays in the pathogenesis of ASD. Neuroimaging studies have found reduced binding affinity of these receptors in limbic and neocortical brain regions of individuals with ASD (Murphy et al., 2006; Oblak et al., 2013; Brandenburg and Blatt, 2019). Accordingly, mice with impaired 5-HT_{1A} or 5-HT_{2A} receptor expression or function display increased anxiety-like behaviour which is rescued with the selective genetic restoration of the respective receptor (Ramboz et al., 1998; Gross et al., 2002; Weisstaub et al., 2006; Piszczek et al., 2015). LSD administration increases brain serotonin levels (Freedman,

1961) and potentiates the excitatory response of 5-HT_{2A} receptor agonism (De Gregorio et al., 2021). Given that psychedelics are agonists of the 5-HT_{1A} and 5-HT_{2A} receptors (De Gregorio et al., 2016a; Inserra et al., 2021a), their pharmacological effects may help restore the altered serotonergic signaling observed in ASD.

Fenfluramine, a serotonin-releasing agent, enhances serotonin signaling in the brain. While few small-sample, placebo-controlled studies found moderate efficacy in fenfluramine's ability to increase IQ in individuals with ASD (Geller et al., 1982; Ritvo et al., 1984), far more have found that this treatment is only effective in mildly reducing some of the motor and attentional atypicalities in people with ASD. This data suggests that increasing brain serotonin levels (and consequently serotonin signaling) is generally ineffective in improving the behavioural condition of individuals with ASD. Thus, the mechanisms of action of psychedelics must be better characterized in order to assess how they may interact with the altered serotonin signaling observed in ASD.

Prefrontal Cortex

The prefrontal cortex (PFC), and especially the medial PFC (mPFC), mediates social behaviours and cognition (Grossmann, 2013). Indeed, lesion of the PFC, which is clinically referred to as "frontal lobe syndrome," induces profound deficits in social interaction (Anderson et al., 1999; Eslinger et al., 2004; Kim et al., 2015; Kirsch et al., 2020). Accordingly, reduced PFC activity is observed in various preclinical models of ASD (Krueger et al., 2011; Duffney et al., 2015; Brumback et al., 2018). Aberrant mPFC activity is also observed in human neuroimaging studies, which report altered mPFC recruitment and connectivity in individuals with ASD compared to neurotypical individuals (Kennedy and Courchesne, 2008; Lombardo et al., 2010; Li et al., 2020). Human post-mortem studies have also found that the PFC of children with ASD have greater neuronal disorganization and differences in neuronal composition compared to neurotypical children (Stoner et al., 2014; Hashemi et al., 2017).

Due to its high 5-HT_{2A} receptor expression, the PFC is highly modulated by the effects of serotonergic psychedelics (De Gregorio et al., 2021; Inserra et al., 2021b; Jakab and Goldman-Rakic, 1998). Indeed, psychedelics activate unique 5-HT_{2A}-mediated transcriptional responses in the mouse mPFC (Martin and Nichols, 2016). Corroborating a crucial role of the mPFC in social behaviour, we demonstrated that the photo-inhibition of mPFC excitatory neurons decreases sociability and blocks LSD's prosocial effects (De Gregorio et al., 2021). Accordingly, in humans, mPFC activation was associated with LSD's ability to enhance social adaptation to others whose opinions are similar to one's own (Duerler et al., 2020). Another neuroimaging study revealed that psilocybin dampens mPFC neural activity, an effect correlated with the intensity of the subjective effects (Carhart-Harris et al., 2012). Similarly, LSD reduced the activity of the right mPFC in individuals presented with fearful faces (Mueller et al., 2017).

Although it is not clear which specific biological processes in the PFC may be targeted in ASD by psychedelics, signaling in this

brain region plays an important role in the mechanism through which these compounds modulate social behaviour.

Thalamocortical Circuit

The thalamus plays a significant role in the integration of external and internal stimuli, and its projections to the cerebral cortex are believed to play a vital role in consciousness (Llinas et al., 1998; Redinbaugh et al., 2020). Thus, thalamocortical dysfunction can interfere with complex human behaviours, such as social functioning. Recent studies have employed large, multi-site neuroimaging datasets to assess thalamocortical functional connectivity in ASD.

Given the vast heterogeneity of the ASD spectrum and that some of these studies considered the thalamus with other brain regions as a single subcortical structure in their analysis (Cerliani et al., 2015; Maximo and Kana, 2019), there are some inconsistencies in the literature. Nevertheless, two main connectivity trends are appreciable in individuals with ASD: 1) hyperconnectivity between the thalamus and sensorimotor cortex (Di Martino et al., 2014; Cerliani et al., 2015; Woodward et al., 2017; Maximo and Kana, 2019; Tomasi and Volkow, 2019; Ayub et al., 2021), suggesting an anomalous filtering of sensory information; and 2) hypoconnectivity between the thalamus and multimodal association cortices (Nair et al., 2013; Chen et al., 2016; Maximo and Kana, 2019), suggesting an aberrant integration of sensory information.

The effect of psychedelics on functional thalamocortical connectivity in humans has recently been investigated. Some studies demonstrate a general 5-HT_{2A}-mediated increase in thalamocortical connectivity following LSD (Tagliazucchi et al., 2016; Müller et al., 2017), while others show that psychedelics increase or decrease thalamocortical connectivity depending on the cortical region observed (Preller et al., 2018; Preller et al., 2019). Specifically, Preller and others (2018) revealed that LSD increases thalamic connectivity to cortical sensory regions while decreasing its connectivity to associative areas. This specific finding suggests that LSD may potentially exacerbate the abnormal thalamocortical connectivity in individuals with ASD. Thus, more investigation is required to elucidate the link between thalamocortical connectivity and social behaviour in ASD, and the way that psychedelics mediate this link.

In addition to thalamocortical connectivity, the effects of psychedelics on social behaviour may involve the regulation of spontaneous firing of thalamic neurons. The mediodorsal nucleus of the thalamus (MDT) has extensive reciprocal projections to the mPFC and is implicated in various cognitive functions, including sociability (Ferguson and Gao, 2018; Parnaudeau et al., 2018). Individuals with ASD present with morphological thalamic alterations, such as decreased global thalamic volume (Tsatsanis et al., 2003; Waiter et al., 2004), and increased surface area of the MDT specifically (Schuetze et al., 2016). Interestingly, the pharmacogenetic inhibition of MDT projections has been shown to reduce social preference in rats (Ferguson and Gao, 2018), further supporting this nucleus's role in mediating social behaviour. We recently discovered that LSD increases neuronal firing in the MDT (Inserra et al., 2021b), suggesting that LSD's effects may partly be mediated by its modulation of MDT projections.

TABLE 1 | Recent (2008–2021) clinical trials assessing social behaviour-related effects of psychedelics in neurotypical (non-ASD) individuals

Year	Title	Cohort	Design	Compound	Regimen (dose, frequency, route of administration)	Main outcomes	Side effects	Ref
2008	Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later	Healthy volunteers with regular participation in religious/spiritual activities	Randomized, double-blind, placebo-controlled, within-subject	Psilocybin	30 mg/70 kg once, twice or three times	Psilocybin increases altruistic/positive social effects at 14 months follow-up	None reported	Griffiths et al. (2008)
2009	A six-month prospective evaluation of personality traits, psychiatric symptoms and quality of life in ayahuasca-naïve subjects	Volunteers participating in religious Ayahuasca rituals (18–57 y/o, average 35.7 y/o, $n = 23$, 8 males, 15 females)	Observational naturalistic study	Ayahuasca	Up to 12 times over 6 months	Regular ayahuasca users have higher “social functioning” scores in the Short Form-36 Health Survey Questionnaire Ayahuasca might lower social reward dependence by decreasing sensitivity to signals of social approval	None reported	Barbosa et al. (2009)
2011	Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects	Healthy volunteers (29–62 y/o average 46 y/o, $n = 18$, 8 males, 10 females)	Randomized, double-blind, placebo-controlled, within-subject	Psilocybin	0, 5, 10, 20, 30 mg/70 kg, per oral solution	Psilocybin increases altruistic/positive social effects at all doses tested The increase in altruistic/positive social effects elicited by psilocybin 20–30 mg/70 kg are greater than those elicited by psilocybin (0.5–10 mg/70 kg) The increase elicited by psilocybin (20–30 mg/70 kg) in altruistic/positive social effects remains present at 14 months follow-up Volunteers reported better social relationships with family and others	Psilocybin induces dose-dependent acute anxiety/fear 44% of volunteers report delusions or paranoid thinking sometime during the session (especially at 30 mg/70 kg). Effects managed with reassurance in the supportive setting	Griffiths et al. (2011)
2015	Acute effects of lysergic acid diethylamide in healthy subjects	Healthy volunteer (25–51 y/o, average 28.6 y/o, $n = 16$, 8 males, 8 females)	Randomized, double-blind, placebo-controlled, within-subject	LSD	200 µg, once, gelatin capsules	LSD increases ratings of “empathogenic drug effects” such as “closeness to others,” “openness,” and “trust” LSD increases circulating oxytocin level	No severe acute side effects Most frequent acute or sub-acute mild side effects (up to 72 h): difficulty concentrating, headache, exhaustion, dizziness, lack of appetite, dry mouth, imbalance, nausea	Schmid et al. (2015)
2016	LSD Acutely Impairs Fear Recognition and Enhances Emotional Empathy and Sociality	Healthy volunteer and mostly hallucinogen-naïve (25–65 y/o) volunteers, $n = 40$, 20 males, 20 females)	Randomized, double-blind, placebo-controlled, within-subject	LSD	100 µg, once, per oral solution 200 µg, once, per oral solution	LSD enhances explicit and implicit emotional empathy LSD increases prosocial behaviour LSD enhances the desire to be with other people LSD decreases cognitive empathy	None reported	Dolder et al. (2016)
2016	Effects of serotonin 2A/1A receptor stimulation on social exclusion processing	Healthy volunteers (20–37 y/o, average 26.48, $n = 21$, 12 males, 9 females)	Randomized, double-blind, placebo-controlled, within-subject	Psilocybin	0.215 mg/kg, once, per oral solution	Psilocybin reduces the feeling of social rejection Psilocybin decreases the neural responses to social exclusion in the dorsal anterior cingulate cortex and the middle frontal gyrus	None reported	Preller et al. (2016)
2016	Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial	Individuals with advanced (stage III or IV) cancer ($n = 29$)	Randomized, double-blind, placebo-controlled, within-subject	Psilocybin	0.3 mg/kg, per oral solution, once	Psilocybin immediately reduced anxiety and depression symptoms for up to 7 weeks post-treatment Psilocybin decreased cancer-related demoralization and hopelessness while increasing spiritual well-being and quality of life for up to 6.5 months post-treatment Psilocybin produced positive social effects (ex: increased altruism), positive mood changes and positive changes on attitudes about life and self	None reported	Ross et al. (2016)
2016	Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial	Individuals with a life-threatening cancer diagnosis (average age: 56.3 y/o, $n = 51$, 26 males, 25 females)	Randomized, double-blind, crossover	Psilocybin	Low dose: 1 or 3 mg/70 kg High dose: 22 or 30 mg/70 kg Either low or high dose was administered, then after 5 weeks the other dosage was administered	High-dose psilocybin elicited a clinician- and self-rated decrease in anxiety (including death anxiety) and depressed mood, and an increase in quality of life and optimism Effects were still present in >80% of individuals at a 6-months follow-up evaluation	No serious adverse effects Some minor adverse effects (such as psychological discomfort, elevated blood pressure, nausea) occurred during the psilocybin session	Griffiths et al. (2016)
2017	Effect of Psilocybin on Empathy and Moral Decision-Making	Healthy volunteers (20–38 y/o, average 26.72 y/o, $n = 32$, 17 males, 15 female)	Randomized, double-blind, placebo-controlled, within-subject	Psilocybin	Psilocybin 0.215 mg/kg, per oral solution	Psilocybin increases explicit and implicit emotional empathy compared with placebo Psilocybin does not modify cognitive empathy compared to placebo	None reported	Pokorny et al. (2017)

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TABLE 1 | (Continued) Recent (2008–2021) clinical trials assessing social behaviour-related effects of psychedelics in neurotypical (non-ASD) individuals

Year	Title	Cohort	Design	Compound	Regimen (dose, frequency, route of administration)	Main outcomes	Side effects	Ref
2017	Psilocybin-occasioned mystical-type experience in combination with meditation and other spiritual practices produces enduring positive changes in psychological functioning and in trait measures of prosocial attitudes and behaviours	Healthy volunteers, support for spiritual practice ($n = 75$)	Randomized, double-blind, placebo-controlled	Psilocybin	Very low dose - Psilocybin 1 mg/70 kg (0.0143 mg/kg) per oral solution, twice 1 month apart $n = 25$ High dose - Psilocybin 20 and 30 mg/70 kg (0.29 mg/kg and 0.43 mg/kg) respectively in session 1 and 2, 1 month apart (+standard support for spiritual practice, $n = 25$, + high support for spiritual practice, $n = 25$)	Individuals receiving high dose psilocybin score higher for altruistic/positive social effects than those receiving low dose psilocybin Individuals receiving high dose psilocybin + high support for spiritual practice score higher for altruistic/positive social effects acutely than dose receiving high dose psilocybin + standard support At 6 months follow-up, individuals who received high dose psilocybin score higher for altruistic/positive social effects than those receiving low dose psilocybin on altruistic/positive social effects At 6 months follow-up, individuals receiving high dose psilocybin + high support for spiritual practice score higher than those receiving high dose + standard support on altruistic/positive social effects	None reported	Griffiths et al. (2018)
2017	Long-term follow-up of psilocybin-facilitated smoking cessation	Individuals with tobacco addiction (average 51 y/o, $n = 15$, 10 males, 5 females)	Open label pilot study (follow-up)	Psilocybin	20 and 30 mg/70 kg, two-three times	Altruistic/positive social effects scores remain significantly higher compared to baseline at 12 months follow-up after the first administration	Physiological adverse effects limited to mild post-session headache, and modest acute elevations in blood pressure and heart rate Some participants experienced challenging (fearful, anxiety-provoking) psilocybin session experiences. These effects resolved by the end of the drug session via interpersonal support from study staff	Johnson et al. (2017)
2018	Role of the 5-HT _{2A} Receptor in Self- and Other-Initiated Social Interaction in Lysergic Acid Diethylamide-Induced States: A Pharmacological fMRI Study	Healthy volunteers (20–34 y/o, mean age 25.42 y/o, $n = 24$, 18 males, 6 females)	Randomized, double-blind, placebo-controlled, within-subject	LSD	LSD 100 µg, once, per oral solution	LSD loosens self-boundaries, reducing neural response to self- versus other-initiated real-time social interaction LSD's reduction in brain activity in regions implicated in self-processing and social cognition was correlated with subjective drug effects LSD alters joint attention processing in the mPFC	No serious adverse events Transient mild headaches after drug effects wore off ($n = 4$ participants) Transient sleep disturbances for the first 2 nights after drug administration ($n = 1$ participant)	Preller, Schilbach, et al. (2018)
				Ketanserin	Ketanserin 40 mg/kg, per oral solution, once prior to LSD 100 µg	LSD increases positive and negative affect scores Ketanserin blocked the LSD-induced changes in self-processing and social cognition	No further side effects reported after 3 months	
2018	Long-lasting subjective effects of LSD in normal subjects	Healthy volunteers ($n = 16$)	Randomized, double-blind, placebo-controlled, within-subject (follow-up)	LSD	200 µg, once, per oral solution	LSD increases ratings of altruistic/positive social effects after 1 and 12 months	None reported	Schmid and Liechti, (2018)
2019	Psilocybin and MDMA reduce costly punishment in the Ultimatum Game	Healthy volunteers (male, $n = 20$)	Open-label, within-participant design	Psilocybin	2 mg per intravenous infusion over 2 min (test performed 60 min later)	Psilocybin increases one's concern for the outcome of interacting partners	None reported	Gabay et al. (2018)
2019	Acute subjective and behavioural effects of microdoses of LSD in healthy human volunteers	Healthy volunteers (18–40 y/o, $n = 20$, 8 males, 12 females)	Randomized, double-blind, placebo-controlled, within-subject	LSD	LSD 6.5, 13, or 26 µg, per oral solution with tartaric acid (0.5 ml, sublingual)	Dose-related subjective drug effects LSD (26 µg) increased vigor and marginally decreased the positivity ratings for positive pictures No other effects on mood, cognition or physiological measures	Trend towards increased anxiety with 26 µg dose	Bershad et al. (2019)
2019	Replication and extension of a model predicting response to psilocybin	183 valid responses ($n = 97$ males, $n = 86$ females). Average age 31.9 y/o, range 18–70 years	Retrospective survey	Psilocybin (dried mushrooms in pieces, dried powdered mushrooms, fresh mushrooms, synthesized psilocybin) Other unprescribed (such as cannabis, opiates, alcohol, stimulants), and prescribed (antidepressant, anxiolytic, blood pressure medications) substances ingested by some of the respondents	Various amounts ingested in the previous 12 months	Having a complete mystical experience is associated with higher post-treatment scores of empathy and social concern Surrender and preoccupation are the psychological states that produce the greatest (respectively positive and negative) responses	None reported	Russ et al. (2019)

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TABLE 1 | (Continued) Recent (2008–2021) clinical trials assessing social behaviour-related effects of psychedelics in neurotypical (non-ASD) individuals

Year	Title	Cohort	Design	Compound	Regimen (dose, frequency, route of administration)	Main outcomes	Side effects	Ref
2019	Sub-Acute Effects of Psilocybin on Empathy, Creative Thinking, and Subjective Well-Being	Volunteers attending a psilocybin retreat (average 34.8 y/o, $n = 55$, 24 males, 26 females)	Observational naturalistic study	Psilocybin-containing truffles	34.2 g average of psilocybin-containing truffles in tea form, once. Psilocybin content 0.127 mg/G of truffle (content in 34.2 g = 4.34 mg psilocybin) Psilocin = 0.7 mg/G of truffle (content in 34.2 g = 23.9 mg psilocin) Truffles crushed and boiling hot ginger tea added. Truffles remains in the cup eaten optionally	Increased emotional empathy (concern for faces depicting negative emotions) sub-acutely (the morning after) but not after 7 days Increased implicit arousal in response to faces depicting positive and negative emotional content the morning after Increased implicit arousal in response to faces depicting negative but not positive emotional content after 7 days	None reported	Mason et al. (2019)
2019	Exploring ayahuasca-assisted therapy for addiction: A qualitative analysis of preliminary findings among an Indigenous community in Canada	Indigenous members of a rural Coast Salish community in British Columbia (BC), Canada (19–56 y/o, mean 38 y/o, $n = 11$, 6 males and five females)	Observational naturalistic study	Ayahuasca	Ayahuasca (50–100 ml, twice over 2 days)	Some of the participants reported improved emotional openness at 6 months follow up Some of the participants improved their social relationships and had better communication with friends and family at 6 months follow-up	None reported	Argento et al. (2019)
2020	LSD-induced increases in social adaptation to opinions similar to one's own are associated with stimulation of serotonin receptors	Healthy volunteers (male and female, 20 y/o to 40 y/o, average 25.25 y/o, $n = 24$, 18 males, 6 females)	Double blind, placebo controlled, within subjects	LSD ketanserin	LSD 100 μ g, once, per oral solution ketanserin pretreatment (60 min prior) 40 mg, once, per oral solution	LSD increases the adaptation to the opinions of others if they are similar to one's own LSD modulates neuronal activity in the mPFC during social feedback processing and not during social decision-making (blocked by ketanserin) The magnitude of LSD-induced social adaptation change is associated with personality Patients with higher neuroticism scores adapt more strongly after LSD administration LSD has the strongest impact on social cognition in patients with lower sociability and higher neuroticism scores at baseline	No substantial side effects acutely and after 3 months Transient mild headaches (4 participants) after drug effects had worn off Transient sleep disturbances for the first two nights after drug administration (1 participant)	Duerter et al. (2020)
2021	Role of the 5-HT _{2A} Receptor in Acute Effects of LSD on Empathy and Circulating Oxytocin	Healthy volunteers (25–52 y/o, average age: 29 y/o, $n = 16$, 8 males, 8 females)	Double-blind, placebo-controlled, crossover design	LSD ketanserin	LSD 25, 50, 100, or 200 μ g, once, per oral solution ketanserin 20 mg, once, per oral solution	LSD dose-dependently increased explicit and implicit emotional empathy LSD 200 μ g significantly increased emotional empathy compared to placebo ketanserin did not significantly reduce the LSD-induced increase in empathy LSD increased blood oxytocin levels 1 and 3 h after drug intake, and this effect was blocked by ketanserin administration	None reported	Holze, Avedisian, et al. (2021)

TABLE 2 | Early clinical trials (1961–1970) assessing the use of psychedelics in “autistic schizophrenic” children. The terms “autistic” and “schizophrenic” do not reflect the currently approved terminology of the DSM-V, but rather the terminology that was used at the time of these early studies.

Year	Title	Cohort	Design	Compound	Regimen (dose, frequency, route of administration)	Main outcomes	Side effects	Ref
1961	Treatment of Autistic Schizophrenic Children with LSD-25 and UML-491	Hospitalized “autistic-schizophrenic” children (<i>n</i> = 14, 11 boys, 3 girls, 6–10.5 years old)	Open label	LSD L-methyl-D-lysergic acid butanolamide (UML-491)	LSD Acute–25 µg, intramuscular Repeated–100 µg, per oral solution, once per week in the early morning Subsequently increased to 100 µg per oral solution 2 to 3 times per week Finally, 100 µg per oral solution daily for 6 weeks UML-491, 8 mg divided in 4 doses daily Other pharmacological treatments interrupted at the onset of treatment with LSD and UML-491	LSD Acute–Improved behavioural patterns. Children unusually interested in the surrounding environment and seeking physical interaction. Children engaged in playful activities such as hand clapping and body swaying. Decreased appetite Repeated - When given 2–3 times per week, effects persist: decreased aggressive behaviour towards peers, increased interaction-seeking and emotional and physical closeness with peers and adults, more spontaneously playful, improvements in physical condition, “rosy” color rather than “blue” or “gray” and increased weight gain, enhanced understanding of environmental stimuli and more appropriate reactions to them, higher maturity in the Vineland Maturity Scale rating. Increased inorganic phosphate blood level. Changes appear to become chronic with continuous administration of the drug UML-491 Enhanced mood, relief of episodic headaches, relief of perceptual hypersensitivity in visual, auditory, olfactory, and skin sensations, general sense of wellbeing with improved sleep patterns	LSD No severe side effects reported. 2 prepubertal (10-year-old) children displayed disturbed anxious behaviour and were dropped from the study UML-491 Motor restlessness, irritability, localized muscle tensions or spasms, mild “crawling” skin sensations Episodes of changing muscle tensions and kinesthetic sensations with clowning, staggering gait, and twisting of the neck, back, and arms	Bender et al. (1961)
1962	Autistic Schizophrenic Children. An Experiment in the Use of D-Lysergic Acid Diethylamide (LSD-25)	“Autistic-schizophrenic” children (<i>n</i> = 12, 10 boys, 2 girls, aged 5 years 11 months to 11 years 10 months)	Open label	LSD	100 µg (1 girl 50 µg, 1 boy 200 µg), per oral solution, once or twice. Other Pharmacological treatments (unspecified tranquilizers, interrupted 24 h prior to LSD treatment)	Increased body awareness Desire for increased physical contact Repetitive behaviours disappeared and then reappeared as LSD wore off Two of the non-verbal children seemed to experiment with new sounds Decreased appetite	Sharp and rapid mood swings Severe anxiety (4 children) Moderate anxiety (3 children) Panic-like state (1 child) Children seemed to be experiencing auditory and visual (the latter more predominant) hallucinations Catatonia (3 children) Acute ataxia (1 children) Acute mild ataxia (4 children)	Freedman et al. (1962)
1963	Interim report on Research project: An Investigation to Determine Therapeutic Effectiveness of LSD-25 and Psilocybin on Hospitalized Severely Emotionally Disturbed Children	Hospitalized Severely Emotionally Disturbed Children (<i>n</i> = 12, 4 y 10 m–12 y 11 m, average 9 y 10 m)	Unknown	LSD Psilocybin	LSD alone (50–400 µg, typical dosage 200–300 µg) Psilocybin alone (10–20 mg, typical dosage 14–16 mg) LSD (100–300 µg, typical dosage 200 µg) + psilocybin (10 mg) Librium (10 mg) and Methedrine (5 mg) were used as pre-treatment medication in some sessions “3 grains of dilantin” administered the night before treatment to reduce the likelihood of seizures “Boosting” dose (LSD 25–100 µg) available if the child seemed to be a) caught in a problem or area that he could not break through, b) regressing to psychotic and stereotyped behaviour, c) defending themselves from new experiences 1–11 treatments, every 14 days–1 month	Increased sociability Increased face gazing Decreased anger outbursts Increased parent relatedness Increased relatedness to peers and adults Increased desire to communicate Decreased anxiety and compulsive behaviour for about 1 day following the treatments 1 self-harming girl who was in continuous restraint to prevent fatal self-harm stopped self-harming, did not need restraints anymore and became toilet-trained Children who respond better - Have speech - Are more “schizophrenic” than “autistic” - Are older (10–12 y/o)	2 episodes of seizures (1 girl) developed during treatment which was discontinued in this child	Fisher and Castile, (1963)
1963	LSD and UML treatment of hospitalized disturbed children	Hospitalized children (<i>n</i> = 50). Half displayed autism spectrum disorder features and half displayed psychotic features	Open label	LSD UML	LSD gradually increased from 50 to 150 µg daily, divided in two doses UML gradually increased from 4 to 12 mg daily, divided in two doses Daily administration, duration of treatment: 2–12 months	Increased responsiveness to environmental stimuli Increased alertness, awareness, and affectionate behaviour Some of the more aggressive children became remarkably quieter after LSD treatment Decrease of regressive behaviour in some “autistic” children Improved food habits and interest in new foods Improved vocabulary in some of the children After taking the children off LSD their behaviour regressed but to a lesser extent	No serious adverse events Some of the quieter “autistic” children became mildly aggressive	Bender et al. (1963)
1966	Modification of autistic behaviour with LSD-25	“Autistic” twin males (4 years 9 months old at study start, 5 years 2 months at study end)	Double-blind placebo-controlled	LSD	LSD 50 µg per oral solution 9 treatments, twice weekly 50 mg oral. chlorpromazine to terminate the LSD effects after 3 h	Increased eye-to-face contact during LSD sessions Increased responsiveness to adults Increased movements towards the experimenter, decreased movements away from the experimenter Decreased repetitive behaviours during LSD sessions Increased smiling and laughing behaviour	None reported	Simmons et al. (1966)

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TABLE 2 | (Continued) Early clinical trials (1961–1970) assessing the use of psychedelics in “autistic schizophrenic” children. The terms “autistic” and “schizophrenic” do not reflect the currently approved terminology of the DSM-V, but rather the terminology that was used at the time of these early studies.

Year	Title	Cohort	Design	Compound	Regimen (dose, frequency, route of administration)	Main outcomes	Side effects	Ref
1966	The Treatment of Childhood Schizophrenia with LSD and UML	“Autistic”, regressed, verbal, psychotic and “schizophrenic” (different groups) pre-and post-puberty male and female children 6–15 years of age (total $n = 54$)	Open label	LSD UML	LSD 100–150 μg , daily in 2 doses UML 12 mg daily, divided in 2 doses Duration of treatment: 2–18 months, with an average of 9 months	<i>Prepuberty “autistic” boys</i> All participants show some mild (variable) degree of favorable response with slow and steady progression Participants were happier following the ingestion of the drug and this tended to carry over through the whole day Participants became spontaneously more playful with toys, other children and adults Participants sought and responded to physical contact and affection Decreased overall aggressive behaviour Food habits and toilet-training improved in some participants Improved skin color and overall physical health Decreased rhythmic and stereotyped behaviour Increased responsiveness to environmental cues, stimuli and patterns Increased laughing behaviour Increased maturity in the Vineland Social Maturity Scale (the authors suggest that the real improvements are underestimated by this scale) <i>Prepuberty “autistic” girls</i> No detectable improvement in maturation or social maturity Two of the three girls seemed brighter and improved in color, weight gain, and eating and toilet habits <i>Postpuberty “autistic” boys</i> Similar responses to younger “autistic” children although responses are attenuated compared to prepuberty “autistic” boys Increased typical behaviours such as climbing, ball bouncing and rocking Strong improvement in verbalization and speech appropriateness in one boy For the first time, some children attempted to contact/approach adults	In “autistic” prepuberal boys, no regressions were observed although some children had episodic occurrences of aggressive contact with other children and feces smearing One of the “autistic” prepuberal girls became too active and aggressive towards other children (reserpine was administered with LSD to counteract these effects) Some of the “autistic” postpuberal boys attempted to interact with others via biting and pinching	Bender et al. (1966)
1970	The Psycholytic Treatment of a Childhood Schizophrenic Girl	Case report (1 of the “autistic-schizophrenic” girls of the clinical trial by Freedman et al., 1962)	Open label	LSD Psilocybin	16 treatments over 11 months with LSD alone (50–300 μg , $n = 13$ treatments), psilocybin alone (10–20 mg, $n = 2$ treatments), or LSD (200 μg) + psilocybin (10 mg, $n = 1$ treatment) Methedrine (5 mg) and Librium (10–25 mg) given in some instances in combination with LSD (200–300 μg) and psilocybin (10 mg) + LSD (200 μg)	Increased motor and verbal behaviour, increased desire for physical contact, the child was delighted and excited with perceptual changes. Decreased repetitive movements. Enhanced sense of humor; she was able to feel and relate to others in a “normal” way At the end of the treatment she reached a state of deep acceptance and profound feelings of love and personal integration. She ceased her isolated, “autistic” behaviour, talked rationally, and helped other children. Despite scarce follow-up records, she seemed to have stabilized at 5 years follow-up	Mood swings including Anxious behaviour, restless behaviour, angry behaviour, stuffing objects in her mouth Emergence of internal conflict and anger led to anxious, agitated, and self-harming behaviour At the end of treatment 4, she became very violent and tried to choke herself as well as others	Fisher, (1970)

Altogether, we suggest that psychedelics may target the dysregulated thalamocortical connectivity and thalamic neuronal firing in individuals with ASD. However, it is also true that the thalamocortical dysregulations in individuals with ASD may concurrently limit the behavioural effects of psychedelics (such as changes in social behaviour) that are mediated by thalamocortical signaling. For instance, mice with embryonic-stage deletions of the Tuberous Sclerosis Complex 1 (*Tsc1*) gene (a standard preclinical model of ASD) had an overabundance and greater diffusion of thalamic projections to the somatosensory cortex (Normand et al., 2013). Since structural thalamocortical connectivity is profoundly altered in this ASD model, the response of this circuit to the administration of psychedelics may also be altered. Thus, any cognitive effects of psychedelics mediated by their ability to modulate thalamocortical signaling may be significantly different in people with ASD, potentially limiting their therapeutic effects.

CLINICAL TRIALS OF PSYCHEDELICS IN CHILDREN WITH ASD (1961–1970)

Prior to the classification of psychedelics as Schedule I Controlled Substances in 1970, these substances were tested in the treatment of children with ASD in order to assess their efficacy in relieving treatment-refractory ASD-like behaviours. Importantly, these individuals were classified as “autistic-schizophrenic” (Bender et al., 1961; Freedman et al., 1962; Bender et al., 1966; Fisher, 1970), and “severely emotionally disturbed” (Fisher and Castile, 1963). Thus, they may not have necessarily been diagnosed with ASD using contemporary diagnostic criteria, imposing a significant limitation on these findings (reviewed and summarized in **Table 2**). Although significant methodological and ethical shortcomings are evident through the lens of modern clinical and ethical research standards, this early work is being re-scrutinized to extrapolate potentially meaningful data which could inform contemporary research.

Most of these studies involved a regimen of LSD given at medium to high doses (25–400 µg), with schedules ranging from a single administration to daily administrations for up to 18 months. The most effective results were observed when daily or weekly LSD was given over relatively extended periods of time (Bender et al., 1961). Greater improvements were observed when the therapist was more actively involved with the children; when they were given the possibility to experience meaningful interpersonal psychotherapeutic interactions; and when the settings were free of artificial or experimental restrictions. When the children were taken off the drug, their behaviour regressed, but not to the extent observed previously (Bender et al., 1963).

Psychedelic-assisted therapy in children with ASD resulted in a variety of clinical improvements: enhanced mood, sociability, and affectionate behaviour; increased emotional closeness, relatedness, and responsiveness to others; increased desire to communicate and interest in the surrounding environment; relief of perceptual hypersensitivity; improved speech and vocabulary; increased playfulness, smiling,

and laughing; increased eye and face-gazing behaviour; decreased aggressive and repetitive behaviours; and improved sleep patterns.

Although the aforementioned effects of psychedelics are desirable in the treatment of ASD, adverse effects of varying severity were also reported. Some of the children experienced rapid mood swings, ataxia, and moderate to severe anxiety, with at least one case of a “panic-like state” (Bender et al., 1961; Freedman et al., 1962). One girl experienced two episodes of seizures during LSD treatment (Fisher and Castile, 1963). Some of the children displayed increased biting and pinching behaviour, some engaged in aggressive behaviour even after the effects of the drug had worn off, and some had difficulty sleeping in the days following administration (Bender et al., 1961; Freedman et al., 1962; Bender et al., 1963; Fisher and Castile, 1963; Bender et al., 1966; Fisher, 1970). In one “autistic-schizophrenic” girl receiving LSD and psilocybin, the emergence of internal conflict led to acute anxious, aggressive, and self-harming behaviour (Fisher, 1970).

Given that certain individuals with ASD present atypical behavioural characteristics such as increased aggression (Fitzpatrick et al., 2016) and epilepsy (Tuchman and Rapin, 2002), it is not entirely surprising that psychedelic treatment triggered aggressive behaviour (Bender et al., 1966) and seizures (Fisher and Castile, 1963) in some of the children. Consequently, serious precautions must be taken when using psychedelic treatments in these vulnerable populations.

Another potential risk is the potential for psychedelics to induce psychosis and/or schizophrenia. The prevalence of schizophrenia is significantly higher in people with ASD compared to neurotypical individuals (Zheng et al., 2018). Since psychedelic use is associated with the development of psychosis in people with genetic predispositions (Breakey et al., 1974; Vardy and Kay, 1983), the risk of psychosis and schizophrenia must be carefully considered when assessing the potential adverse effects of psychedelic administration in this population. Altogether, although some therapeutic effects of psychedelics in children with ASD have been reported, the extended list of reported adverse effects demands caution.

CONCLUSION

Due to the limited treatment options for ASD, the development of novel therapies is warranted. Clinical and preclinical trials suggest that psychedelics may improve social behaviour and decrease the burden of co-occurring diagnoses in ASD by targeting synaptic function, serotonin signaling, PFC activity, and thalamocortical signaling. Early clinical trials in childhood ASD suggest that psychedelics might hold therapeutic potential; however, the side effects encountered represent potential limitations to this treatment. It is possible that psychedelics may alleviate a few core social-behavioural features in individuals with ASD, such as social anxiety, but carefully performing a risk-to-benefit assessment is crucial due to the severity of their potential side effects.

Individuals with ASD represent a highly heterogeneous demographic; therefore, only certain subsets of individuals

with ASD may respond well to psychedelic treatment options. Clinical trials must proceed with caution because this population is also comprised of children and some individuals with intellectual disabilities, for which obtaining informed consent is a challenge. Future studies must make these considerations when determining if some of the positive findings obtained in the “first wave” of psychedelic research in ASD can be validated when employing contemporary scientific and ethical standards.

AUTHOR CONTRIBUTIONS

Participated in Research Design: AM, AI, DDG, and GG. Wrote or contributed to the writing of the article: AM, AI, DDG, and GG.

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The remaining author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Therapeutic Alliance and Rapport Modulate Responses to Psilocybin Assisted Therapy for Depression

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Background: Across psychotherapeutic frameworks, the strength of the therapeutic alliance has been found to correlate with treatment outcomes; however, its role has never been formally assessed in a trial of psychedelic-assisted therapy. We aimed to investigate the relationships between therapeutic alliance and rapport, the quality of the acute psychedelic experience and treatment outcomes.

Methods: This 2-arm double-blind randomized controlled trial compared escitalopram with psychedelic-assisted therapy for moderate-severe depressive disorder ($N = 59$). This analysis focused on the psilocybin condition ($n = 30$), who received two oral doses of 25 mg psilocybin, 3-weeks apart, with psychological preparation, in-session support, and integration therapy. A new psychedelic therapy model, called “Accept-Connect-Embody” (ACE), was developed in this trial. The primary outcome was depression severity 6 weeks post treatment (Quick Inventory of Depressive Symptomatology, QIDS-SR-16). Path analyses tested the hypothesis that therapeutic alliance (Scale To Assess the Therapeutic Relationship Patient Version, STAR-P) would predict depression outcomes via its influence on the acute psychedelic experience, specifically emotional-breakthrough (EBI) and mystical-type experiences (MEQ). The same analysis was performed on the escitalopram arm to test specificity.

Results: The strength of therapeutic alliance predicted pre-session rapport, greater emotional-breakthrough and mystical-type experience (maximum EBI and MEQ scores across the two psilocybin sessions) and final QIDS scores ($\beta = -0.22$, $R^2 = 0.42$ for EBI_{Max}; $\beta = -0.19$, $R^2 = 0.32$ for MEQ_{Max}). Exploratory path models revealed that final depression outcomes were more strongly affected by emotional breakthrough during the first, and mystical experience during the second session. Emotional breakthrough, but not mystical experience, during the first session had a positive effect on therapeutic alliance ahead of the second session ($\beta = 0.79$, $p < 0.0001$). Therapeutic alliance ahead of the second session had a direct impact on final depression scores, not mediated by the acute

experience, with a weaker alliance ahead of the second psilocybin session predicting higher absolute depression scores at endpoint ($\beta = -0.49$, $p < 0.001$)

Discussion: Future research could consider therapist training and characteristics; specific participant factors, e.g., attachment style or interpersonal trauma, which may underlie the quality of the therapeutic relationship, the psychedelic experience and clinical outcomes; and consider how therapeutic approaches might adapt in cases of weaker therapeutic alliance.

Clinical Trial Registration: This trial is registered at <http://clinicaltrials.gov>, identifier (NCT03429075).

Keywords: psilocybin, therapeutic alliance, therapeutic relationship, emotional breakthrough, mystical experience, depression, acute psychedelic experience, psychedelic assisted therapy

INTRODUCTION

Psychedelic-assisted therapy is a mental health intervention that involves the administration of a psychedelic substance, such as psilocybin, in combination with therapy or psychological support (Nutt and Carhart-Harris, 2021). Use of psychedelic substances within indigenous sacramental and healing rituals dates back thousands of years (Schultes et al., 2001). Psychedelic-assisted therapy was widely researched, and noted for its promise, during the 1950s and 60s, until it was shut-down due to restrictive governmental regulations (Nutt et al., 2020). Over the past decade, psychedelic-assisted therapy research has re-emerged with a growing body of evidence supporting its efficaciousness for a wide range of mental health presentations (for a review, see Andersen et al., 2021), including distress associated with a life-threatening illness (Grob et al., 2011; Griffiths et al., 2016; Ross et al., 2016; Anderson et al., 2020), substance misuse (Krebs and Johansen, 2012; Johnson et al., 2014, 2017; Bogenschutz et al., 2015), and major depressive disorder (MDD) (Carhart-Harris et al., 2016; Carhart-Harris L. et al., 2018; Palhano-Fontes et al., 2019; Carhart-Harris et al., 2021a; Davis et al., 2021). Most relevantly for the present work, in the recently published results of a double-blind randomised controlled trial (DB-RCT), analysed here in this paper, there was no significant difference found between the psilocybin-assisted therapy versus a treatment arm that featured 6 weeks of daily ingestion of a selective serotonin reuptake inhibitor (SSRI) antidepressant, escitalopram, in the primary outcome (change in QIDS from baseline to primary endpoint), with the same psychological support (Carhart-Harris et al., 2021a). However, we found more rapid and wide-ranging mental health improvements in the psilocybin arm. Given these findings, alongside the growing evidence base for the efficacy of psychedelic-assisted therapy, there is a need to better understand its therapeutic mechanisms of action.

Extant research suggests that the quality of the acute psychedelic experience is predictive of psychedelic-assisted therapy's positive therapeutic effects (Roseman et al., 2018; Romeo et al., 2021). To date, the most extensively researched dimension of the acute psychedelic experience is the so-called 'mystical-type' or 'peak' experience, which includes deeply felt positive mood, ineffability, a sense of sacredness and unity, and

transcendence (see Johnson et al., 2019). Several studies have provided evidence for the role of the mystical-type experience as a predictor of positive treatment outcomes following psychedelic-assisted therapy (Bogenschutz and Johnson, 2015; Carhart-Harris et al., 2018; Garcia-Romeu et al., 2014; Griffiths et al., 2016; Johnson et al., 2017; Roseman et al., 2018; Ross et al., 2016; for a review, see; Romeo et al., 2021). Beyond the mystical-type experience, recent prospective research (Roseman et al., 2019) and published accounts of trial participant's psychedelic therapy experiences (Gasser et al., 2014; Watts et al., 2017) have also highlighted the importance of emotional breakthrough; i.e., experiencing emotional release or catharsis after facing and overcoming difficult or previously inaccessible emotions or memories, and gaining personal and interpersonal insights; therapeutic mechanisms well established within traditional psychotherapeutic schools (Foa and Kozak, 1986; Jackson, 1994; Samoilov and Goldfried, 2000; Greenberg and Pascual-Leone, 2006; Pascual-Leone et al., 2015). One of the proposed mechanisms of psychedelics is that they weaken ego boundaries and allow access to the 'unconscious mind' (Frederking, 1955; Grof, 2008), and in line with this, many psychedelic therapists have written about the importance of emotional breakthrough as a therapeutic mechanism (see Roseman et al., 2019 for a comprehensive background). Results of survey-based data of individuals planning to use a psychedelic suggested that higher levels of emotional breakthrough are associated with improved mental health in the weeks following psychedelic use (Roseman et al., 2019; Spriggs et al., 2021). Importantly, however, the role of emotional breakthrough in facilitating treatment outcomes has not yet been evaluated within a clinical sample or in the context of a controlled psychedelic-assisted therapy clinical trial.

Empirical research to date has focused primarily on the role of the acute psychedelic experience as a mediator of treatment outcomes, with relatively less focus on the role of other important components of psychedelic-assisted therapy that may serve to promote certain acute experiences supportive of clinical improvements. There is some evidence to support a strong and long-held assumption in psychedelic-assisted therapy research that psychological and clinical outcomes are critically dependent upon the surrounding context in which they are taken (Leary et al., 1963; Hartogsohn, 2016, 2017; Carhart-Harris and Nutt, 2017; Carhart-Harris et al., 2018).

One key contextual component in this regard is the relationship between the individual receiving psychedelic-therapy and the treatment provider(s) i.e., the ‘guides’ or therapists (Grinspoon and Doblin, 2001; Grof, 2008; Johnson et al., 2008; Richards, 2016; Carhart-Harris and Nutt, 2017; Brecksema et al., 2020; Nayak and Johnson, 2020; Watts and Luoma, 2020). Across a range of cultural and historical contexts there has always been a strong emphasis on the importance of the guide, therapist or shaman in supporting psychedelic experiences (Walsh and Grob, 2005; Grof, 2008; Richards, 2016; George et al., 2020). In contemporary psychedelic research, these individuals are most often referred to as “guides” but can also be referred to as “sitters” or “therapists”. Similarly, the terms “participants” and “patients” tend to be used interchangeably depending on the specific context in psychedelic literature. Therapeutic approaches in psychedelic-assisted therapy are evolving and vary across different clinical trials, as does the emphasis on the importance of the role of the therapist or guides [see methods for details of the Accept Connect Embody (ACE; Watts and Luoma, 2020) therapeutic protocol], but typically these guides take a supportive, open and non-directive approach and aim to provide a safe and containing setting with a view to allowing unconscious psychological material, emotions, memories and difficulties to emerge (Grinspoon and Doblin, 2001; Grof, 2008; Brecksema et al., 2020; Nayak and Johnson, 2020; Watts and Luoma, 2020). The standard model is to allocate two such guides to each participant (Walsh and Grob, 2005; Grof, 2008; Richards, 2016), who are typically mental health professionals, ideally with personal and/or professional experience with the effects of psychedelic compounds or other non-ordinary states. In this trial participants had approximately 35–40 h of contact with their guide, 16 of which were the two psilocybin session days.

The therapeutic relationship, i.e. the relationship between therapist and patient, is recognised to be of fundamental importance across different psychotherapeutic models or approaches (Horvath, 2000; Lemma, 2015; Baier et al., 2020). Some particularly relevant constructs or phenomena for psychedelic-assisted therapy include: the ‘therapeutic alliance’—i.e., the presence of a collaborative relationship that includes agreement on treatment goals/tasks and a positive emotional bond (Bordin, 1979; Martin et al., 2000), and the psychoanalytic concept of “transference” or the unconscious ways that a person’s experience of past relationships influences their perception and experience of the therapeutic relationship and “countertransference” which refers to the reciprocal feelings evoked in the therapist (Horvath, 2000; Lemma, 2015). Contemporary thinking acknowledges the complexity of trying to theoretically define the therapeutic relationship as it is intersubjective and dynamic, influenced consciously and unconsciously by both therapist and patient (Horvath, 2000; Safran et al., 2001; Lemma, 2015). Compelling evidence exists that the quality of the therapeutic alliance is an important predictor of treatment outcomes in psychotherapy (for a review, see Baier et al., 2020). The therapeutic alliance is also recognised to be a dynamic phenomenon that is sensitive to change over the course of therapy; with a bidirectional and

reciprocal relationship with symptom improvement; and which is influenced by pre-treatment patient characteristics e.g., complex relational trauma (Falkenström et al., 2013; Baier et al., 2020; Flückiger et al., 2020); and therapist characteristics and qualities (Ackerman and Hilsenroth, 2003; Phelps, 2017). The term “therapeutic rapport” is sometimes used synonymously with “therapeutic alliance”, albeit with a more specific stress on the *positive* nature of the emotional bond between the therapist and patient (Leach, 2005).

Despite strong theoretical assumptions surrounding the importance of the therapeutic relationship within psychedelic-assisted therapy, and strong evidence for its importance within psychotherapeutic interventions broadly, little empirical research has been done to examine its role in shaping psychedelic experiences and psychedelic-assisted therapy treatment outcomes. One prospective, observational survey study looking at people taking psychedelics in non-clinical settings found that having a “good feeling” or a “good relationship” with the people that an individual was taking a psychedelic with, or who would be taking care of them during the experience, was predictive of a reduced likelihood of challenging experiences and greater subsequent improvements in psychological well-being (Haijen et al., 2018). A similarly designed study of psychedelic use in communal settings, e.g., retreat centres, found that the positive relationships between rapport and increases in well-being and social connectedness, were mediated by experiences of togetherness and shared humanity (Kettner et al., 2021).

Although many psychedelic therapists have published qualitative reports of intensified transference in psychedelic-assisted therapy (Walsh and Grob, 2005; Grof, 2008; Fisher 2015), there has been no published quantitative research into the matter of more concrete questions, such as whether the quality of the therapeutic relationship is predictive of the quality of the acute psychedelic experience (e.g., mystical-type or emotional breakthrough experiences) en route to positive treatment outcomes. It is also important to consider what impact a weaker therapeutic alliance has on the psychedelic experience and clinical outcomes, as this may have implications for screening and therapeutic approaches e.g., considering who and at what point in a therapeutic process participants will benefit from the experiences, identifying those at risk of harm and to consider how the therapeutic framework might need to adapt in certain cases. Furthermore, research has not yet examined whether the strength of the therapeutic relationship leads to treatment outcomes *through its influence* on acute psychedelic experiences. Additionally, despite evidence for the dynamic nature of the therapeutic relationship and suggestions that psychedelic experiences and psychedelics themselves may intensify and potentially enhance the therapeutic relationship (e.g., Grinspoon and Bakalar, 1986; Grinspoon and Doblin, 2001; Walsh and Grob, 2005; Grof, 2008; Fisher 2015; Dolder et al., 2016), research has not yet examined whether psychedelic experiences are associated with subsequent improvements in the therapeutic relationship.

The present article uses data from a recently published DB-RCT (Carhart-Harris et al., 2021a) in which individuals with MDD received two treatment sessions of psilocybin (25 mg) plus

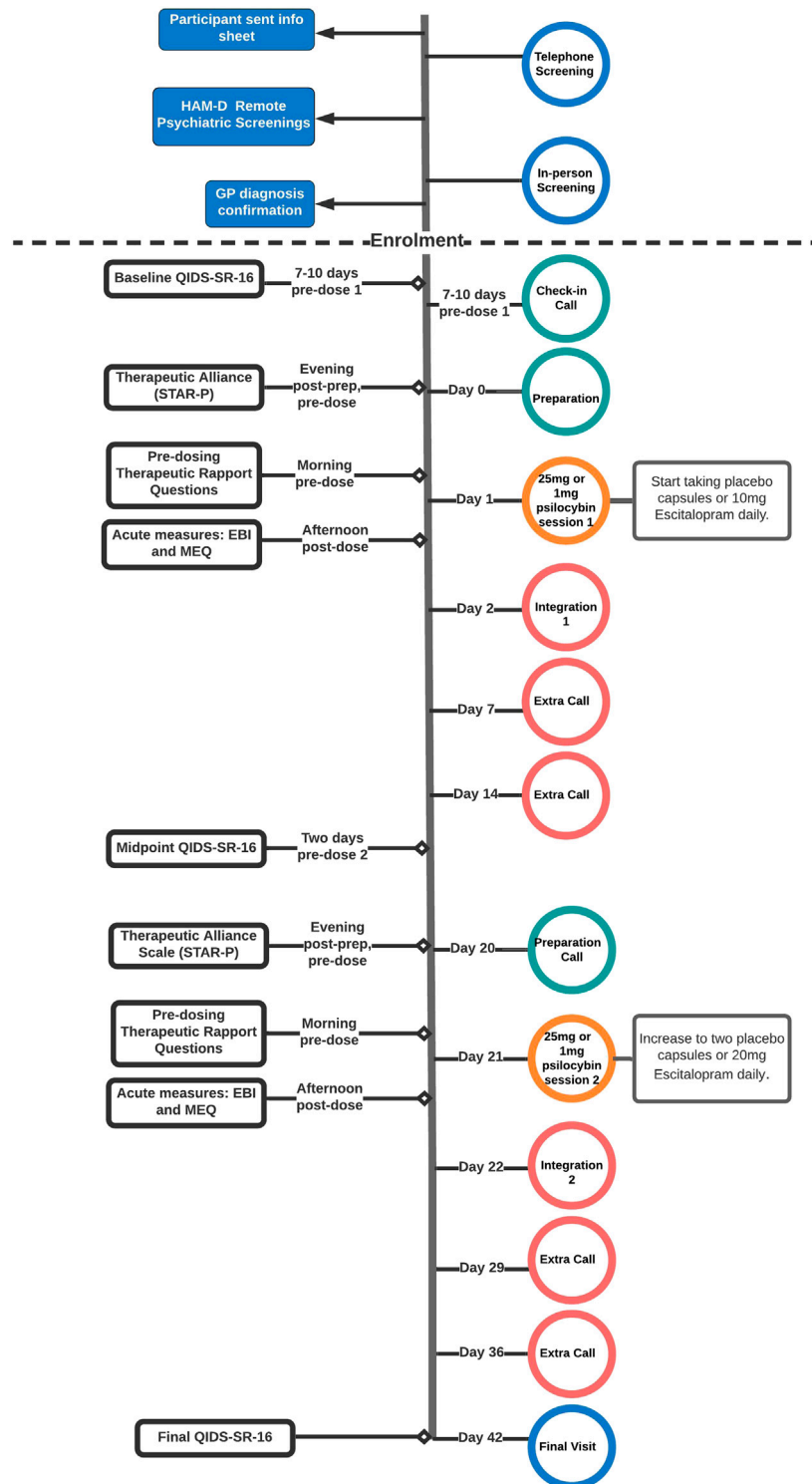


FIGURE 1 | Flow-chart outlining study procedures for the psilocybin and escitalopram arms of the trial featured in this article, outlined in "Design and Procedures".

All participants included in this analysis followed the outlined procedures, unless otherwise stated in the "Descriptives" section of the results. After the 6-weeks key endpoint, participants completed remote monthly follow-up assessments until 6 months post-study. The dotted line separates pre-enrolment screening procedures (above line) from post-enrolment study procedures (below line). Info Sheet: Participant Information Sheet, HAM-D: 17-item Hamilton Depression Scale (clinician-rated), GP: General Practitioner, STAR-P: Scale To Assess the Therapeutic Relationship (participant-rated version), QIDS-SR-16: 16-item Self-Reported Quick Inventory of Depressive Symptomatology (primary outcome), EBI: Emotional Breakthrough Inventory, MEQ: Mystical Experience Questionnaire.

6 weeks of daily placebo; or two treatment sessions with a *de facto* placebo, plus 6 weeks of daily escitalopram. Both arms received therapeutic support as described below (see Methods). Due to our strong prior hypotheses in relation to the role of therapeutic alliance and rapport in mediating the quality of the psychedelic experience and subsequent key clinical outcomes, we chose to focus specifically on the psilocybin condition, but analysis of the escitalopram arm is available in the supplementary material. Our specific main aims were to:

1: Examine whether the quality of the acute experience (specifically, mystical-type experiences and emotional breakthrough) serves as a mediator of the relationship between the strength of the therapeutic relationship (specifically, therapeutic alliance measured here using the participant version of Scale To Assess the Therapeutic Relationship (STAR-P) and rapport which was measured via a single, self-constructed visual analogue scale) and changes in depression.

2: Explore the relationship between the strength of the therapeutic relationship (therapeutic alliance and rapport), the acute experience (mystical-type experience and emotional breakthrough) and changes in depression score (measured via the 16 item self-rated Quick Inventory of Depressive Symptomatology or 'QIDS') and the interplay between these factors on a session-by-session basis, given there were two psilocybin dosing sessions in this trial.

METHODS

Trial Oversight

This study received approval from the Brent Research Ethics Committee (REC), the Medicines and Healthcare products Regulatory Agency (MHRA), the Health Research Authority (HRA), and the Imperial Joint Research Compliance (study sponsors) and General Data Protection Regulation offices. It also received a study-specific Schedule I license approval from the United Kingdom Home Office to prescribe psilocybin. All clinical visits took place at the National Institute for Health Research (NIHR)-funded Imperial Clinical Research Facility. The psilocybin for this trial was provided by COMPASS Pathways and the placebo tablets by the Pharmacy Manufacturing Unit at Guy's and St. Thomas' Hospital.

Participants

Detailed information about recruitment and the screening process including full exclusion criteria can be found in the supplementary material and clinical protocol published in Carhart-Harris et al. (2021a). The following summary is provided for ease of reference (see **Figure 1** for a visual summary), however:

This study was advertised to General Practitioners via the NIHR Clinical Research Network and to the public online, recruiting men and women aged 18–65 years old. Telephone screening was followed by a remote Hamilton Depression (HAM-D; Hamilton, 1960) assessment with a minimum score of 17, indicating moderate-to-severe MDD, was required in order to proceed. Exclusion criteria included an immediate family or

personal history of psychosis, major physical health conditions, a history of high risk suicide attempts, pregnancy, contraindications to selective-serotonin reuptake inhibitors (SSRIs) or magnetic resonance imaging (MRI), having failed a previous full course of escitalopram or having already taken psilocybin for therapeutic purposes.

Ahead of potential enrolment, the final stage was a face-to-face screening visit involving physical and psychiatric assessments with the study clinicians. After this, the participants met with their guiding pair for an hour. Discussion topics were typical of a psychotherapy initial assessment including current difficulties, salient early life experiences, family and interpersonal history, previous traumas and experiences of therapy. Participants had only two face-to-face contacts and one phone call with their therapists prior to dosing, thus, an ability to build sufficient therapeutic alliance and rapport relatively quickly was deemed necessary for inclusion. This was assessed by the team clinically as in traditional therapy assessments based on how they related during the screening process e.g. their ability to speak openly about their difficulties; to be emotionally vulnerable; an awareness of and ability to speak about their own relational patterns and how this might impact on the therapeutic relationship. Information around current and historical relationships and previous experiences of therapy was also gathered. More concretely those with a suspected or known diagnosis of any conditions which would significantly impact on rapport such as emotionally unstable personality disorder or complex post-traumatic stress disorder (as assessed by the screening psychiatrist) were excluded.

All participants withdrew from psychiatric medication for at least 2 weeks before starting the trial (**Table 1** for detailed demographics) and psychotherapy for at least 4 weeks.

Design and Procedures

This was a phase II, double-blind, two-armed, randomised controlled trial. In this study, participants with moderate-severe MDD were randomised either to an 'escitalopram arm' or to a 'psilocybin arm'. The analyses in this paper focus primarily only on the latter arm, but full trial procedures and main clinical results for both arms have been reported in Carhart-Harris et al. (2021a). In order to validate our findings, we ran the same models used in our primary confirmatory analysis for the escitalopram arm. This data is available in the supplementary material of this paper.

Each participant was assigned two guides (see introduction). These were mostly trained or training clinical psychologists, psychotherapists or psychiatrists with therapy experience. All guides had experience of working with psychedelics or non-ordinary states. One of the pair was assigned the role of 'main guide' and was present in all six of their face-to-face visits and five calls post-screening (plus the option of four additional if clinically indicated). One of the two guides could be a clinical trainee if accompanied by an experienced mental health professional.

See **Figure 1** for a visual summary of all clinical contacts. Approximately 1 week (seven to 10 days) prior to the first psilocybin dosing session guides rang participants (Check-in Call) to discuss practicalities, answer questions and to discuss

TABLE 1 | Demographic information of participants in the psilocybin arm of the trial.

Overall	
Total patient number included in model	29
Total patient number excluded from model	1
Demographics of those included	
Age, years—mean, SD (range)	42.8, 11.6 (21–64)
Females, number (%)	11 (38)
Caucasian Ethnicity, number (%) ^a	27 (93)
Employment status—number (%)	
Employed	20 (69)
Unemployed	7 (24)
Student	2 (7)
University-level education, number (%)	22 (76)
Past psilocybin use, number (%)	7 (24)
Weekly alcohol (United Kingdom units)—mean, SD (range)	4.8, 5.4 (0–20)
Clinical	
Illness duration, years—mean, SD (range)	22.2, 10.9 (3–44)
HAMD-17 scores at pre-treatment baseline—mean, SD (range) ^b	19.2, 2.3 (16–23)
QIDS-16 scores at pre-treatment baseline—mean, SD (range) ^c	14.7, 3.9 (7–23)
No. past psychiatric medications—mean, SD (range)	2.2, 1.7 (0–6)
Discontinued psychiatric medication for trial, number (%)	11 (38)
Past psychotherapy, number (%)	27 (93)

Pre-treatment baseline was 7–10 days before dosing-day 1.

^aRace was reported by the patients.

^bThe scores on the 17-item Hamilton Depression Rating Scale (HAM-D-17) range from 0 to 50, with higher scores indicating Greater depression. At screening, which was typically a few weeks before pre-treatment baseline, all the patients. Had a score of at least 17 on the HAM-D-17. The depression scores reported in this table are from pre-treatment baseline. And not screening.

^cThe scores on the 16-item Quick Inventory of Depressive Symptomatology—Self-Report (QIDS-SR-16) range from 0 to 27, with higher scores indicating greater depression.

the music playlist as participants were given the option to add three personal music choices to play at the end of the session. In visit 1 (“Prep”) all participants were given approximately 5 hours of preparation by their guides for the next day’s psilocybin session. In visit 2 (Dosing Day 1), participants in the psilocybin arm were given 25 mg of psilocybin and participants in the escitalopram were given 1 mg of psilocybin, accompanied and supported by their two guides throughout the day. All participants were told that they would definitely be given psilocybin, but they were not told the doses in an effort to standardise expectations. After psilocybin administration, the guides provided the participant with psychological support throughout the day. The acute effect of a 25 mg psilocybin dose lasts approximately 6 hours. The morning after dosing, participants returned for an ‘integration’ session (visit 3), where they discussed their psilocybin experience with their guides for two to 3 hours. At the end of the dosing day, patients on the psilocybin arm were given a 3-week course of placebo capsules and the escitalopram arm were given capsules containing 10 mg of escitalopram. All patients were instructed to take them every morning for the duration of the trial. Patients had

the option of weekly 1-h integration or therapy calls with their main guides for the duration of the trial, as clinically indicated.

Three weeks after the first psilocybin session, patients had a second 25 mg (psilocybin arm) or 1 mg (escitalopram arm) psilocybin dosing day (visit 4) and a next day integration session for two to 3 hours (visit 5), preceded by a shorter preparation call over the phone. Patients on both sides were instructed to start taking two tablets every day, increasing the escitalopram dose to 20 mg for the escitalopram arm.

Three weeks after the second integration session, patients returned for a 3-h final visit [visit six; final follow-up (FFU)]. This was their final formal integration with their guides within the 6-weeks trial, where they could discuss their experience of the trial and their current mood state. After performing key assessments, patients and clinicians were unblinded at this key endpoint so that the clinical team and patients could consider future treatment options and support.

Therapy Protocol

Detailed information about the role of the guides and the therapy protocol can be found in the supplementary material of Carhart-Harris et al. (2021a). See (Watts and Luoma, 2020) for the original publication of the Accept-Connect-Embody (ACE) therapy model, and (Watts, 2021) for an associated manual.

In keeping with standard practice in psychedelic-assisted therapy (Grinspoon and Doblin, 2001; Grof, 2008; Johnson et al., 2008; Richards, 2016; Nayak and Johnson, 2020), the therapeutic protocol used in this trial consisted of preparation, support during psilocybin sessions, and integration therapy. Principles of Acceptance and Commitment Therapy and psychological flexibility (Hayes et al., 2012), which are being increasingly utilised in the psychedelic therapy field (Walsh and Thiessen, 2018; Luoma et al., 2019; Sloshower et al., 2020), provided a particular source of inspiration for the therapy team, where the latter construct, in particular, has been shown to be an important mediator of therapeutic outcomes in psychedelic-assisted therapy (Close et al., 2020; Davis et al., 2020; Zeifman et al., 2020). A psychedelic-specific therapy model, informed, in part, by ACT, emerged during the trial, and is referred to as The ACE model (Watts and Luoma, 2020). The ACE model emphasises building trust between participants and their guides, engaging with and accepting difficult emotions (in contrast to experiential avoidance); connecting to personal meaning, values, self and others; and giving mindful awareness to embodied or somatic experiences (Watts and Luoma, 2020). Guides were encouraged to support participants in a non-directive and open manner, showing unconditional positive regard throughout (Rogers, 1951).

A primary aim of the preparation session was building trust and rapport, setting intentions and sharing information about psychedelic experiences. Emphasis was placed on ideas of moving towards difficult experiences and painful content. Prior consideration was given to how the guides would support the participant during the sessions. The participants feelings in relation to asking for help were explored. Discussions were had around physical contact, such as the use of hand holding to provide non-verbal grounding and support during the

experience. Visualisation exercises were used as a preparation and integration tool to support processes of attuning to their bodies, moving towards difficult emotions, and connecting to self and others, details of which can be found in the original publication on the ACE model (Watts and Luoma, 2020; Watts et al., 2021).

For the psilocybin sessions themselves, participants wore eye masks and earphones through which they listened to a pre-selected playlist. This playlist was informed by research demonstrating the influence of music, i.e. “the hidden therapist”, on the subjective experience and clinical outcomes (Kaelen et al., 2018). Therapists aimed to provide a safe and containing setting with a view to allowing unconscious material, emotions, memories and difficulties to emerge. Participants were encouraged to direct their attention inwards and share their experiences towards the end of the day, if they wished. Integration sessions took place in person the following day and in subsequent weekly calls if indicated. Integration sessions involved open and attentive listening to participants’ accounts of their experiences and reflections. The role of the guide during integration is to provide compassionate support and recognition of any psychological insights or changes.

Monthly group supervision was provided by a consultant psychiatrist and psychotherapist, with extensive experience of working with non-ordinary states.

Measures

Participant Demographics and Histories—Age, gender, ethnicity, education, employment, and clinical history including illness duration, past psychotherapeutic and pharmacological treatments were collected at screening.

Primary Outcome—The 16 item self-rated Quick Inventory of Depressive Symptomatology (QIDS; Rush et al., 2003) was used to assess changes in depression severity (range of scores = 0–27). The QIDS was administered at three timepoints: 1) baseline, seven to 10 days ahead of the first psilocybin session; 2) mid-treatment, 3 weeks after the first dosing and 2 days ahead of the second psilocybin session; 3) post-treatment/primary endpoint, 3 weeks after the second psilocybin session.

Therapeutic Relationship—The participant-rated Scale To Assess the Therapeutic Relationship (STAR-P; McGuire-Snieckus et al., 2007) was used to assess the therapeutic alliance (specifically the constructs of positive collaboration, positive clinician input and non-supportive clinician input) 1-day pre-dose one and 1-day pre-dose two. A self-constructed single-item measure of rapport (“*I have a good relationship with the main person/people who will look after me during the upcoming experience*”) rated on a 0–100 Visual Analogue Scale (VAS) assessed the extent of rapport in the hours immediately before the psilocybin session, part of the Psychedelic Predictor Scale (Hajjen et al., 2018).

Acute Experience Measures—On the afternoon of each dosing day, after psychedelic effects had worn off, participants completed the Mystical Experience Questionnaire (MEQ; Barrett et al., 2015), which assesses mystical-type peak experiences using 6-point Likert scale, as well as the Emotional Breakthrough Inventory (EBI; Roseman et al., 2019), a 6-item (0–100 VAS) measure of cathartic release and resolution of difficult emotions or trauma.

Statistical Analyses

Primary Confirmatory Analysis—Longitudinal path modelling was employed to test the primary hypothesis, that therapeutic alliance would affect treatment outcomes by modulating the intensity of acute subjective effects. Based on previous research (Roseman et al., 2018; Roseman et al., 2019), mystical-type (MEQ) and emotional breakthrough experiences (EBI) were chosen as acute predictors of depression outcomes. Therapeutic alliance was measured on the day before each psilocybin session using the STAR-P. The single-item participant-rated measure of their felt rapport with their guides was taken within 3 hours prior to dosing. These values were included in the path model to account for variation in therapeutic rapport experienced by participants on the day of the session.

In order to simplify the analysis across the two separate psilocybin sessions while still taking into account all available data, the respective maximum MEQ and EBI score across the two sessions was used to predict depression outcomes. This was done based on the hypothesis that the predictive function of subjective effects on outcomes would depend on the single most intense experience across the two sessions (rather than accumulative). Due to expected multicollinearity between the EBI and MEQ ($r = 0.61$ across both sessions), separate models were fitted including maximum EBI and MEQ scores, respectively, as well as the relevant STAR-P and Rapport scores (i.e., from the same respective dosing day on which the higher EBI or MEQ score was reported). Models with the same structure (using maximum EBI and MEQ) were constructed and analysed including subjects in the escitalopram arm, which are reported in the supplementary material.

Secondary Exploratory Analyses—In order to investigate session-specific mechanisms of therapeutic alliance and the acute psychedelic experience, additional (near-) saturated sequential mediation analyses were conducted for the first and second psilocybin session, a special case of path model in which all possible paths between all variables are specified. Saturated models by definition reproduce the data perfectly but are also more susceptible to random noise in the data. The specification of all possible paths between variables makes this type of model especially useful for exploratory analyses that are not hypothesis driven. For both the first and second session, covariates included therapeutic alliance, rapport, MEQ and EBI (the latter two in separate models to mitigate multicollinearity issues). Outcomes in both sessions included depression severity at the key endpoint, corrected for baseline depression severity in case of the first, and intermediate depression severity in case of the second psilocybin session. This was done in order to investigate to what extent the subjective effects during the first and second session would independently contribute to overall changes in depression severity. As an additional outcome in the first psilocybin session, therapeutic alliance ahead of the second session was included to assess whether participant experience during the first psilocybin session would impact the therapeutic relationship and thereby indirectly affect the second psilocybin session. Additional paths between baseline (or in the case of session two, intermittent) QIDS scores and other included covariates led to

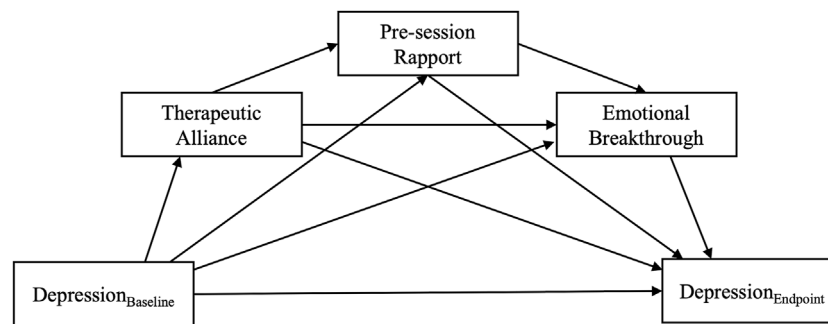


FIGURE 2 | Directed Acyclic Graph (DAG) displaying the path structure of a fully saturated sequential mediation model testing the serial mediation effect of therapeutic alliance on depression outcomes via the active psychedelic experience. The model is completely unrestricted, meaning that all possible paths between all variables are specified.

(near-) saturation of the models, taking a general shape as displayed in **Figure 2**.

For all path analyses, maximum likelihood estimation was chosen as the estimation method, since all endogenous variables were continuous. Following the recommendation by Kline (2015), multiple indicators of model fit are reported for confirmatory analyses, including model Chi-Square, Comparative Fit Index (CFI) and Root Mean Square Error of Approximation (RMSEA). Simulation studies have shown that small sample sizes lead to an overestimation of fit for Chi-square, and an underestimation of fit for CFI and RMSEA (Shi et al., 2019), the latter thus being more conservative indicators in the present study. Thresholds for acceptable and good fit were taken from the extant literature, where less stringent cut-offs were chosen for RMSEA to account for sample size biases (Hooper et al., 2008; Hair et al., 2010; Awang, 2014). Effect strengths of standardized regression coefficients were interpreted following Acock and Oregon (2018), $\beta < 0.2$ being weak, $0.2 < \beta < 0.5$ moderate, and $\beta > 0.5$ a strong effect.

While the trial, including primary and secondary outcomes published in Carhart-Harris et al. (2021a) was registered at Clinicaltrials.gov, 2021 (Identifier NCT03429075), the specific analyses presented here had not been pre-registered.

RESULTS

Demographic Information

Approximately, 1,000 individuals were screened by telephone and/or email. This number is large due to the large volume of interest in the trial, due to high public awareness of our psychedelic research programme and demand for psilocybin-therapy in particular. 891 did not meet inclusion criteria and 50 chose not to participate. A total of 103 individuals were invited to an in-person screening visit. At the point of face-to-face screening, 44 participants were excluded because of potential difficulties in building alliance and rapport. Finally, 59 participants with moderate-severe major depressive disorder were enrolled onto this trial. They were randomised to one of two groups (see Procedures section): 30 into the psilocybin arm

and 29 into the escitalopram arm. As the analyses in this paper focus solely on the psilocybin arm, demographics for this subgroup are provided in **Table 1** below and demographics for the escitalopram arm is available in the supplementary material. One participant has been excluded from this analysis because they did not comply with required restrictions on drug-taking throughout the trial which was felt to impact on the therapeutic relationship, acute experience and outcomes. Other protocol deviations include two participants who were unable to complete their second psilocybin dosing and integration visits due to Covid-19-related restrictions, and one participant who stopped taking their placebo tablets after guessing their content. These individuals have, however, been included in this paper's analyses as the nature of their deviations from the protocol does not corrupt or invalidate their data meaningfully.

Primary Confirmatory Analysis: Therapeutic Alliance Predicts Outcomes via Acute Subjective Effects

As displayed in **Figure 3**, depression severity at the key endpoint was significantly predicted by both EBI and MEQ scores, but the standardised effects were slightly larger for EBI ($\beta = -0.56$, $p = 0.03$) as compared with MEQ ($\beta = -0.45$, $p = 0.04$) scores, suggesting that emotional breakthrough was a more reliable predictor of depression improvements in this trial, than MEQ assessed "mystical-type experience". This difference was also reflected in a higher amount of explained variance in the final depression severity outcome in a model that included the EBI, vs one that replaced it with the MEQ: $R^2 = 0.42$ vs 0.32 , respectively. After subtracting the amount of variance explained by baseline depression severity alone, the EBI-based model explained $42-12\% = 30\%$ and the MEQ-based model explained $32-12\% = 20\%$ of variance in depression severity at the key endpoint. In both cases, the cumulative indirect effect of STAR-P on depression outcome was significant ($\beta = -0.22$, $p = 0.02$ for EBI-based model; $\beta = -0.19$, $p = 0.03$ for the MEQ-based model), although this effect would have been reduced to trend level ($p = 0.06$) in case of the MEQ after applying Bonferroni correction for the two

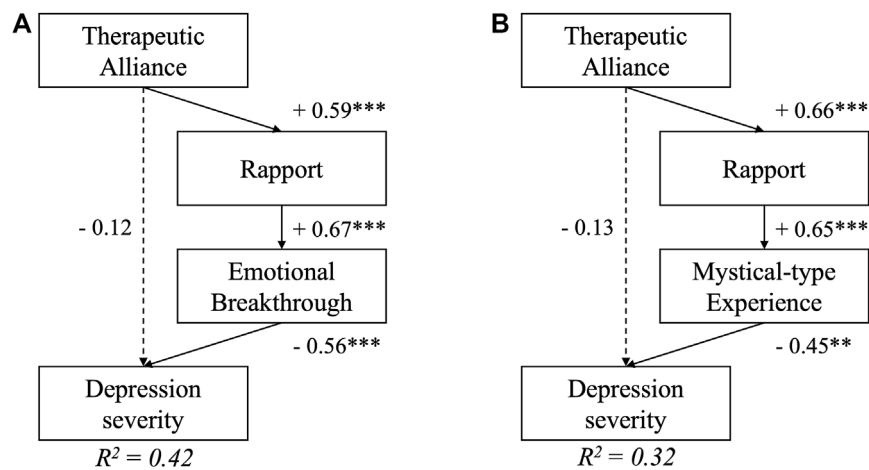


FIGURE 3 | Path models testing the primary hypothesis that therapeutic alliance would lead to better depression scores 6 weeks following psychedelic-assisted psychotherapy. Serial mediation of therapeutic alliance via pre-session rapport and A) Emotional Breakthrough and B) Mystical-type experiences were supported by the models. Depression severity at the 6-weeks Endpoint was adjusted for baseline depression scores ($p > 0.1$, not displayed in the figure), which by itself accounts for $R^2 = 0.12$, i.e., 12% of variance in the final outcome. Numbers represent standardised regression coefficients for significant (solid) and non-significant (dashed) paths. **indicates $p < 0.01$, *** $p < 0.001$.

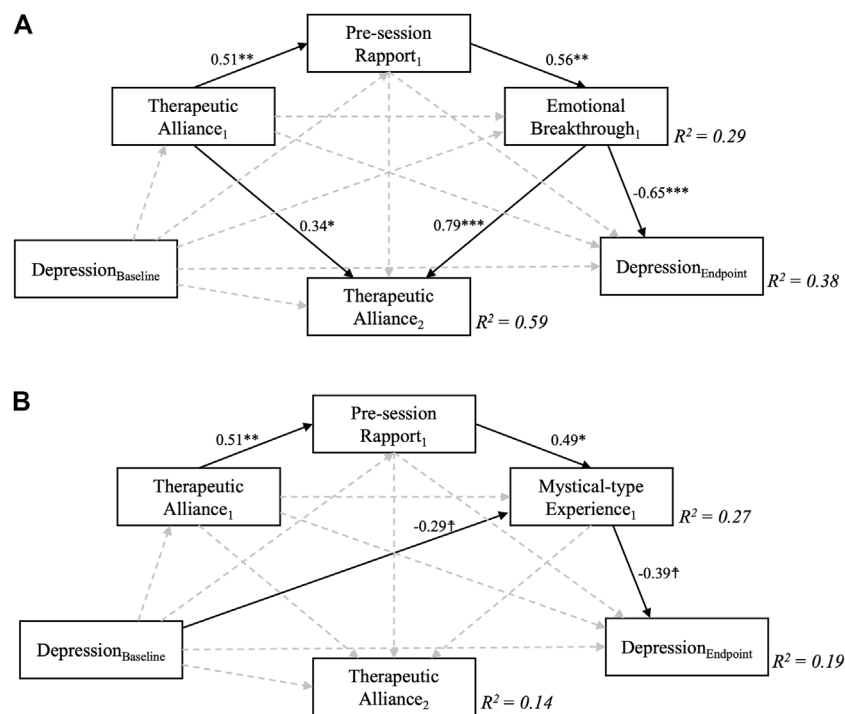
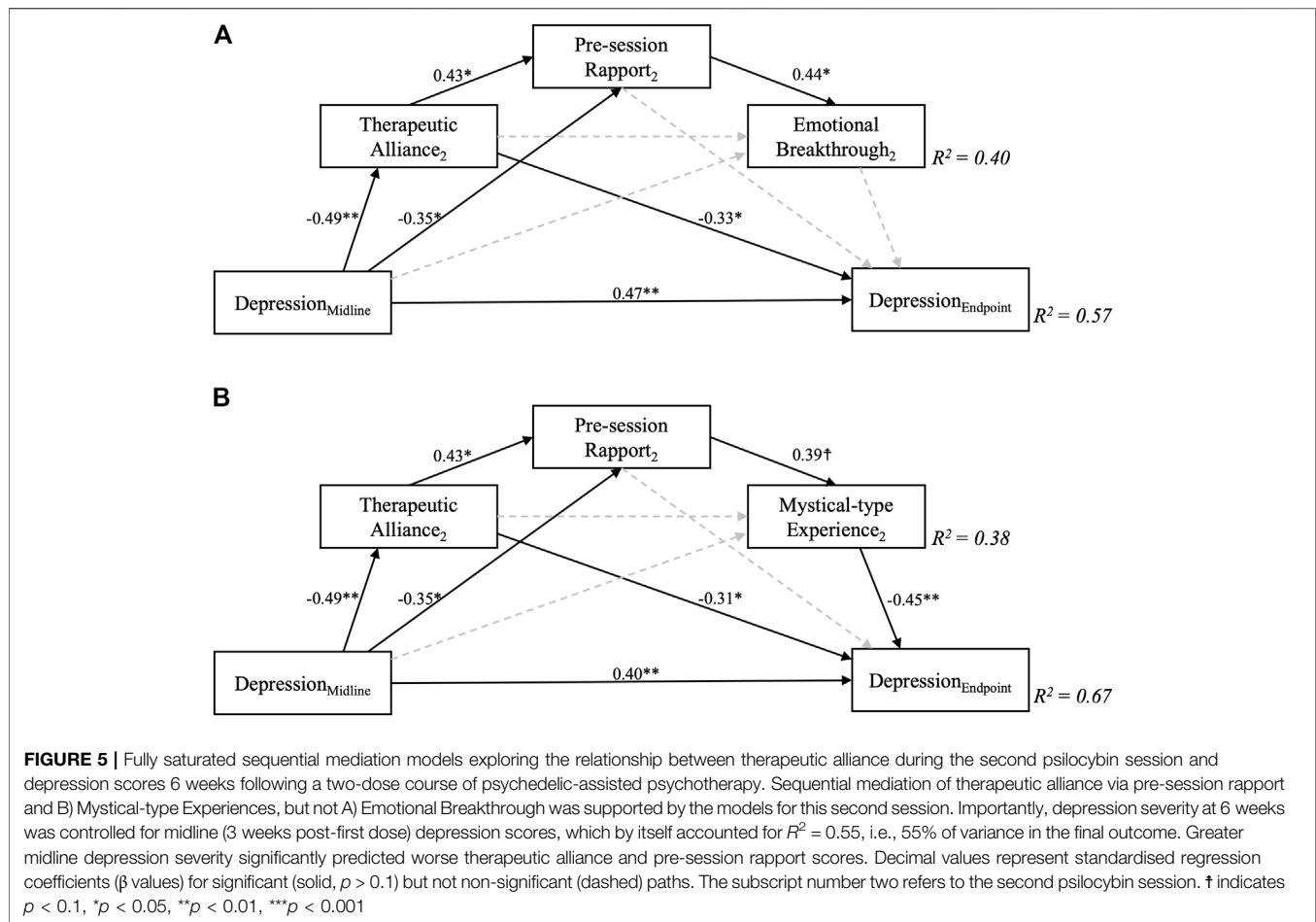


FIGURE 4 | Near-saturated sequential mediation models exploring the relationship between therapeutic alliance during the first psilocybin session and depression scores 6 weeks following a two-dose course of psychedelic-assisted psychotherapy. Sequential mediation of therapeutic alliance via pre-session rapport and A) Emotional Breakthrough and B) Mystical-type Experiences were supported by the models in the case of depression severity, but not for intermediate therapeutic alliance measured ahead of the second psilocybin session, which was only significantly predicted by Emotional Breakthrough scores. Depression severity at 6 weeks was controlled for baseline depression scores, which by itself accounted for $R^2 = 0.12$, i.e., 12% of variance in the final outcome. MEQ, but not EBI scores were furthermore affected by baseline depression severity, although only at trend level. Numbers represent standardised regression coefficients for significant (solid, $p > 0.1$) but not non-significant (dashed) paths. Subscript numbers refer to the different psilocybin sessions, one and two; e.g., Therapeutic Alliance₁ refers to STAR-P scores ahead of psilocybin session one and Therapeutic Alliance₂ refers to STAR-P scores ahead of psilocybin session 2. † indicates $p < 0.1$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.



comparisons. Both models had acceptable to good fit on all estimated fit indices (see Table 3 for fit estimates of all included path models).

Secondary Exploratory Analyses: Psilocybin Session-specific Effects

Results for the near-saturated mediation models for the first psilocybin session are displayed in **Figure 4**. The EBI ($\beta = -0.65$, $p < 0.001$) significantly mediated the effect of therapeutic alliance on depression severity but the same was not quite true for the MEQ ($\beta = -0.39$, $p = 0.06$). Therapeutic alliance ahead of the second psilocybin session was significantly affected only by EBI ($\beta = 0.79$, $p < 0.001$), but not MEQ scores ($\beta = -0.02$, $p = 0.94$). Thus, while 59% of variance in STAR-P scores was explained in the EBI model, the MEQ-based model only explained 14% of variance in STAR-P scores, which approximately corresponds to the amount of variance accounted for by baseline STAR-P scores. A trend-level relationship was found between baseline QIDS scores and MEQ scores, meaning that higher baseline depression severity was associated with lower mystical-type experience scores for the first psilocybin session ($\beta = -0.29$, $p = 0.09$).

Results for the saturated mediation models for the second session are displayed in **Figure 5**. When controlling for intermediate QIDS scores, only MEQ ($\beta = -0.45$, $p = 0.002$) but not EBI ($\beta = -0.18$, $p = 0.27$) scores significantly affected final depression outcomes. Instead, significant direct effects between therapeutic alliance and depression outcomes emerged for each model ($\beta = -0.33$, $p = 0.049$; $\beta = -0.31$, $p = 0.033$, for MEQ and EBI-based models, respectively). A large overall amount of variance in final depression outcomes was explained in each of the fully-saturated mediation model ($R^2 = 0.67$, and 0.57), but it is important to note that the correlation between depression severity at the intermediate and the final endpoints was very high at $r = 0.74$, thus already accounting for $0.74^2 = 55\%$ of variance. The implication is that most of the mediation occurs in relation to the first dosing session, after which depression severity prior to session two is a strong predictor of depression severity at the 6-weeks endpoint. The additional amount of variance in final depression severity outcomes explained by inclusion of other covariates than midline depression was thus only approximately $67 - 55 = 12\%$ for the MEQ-based model, while the inclusion of EBI scores and other covariates during the second session only explained $65 - 55 = 10\%$ of additional variance. Of interest, significant negative effects between midline QIDS and therapeutic alliance ($\beta = -0.49$, $p = 0.004$), as well as pre-session rapport ($\beta = -0.49$, $p = 0.036$) were

revealed - both in the EBI- and MEQ specific models, meaning that higher depression severity at the intermediate (3 weeks post-session 1) timepoint were associated with worse therapeutic alliance and rapport ahead of the second session. Again, this finding could be viewed as highlighting the importance of processes leading up to and including dosing session one as being the major determinants of eventual outcomes at the study endpoint.

Supplementary Result

See supplementary material for the path models for the escitalopram arm (**Supplementary Figure S1**), the histograms comparing the acute scores between the psilocybin and escitalopram arm, i.e., EBI and MEQ for dosing one and two (**Supplementary Figure S1**), the demographics of this arm (**Supplementary Table S1**), Pearson correlations between all measures that included in the path models (**Supplementary Table S2**) and a correlation matrix of all included variables on the psilocybin arm (**Supplementary Table S3**).

DISCUSSION

The importance of the therapeutic relationship in psychedelic-assisted therapy has long been treated as a matter of conventional wisdom, both traditionally and in contemporary research (Grof, 2008; Johnson et al., 2008; Richards, 2016; Carhart-Harris and Nutt, 2017; Breeksema et al., 2020; Nayak and Johnson, 2020; Watts & Luoma, 2020) but has never been empirically tested. Here, via a sequential path model, we have demonstrated how a strong therapeutic alliance predicts pre-session rapport, which predicts greater emotional breakthrough and “mystical type” experience towards improved clinical outcomes in a trial of psilocybin-assisted therapy for depression. This work shows how the acute experience, previously established as critical to outcomes (Watts et al., 2017; Roseman et al., 2018; Johnson et al., 2019), is influenced by pre-session therapeutic alliance and rapport, supporting the idea that participants need to feel safely contained within the therapeutic relationship in order to surrender to the psychedelic experience and the vulnerabilities it may open up.

As the field of psychedelic-assisted therapy develops, it is essential to test even the most confidently held assumptions, such as the importance of the therapeutic relationship, to optimise clinical outcomes and challenge economic or commercial imperatives that might lead to risky cutbacks in therapeutic support, as well as its supervision and training (Noorani 2020; Marseille et al., 2020; Carhart-Harris et al., 2021b). It is also important to consider how the nature and quantity of therapy might need to adapt to more complex clinical populations. Such individuals e.g., with greater personality and attachment difficulties, may struggle to build trust or to feel safe in relationships. No research to date has looked at using psychedelics in patients with emotionally unstable or borderline personality disorder (Zeifman and Wagner, 2020). As in many psychedelic clinical trials, a diagnosis of a personality disorder, complex trauma or an inability to build early alliance or rapport were exclusion criteria in this trial (Carhart-Harris et al.,

2021a). Whether such complexity is a contraindication for psychedelic-therapy is an important question. If it is not, then how might therapeutic models adapt to accommodate and support these participants? These matters are important, particularly given the complexity of treatment-resistant populations, the treatment of which both MDMA and psilocybin trials have been exploring, where e.g., there are high rates of comorbid personality disorders and complex relational trauma (Thase, 1996; Carhart-Harris et al., 2021b).

The finding of our stage-by-stage analysis may bear relevance to a stage and relationship sensitive adaptive treatment approach going forwards. For example, in the first psilocybin session, emotional breakthrough appears to be the most potent predictor of subsequent improvements in depressive symptoms and this relationship is mediated by pre-session therapeutic alliance and rapport (see **Figure 4A**). The implications of this model are relatively straightforward therefore, merely highlighting the importance of the therapeutic alliance, in line with prior assumptions, but also placing a significant emphasis on the clinical importance of emotional release or catharsis in the first session.

A second major implication of the model results is that the picture changes somewhat ahead of the second psilocybin session, with emphasis placed less on emotional breakthrough and more on the mystical-type experience as a means to further therapeutic progress. Also, of note, the therapeutic alliance ahead of the second session has a direct impact on final depression scores, now in a manner that is *not* mediated by the acute experience. Perhaps the most interesting nuance in this regard is that if depression scores are high at this treatment midpoint, therapeutic alliance and rapport is weak—and this is critical, as weaker alliance at this key treatment mid-stage translates into poor depressive outcomes at the end of the trial, as well as lower levels of mystical-type experience and emotional breakthrough (**Figure 5B**). These findings have significant clinical implications, further discussed below.

The Therapeutic Relationship

On a broader level, our results consolidate, but now in the context of psychedelic-assisted therapy, the view that having a strong therapeutic relationship shapes the quality of the therapeutic process en route to better clinical outcomes. An important caveat prefacing this discussion is the particular context of the present trial’s double-blind and randomised design, and the “promissory culture” surrounding psychedelic-assisted therapy at present. This can impact on scientific research in an unhelpful way, e.g., causing exaggerated expectations and an idealisation of researchers and guides. Inflated expectations can increase the risk of disappointment, as well as feelings of neglect or rejection if expectations are not met.

In the present study, the therapeutic alliance was either stronger (e.g., McGuire-Snieckus et al., 2007) or similar (e.g., Knittle et al., 2019) to that observed in previous clinical samples. More research is required to examine what factors determine the strength of therapeutic alliance and rapport. Some candidates include therapist experience, training and interpersonal disposition; the length and quality of the pre-dosing

preparation work (e.g., early alliance and rapport building); and specific patient factors (Horvath, 2000; Grof, 2008). The latter might be assessed by looking at patterns of relating, such as attachment style or the influence of internalised early relational experiences on lifelong patterns of relating (i.e. quality of object relations; Goldman and Anderson, 2007; Horvath, 2000). A link between early relational experiences and depression is well established, with attachment difficulties suggested to partially mediate the relationship between early interpersonal trauma and depression (Fowler et al., 2013). Recent research examining the relationship between insecure attachment styles and responses to individual psilocybin therapy sessions with group preparation and integrative group therapy sessions (Stauffer et al., 2021), found that high attachment avoidance was associated with more intensely challenging psychedelic experiences, whereas high attachment anxiety was associated with higher levels of mystical experience in the psilocybin sessions. Furthermore, attachment anxiety was significantly reduced by the trial endpoint.

In the present study, it is worth noting that nearly half of the variance of both maximum EBI and MEQ was explained by baseline depression, therapeutic alliance and rapport (**Figure 2**). Looking at the exploratory analysis, the results suggest that a strong therapeutic alliance and rapport prior to the first psilocybin session resulted in more emotional breakthrough, as well as better alliance and rapport before the second session, and better eventual clinical outcomes. This finding suggests the clinical importance of having a strong pre-session therapeutic alliance and rapport in place to support a participant in accessing and working through previously unprocessed memories, emotions or traumas during this first psilocybin session.

Focusing next on the second session, therapeutic alliance after the first session had a direct impact on final outcome in our second dosing model. That is, as shown in the top-left to bottom right diagonal in **Figure 5**, post session one (pre session two) therapeutic alliance predicted final depressive symptom severity independent of the nature of the acute experience within the second psilocybin session. This may speak to an enhanced importance of the therapeutic relationship as the main vehicle of change after a first psychedelic-assisted therapy session, perhaps due to a sub-acute intensification of transference (Walsh and Grob 2005; Grof, 2008; Fisher, 2015). Some consideration could be given here to prolonging the gap between psilocybin sessions, so as to develop the therapeutic relationship, giving it priority ahead of another psilocybin therapy session.

Having a strong therapeutic alliance appears to support participants towards more powerful emotional breakthroughs and mystical experiences, but the experience of coming into contact with old traumas and working through difficult emotional material in the context of a containing and supportive therapeutic relationship may be a key component of the healing *process*. Our data revealed that emotional breakthrough after session one was a significant predictor of therapeutic alliance prior to session two, but the same was not true for mystical-type experiences linked to session one. One speculative explanation for this could be that emotional

breakthroughs are more inter-personal or relational in content and nature; whereas mystical-type experiences are more transpersonal, solitary experiences which transcend the personal or relational.

Gaining insight into relational patterns and narrative building at an explicit verbal level is considered a fundamental aspect of many psychological therapies, but alongside this, the experience of the relationship with the therapist(s) or guides(s) themselves can result in changes in relational knowing that occur at an unconscious or procedural level (Lachmann and Beebe, 1996; Lemma, 2015). The latter process may be particularly relevant to psychedelic-assisted therapy, with early psychedelic-assisted therapy and more recent therapy models emphasising more embodied, non-verbal experiential processes (Grof, 2008; Watts and Luoma, 2020). Psychedelics can induce heightened affective and age-regressed states (Grinspoon and Doblin, 2001; Grof, 2008; Watts et al., 2017; Carhart-Harris and Friston, 2019) in which care can be experienced in an intensified way, potentially recapitulating the early care and attachment processes of infancy (Lachmann and Beebe, 1996; Grof, 2008; Watts and Luoma, 2020). The neuroplastic brain state associated with psychedelics (Carhart-Harris and Friston, 2019; Murphy-Beiner and Soar, 2020; Olson, 2021) may serve to catalyse deep processes of change, including changes in implicit relational being and knowing, which may, in turn, support further therapeutic progress.

In a study where as many as 40% of participants in either trial arm failed to achieve remission and 30% failed to respond to psilocybin-assisted therapy, it is important to acknowledge that one implication of our results is that participants who reported *weaker* therapeutic alliance and rapport experienced *less* therapeutic breakthrough during sessions which appear necessary for improvement in core symptomatology by the trial end-point. One possible interpretation of this study's results is that early warning signs of poor response, such as poor initial therapeutic alliance, perhaps combined with a lack of emotional breakthrough in a participant's first psilocybin session, might signal a postponement of any subsequent psilocybin sessions. At such a juncture, the therapeutic focus might move towards working on aspects of the therapeutic relationship or trying to understand other unconscious factors that may be maintaining the illness - with a view to improving alliance and/or enhancing the likelihood of an emotional breakthrough. Arguably, the earlier clinicians can intervene in an adaptive, evidence-based way, the better. More concretely, this could imply assessing baseline predictors of poor therapeutic alliance.

Here we have shown that poor therapeutic alliance led to less emotional breakthrough and mystical experience during the psilocybin sessions. One might consider how specific patient factors might underlie both the quality of the therapeutic relationship and the psychedelic experience itself. What might look like a participant resisting the experience or not responding to psychedelics might just be a different kind of psychedelic experience. Further research is needed to better understand the quality of the psychedelic experience in cases of a weaker therapeutic alliance, e.g., is it associated with more challenging

experiences (Stauffer et al., 2021), amplified psychological defences or intensified transference (Grof, 2008)? Moreover, how might these experiences be best supported and worked with therapeutically? Participants who experience more challenging therapeutic processes may need a different therapeutic approach, which could entail e.g., a longer preparation period to build trust and safety, greater number of psilocybin-therapy sessions and/or more integration therapy (Carhart-Harris et al., 2021b). There is a precedent of endeavouring to work with more challenging experiences e.g. amplified negative transference (relational difficulties); states of intensified shame, hopelessness, despair; in psychedelic-therapy dosing sessions (Grof, 2008), as there is a long tradition of in traditional psychological therapies (Piper et al., 2004; Yakeley, 2014; Lemma, 2015). However, this may be more challenging in the context of tightly controlled and constrained short-term clinical trials; compared to real-world clinical care contexts, permissive of greater flexibility, adaptability and longer-term care (Grof, 2008). Future studies may consider alternative clinical trial designs and therapeutic approaches that are more responsive and adaptive, potentially allowing for longer gaps between dosing sessions and more flexibility on dosage amount, regularity (Carhart-Harris et al., 2021b) and perhaps even drug—where e.g., MDMA-therapy could be explored as a switch option if clinically indicated (Mitchell et al., 2021).

The Acute Experience

Our results demonstrate that depression severity scores following psychedelic-assisted therapy were significantly reduced in relation to the intensity of both emotional breakthrough and mystical type experiences. Greater standardised effects were seen for maximum EBI, reflected in a higher amount of variance in depression severity explained by mediation models including the EBI (see **Figure 2**). The predictive value of the acute experience on clinical outcomes demonstrated here is in line with previous research (for a review, see Romeo et al., 2021). This finding enriches recent debates about the necessity of the subjective psychedelic experience for enduring therapeutic effects (Olson, 2021; Yaden and Griffiths, 2021) and the increasing interest in developing non-hallucinogenic analogues of psychedelic compounds (Cameron et al., 2021).

Emotional breakthrough is arguably a more intuitive and familiar construct as a therapeutic mechanism, which may be more easily integrated into mainstream neuroscience and mental health care. Whilst recent advocacy for the secularisation of psychedelic treatment spaces (Johnson, 2021) is a welcome call to prevent potential patients turning away from what might be an effective treatment, it fails to address the complex role of therapists' ontological assumptions in shaping their patients' experiences. The field must grapple with the tension of holding onto the uniqueness of these ineffable experiences including its roots in indigenous practices and underground work; whilst trying to move into the medical and therapeutic mainstream (Williams and Labte, 2019; George et al., 2020; Noorani, 2020; Gerber et al., 2021).

The so-called “Grofian model”, devised by psychiatrist, Stanislav Grof, suggests a stage-wise process via which people first “work through” personal, biographical material prior to moving to the so-called transpersonal realm (Grof, 2008). This model might help explain the stage-wise influence of emotional breakthrough (dose 1) and mystical experiences (dose 2) in the present study's path models. It is notable that higher baseline depression was associated with less mystical experience but had no impact on emotional breakthrough in the first session. One speculative explanation, for this is that more severely depressed patients often have a more complicated history of adversity that naturally lends itself to a stage-wise process of first working through personal material before progressing to a transpersonal stage. It is worth noting that anecdotal evidence also exists for the idea of an initial mystical experience allowing an opening to more biographical work, and of course psychedelic experiences can contain a multitude of different experiences (Grof, 2008), but these ideas could be tested in the future.

Specificity

The supplementary path models for the escitalopram arm differed from those of the psilocybin arm in most respects, serving to support the specificity (to psychedelic assisted-therapy) of the main models presented above. A stronger relationship between depression severity at baseline and endpoint was observed for the escitalopram arm, compared to the psilocybin arm. This indicates that treatment responses after psilocybin treatment are less dependent on the severity of baseline symptoms and that a larger extent of variability in final outcomes is explained by treatment-specific variables such as acute subjective effects and the therapeutic relationship compared to treatment with SSRI's. Baseline depression also accounted for a greater amount of the explained variance in the escitalopram arm. The therapeutic relationship (therapeutic alliance or rapport) did not predict either the acute experience or final outcomes in the escitalopram arm, indicating that the therapeutic relationship was of greater clinical importance in the psilocybin arm. There was non-significant effect from the acute experience (EBI and MEQ) on final outcomes in the escitalopram arm.

Strengths and Limitations

This is the first study to provide quantitative evidence supporting the importance of the role of the therapeutic relationship in shaping both the nature of the acute psychedelic experience and subsequent treatment outcomes in a clinical trial of psychedelic-assisted therapy. It is also the first study to validate the importance of emotional breakthrough in mediating therapeutic outcomes in a clinical population or trial.

As pointed out previously (Baier et al., 2020; Kangaslampi, 2020), the nascent field of mechanistic studies in psychedelic research suffers from several methodological limitations, including the lack of appropriate testing of putative causal relationships. By implementing sequential mediation analyses on variables that were measured across successive time points, the current study was able to inform on causal relations in the treatment process. Importantly however, the path analyses applied here, usually require large sample sizes to be

considered reliable (Kline, 2015); although rules-of-thumb for sample size estimations in structural equation modelling have been found to be insufficient (Wolf et al., 2013). An important limitation of the current study therefore arises from the small sample size available for the present analyses. Even though models consistently converged and showed acceptable fit, which is normally underestimated in small samples (Ullman, 2001), it is possible that the established parameter estimates are biased by participant characteristics specific to the trial. Future studies should therefore focus on replicating the causal pathways found here in larger samples from psychedelic trials.

One should also note that the present sample was a specific population of individuals with current major depressive disorder. Therefore, we caution against extrapolating to other populations. All participants in this trial were under primary care (i.e. their GP) and were able to demonstrate an ability to build rapport, deemed necessary because of the constraints of the trial design. It is important to consider that many patients with chronic depression have significant comorbidities and complexity (Westen et al., 2004). The demographic in our trial was one typical of clinical research - predominantly white, male and university educated - which does not represent the diversity of patients suffering from depression in the United Kingdom or those most vulnerable to depression (Public Health England, 2019). Lack of diversity and minority exclusion in psychedelic research is a recurrent issue which needs to be addressed (George et al., 2020; Williams and Labate, 2019). Unfortunately, no demographics are available for those who applied to participate (information which should be collected going forward) but the experience of the team was that there was a notable lack of diversity in those applying to participate. Future research should consider diversifying clinical teams, specific culturally-sensitive and targeted recruitment strategies, and appropriate training (Williams et al., 2020). Ongoing and planned studies from the research group have been utilising Patient and Public Involvement (PPI) to address these issues (Close et al., 2021). Furthermore, stigma in relation to sexuality, gender or race has been shown to negatively impact the therapeutic alliance, especially when therapists are not appropriately trained or multiculturally competent (Anderson et al., 2019; Williams et al., 2021), an area future research should explore.

A finding worth reflecting on is the low correlation between therapeutic alliance prior to the first psilocybin session and the acute experience of that session (see **Supplementary Table S3**). This may be a spurious finding as measures of rapport prior to the first psilocybin session correlated highly with measures of alliance and the acute experience; nevertheless, it is worth considering some possible implications of this. The STAR-P, used here to measure therapeutic alliance, speaks to ideas of the working relationship between patient and therapist (McGuire-Snieckus et al., 2007). Hence it may be that data on this aspect of the therapeutic relationship was less accurate initially, since participants had only three clinical contacts with their therapist at this point, only two of which were in-person. Perhaps the most constructive interpretation here with regards to future research is that pre-session rapport (measured shortly

before dosing) may be a more informative predictor of the nature of session one (and thus, longer-term outcomes) than an earlier measure of therapeutic alliance. The downside of this, however, is that pre-emptive action is arguably easier to take at an earlier stage in a process than in the minutes prior to dosing itself. Beyond psychedelic therapies, measures of mean therapeutic alliance across psychotherapeutic sessions has been shown to be a stronger predictor of outcome than early alliance alone (Krupnick et al., 2006).

The primary endpoint of this trial was at 6 weeks, so the present results are only relevant to this relatively brief window of time. It is possible that findings may change, if we were to include longer-term follow-up assessment results in our models or more regular sampling of therapeutic alliance and rapport. Indeed, critics of the proposed 2017 (now delayed to 2022) National Institute of Health and Care Excellence (NICE, 2009) guidelines for depression pointed to the inadequacy of short-term outcome data for informing on long term and persistent conditions such as depression (McPherson et al., 2018).

Another important limitation of the present work was that we did not assess countertransference or clinician rated therapeutic alliance, i.e., the feelings of the guides towards their participants. This might not be considered a major limitation as most evidence suggests that the patient's perception of the alliance is as good as, if not a more accurate predictor of outcomes (Baier et al., 2020). However, future research might consider including relevant assessments in order to compile a more complete, bidirectional picture of the therapeutic relationship. Assessments of individuals therapists' ontological assumptions might also yield interesting findings, such as how they may unconsciously influence outcomes. Furthermore, the therapy manual has not been peer reviewed.

Clinical Implications and Future Directions

These findings highlight the importance of the therapeutic relationship in the psychedelic-assisted therapy treatment process. Development of the required skills for psychedelic-assisted therapy requires appropriate training and experience. Aspects of the therapeutic relationship are likely to be intensified in this work; meaning that in our opinion understanding of ideas such as transference and countertransference dynamics, enactments, boundaries and working with endings is vital; especially when working with clinical populations. Most psychotherapy training programmes require that training psychotherapists undergo their own personal work, often receiving psychotherapy themselves as part of the training process. Future research might consider assessing the impact of the guide's professional and personal experiences of both standard therapy and of non-ordinary states on clinical outcomes. Our results indicate that factors such as the expertise of the clinical team, and the flexibility and design of the clinical protocol should be carefully considered when deciding to work with participants who may find it more challenging to build a strong therapeutic alliance and rapport. The guides involved in the present trial all received supervision from an experienced psychotherapist, who had extensive experience with therapy in the context of non-ordinary states of consciousness. It is our opinion, that as in traditional psychotherapy, supervision with an experienced clinician is invaluable in order to

support high quality therapeutic practice. These and related principles are broadly reflected in published training programmes for psychedelic-assisted therapy (Mithoefer et al., 2017; Phelps, 2017; Tai et al., 2021).

In the United Kingdom traditional psychotherapies are delivered both privately and in the NHS, and so psychedelic-assisted therapy could function as an occasional catalyst to such practices, e.g., to resolve therapeutic impasses, and empirical evidence - such as our results here - may help clinicians and services decide on patient selection and when in a treatment process they might consider a psychedelic experience. Our results could suggest that, within the context of this particular trial design and therapeutic framework, one might consider delaying a dosing session until a sufficiently strong therapeutic alliance is in place. This may apply either before the first or any subsequent dosing sessions. The present findings also suggest that if someone has not responded to the first session (here indicated by low EBI and MEQ scores and high QIDS) that a second session may not confer any additional benefit. One could also infer from the minimal variance explained by the second dosing session, and the direct effects of therapeutic alliance on final outcome, that longer time frames with more therapy between dosing sessions could be considered. Questions of how much preparation, how many dosing sessions, how far apart, and with how much integration, are important—and have significant economic implications for developing plans for psychedelic medicine (Carhart-Harris et al., 2021b). Further research comparing different designs is needed to explore these matters.

It has been suggested that the field of psychotherapy in general should move its focus away from outcome to “process-outcome” research, focussing on specific processes and mechanisms of change (Cohen and DeRubeis, 2018; Yakeley, 2014). Currently, much of the focus of psychedelic-therapy research is understandably on evidencing efficacy and safety in well-controlled and standardised trials, but questions of *who* can benefit most, and *how*, are important for the field, especially when working with clinical populations. Qualitative data and case reports may do well to focus on non-responders in order to better understand how to improve treatment for these individuals going forwards. Observer ratings of the therapeutic relationship e.g., on filmed exchanges for training purposes, may be worth exploring, and case studies and qualitative analyses could also be used to good effect. Future research should include consideration of specific patient factors such as attachment style, defensive organisation, and the quality of object relations, as these factors may underlie a person’s ability to form a strong therapeutic alliance; to feel safely contained in order to surrender to a psychedelic experience and the vulnerabilities it may open up; and to safely work through feelings evoked by the ending of the therapeutic relationship post-trial.

Relatedly it is worth considering the limitations of standardised measures and fixed time frames, i.e. a rapid change in QIDS scores, in capturing the complexity of psychological change and the therapeutic process. It is well established that addressing and working through emotionally challenging biographical material may result in a worsening of symptoms in the short-term but may ultimately enable a deeper

understanding and connection to oneself and others in the long term (Lemma, 2015; Olson, 2021). As discussed, clinicians need to be mindful of the idealisation of this new treatment and those that offer it, and the impact this might have on the therapeutic process, tempering unrealistic expectations, and working with the disappointment that may follow as the reality of a more long-term process of healing is recognised if difficulties remain or re-emerge. In our trial, we suspected that many of the participants in this trial would have benefitted from further integration or therapeutic work. Indeed, many went on to work with private psychedelic integration therapists or psychedelic integration groups after the core trial period. This would again indicate a need for more flexible treatment protocols with longer-term follow-up and support.

CONCLUSION

In this paper, we have found evidence of an effect of therapeutic alliance and rapport on the quality of the psychedelic experience, which in turn was associated with changes in depressive symptom severity 6 weeks later. More specifically, improvements in depressive symptom severity were more strongly affected by emotional breakthrough experiences during the first, and mystical-type experiences during the second session, respectively. The strength of the therapeutic relationship after the first, but before the second psilocybin session, predicted final depression scores directly, with better alliance predicting lower eventual depression scores. Higher levels of emotional breakthrough during the first psychedelic session was a predictor of therapeutic alliance at this critical intermediate stage, implying the existence of early prognostic predictors that could inform treatment adaptation at any early stage of the therapeutic process. Importantly on the converse, a weaker alliance led to less emotional breakthrough or mystical experiences, and lower depression scores. Further qualitative and quantitative research will be needed to inform on an evidence-based personalized and adaptive, psychedelic-therapy.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available due to human subjects being involved. Requests to access the datasets should be directed to roberta.ni.mhurchu@gmail.com.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by This study received approval from the Brent Research Ethics Committee (REC), the Medicines and Healthcare products Regulatory Agency (MHRA), the Health Research Authority (HRA), and the Imperial Joint Research Compliance (study sponsors) and General Data Protection Regulation offices. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

RM directed the project. RM, HK, RZ, BG, and LK worked collectively throughout including planning the manuscript, conceiving of the theoretical model, planning the analyses and interpreting the results. HK designed and carried out the statistical analyses and led on all aspects of this including interpretation of results. RM wrote the manuscript along with RZ (introduction), BG (trial oversights, participants, designs and procedures, and references), HK (measures, statistical analyses and results) and LK. JM, RZ, and HK also contributed to the discussion. RCH supervised the writing of the paper including planning of the statistical models, feedback and editing of the manuscript. BG, JM, MB-J, AM-B, RW, and RM worked as the clinical team for the research trial. RW was the clinical lead for the team and designed the therapeutic model. TR provided group therapy supervision during the trial. Many of the ideas in this paper come from this clinical work, discussions within the team and in supervision. DE, DN, and RC-H were all investigators for the trial and planned, designed and oversaw it. All authors provided feedback on the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fphar.2021.788155/full#supplementary-material>

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Virtual Daime: When Psychedelic Ritual Migrates Online

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During the 2020 COVID-19 epidemic a variety of social activities migrated online, including religious ceremonies and rituals. One such instance is the case of Santo Daime, a Brazilian rainforest religion that utilizes the hallucinogenic brew ayahuasca in its rituals. During the pandemic, multiple Santo Daime rituals involving the consumption of ayahuasca took place online, mediated through Zoom and other online platforms. The phenomenon is notable since the effects of hallucinogens are defined by context (set and setting) and Santo Daime rituals are habitually governed by punctilious regulations aimed at directing the experience of participants. The abrupt move to online space thus augurs significant implications in the context of hallucinogenic rituals. This paper looks at this development and its repercussions for entheogenic rituals, as it asks how do psychedelic rituals change when they move online? Building on the author's previous work on set and setting in the Santo Daime religion, the paper introduces accounts from 12 semi-structured interviews with daimistas participating in online daime rituals, approached through the prism of set and setting, and the study of online religiosity. The analysis points at several key dynamics emerging in the context of virtual rituals. The migration online allowed for the continuation of Santo Daime entheogenic rituals at a time of social distancing, fostered a sense of global brotherhood and opened new possibility for religious participation and learning. Concurrently, online ritual produced an impoverished ritual experience and novel types of challenges including a higher potential for distractions, technical difficulties, and low sensory fidelity. Other novel challenges included social anxiety and an in-built tension between the social and spiritual dimensions of ritual. Finally, some participants were concerned by the cultural context of online rituals: technological mediation, consumerism, commodification, and digital divide. The limitations of digital technology appear amplified by the highly immersive, body oriented, experientially intensified context of the psychedelic experience. This paper contributes to the literature on the extra-pharmacological factors shaping experiences with psychedelics, as well as to the literature on the consequences of the adoption of digital media technologies during the COVID-19 pandemic.

Keywords: Santo Daime, psychedelics, entheogens, set and setting, online psychedelic ritual, online religion, online ritual, ayahuasca

INTRODUCTION

The global eruption of the COVID-19 coronavirus pandemic in early 2020 has brought about a rapid wave of digitalization. With growing restrictions on assembly, diverse types of activities including shopping, learning, working, meeting and entertainment were moved online, a phenomenon that led to distinct challenges and adaptations (Dhawan, 2020; Okabe-Miyamoto et al., 2021; Vargo et al., 2021; Yan et al., 2021). A particularly interesting case in point is the story of the online rituals of the Santo Daime ayahuasca religion.

Santo Daime (henceforth referred to as SD) is a Brazilian rainforest religion that utilizes the hallucinogenic brew ayahuasca in its elaborate multiple-hour rituals that regularly evoke personal insight, communal intimacy and spiritual transformation (MacRae, 1992; Couto, 2004; Cemin, 2010; Blainey, 2021; Hartogsohn, 2021). As the COVID-19 pandemic spread across Brazil and the world in early 2020, SD churches were forced to cease their communal, on-site ritual service, with some of these churches convening on virtual platforms like Zoom. By May 2020 online SD rituals were rapidly institutionalizing. SD church leader, Alfredo Gregório de Melo (henceforth referred to by his common title *Padrinho Alfredo*), was leading virtual SD rituals of unprecedented scale, involving thousands of participants worldwide. These rituals, which were held under the banner of *Live Works*, raise a series of intriguing questions: What happens when entheogenic rituals migrate online? How are communal psychoactive rituals adapted to suit the pandemic reality of solitary, remote, computer-mediated participation? Which types of possibilities do online rituals open, and what types of challenges to they pose?

This paper can be read as a sequel paper to a previous one by the author that looked at the role of set and setting (context) in the shaping of Santo Daime entheogenic experience (Hartogsohn, 2021).¹ The prior paper sought to provide a high-resolution description of the ways in which elements of ritual context (e.g., preparation, intention, visual, musical, social, and symbolic elements) shape the experiences of participants in SD Ceremonies. This sequel paper explores the transformation of the features of SD entheogenic ritual work as it migrates online, and how these transformations remold ritual dynamics and participant experiences.

As the mediatization of everyday life continues, a growing number of human activities migrate online (Hjarvard, 2013a,b; Couldry and Hepp, 2018; Hepp, 2019). The history of this process presents us with a Janus face. Digitalization and mediatization open new and liberating potentials (Turkle, 1997; Jenkins, 2006; Rushkoff, 2011) while also giving rise to experiences of loss, confusion, and despair (for prominent accounts see Carr, 2010, 2015; Turkle, 2011; Twenge, 2017a; Zuboff, 2019). As religious service, including entheogenic religious service, migrates online, its features and characteristics are reshaped, following the logic of mediatization. To understand the meaning of these new forms of

digitally mediated religious life, it is crucial to keep a keen eye on the range of effects produced by the move online, and to tease out their implications for ritual dynamics, participant experiences, and religious institutions.

Santo Daime provides a particularly instructive case to explore since it employs elaborate ritual techniques that have been thoroughly described and analyzed elsewhere (MacRae, 1992; Cemin, 2010; Hartogsohn, 2021), and also because of the unique features of the psychedelic experience. Psychedelic compounds are distinguished by their tendency to amplify experiential intensity and enhance diverse features of sensory, emotional, and cognitive experience (Hartogsohn, 2018, 2020; Timmermann et al., 2020). The experience-enhancing effects of psychedelics serve to vividly highlight the characteristics, strengths, limitations and unique dynamics of online rituals.

Based on a comparison of the set and setting conditions of traditional SD rituals and their online equivalent, this paper draws on relevant insights from the field of media studies and on semi-structured interviews with 12 participants in *Live works*. It explores key features, tensions, and dimensions of online SD ritual, and sets out to answer the crucial question: can the ritual entheogenic experience be recreated online?

A Brief Introduction to Santo Daime Religion

Santo Daime religion is a Brazilian ayahuasca religion, which emerged in the Amazonian state of Acre in the 1930s. Founded by Raimundo Irineu Serra, SD rituals developed throughout the mid-twentieth century, until 1971 and the death of its founder (Moreira and MacRae, 2011). Following this event, the group split into several distinct lines. One of these lines, led by Sebastião Mota de Melo (henceforth referred to using his common title *Padrinho Sebastião*), went on to establish itself across Brazilian urban centers, and eventually became internationalized with centers in Europe, Asia, Australia, and the Americas.² This paper concerns itself exclusively with Sebastião's line, which achieved dominance over the past decades. Formally known as ICEFLU (Igreja do Culto Eclético da Fluente Luz Universal), this line will henceforth be identified simply as Santo Daime (or SD).

Several key terms crucial to SD religion need to be introduced at this point. At the center of SD religion stands the ritual consumption of the ayahuasca beverage (referred to as *daime*) in a carefully organized context, centered around the joint musical performance of ritual hymns (*hinos*), within a ritual space referred to as the salon (*salão*). SD rituals are collective endeavors performed by congregations (churches) and referred to as works (*trabalhos*). During such works, members wear ritual uniform (*farda*) and believe to be receiving visions and guidance from the astral—a higher order spiritual realm, which becomes accessible under the force of *daime*. During works members believe to be creating a communal spiritual current (*corrente*) which binds participants together and elevates their spiritual work. They jointly face physical, mental, and spiritual hardships and traverse them by practicing firmness (*firmeza*) – a

¹Set and setting is a key term in the field of psychedelic science, pointing to the crucial dependency of the psychedelic effects on contextual factors including expectancy, intention, physical, social and cultural environment (Hartogsohn, 2017).

²See Dawson (2013 p. 35). The similarities and crucial differences between these lines are discussed extensively by Orgad (2012).

fortitude of spirit. SD works take place under the more general symbolic and religious framework referred to as “the doctrine” (*doctrina*), a “multi-vocal” term (Groisman and Sell, 1995, p. 250) invoked repeatedly despite never being properly defined, but generally pointing to the fundamental spiritual and metaphysical principles underlying and validating SD practice. Finally, a particularly important concept in terms of sociality and the introduction of the *Live* works is the concept of *Irmandade* (brotherhood). The SD *irmandade* consists of all members of the SD church. It portrays the members of the church as brothers and sisters, all parts of the “family of Juramidam.”³ As we will see further on, the commitment to the preservation and cultivation of the *irmandade* played a key role in the decision to initiate online works.

The Initiation of *Live* Works During the COVID-19 Pandemic

The year 2020 was supposed to be a festive, propitious year for the SD. For several years, the church has been preparing to celebrate the 100th year anniversary of its founding figure, Padrinho Sebastião (1920–1990), father of SD’s current spiritual leader, Padrinho Alfredo. Thousands of visitors from across the world were expected to travel to SD’s home community Céu do Mapiá in the Brazilian Amazon to commemorate the event in an unprecedented gathering of massive proportions branded as the *Centenario* (centenary).

The eruption of the 2020 COVID-19 Pandemic pulverized these plans. As the pandemic spread across Brazil and the world, international flight routes were suspended and Céu do Mapiá closed its gates to outside visitors. Meanwhile, SD churches worldwide began searching for solutions to the limitations put on SD religious practice by restrictions on congregation. As multiple religious congregations moved their services online (Campbell, 2020), SD churches too began organizing SD works using the Zoom videotelephony platform.

Santo Daime turn online was the result of dire religious exigency, a moment when religious communities worldwide were searching for ways of coming to terms with new restrictions on assembly (Lathrop, 2020). It posed distinct challenges. SD rituals are firmly grounded in the physical world and the possibilities it affords for immersive and immediate sensory experience, social copresence and interaction. The withdrawal from physical space was therefore potentially disruptive. It was nevertheless embraced by SD leader Padrinho Alfredo as a novel way of maintaining the SD *irmandade* and allowing its members to convene, sing, and pray together. Another factor which might have facilitated this openness to introducing digital media into the center of SD ritual might have been SD’s pronounced millenarian tendencies, reflected in the anticipation of a new era of great and unprecedented transformations (Orgad, 2012; Dawson, 2013). Like many other religious communities around the world, SD figures approached the COVID-19 pandemic as an event of religious significance (Dein, 2021). The insertion of

digital tools into ritual work were thus readily understood by some as characteristic of an ominous time.

The first international live work headed by Padrinho Alfredo took place on the 26th of April, 2020. Crucially, the work chosen to start the *Live* era was a Saint Michael (Sao Miguel) work, a mediumship type work that was introduced into the doctrine by Padrinho Alfredo. The event was promoted across the entire worldwide SD brotherhood, many of which viewed this as an historic event demanding their recruitment. As one of my informants told me: “then came this invitation to do a *Live* work with Padrinho Alfredo (...) Doing a ceremony online wasn’t something I eagerly wanted to do, but this was an invitation from our Padrinho, and I felt like: ‘it’s not really a question’. We participate in whatever our Padrinho asks us.”

The ritual, which was organized by the NYC SD group Casa Cocar, was held on Zoom, and transmitted over Facebook Live and YouTube Live in collaboration with Canal Jagube, a Brazilian media organization involved in the dissemination of SD music and videos. According to the organizers, the event, which lasted 8 hours, attracted twenty thousand visitors, easily the biggest SD work in history (Canal Jagube, 2020a).

The months following that historical work saw a rapid succession of *Live* works. These events culminated in the *Centenario* celebrations which took place in October 2020. These events highlighted the *Lives*’ potential to draw SD’s global community together. SD members were originally expected to travel to the Amazon to participate in the *Centenario* celebrations, yet most of SD’s global community would not have been able to make the costly and arduous trip. Through the *Live* works, an unlikely vision was realized: the entire global *irmandade* was suddenly able to participate together.

As *Live* works became a regular feature for global SD community their execution underwent rapid institutionalization. This institutionalization included the establishment of a core group of church members involved in the production of the *Live* works and their many technical, organizational, and promotional aspects, some of which are conducted in cooperation with Canal Jagube.

Online rituals can be divided into three major genres. The first and best known one, with which this article is primarily concerned, are the *Live* works organized by a dedicated group within ICEFLU. These official *Live* works take place on Zoom and are broadcast to two other platforms: Facebook Live and YouTube Live. They typically attract a viewership of several thousands.

Another type of zoom works is held by individual, local churches. In these smaller-scale rituals, which are not broadcast outside of zoom, church members are able to convene and consecrate the SD ritual beverage in the safety of their homes, without violating social distancing codes.

In addition to these, informants have also reported on hybrid type works where some church members convene to perform an on-site work, while others join them virtually, either for reasons of social distancing (for instance when there is a cap on the number of participants allowed to convene due to COVID-19 restrictions), or because of being away from the country (For

³The term ‘Juramidam’ is a native SD term which denotes both God (Jura) and his soldiers (midam) thereby emphasizing the collective nature of SD work (Vasconcelos, 2017).

non-SD accounts of such models see Cocco and Bertran, 2021; Garner, 2021).

The Ritual Status of Virtual Santo Daime Works

The question regarding the validity and authenticity of online rituals has stood at the center of much scholarly debate (O'Leary, 1996; Dawson, 2005; Helland, 2005). *Live* works have since their beginnings been surrounded by ambiguity. On the one hand, they have enabled the maintenance of community during calamitous times of social distancing and allowed the continued upholding of the SD calendar of spiritual works. Concurrently, the move online was met with the suspiciousness with which some in the global SD community approach modern technology.

The decision to reinvent the firmly established guidelines of Santo Daime ritual, honed over a period of almost a century, might have been contentious, yet, at a time of global pandemic, with the threat of social isolation and disruption to communal rituals, the choice was made, stimulated in part by local initiatives of Zoom-based daime rituals that began appearing as COVID-19 took hold. The considerable millenarian features of SD religion might have facilitated this transition. The COVID-19 pandemic, particularly in its beginning, carried biblical undertones, of a Godly reckoning and a fulfillment of ancient prophecies (Dein, 2021). To many of my informants, the switch online seemed to strangely make sense, perceivably becoming of the extraordinary nature of calamitous times. Still, despite this apparent embrace of the *Live* works, a certain ambiguity persisted. For one thing, it was never explicitly stated just what these works were or how they stood in relation to on-site works.

Theoretically, *Live* works can be considered entirely valid. If participants utter their opening and closing prayers and join in for the entirety of ritual, such works can be considered plainly as works at a distance. Practically, however, key differences emerge. Participants in *Live* works drink reduced amounts of daime (or, in most cases, none at all), are unbound from the ritual conventions enforced in on-site works and exhibit lower levels of commitment to ritual. *Live* works are therefore *not* the same as traditional, on-site works, as my informants confirmed. But if *Live* works are not "real" works, what are they then? Are they a temporary substitute? Do they aim to replace the 'real' thing? And if they are but a temporary substitute, will they persist in a hypothetical post-corona world? These are some of the questions this paper seeks to answer.

On the Study of Online Religion and the Surprising Relationship Between Media Studies and the Study of Set and Setting

My study of online psychedelic rituals draws from two main bodies of knowledge. The first is the study of set and setting and their role in shaping psychedelic experiences, particularly in ritual context (Dobkin de Rios, 1984; Hartogsohn, 2017; Dupuis, 2021). The second is the field of media studies, in particular the media ecology approach which interrogates the effects on media on personal and social life (Strate, 2006, 2017; Cali, 2017).

The subject of set and setting and the field of media studies are closer abreast than one tends to suppose. This is readily perceivable when one appreciates that a crucial definition of the term 'media' is environment (Strate, 2017). Media ecologists have long approached the study of media as the study of environments, arguing that diverse media including writing, print, electronic media, and urban planning can be understood as environments shaping the features of human experience (McLuhan, 2003). Similarly, the study of set and setting is the study of (psychological, social and cultural) environments and their effects on shaping psychedelic experiences. Studying set and setting therefore means studying media (environment) in the context of psychedelic experimentation. Moreover, the study of the set and setting of computer-mediated, online rituals compatibly brings together these two seemingly disparate fields of study. It invites us to consider not only how media shape human interactions and experiences (the prerogative of media ecology) but also how our understanding of media effects might inform our analysis of the set and setting of online psychedelic rituals (a prerogative of psychedelic studies).

A key concept connecting the fields of media studies and the study of set and setting is the concept of affordance (Davis and Chouinard, 2016; Evans et al., 2017). Simply stated, affordances are defined as those possibilities which a certain medium renders available or unavailable. Affordances can be recognized each time an artifact requests, demands, allows, encourages, discourages, or refuses certain activities (Davis and Chouinard, 2016). While affordances may be fluid, non-binary, non-deterministic, and context-dependent, the concept does point to technological agency and the way structural features of a technology shape diverse aspects of the human world (Davis and Chouinard, 2016; Strate, 2017). Thus, for instance, the one-way, one-to-many affordances of television discourages the type of interactive, many-to-many, non-hierarchical public discourse facilitated by the affordances of digital social media, which in turn has profound implications for political and social life (Turner, 2006, 2019; Hopkins, 2016).

Migrations across media invariably lead to new constellations of affordances and constraints. The transition between on-site ritual work and computer-mediated ritual is no exception. As this paper demonstrates, migration online radically reconfigures entheogenic ritual dynamics. It opens a range of attractive affordances: the transmission of the work across time and space, the possibility for massive rituals, the recording, replay and re-experience of rituals. Yet, the new computer-mediated environment also entails new and at times uneasy constraints. Sound and video quality is inferior. Voice synchronization is impossible. Ritual leader is unable to survey his flock and offer individual support.

By thinking in terms of affordances we can better understand just what is gained and what is lost when SD entheogenic rituals migrate online. Affordances and constraints, in other words, are measures of set and setting, of opening and foreclosing psychic, social and spiritual landscapes.

This paper also converses with an additional field of scholarly investigation: the study of online religion. This field has been evolving since the 1990s and the rise of the internet, which

became a formative force for contemporary religion (Højsgaard and Warburg, 2005; Campbell, 2011). Scholars of online religion have long been engaged in the study of online rituals and their relationship to embodied rituals (Grieve, 1995; O'Leary, 1996; Radde-Antweiler, 2006; Miczek, 2008). They have, among other things, developed theories of ritual transfer which argue that contextual changes to rituals (such as moving between media) lead to changes in their internal dynamics (Lüddeckens et al., 2005; Radde-Antweiler, 2006; Miczek, 2008), a fact amply demonstrated in the current study. Enlisting the findings of online religion scholarship to contextualize its results, this study also offers a unique contribution to this field by providing an examination of the distinct results of online ritual transfer in the case of psychedelics.

METHODOLOGY

While participating as an observer in several *Live* works, I conducted in-depth semi-structured interviews (of between 30 and 60 min) with 12 daimistas from 6 churches in Europe, Asia, and Brazil, recruited partly through initial personal acquaintanceship and partly through further networking in a snowball manner.⁴ The interviewees had differing levels of experience with virtual daime works, with several who participated in a few dozen virtual SD works, and others who frequented only a few (often those voicing more critical views). The participant pool is not intended to be a statistically representative of the global SD community, but is rather used to portray, using personal testimonies, some of the significant issues arising through the online migration of SD ritual. The materials were analyzed for common themes, and against the literature on set and setting, media ecology, and online religiosity, as well as the author's personal impressions and informal discussions with other visitors of these ritual, which all served as the basis for the examination.

A COMPARISON OF SET AND SETTING IN ON-SITE VS. *LIVE* SANTO DAIME WORKS

The following sections build on my previous paper "Set and Setting in the Santo Daime." What follows is a comparison of the set and setting of virtual SD rituals vs. traditional SD works, pointing to the fundamental ways in which the transition online alters the meaning of SD ritual.

PREPARATION AND INTENTION

The elements of preparation and setting of intention are essential for determining the quality of psychedelic experiences (Johnson et al., 2008; Danforth, 2009). In "Set and Setting in the Santo Daime" I pointed to key elements of preparation and intention

⁴Due to the precarious legal situation of many SD communities, the specific location of churches is kept confidential.

setting in SD works including the perception of ritual order as divine in origin, the sanctified status of the daime beverage and the use of symbolism, and ritual calendar. Some of these elements remain unchanged (sanctified status of daime, symbolism). Other elements are modified by the move online. The divine origin of digitally mediated rituals, for instance, is not established as that of traditional SD ritual, a fact evident in the critical views expressed by some informants. The meaning of calendar is modified too, with users now able to access ritual recordings at any time.⁵

The Paramount Role of Intention in the Home Environment

One point that recurred in many of my interviews is the paramount significance of personal preparation and intention in the context of a virtual rituals. Dawson, writing about SD ritual before the era of social distancing, observed: "collective ceremonial practice (...) furnishes a return on subjective cultic action far greater than that ordinarily available to an individual working in ritual isolation" (Dawson, 2013, p. 75). As ritual moves to a personal, isolated space, a massive loss of communal context results. Ritual participants are called forth to make up for these lost dimensions by preparing properly, adhering to ritual prescriptions, and cultivating a firm intention and commitment. Elements of proper preparation include, most prominently, putting on one's ritual uniform (*farda*) and setting up an altar, like the one used in on-site SD works, including candles, flowers, water and a *cruzeiro* (caravaca cross). Importantly, in the beginning of each work a slide with the title "OFFICIAL PROTOCOL FOR PARTICIPATION IN ONLINE MEETINGS" is presented on the screen, wherein virtual participants are advised to follow certain guidelines: "Prepare the place with doctrinal references with a *Cruzeiro* and candle" "Stay in positions recommended in our rituals (sitting or standing), with appropriate clothing: blue or white *farda*, or white clothes" "Do not consecrate the Santo Daime or any medicine in front of the camera, during meetings." (Canal Jagube, 2020b, min. 34:00). Such guidelines can be viewed as a drastically diluted and abbreviated version of ICEFLU's "Norms of Ritual" document, which proscribes the proper execution of SD rituals, adjusted to the online environment (CEFLURIS, 1997; Hartogsohn, 2021).⁶ These guidelines gesture toward a proper manner of approaching virtual rituals. Yet, as several of my informants shared, commitment is often difficult to maintain due to the nature and constraints of the isolated home environment.⁷

⁵In practice, few daimistas will realize such interest. My informants repeatedly pointed out that the live, in-time, quality of *Live* works is a key part of their attraction. Moreover, some of the *Live* works have been removed from the web following requests by organizing churches of particular works, or to because of errors in musical renditions of some hymns.

⁶According to my sources these guidelines were introduced after some participants in early *Live* sessions appeared on screen involved in unrelated activities like "eating, talking or frying eggs."

⁷Importantly, the protocol fulfills a legal function too. Paragraphs from Brazil's General Law of Data Protection (LGPD) are presented as part of the protocol in order to ensure that the work complies with privacy mandates specified by this law. It is interesting to think about the contextual difference of opening a spiritual work by reciting prayers, as commonly done in on-site SD works, and opening it by reading official legal code, as happens in *Live* works. Such legal considerations

A major component lacking from online ritual work and rendering it exceedingly more demanding to commit to is the absence of the communal observing gaze. In traditional works, daimistas sit/dance facing each other for the duration of ceremony. This creates an all-see-all, surveilling environment where a person is visible and potentially observed at all times, boosting participants' level of ritual commitment. Daimistas will go to great lengths to avoid violating the rules and harmony of ritual space. Inspired by the SD's spiritual-military dialect and the injunction to be loyal soldiers and hold the line during communal trials, participants may, for instance, resist bodily and mental impulses to lie down or visit the restroom, keeping themselves firmly seated even at times of great discomfort (Hartogsohn, 2021).

The solitary nature of online works often blurs such ritual boundaries, a fact that recurred in informant reports. Consider this report, by an informant that decided to join a long Zoom work but found that the home environment challenged her determination.

"I drank. I consecrated and I logged in [...] About a hundred songs later I'm already at a different place. The phone keeps flickering, and I'm getting hungry. So I said to myself 'Ok, I'll go prepare something to eat' and while I'm at it, I smoked a pito [rolled cannabis joint], and then looked at my phone. And then I said to myself 'Okay, am I in a work or am I going log off?' And you see this happening all the time. People log in and log off with their cameras. [...] But then at some point I told myself: 'wait a moment, but I'm sitting in this work now. So, what's that about? Can I really do this just because I'm at home?' where do you draw the line?"

Some informants found the freedom from the monitoring gaze liberating, allowing them to join in or leave the work as they pleased. Digital participants gain all sorts of liberties unavailable in on-site works: they may sit as they please, visit the bathroom, chat online, snack, or take a nap. The move online signals the end of the heteronomous order of SD ritual, where the daimista is subject to external control, and signals the recentralization of ritual around individual preferences. Radde-Antweiler proposes the concept of patchwork ritual, as ritual involving selection, transfer and combination of ritual elements (Radde-Antweiler, 2006). By allowing participants greater freedom, virtual SD works open the possibility of such patchwork rituals that cater to participant preferences in line with digital logics of customization and personalization of experience (Bennett, 2012; Kant, 2020).

At the same time, the new freedom presents new types of challenges. Participants face a growing number of choices regarding their level of participation: Which platform to use, what to wear, whether to open one's camera, etc. This wider range of choices and optionality runs the risk of lowering satisfaction and inducing disquiet, as amply evidenced by the literature on choice overload (Schwartz, 2004; D'Angelo and Toma, 2017; Thai and Yuxsel, 2017). Moreover, the spiritual benefit of SD works often arises from undergoing arduous trials. The strength to withstand such trials is often inspired by the social environment of the

collective on-site work, where one is strongly encouraged to hold the line. As our informant found out, persisting in a work for an entire night is exceedingly more challenging when one is alone and unseen by others, highlighting the paramount importance of preparation and intention for those attempting virtual works.⁸

Ritual Platformization and Its Consequences

A particularly interesting element of preparation and intention in virtual SD rituals is the relationship between the choice of media platform and participants' level of engagement and commitment. One of my informants highlighted a distinction between joining in on massive *Live* works vs. small zoom works held by their local church.

"When I join a work by myself [*Live* work], I'm less observant about *cruzeiro* or *farda*. I care less. With the camera off nobody sees you. You can do what you want. But when I'm with my own church, even when I'm alone I'll at least be wearing *farda*, and (...) everybody wears *farda*. There's flowers, Candles. The whole shebang is there – to keep it as official as possible."

My informants ascribed essential importance to the decision of joining works over Zoom vs. watching them on Facebook Live or YouTube Live. These three different media, all streaming similar content, furnish different types of affordances, leading to different types of experiences. Most crucially, while Zoom allows users to broadcast their own video stream and chat with other ritual participants, such possibilities are considerably more limited for YouTube Live and Facebook Live viewers, though a live comment option is available on both platforms, and was quite popular on YouTube during works. Helland (2000, 2005) drew a seminal distinction between the one-to-many, passive character of *Religion Online*, and the interactive, participatory character of what he terms *Online Religion*. Drawing on Helland's distinction, which admittedly reveals a spectrum rather than a dichotomy (Helland, 2005), Zoom works are closer to the participatory *Online Religion* type in comparison with the more passive, viewership fostered by the Facebook and Youtube Live platforms.

Informants ascribed varying levels of spiritual merit to participation through different platforms. Connecting through Zoom was held in highest regard, while watching through YouTube or Facebook was considered second-rate. Importantly, though, both modes had their advantages and disadvantages:

"When I enter in zoom, I really enter. But if I play it on Facebook or YouTube, it's like playing a hymnal. I can make dinner. I can be in bed. It's just to watch."

In the above quote the informant indicated the advantages of being able to join works through a secondary platform where they are not subject to ritual demands. The possibility to choose one's level of engagement was viewed by some as a valuable affordance of digital space:

are notably also responsible for the proscription around drinking daime in front of the camera during *Live* works.

⁸Importantly, several of my informants indicated that their commitment to virtual rituals was strengthened when joining in the company of friends, either physically co-present or even just virtually co-present in the event.

“You can choose your level of involvement. It’s not like going to a work. You can choose whether to watch on Youtube or enter the Zoom. When you enter the Zoom then you’re really participating.”

“You can be on Facebook, or peaking on Canal Jagube while you’re surfing [the web], or you can be on Zoom, but not open your camera. Stay in the background. Or on Zoom with open camera, or even performing. These are like different perspectives. Every position implies a different level of participation. [...] Your choice of clothes will be in accordance with your level of commitment and motivation. You can either be watching Facebook wearing your pajamas, or you’re on Zoom, with trousers and a white shirt, or putting on the whole Farda.”

The ability to choose one’s level of involvement might be liberating. However, the liberatory affordances of digital media also presents a challenge. When participants opt for a lower level of exposure their commitment tends to be lower, and they may find it harder to engage with the communal current of the work. The solitary nature of digital works puts the onus on the participant to connect. One’s intention and commitment become paramount:

“You need to act. You need to participate on some level. That is fundamental to SD work in general. You can’t just come, drink daime and say ‘Well, what have you got to show me.’ If you want to work correctly, for your own sake, bring your energies either through singing or playing the maraca or other instruments. When I didn’t know anything, I’d tap my lap.”

The issues of preparation and intention are exceedingly acute in virtual SD works. Without the collective support of the *irmandade*, ritual participants are basically on their own. Without the presence of a ritual leader, or community, they can count only on themselves and their own intention setting. They are the ones in charge:

“It’s a very individual work. There’s no interference . . . So there’s no one else to whom you relegate responsibility. It’s all you yourself. You have nowhere to run.”

Asked about the challenges of *Live* works one of my observants summed this up the following way:

“The challenge is taking the work seriously, and concentrating to feel the force, receive the instructions, sing, and enter the current (...) the *Live* is an individual type of work of finding the firmness and the will to make yourself truly present independently of where you are (...) I believe that it depends on how each behaves during the *Lives*. If the person is connected and concentrated, drinking daime and singing, they are going to feel the force and receive the instructions in the same way as in the church. To my mind, it is a personal study of the force, of the will, and of firmness, for searching the divine within oneself.”

A final note on platformization, set and setting, and drug effects. As demonstrated above, choice of media has profound implications for participants’ experiences in virtual SD works. Informants viewed specific media platforms (Zoom) as more conducive to spiritual work than others (Facebook/YouTube). This view sits well with key insights from the literature on media ecology, which demonstrate that media types from writing

to print and electronic media produce their distinct effects on the minds of users (Havelock and Havelock, 1963; Goody and Goody, 1977; Innis, 2007, 2008; Abram, 2012). Like drugs in the past, smartphones and social media apps have lately attracted scrutiny as potential catalysts and aggravators of mental pathologies (Twenge, 2017b; Haidt and Twenge, 2021). Considering the growing body of research interrogating the analogies, similarities, and interrelationships between media and drugs (MacDougall, 2012; Hartogsohn and Vudka, 2022), opens the intriguing possibility of conceiving of the interaction between drug use (ayahuasca and cannabis in the case of SD) and digital media use as linking two distinctly psychoactive levels – a pharmaceutical level and an electronic level, with the electronic level modulating the set and setting of the user, and therefore shaping pharmacological effects.

PHYSICAL (SENSORY) SETTING

Physical (sensory) environment plays a crucial role in shaping experiences with psychedelics (Leary et al., 1964; Hartogsohn, 2015; Kaelen et al., 2018; Gukasyan and Nayak, 2021). The importance of sensory setting is largely a function of the heightened suggestibility characteristic of psychedelic states (Sjoberg and Hollister, 1965; Carhart-Harris et al., 2014; Hartogsohn, 2018). Within these highly suggestible states sights, sounds and scents are enhanced in meaning and may elicit positive experiences of absorption and epiphany next to harrowing experiences of anxiety and distress. Contemporary psychedelic therapy thus encourages the skilled use of visual elements and careful arrangement of musical selections (Johnson et al., 2008; Kaelen et al., 2018).

Santo Daime religion is meticulous in its management of sensory impressions (Hartogsohn, 2021). Prominent visual features of SD ritual space include the symmetric arrangement of participants in a hexagonal shape, at the center of which stands a star-table laid with candles, flowers, water, and the *cruzeiro* cross. This carefully arranged altar functions as a centripetal hub to which participants turn both physically and spiritually. Ritual space is habitually adorned with devotional objects such as the SD flag and religious icons. Members are dressed in festive uniforms (*farda*) (Dawson, 2013; Hartogsohn, 2021). The audial experience is defined by the musical performance of santo daime hymns, which guide the participants in their inner Journey (Labate et al., 2017). Olfactory dimensions, meanwhile, are engaged using incense and perfumes (Hartogsohn, 2021).

On Disorder and Distractions in Domestic Space

Virtual SD works radically alter the established order of on-site SD rituals. Instead of a carefully arranged ritual environment, participants now find themselves at home, which entails a higher potential for encounters with the disorder and distractions endemic to domestic space. Rather than facing an altar and other ritual participants, participants now face a screen. An informant described the rearrangement of space in wistful terms:

“You invest all of your energies to make sure your screen is nice [to watch] and it means that instead of sitting in front of a photo of your padrinho or madrinha your photos actually face the cameras. (...) we’re used to sit in front of pictures of Master Irineu or Padrinho Sebastião or Madrinha Rita. And now we’re sitting in front of a screen. (...) it is like you’re worshipping a screen.”

Virtual ritual environment was described by informants as more distracting and social:

“You’re in front of a screen, usually a phone. There’s a lot of stuff [notifications appearing] that you don’t have in an official work, because you shut-off the background noise [of everyday life]. (...) There’s something social about it. Like using social media. It’s different than when you just meditate and concentrate and sing.”

The informant also shared a story of how her intention to participate in a work was thwarted by the pull of everyday life.

“*Dia das Mães* [mother’s day] was a work I really wanted to do. I set up the table and put the computer on it and started playing the guitar. But then in the middle, a friend came to visit, and it kind of cut my flow. It made me tired. And then after that break, I couldn’t come back. So I went to bed and opened it [the work] there and then I fell asleep.”

In this example, an event (a visit from a friend) which could not have occurred within the strictly regulated context of a church-based ritual subverted the informants’ plans to perform the work online. Several similar accounts were given by informants, who noted the difficulty of unlinking themselves from their web of digital and social relations when performing rituals from home.

Sensory Fidelity

Participants in on-siteentheogenic rituals take the high-fidelity of sensory impressions for granted. Physical space still reigns supreme in terms of richness of sensory experience. Some sensory dimensions, such as the olfactory impressions (e.g., from the burning of incense) or the kinetic, bodily experiences induced by lengthy dance works, vanish completely in virtual daime works. Other sense-organs are left radically impoverished. Popularly available screen- and streaming-based simulations of the human sensory experience pale next to immediate perception of sight and sound. Streaming is often choppy and disrupted. Some churches use inferior technical equipment producing pixelized images and grating sounds. In other moments uneven streaming causes peculiar and unsettling effects. The video and audio stream slow down or stop altogether, but then, as data finally arrive, the videostream speeds up to make up for lost time. The rhythmic disturbance may prove confusing and unnerving to those singing or playing at home.

“There are different types of technical problems. There’s sound drop [a faulty change of pitch]. Then there are gaps and getting stuck. ... it can be annoying when buffering occurs. He [the guitarist] plays, then it gets stuck, then it plays the phrase super quick to connect [with the tempo], and this pulls you out of your natural current. Sometimes you’ll go on. Other times you’ll say. ‘Well, this is getting on my nerves. I don’t want it.’”

Whether or not the ritual participants are able to stomach such technical lapses, the quality of ritual unquestionably suffers. The transformational effects of SD rituals are based to no small effect on the possibility of surrendering oneself to the sublime beauty of ritual space, including the rich acoustics of live voices and musical instruments. The experience of sensory enhancement, common in psychedelic states, further enhances such pleasures. However, the choppy, low-bandwidth, nature of online video and audio curbs the potential for such elevating sensory experiences and often proves unnerving.

Lack of voice synchronization is particularly detrimental to ritual dynamics. The poignant challenges of online religious singing have been priorly described (Miczek, 2008). In SD works, which are crucially musical (Labate and Pacheco, 2010; Labate et al., 2017), synchronization is a central element of ritual. By synchronizing their voices, participants become one voice. The paramount daimista concept of the current (*corrente*) is predicated on the notion that by meshing and synchronizing, human voices resonate to create a flowing, harmonious current. However, the built-in latency of the web’s architecture renders such synchronization impossible. This constraint of current virtual media has grave implications. As one informant told me: “Zoom has no possibility for synchronization. Instead of harmony, there’s separation. You don’t hear me, and you don’t hear the others. You just hear one source.”

Transgressions of Space and Time

Electronic media is characterized by its ability to transcend boundaries of time and space. The attraction of virtual SD works lies, unquestionably, in their ability to transcend space-time and connect SD members separated by the COVID-19 pandemic and geographical remote locations. Concurrently, the transition to a space beyond space and time creates several unforeseeable, noteworthy effects.

A first point to mention is the increasingly dynamic, sometimes fleeting, nature of visual impressions in virtual SD rituals. In traditional SD works, one’s point of view is stable. One’s distance and angle in relation the altar-table and *cruzeiro* are fixed, the positions and identity of the people sitting or dancing at one’s side are generally immutable.

Virtual daime works offer a completely different experience. Here, a crucial part of the visual landscape appears not in the immediate physical space, but on the screen, in a dynamic videostream that moves around across different homes and churches. Hymnal works are commonly divided between churches in five-song sections, so that every five songs the participant is transported into a new visual and auditory environment. The pace of images rises rapidly in montage sequences. Here, the editing jumps around between participants’ video streams that are spotlighted for several seconds before moving on. Spacetime is thus condensed in a way that jogs the virtual participant across diverse landscapes with different features and characters. Crucially, these views are framed by the logics of mediatization (Hjarvard, 2008). The roving video stream moving between locations cannot but remind one of the new digital ecology of participatory culture (Jenkins, 2006), with its endemic selfies and endless live-streaming – of the

burgeoning world of Facebook, YouTube, Tik Tok, Instagram and the aesthetics featured in web-inspired collective cinematic works like *Viral*, *In My Room*, and *Life in a day* (Bukowski et al., 2011; Bornstein et al., 2021).

A second point to note, is that the migration online transforms the implicit relationship between ritual space and spiritual benefit. In *Santo Daime: A New World Religion*, Andrew Dawson writes about a “Field of power” characterizing SD ritual space. Dawson’s “field of power” references a certain type of hierarchy where those in greater proximity to the physical center of SD ritual space are assumed to draw greater spiritual benefits in their ritual work.

Live works present a comparable but distinct hierarchy, reorganized according to the affordances of virtual space and the platformization of SD work. This hierarchy was described by one of my informants in the following manner.

“There are a couple of levels to the virtual astral. You can watch the *Live* the day after. It still counts. But if you are there live, that’s a different level (...) the next level is your camera is open. This is a much stronger connection. Then there is another level, which is when they spotlight your videostream on the big [main Zoom] screen. All your friends see you. Padrinho Alfredo sees you. Then there is another level, which is you appear on both video and audio [i.e., when performing].”

The informant distinguishes between five levels of ritual work, depending on timing and on one’s level of visibility. According to this logic, which recurred across the interviews, the more one reveals and is exposed on the videostream, the closer they are to the spiritual current of the work.

Another noteworthy way in which space-time are transgressed in virtual SD works concerns the use of pre-recorded performances. As noted above, hymnal works are commonly split into 5-hymn sections performed by different churches. Some of these sections are performed in real time, while others are pre-recorded, often for reasons of time difference (with non-Brazilian churches). These prerecorded sections are often a genre in themselves and are recorded under exceedingly diverse conditions. Participants might be under the influence of daime or not. They might record before, during or after an actual work. Alternatively, they might gather solely for the purpose of recording the short section.

Such considerations are highly consequential for the quality and “current” of the recording. Normally, different parts of works have different qualities, corresponding to their location in the temporal trajectory of the work. Human voices and musical performance sound different in different stages of the work, e.g., in the first hour vs. four or seven hours into a work, when participants are in a state of spiritual ecstasy, or conversely exhaustion and fatigue. These dynamics of traditional SD work are radically circumvented by the logics of pre-recorded performances, which are cut off from their habitual surrounding context, and where participant attempt to present their best selves to the watching audience.

“When we pre-record (...) there’s something very powerful about it, though a bit abrupt and weird. Sometimes you finish the

recording in the force [feeling the force of daime], and then everybody goes their own way.”

The fragmented nature of time in online rituals has been noted by scholars (Grieve, 1995). One of my informants described the uncanny and sometimes disorienting experience of rewatching her pre-recorded video during a work:

“We shoot ourselves, then we send the video, and then they broadcast it and we watch ourselves live, but we can also watch it the next day, and watch ourselves watching ourselves. The work lives endlessly.”

Another informant who participated in a pre-recorded session excitedly shared their feelings of transcending time and space:

“It was very strong, because it’s still two days before the work, and you drink a bit and you sing, and you’re concentrated, and even though it’s pre-recorded you feel it very strong, and sometimes you look inside the camera, and inside the camera you come into contact with all the people who watch you, and Padrinho Alfredo and the comitiva, and Mapia and whoever is watching you. They are over there, inside the lens of the camera, and you can even wave at them, and you know that in a lag of time and space, they will see you (...) it just takes two days to travel to them. But you still waive at them, and two days later, you sit at home, and you watch it, and they wave back at you. You see them waive and you receive it.”

Another more mundane aspect of temporality involved in online works is the issue of time differences, which often make it more difficult for Daimistas from the other side of the ocean to participate in virtual works. It is quite different to enter a work that starts at 16:00 and ends at 23:00 (Mapiá time) than joining a work that starts at 23:00 and ends at 6:00 AM the next day (CET). Such time differences shape engagement levels.

“The hours are not easy, because if they start there in the afternoon here it’s very late. (...) This Saturday I was like ‘Well, I’m here with myself, and I had a really difficult day. I will not put my farda!’ Then I think: ‘but Padrinho Alfredo is there putting his farda. Well, if they see me without farda’ [that’s awkward]. But then I think: ‘for Padrinho Alfredo it’s 12 at noon, and here it’s the middle of the night. I have work. I have other stuff. I cannot be in white farda.’”

SOCIAL SETTING – LIVING IN A VIRTUAL GLOBAL COMMUNITY

Sociality plays a crucial role in shaping experiences with psychedelics (Hartogsohn, 2015). Studies have demonstrated that social environment, levels of amenability and familiarity determine responses to psychedelics, and that sociality plays a key role in enhancing psychedelic effects (Dimascio and Klerman, 1960; Hyde, 1960; Olson et al., 2020). In “Set and setting in the Santo Daime” I discuss the central role of sociality in the SD experience, noting the central place of communitarian values in the SD doctrine, the “familial ideology” (MacRae, 1992, p. 3) embedded in SD culture, the socially cohesive effects of collective entheogenic ritual, and the tight-knit character of

many SD communities (Hartogsohn, 2021). Importantly, a search for sociality has been noted as a primary driver toward online community (Grieve, 1995; Rheingold, 2000), and has played a central role in the turn online of many religious communities in the 2020 COVID-19 Pandemic (Campbell, 2020, 2021c; Cocco and Bertran, 2021).

The Global Irmandade

The notably individual, isolated nature of virtual SD works was noted earlier [preparation and intention, section], and yet sociality is central to virtual SD works and might be considered their primary function. The desire to allow for assembly at a time of pandemic served as the original impetus for organizing *Live* works. Virtual works, despite their many limitations, were described as a way of keeping the irmandade close, and allowing SD members to convene, pray and sing together even at times of social distancing and isolation. Indeed, the one domain where virtual daime works undeniably surpass their on-site equivalent is their ability to bring together individuals from many parts of the world.

“How would people be able to do a work with so many individuals present as in the *Live*? People from Holland, India, Europe, Japan, Australia, United States. How would it be possible to unite all these people in a physical meeting? It would be difficult, don't you think? (...) I'm not a person who is very connected to technology. (...) When I entered the *Live* I was very surprised, because I immediately understood the power of the *Live*. (...) It connected me with the *irmandade* of the entire world.”

The ability of virtual works to produce social connection on a global level was considered by informants as their most valuable feature. Some informants reported that participation in the works, reignited and strengthened their relationships with SD members from other churches. Others described the socially connective aspect of *Live* works as meaningful and uplifting.

“It's good to know that as I start changing clothes [to ritual uniform], I know that another person in Europe is doing that, and another guy from Southern Brazil is doing the same, and then we meet in a way that we wouldn't meet otherwise.”

“It's nice because SD is such an international community and you suddenly have a chance to see people that you know from all over the world, and actually work with them.”

“When you share cyberspace with Padrinho Alfredo and other daime VIPs, that can give you a kind of feeling of closeness. It kind of elevates the session ... and seeing people I know from other churches ... The friendship warms the heart, and that can also be kind of spiritual.”

“These works connect the *irmandade* on a global level. You can be part of it wherever you are. They connect the *irmandade* with Céu do Mapiá. That was something new that we never could have imagined would happen, but it was a way for us to keep ourselves united, in prayer, singing the hymns and connected to the doctrine of SD.”

One of the features of online life is its ability to bring together sparsely spread communities sharing joint interests. For some of my informants being able to connect with Brazilian daimistas was

valued as a way of finding peers and being able to transcend one's sense of cultural marginality:

“We're very esoteric in this country ... here [online] you find many people that are esoteric together. They work with the same materials like me. In many ways they are closer to me than people in my country. ... My everyday life is about daime hymns, so in this sense I'm closer to them [than to compatriots]. ... There are many reasons why I don't go to the [Amazon] forest. The heat, the humidity, mosquitos. Daime travels here. The only thing which doesn't travel are Padrinho and his friends, and now we can be connected to them in this way and see them HD. ... that's an intimacy I wouldn't have been able to achieve in Mapiá.”

An added value of global sociality was being able to celebrate the official dates of the full SD calendar, some of which are not regularly celebrated by smaller communities. “You use this opportunity because you want to commemorate the date, but you don't want to drink alone. This then gives you a chance,” one informant noted.

Finally, for some, the participation in the global sociality of virtual SD works allows for spiritual reconnection to the Amazon Forest and its teachings, which are held in high esteem within SD religion.

“For people who were in the forest ... I basically live with eternal *saudades da floresta* [yearning to the forest]. And [when watching] it's like 'Okay, it's still there. It's alive. They are there.' It made me feel very connected. ... It reinforces the connection to all the churches and the forest ... Every time I saw the *commitiva* of Padrinho Alfredo, or the women in Mapiá, or the people in Colonia 5,000 ... Md. Rita, every time I saw these people that are so deep and central to the doctrine, I was reminded what *firmeza* is, and what essence these people bring to the works.”

The Paradox of Virtual Daime

The central role of sociality in virtual SD works contrasts with the reduced role of another crucial element that traditionally stands at the center of SD works: powerful visions and inner voyages. Participants in virtual works tend to drink less daime. Mustering the courage to brave the ingestion of a second, third or fourth cup of daime is harder without the support of collective SD rituals. Furthermore, in on-site SD works experienced SD members (*fiscais*, guardians) are tasked with overseeing participants and helping them in need. Drinking heroic doses of daime is more daunting without this social safety net. There is, however, another reason why most of my informants found it difficult to surrender themselves to the entheogenic experience during *Live* works.

“Many times, the conclusion is that what I like better is getting together with a friend and doing a concentration work, just the two of us next to a candle, with a guitar. Because you can go deep. You can close your eyes. To go deep, it's better to get together, or do it alone. But for the experience, the togetherness, the holiday, seeing other people – it's [Live works] more in service of this need. ... There's a paradox, because really what's the idea behind the Zoom? Is the idea having a shared experience or is it about going through a deep personal experience?”

The informant's words are indicative of a greater issue at hand. An inherent paradox lies at the heart of the *Live* work which

concerns the very idea of video streaming. Traditional SD rituals are habitually performed with closed eyes. SD members are often advised to keep their eyes closed during rituals to avoid intruding on other people's experiences, and crucially, to connect more strongly with the force of daime and its visions.⁹ To go deep, one is advised to close their eyes and look inwards. However, when participating in a *Live* work it is only natural to open one's eyes and stare at the screen. If not, after all, then why even open one's laptop? The question reveals an unresolved tension between the spiritual and social dimensions of virtual SD rituals. The efficacy of one dimension reduces the efficacy of the other.

The dichotomy between the social elements of the work and the contradicting desire to go deep into the daime experience were evident in the words of another informant:

"When I am in a church, I close my eyes when I sing. But in the zoom works I don't close my eyes. I look at the screen. If I open my camera, people can see me also. So I need to be prepared to be seen. . . . Usually I don't like to be watched when it's very strong."

Does the social aspect of virtual daime works preclude the occurrence of deep spiritual experiences in the virtual rituals? While many of my informants found that sociality of *Live* work runs counter to their ability of deeply dive inward, experiences of spiritual elation and transformation *can* occur in the online contexts. Informants reported a range of spiritual experiences, usually induced by the social nature of works. While most informants felt that virtual rituals offered a diluted version of on-site SD works, in terms of their spiritual intensity, exceptions were noted. Particularly impressive was the report of one informant who said "when I sit down to do a zoom, I enter a church (. . .) I feel myself sitting on the bank next to the wall in the church." The informant shared several spiritually uplifting experiences during *Live* rituals. One of these experiences that occurred in her first *Live* work helped her come to terms with the global situation of the pandemic and her own situation of social seclusion. Significantly, it was triggered by the social aspects of the *Live* work.

"I saw a woman alone. Another sitting next to an altar and a candle. One dancing. Another sitting. Another with a vase of flowers. A man alone playing the guitar. Another praying. It brought such a powerful emotion. It made me realize that each of us is firm with the words we sing like an ivory tower. And this will overcome whatever upheavals are coming. And this is what we're doing during the pandemic: building that place where each can be. And this is the golden unity of these *Lives*. Because you're sitting alone in your house drinking daime. [And you say to yourself] My god, what's going to be? [Then] you see our *Padrinhos*, that which connects. You see the brothers. I saw the reunification of the web, of the earth, of the brothers with the spiritual web that people recognize when it brings people together."

⁹This might at first sight contradict with the above given description of on-site SD works as all-see-all affairs, where one is visible and potentially always observed. No contradiction exists, however. While members are encouraged to keep their eyes closed, some members may keep their eyes open, so that the participant is always potentially observed.

Social Anxiety and Performativity

The above quote demonstrates the power of online sociality to induce spiritual experiences empowered both by psychedelics and the global affordances of virtual environments. At other points, though, the affordances and constraints of the digital social environment were experienced as oppressive and anxiety-provoking.

One distinct affordance of Zoom broadcasting is its unifocality. Unlike embodied SD works, where human voices mix together, and one is able freely move their gaze, here there is one spotlight, one videostream that is presented on the screen for all to see, focusing collective attention. The observing gaze thus becomes overtly noticeable, much like spectators viewing a broadcast performance. When spotlighted ritual participants come to resemble performers, this can have crucial implications. Stage fright is one of the most common human phobias (Narrow et al., 2002; Bodie, 2010). The prospect of suddenly appearing full screen in front of thousands of global viewers easily induces anxiety among many individuals. "It's not easy to be watched by the whole doctrine [i.e., irmandade]" one of my informants told me. Social media has been implicated in enhanced anxiety (Vannucci et al., 2017). Importantly, in virtual SD rituals, the anxiety provoking effects of digital media may interact with the effects of other mind-altering plants that may aggravate anxiety, thus creating a second layer that reshapes the effects of the digital pharmakon (Hayatbakhsh et al., 2007; Hser et al., 2017). One of my informants, a guitarist, described his challenges knowing that his image and sound are broadcast to thousands.

"You're exposed visually. How you look. Your guitar playing. I do these faces when I play the guitar. Suddenly all these twisted faces you're making while you're trying to reach F#, or something – Everybody sees that. It doesn't matter that much in [traditional] works . . . When I view myself [on screen] there's a whole range of emotions. A lot of self-critique about how I look, my guitar faces, every little thing. First, you're overly self-conscious, then you realize it's okay, not everybody are looking at you the same way you're looking at yourself. I remember everybody [participating in a video recording] were anxious about it. Particularly when the video quality is high and the camera is directed at your face."

While some agonize under the spotlight, others relish it. Next to social anxiety, another effect of the virtual unifocality is performance. The common element to both anxiety and performance is that both potentially distract ritual participants from the ethos of concentration in ritual. This is evident in montage sequences where the videostream roams between participant cameras. Spotlighted participants regularly recognize themselves on the screen. Some wave their hands at the camera, others bring their two hands together and gesture the heart sign. One of my informants found this type of performance anathema to daimista ethic:

"Even when you drink normal amounts [in *Live* works], something in the energy gets scattered. One obvious reason is people waving their hands [. . .] or people doing the heart sign. Our comandante [church leader], forbids any waving. It's less focused . . . It doesn't have the kind of *firmeza* [firmness] that our doctrine requires."

The informants' remark against all types of waving and gesturing touches on a key point regarding the performative aspects of *Live* works. Participants in SD works are encouraged to close their eyes and explore themselves from within. One sings and plays musical instruments, but the emphasis is on being with the hymn, rather than on performance and self-consciousness. It is unthinkable for a daimista to wave their hands or gesture the heart sign during a traditional SD work. When *Live* participants wave their hands or gesture at the camera, they are in fact stepping out of their role as participants supporting the work through singing and concentrating. Instead, they are drawing attention away from the hymnal and toward themselves and inter-personal communication. Nevertheless, as lack of interaction can be interpreted as lack of engagement and care, such performative acts of waving and sending kisses to the camera are often encouraged. This type of behavior is therefore better tolerated because of the *Live* context where social function is central, though, as noted above, not everybody condones it.

Finally, one of my informants revolted against the amplified role of performance in its entirety, considering it to be blasphemous and opposed to the core of SD's doctrinal teachings:

"You realize that you're on a show. That you're going to perform. I came to SD seeking for something that is not of the ego, that is not about performance, and not about showing myself to anybody. I felt like we're in a movie, or a TV reality show. (...) the effort that we are used to put in our spiritual work is transformed into an effort that we put to show ourselves at our best."

Changes in the Irmandade

One final note on sociality. The rise of online SD works leads, among other things, to a shift in the constitution of the Santo Daime irmandade. As is evident from informants' replies, daimista responses to virtual works vary. While some are open and welcoming to online rituals, others are more critical and less inclined to participate, because of ideological reasons, personal preferences, or technical limitations. SD members in areas under lockdown are more likely to join virtual works than those able to join on-site works. The make-up of participants in virtual SD works is therefore quite different from the make-up of traditional SD works. Compared to these traditional SD works some populations are excluded, other self-exclude, and other are over-represented. Since the initiation of *Live* works there emerged a distinct group of individuals regularly participating in these rituals. Virtual SD works therefore not only strengthen the connections within the *irmandade*. They also forge a new *irmandade* with an altered composition.

CULTURAL SETTING

The concept of cultural setting relates to impact of broad cultural forces on the character of psychedelic experiences (Hartogssohn, 2020). Wallace, for instance, argues that the Western association of hallucinations with mental illness raises the likelihood of negative experiences with hallucinogens for Westerners (Wallace, 1959). More recently, the concept has been used to explore the ways in which COVID-19, climate change, and political

populism shape experiences with psychedelics for contemporary users (Prideaux, 2021).

The migration of SD works from the on-site church environment to platformized, digital environments entails a transformation of the cultural set and setting. One obvious way in which the cultural environment changes is the transition from the symbolically safeguarded environment of the church (perceived by daimistas to be protected by carefully arranged *puntos* with candles surrounding the church structure) into the suspect, exposed and perennially surveilled digital environment, mediated by corporate technology. On-site rituals are safeguarded not only by individual guardians taking care of the space and participants, but also by symbols and incantations. These elements are missing from online works, raising the question, how are virtual rituals protected?

The move online, implies that participant's relationship with SD ritual is no longer immediate, but framed by digital media. Like many global citizens in the early 2020s, some in the contemporary global SD community are critical and suspicious of corporate dominated digital space, tarnished by association with massive online surveillance, rising inequality, voter manipulation, tech-addiction and mental pathologies (O'Neil, 2016; Alter, 2017; Bridle, 2018; Lanier, 2018; Eubanks, 2019; Zuboff, 2019). SD's foundational story contains a strong primitivist message of return to nature and romantic simplicity. It tells of Padrinho Sebastião who, in the early 1980s, led his flock away from the Amazonian city Rio Branco and back to the depths of the forest. There, they were promised to find freedom and happiness in harmony with nature (Mortimer, 2018). The institutionalization of virtual SD works mars this narrative. The return to the forest ironically ends up leading back to the virtual. Instead of connecting directly with divine astral realm, participants (now users) must access it through the servers of disreputable tech corporations. Connection to divinity is now dependent on a proxy server and technological media, of which some participants are wary and distrustful:

"Sitting in front of the computer, I don't like that. I sit all day in front of the computer. I don't want my spiritual work to also be in front of the computer. This medium has the advantage that it can cross temporal and spatial boundaries, but it's still sitting in front of the computer, with latency, and pixelization, and a quality [level] that has an unhealthy effect on my [somatic and mental] system. It can bring stress when things [in the videostream] get stuck."

"I consider myself a millennial, so the world of commenting, reactions and live stories on Instagram is part of my world. But I don't like to see a work transmitted on YouTube with all the comments ... you see sides of daime people that you don't really want to see."

"The screen produces separation, which is something that's not natural to us, considering the messages of the doctrine. Finding unity and connection in all of this is hard. We're very used to the screen as something that turns us into spectators."

Informants' views of the virtual realm were often negative. One informant even referred to the digital dimensions as "the dark side of the astral." Another informant argued that their participation in *Live* works is proof of their devotion to SD

doctrine. They confessed to intensely disliking Zoom and video conferencing. To this informant, willingly participating in Zoom works meant that “this is a place I care so much about that I am willing to tolerate the medium, which I find difficult.”

The technological framing of virtual SD works also runs the risk of depreciating their value in the eyes of participants. As SD works become a consumable media experience, they run the risk of being commoditized and losing their aura effect. Walter Benjamin's classic paper *The work of art in the age of mechanical reproduction* argues that the reproduction of artistic objects diminishes their aura effect (Benjamin, 2008). For example, whereas priorly one had to put on a frack and ride to the opera to listen to Beethoven, today one may listen to Beethoven on YouTube in the privacy of one's home, wearing nothing but underwear. In this way, art loses its ritualistic resonance and potency. A sense of transcendence is lost with the change in context. A parallel can be found in the case of virtual SD rituals. Priorly, SD members needed to take an arduous pilgrimage to Céu do Mapia to participate in works with Padrinho Alfredo. Members' commitment and struggle gave rise to reverence toward that which was reachable only with great difficulty and sacrifice. How might that change when one is able to frequent works led by Padrinho Alfredo on a regular basis, from the comfort of one's own home? What changes when the *Live* stream of a spiritual leader appears next to other videos placed there by Facebook's and YouTube's algorithms, some of them blatantly inappropriate to religious service? In sum, how do the flattening, de-hierarchal features of digital technologies (Castells, 2003; Turner, 2006) change participants' modes of approaching religious authorities and do they corroborate reports of erosion of religious authority in digital environments? (Piff and Warburg, 2005; Hjarvard, 2008; Cheong et al., 2011). Some of my informants' reports imply that the *Live* context may introduce acrid alterations in one's relationship with their spiritual guide and spiritual work.

“It's like the gentrification of the doctrine. There's this Hollywood vibe. I want my Padrinho looking me in the eyes and serving me daime, not somewhere on a screen. It creates *rebeldia* (rebelliousness) in me”

“SD is becoming something you consume. You have products to consume. You have webinaros [webinars]. You have recordings. You have merchandise of SD.”¹⁰

A related issue that came up was the culturally delicate issue of class differences. The question of digital divide has cropped up in recent discussions on the virtual turn in online religiosity (Campbell, 2021b). Such differences may play a role in on-site SD works, as evident when comparing the material conditions of SD congregations: the architecture of SD churches, the use of makeshift vs. permanent constructions, the fee paid for participation and the type of ayahuasca procured.

¹⁰Importantly, this perspective, which was voiced by some Western interviewees, is quite different from that of Brazilians. Missionary trips and international tours have represented a major source of economic income and stability for some families of daimistas. This system of exchange was abruptly interrupted with the pandemic. Brazilians, particularly from Céu do Mapia, therefore often view *Live* works as an opportunity to conduct campaigns to raise money for the support of their families and communities in the Amazon. See Viridi (2020).

Still, while important on a macro level, such factors tend to be subdued within the person to person level of an on-site work, where participants operate within the same conditions (occupying the same space, using the same equipment, drinking the same beverage, etc.). In online works, where participants exist and transmit from distinct types of environments, such differences become more apparent, as reflected by the quality of one's technical equipment and conditions: internet connection, speakers, screen, and personal space. As one of my informants argued:

“In the doctrine we are 'todos iguais' [all equal] and you can give in to a sense of oneness, but technologically we're not all equal. If I have a Mac and I'm sitting in my penthouse connected by an optic fiber, and you have a small apartment with a sleeping baby then we're not 'todos iguais'. There are class differences, and this is in a sense a privatization of the Salão.”

Finally, another form of commodification regards the concern that the logics of SD work might become subordinate to the logics of digital consumption. Writing about the mediatization of religion, Hjarvard observes that “through the process of mediatization, religion is increasingly being subsumed under the logic of the media” (Hjarvard, 2008, p. 11). In the case of SD online ritual, by entering the video player ecology, the spiritual arguably becomes manipulable. The viewer (formerly participant) may opt to skip certain less compelling sections of the work (e.g., lengthy prayers, breaks, concentration sessions), rewatch highlights or fast forward through other sections. Religious ritual is transformed from lofty and awe-inspiring to a pliant, manipulable media object which users can use as they like, and even binge on.

INTEGRATION

Integration is the post-session work of constructively processing and assimilating the experiences and insights that arose during a psychedelic experience (Godasi, 2019; Westrum and Dufrechou, 2019; Watts and Luoma, 2020). In on-site SD rituals, informal integration habitually takes place after the work. Participants often linger in ritual space exchanging hugs, impressions, and engaging in reinterpretations of their experiences. This dimension is lost with the migration online. While Zoom participants are able to remain in the Zoom room as long as it is open, the possibility to freely converse is limited by the unifocality of the Zoom platform: the inability to have discrete conversations without being heard by all. For *Live* viewers, even this is impossible. Once the *Live* videostream ends, participants find themselves alone in their home environments. Participating in a *Live* work as a group may mitigate the sudden cutoff and allow participants to integrate with their close group, as noted in footnote no. 8.

SKILLSET

The concept of skillset is defined as a set of cultivable techniques, strategies and approaches for navigating experiences with psychedelics (Godasi, 2019). On-site SD rituals offer participants

diverse opportunities to cultivate skillset including studying hymns, practicing concentration, and fulfilling diverse ritual roles such as playing musical instruments, acting as guardians, or serving daime. Each of these roles offers distinct challenges, curricula and skills to be perfected (Hartogsohn, 2021). In virtual SD works, however, many of these dimensions are lost, as one informant argued.

"In our rituals we have alter egos that emerge, and people can access powers that are not necessarily available to them in their everyday life. . . . The relationships between the brothers and sisters are powerful because we tend to produce some other versions of ourselves during the work, which we do not do on zoom."

Because of the affordances of video transmission (i.e., the unifocality of video and audio streams), and because there is no common ritual space, participants' ability to contribute to the collective ritual (e.g., by singing, dancing, or facilitating other aspects of ritual) are limited. This changes the nature of skillset, which is achieved not in communal work, but in solitary work, developing the ability to stay firm, intent, and concentrated away from the supportive networks of social ritual work.

Another dimension of skillset that may develop in virtual SD works is the pedagogic deepening of knowledge and familiarity with SD's hymnal repertoire and manners of ritual. By participating in works led by SD dignitaries of international renown, participants may learn from others, more knowledgeable in the SD work:

"It's an education. It's learning the hymns, the musicality, the energy . . . you see how other churches play, their way of working with different musical instruments . . . with the singers . . . there are many aspects to this."

CAN VIRTUAL SANTO DAIME WORKS REPLACE ON-SITE WORKS?

A central question raised in this paper, regards the future of *Live* works in a post-pandemic world. As noted, the COVID-19 pandemic has led to a rapid wave of digitalization in diverse areas of life, including business, education, culture, and therapy. In many cases, digitalization has been presented as irreversible. The world of business, education, and culture, some argue, will never revert back to 'normal.' Similarly, in the ecclesial domain, some argue that the church cannot return to the life and practice of pre-pandemic days (Campbell, 2021b; Garner, 2021; Rieimann, 2021). Can the same be said regarding with entheogenic rituals?

The challenges of translating religious rituals into online environments have been noted by early scholars of online religiosity, some of whom opined that current internet technology will struggle to replace ritual performance in physical sacred space (Dawson, 2005; O'Leary, 2005). As argued above, the body oriented, sensory enhanced, and experientially intense nature of the psychedelic experience renders the task of successfully translating it into online realm particularly daunting, given current technical limitations including latency, inferior video-audio fidelity and dependence on non-immersive screen

interfaces. The impoverished, flat and pixelized qualities of online simulation become still more evident under the influence of psychedelics. My informants all agreed that online SD works are no substitute for on-site church-based rituals. Their responses included a variety of litanies about the constraints of virtual works. Compared with traditional SD rituals, virtual works discourage powerful inner voyages of transformation, present new challenges of distraction, and furthermore modify, erase and swaps diverse aspects of SD social and cultural context. In many respects, they represent a radically impoverished version of the 'real thing.' The more critical members of the informant pool were incisive in their judgment. They described virtual works as "a bumming experience" and "a way to connect that keeps us separate."

Nevertheless, not all is negative. Some told of spiritual experiences had within *Live* rituals and asserted the spiritual authenticity of these works. Moreover, even the more critical voices conceded that virtual SD works had their place in the reality of social-isolation brought about by the COVID-19 pandemic. Pointing to the severity of mental health crisis experienced by Brazilian population in the wake of the pandemic (Goularte et al., 2021), one of my informants spoke of *Live* works as an antidote, allowing individuals to come together in a time of isolation. "It's not a solution, but it's something" told me another informant "my years of being a church member tell me that I need to work to maintain my connection to the SD." For some church members, the realization of *Live* works represents an effort to not abandon one's religion. Being able to join works online at a time when that wouldn't otherwise had been possible allows the maintenance of the connection with one's religious faith and practice.

Live works were generally seen as a fitting, *ad hoc* alternative for a moment of collective exigency. Asked whether *Live* works will continue in a post-pandemic world most of my informants suggested they probably will, but with less regularity, reserved for special occasions, courting to specific groups within the SD irmandade, and fulfilling a mostly social function. Asked whether they consider virtual SD rituals to be "real" works, they argued that online rituals perform a different function. Virtual works, in other words were viewed not as substitutive but rather as complementary, adding interconnection and complexification to SD practice (Sbardelotto, 2021). Importantly, while Campbell notes that some church members prefer online worship for reasons of convenience and flexibility (Campbell, 2021a), none of my informants indicated anything of the sort, a fact that might be explained by the dramatic, spiritually intense, and scarcely reducible character of the psychedelic experience.

Finally, it is important to note that the *Live* genre of works still has a volatile, uncertain, plastic nature. Since August 2021, and as of the writing of these lines (February 2022) the organization of *Live* works by ICEFLU has ceased. Sources I have approached to inquire about the reason for this cessation have cited the more controlled COVID-19 situation in Brazil and the resumption of on-site works in Ceu do Mapiá. The demanding work required to organize multiple *Live* works was also cited. At the same time, non-ICEFLU online SD works are continuing, and ICEFLU organized works may resume in the future. Moreover, new more advanced technologies, such as virtual reality, might enter the

picture in the future rendering the experience more immersive and attractive, and so the shape of online SD rituals is expected to further develop and evolve in the future.

CONCLUSION

This paper contributes to the literature on the extra-pharmacological factors shaping experiences with psychedelics, as well as to the literature on the adoption of digital media technologies during the COVID-19 pandemic. It provides a unique perspective that combines these two fields of scholarship, focusing on the transformation of SD entheogenic rituals with the move online and the consequences for ritual participants.

This examination reveals both strengths and weaknesses. The migration online allowed for the continuation of SD entheogenic rituals at a time of social distancing and fostered a sense of global brotherhood. Concurrently, online ritual produced an impoverished ritual experience and novel types of challenges including a higher potential for distractions, technical difficulties, and low sensory fidelity. Other challenges included social anxiety and an in-built tension between the social and spiritual dimensions of ritual. Finally, some participants were concerned by the cultural context of online works: technological mediation, consumerism, commodification, and digital divide.

The study of online psychedelic rituals draws insights from the study of online religious rituals, the study of mediatization, and the turn online. Nevertheless, the intensified nature of the psychedelic experience (Hartogsohn, 2018; Timmermann et al., 2020) makes these rituals unique when compared with other online activities. Firstly, because of the intensified, sensitive nature of the psychedelic experience, these rituals are particularly high-stakes for participants. Moreover, the limitations of virtual space emerge all the more strikingly in the highly immersive, body oriented, experientially enhanced context of the psychedelic experience when compared with other instances of activities that migrated online (e.g., education, business, office work, non-psychedelic religious rituals). Current technology might be adequate to replace some types of everyday activities but judging from informants' reports it has much to go before it is able to provide a viable alternative for embodied psychedelic rituals.

While this research is limited in scope and focused on the specific example of virtual SD rituals, it has implications for a wider range of issues and domains. Future research may

pursue quantitative analyses of the types of shifts explored in this paper, expanding the number of surveyed individuals, as well as the number of groups and frameworks examined. Researchers may use the template of set and setting factors provided here to analyze other instances where entheogenic, and non-entheogenic religions are transformed by the migration online. Media ecology concepts like affordance may further serve to interrogate the ways of media environments reshape the characteristics of psychedelic experiences in virtual spaces, and religious experiences more generally. As growing parts of religious and entheogenic life move online, the questions what is gained? What is lost? And what possibilities lie ahead? Will continue to be resonate, prompting new investigations into novel forms of virtually mediated entheogenic ritual.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because of sensitive information which includes the illegal use of psychedelics. Requests to access the datasets should be directed to IH, idohartogsohn@gmail.com.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Bar Ilan University Interdisciplinary Studies Unit Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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The influence of ceremonial settings on mystical and challenging experiences occasioned by ayahuasca: A survey among ritualistic and religious ayahuasca users

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Recent studies have recognized the importance of non-pharmacological factors such as setting to induce or promote mystical experiences or challenging experiences among ayahuasca users. This study aimed to evaluate the association between the setting in which ayahuasca is consumed and the intensity of mystical and challenging experiences considering three ayahuasca using traditions (União do Vegetal, Santo Daime and neo-shamanic groups). A cross-sectional analysis was performed on survey data collected online from 2,751 participants. The Setting Questionnaire for the Ayahuasca Experience (SQAE) was used to evaluate six dimensions of the setting characteristics. The Mystical Experience Questionnaire (MEQ) and the Challenging Experience Questionnaire (CEQ) were used to quantify the psychedelic experience. Ratings on every SQAE setting dimension were negatively correlated with ratings of the CEQ (r values between 0.21 and 0.36) for all ayahuasca using traditions. Regression analysis revealed that ratings on four SQAE dimensions (Social, Comfort, Infrastructure and Decoration) explained 41% of the variance in CEQ ratings. Associations between SQAE and MEQ ratings were relatively weak and confined to the dimensions Leadership and Comfort, explaining 14% of the variance in MEQ ratings. Ratings of Social context were higher among members of União do Vegetal compared to Santo Daime and neo-shamanic members. Ratings of Infrastructure, Comfort and Decoration were more consistently correlated with MEQ in the neoshamanic tradition compared to the other traditions. This study shows that the setting is an important moderator of a challenging experience under ayahuasca. Maximizing the quality of the setting in which ayahuasca is taken will reduce the chance of a challenging experience while contributing positively to a mystical experience. The present findings can be considered when designing rituals and the (social) environment of ayahuasca ceremonies, and indicate that the SQAE

questionnaire can be employed to monitor the influence of ceremonial settings on the ayahuasca experience.

KEYWORDS

ayahuasca, setting, Santo Daime, UDV, neo-shamanic, mystical experiences, challenging experiences

Introduction

Ritualistic and religious use of psychedelic substances such as ayahuasca has been reported to occur in several South-American Indigenous cultures (Richards, 2008; Labate and Feeney, 2012; Carbonaro et al., 2016; Santos et al., 2017; Miller et al., 2019). Ayahuasca is a *N,N*-dimethyltryptamine (DMT) and β -carboline-rich decoction, traditionally made from the *Banisteriopsis caapi* vine with leaves of *Psychotria viridis* (Labate and Feeney, 2012). β -carboline alkaloids such as harmine, harmaline and tetrahydroharmine function as monoamine oxidase inhibitors (MAOI) allowing DMT to reach the central nervous system for a prolonged period of time. This leads to intense alterations in perception and sensory integration and the induction of an altered state of consciousness (McKenna et al., 1998; Riba et al., 2001; Tupper, 2008; Palhano-Fontes et al., 2015).

From the 1930s on, ayahuasca consumption expanded to syncretic religious groups. The most widespread today are União do Vegetal (UDV) and Santo Daime (McKenna et al., 1998; De Rios and Grob, 2005). These were mainly established in Brazilian urban centers, and by the end of the 1980s, they had also spread throughout Europe and North America (Metzner, 2014; Hartogsohn, 2021). During this period, neoshamanic rituals— Influenced by Indigenous practices, Eastern religions and the previous syncretic ayahuasquero groups—also spread through Brazil and Europe (Metzner, 2014; Ivanescu and Berentzen, 2020). Consumption of Ayahuasca is allowed in Brazil for religious purposes, but in certain European countries (e.g., Italy, France) ayahuasca is a scheduled substance because of its assumed threat to public health (Labate and Feeney, 2012; Labate and Cavnar, 2014).

Within the UDV, Santo Daime and neoshamanic practices, some common elements can be observed, such as the concepts of healing (either physical or metaphysical) and spiritual growth. All three of these practices have leaders responsible for studying their doctrines and managing the rituals (Goulart, 2006; Hartogsohn, 2021). Doctrines are taught during the ayahuasca ceremony: in the Daime through lyrics (MacRae, 2004; Hartogsohn, 2021), in the UDV through question and answers and singing of *a cappella* chants (Goulart, 2006), and in neoshamanic rituals through chanting, hearing of songs or recordings and shamanic practices such as smoke blowing and herbal sprays (Gonzalez et al., 2021). In both UDV and Santo Daime, Christian symbolism predominates, with influences of other religious groups, such as

spiritists and Afro-Brazilian religions. The latter have added elements of setting and symbolic repertoire, such as the belief in the presence of human and nature spirits (MacRae, 2004; Goulart, 2006). Traditional shamanism can be defined as a set of beliefs and ancestral rites, present in different cultures, each with its own particularities. This set of spiritual practices is centered around the figure of the shaman, who promotes altered states of consciousness in support of physical and emotional healing (Von Stuckrad, 2002; Townsend, 2004). The contact of traditional shamanism with Western culture from the 1970s promoted a series of modifications and syncretism that culminated in the neo-shamanic movement (Von Stuckrad, 2002). Besides the characteristics of traditional shamanism, Neo-shamanism includes elements from Eastern, Pagan, and Christian religions, among others (Townsend, 2004). Furthermore, it focuses on spiritual development from an individual logic, departing from the sense of collectivity that is characteristic of traditional shamanism (Von Stuckrad, 2002).

During these religious rituals, practices are performed aiming to facilitate the occurrence of mystical experiences and to prevent unpleasant or challenging experiences in the participants, such as singing religious music and choosing the space decoration and colors (Hartogsohn, 2021). It has also been noted that mystical experiences contain common elements that occur independent of their historical, cultural and religious context (Stace, 1960; MacLean et al., 2012; Roseman et al., 2018), such as a sense of unity, peace (Garcia-Romeu et al., 2015), sacredness, ineffability and joy, and the absence of time and space (MacLean et al., 2012). In addition, the consumption of psychedelic substances can also produce challenging experiences (Cohen, 1960; Barrett et al., 2016). Negative experiences may vary in intensity and duration and may result in transient outbursts of paranoia, sadness, anger, delirium, depersonalization, dissociation and confusion (Johnson et al., 2008; Barrett et al., 2016).

Specific causes and conditions that induce or promote mystical experiences (MacLean et al., 2012) or challenging experiences (Barrett et al., 2016) are not well understood. However, recent studies have recognized the importance of non-pharmacological factors, such as set and setting, as moderators of the behavioral and psychological effects of psychedelics (Carbonaro et al., 2016; dos Santos et al., 2016; Hartogsohn, 2016; Roseman et al., 2018). Set refers to the psychological state, intentions and expectations of individuals in psychedelic ceremonies, while setting refers to the context in which a ceremony occurs. The parameters of the setting can refer

to sensory modes (e.g., auditory, musical; visual, tactile), the social environment (e.g., being alone or in a group, in nature or in a building, presence of a leader), the set of those present in a ceremony that surround an individual (Leary et al., 1963; Shewan et al., 2000; Hartogsohn, 2016, 2017; Haijen et al., 2018), or group dynamics and leadership (i.e., facilitators or hosts) before, during, and after ceremonies with psychedelics (Trope et al., 2019). Setting parameters may increase an individual's sensitivity to a psychedelic experience and amplify its subjective effects (Carhart-Harris et al., 2018).

A tool to assess an individual's perception of the setting during an ayahuasca ritual was recently developed by our group (Pontual et al., 2021). This Setting Questionnaire for the Ayahuasca Experience (SQAE) was developed from interviews with experienced ayahuasca users and validated using a large survey sample (Pontual et al., 2021) and allows the qualification of six major setting parameters (Leadership, Decoration, Infrastructure, Comfort, Instruction and Social Context).

Considering the attention given to the importance of ritualistic setting for the consumption of Ayahuasca, and its possible effects on mystical and challenging experiences, there is a need to analyze correlations between aspects of predominant ritualistic settings of ayahuasca with occurrences of mystical or challenging experiences. Therefore, the present study applied the SQAE aiming to evaluate the association between setting parameters during ayahuasca ceremonies and the occurrence of mystical and challenging experiences across three ayahuasca using traditions, i.e., UDV, and Santo Daime in religious Brazilian traditions and neo-shamanic practices in Western cultures.

Materials and methods

Participants and procedure

An online questionnaire was developed using Qualtrics. Data were collected in Brazil and the Netherlands. As a recruitment method for the Brazilian participants, invitations with a weblink to participate in the study were sent to members of different ayahuasca churches and neoshamanic communities. An institutional email was also sent by the head office of UDV church in Brazil to all registered members, encouraging them to participate in the study. For the data collection in the Netherlands invitations were sent to Dutch ayahuasca organizations that hosted retreats. The Dutch participants were not linked to an institution, like Daime or UDV.

Participants were asked to complete the questionnaire while thinking about their most recent ayahuasca experiences. Inclusion criteria for this study were: being at least 18 years old; having consumed ayahuasca for at least 6 months before the study. Exclusion criteria were: not having filled out all the fields in the survey; having completed it in less than 5 min (considered insufficient time); or giving the same answer to all the items (interpreted as invalid data). From a total of 3,472 participants,

2,751 were considered valid, 2,263 participants from Brazil and 488 from the Netherlands. Participants were also classified in one of three traditions; (Neo)shamanic (i.e., ayahuasca or an ayahuasca analogue was taken in a setting that was hosted by a shaman or in a shamanic ritualistic tradition), UDV, or Santo Daime.

Instruments

Mystical experience questionnaire

Mystical Experience Scale (Mystical Experience Questionnaire – MEQ-30): is a self-report instrument, developed by Pahnke (1969) and validated by Barrett et al. (2015). Evidence of its validity for the Brazilian population was explored by Schenberg et al. (2017). Its reduced version contains 30 items. Participants were asked the degree to which they experienced a list of phenomena in their last ayahuasca experience ranging from (0 = not at all to 6 = extremely). Example items are: “experience of pure being and pure awareness” and “experience of unity with ultimate reality”. Evidence of its validity for the Brazilian population was explored by Schenberg et al. (2017), who demonstrated a satisfactory internal reliability index by Cronbach's Alpha. The MEQ is a tool that has been widely used internationally to assess unique mystical experiences from the ingestion of psychedelics (MacLean et al., 2012).

Challenging experience questionnaire

The CEQ is a self-report instrument developed and validated in 2016 by Barret and Griffiths (Barrett et al., 2016). It aims to assess the phenomenological profile of psychedelic experiences characterized as challenging. The instrument is composed of 26 items and seven factors: sadness, fear, death, insanity, isolation, physical suffering, and paranoia. Participants were asked to rate the extent to which they experienced a list of phenomena in their most recent ayahuasca experience on a 5-point scale ranging for 0 = not at all, to 6 = extremely. Example items are “isolation or loneliness” and “fear that I may lose my mind or go insane.”

Setting questionnaire for the ayahuasca experience

The SQAE is a self-report instrument developed based on interviews with ayahuasca drinkers from different ritualistic backgrounds and levels of experience. It was developed by Pontual et al. (2021) and it aims to evaluate different elements of the setting of ritualistic ayahuasca consumption. It was validated among a sample of 2,994 Brazilian ayahuasca drinkers, presenting evidence of validity for its theoretical model composed of 6 dimensions with 28 Likert-type statements and supplementary descriptive information about the ritual. The six dimensions include: Social (i.e., how participants felt within the group, e.g., “I felt among equals in that group.” and “Looking at other people bothered me”), Leadership (i.e., how participants saw the organizers as experienced leaders or not; e.g., “The organizers showed themselves to be inexperienced” and “I entrusted all my

concerns to the ritual support group”), Decoration (i.e., how they felt in the space; e.g., “The ceremony was held in a sufficiently open space”), Infrastructure (i.e., facilities and logistical details; e.g., “I found the bathroom to be inadequate”), Comfort (i.e., how comfortable the space was; e.g., “I missed a support for the spine, head or arms” and “The place where I was sitting/lying bothered me”) and Instructions (i.e., how they were given preparatory instructions about the event; e.g., “I was previously instructed about the whole ritual” and “There were times when I felt that there was a lack of instruction”). Scores on each item ranged from 1 (strongly disagree) to 5 (strongly agree), with higher scores meaning higher agreement on the importance of this element during the ritual (negative statements are reverse-scored). In addition, some questions are contained to explore additional ceremony features such as the use of live, recorded, religious, Indigenous and other types of music (participants indicate if those elements were present yes/no), presence of activities such as dancing or text reading, and how enjoyable they felt – answers starting at 0 (This activity was not performed.) and ranging from 1 (It was very unpleasant) to 6 (very pleasant) –, presence of natural elements (e.g., fire, animals, 0 = not present, 1 = present), and other possible disruptive stimuli (e.g., noise, insects 1 = did not bother me, 4 = bothered me a lot). It was originally developed in Brazilian Portuguese and English by Pontual et al. (2021) and translated to Dutch for the purpose of the present study.

Data analysis

Statistical Package for the Social Sciences (SPSS), version 26 (SPSS, Chicago, IL, United States) was used to perform the descriptive and inferential analyses. The calculation of means, standard deviation, kurtosis, and skewness were used for the descriptive analyses. One-way ANOVAs were conducted to analyze differences in setting ratings between traditions. Bonferroni corrected, *post hoc* contrasts were conducted to assess differences between separate traditions. Two-tailed Pearson correlations were performed between SQA ratings and ratings from MEQ and CEQ. Correlations stronger than $r > 0.10$ were considered relevant, and results with a $p < 0.01$ were considered significant. In addition, regression analyses were used to evaluate SQA parameters as predictors of MEQ and CEQ ratings. In a second step, it was investigated whether traditions differed in their ratings and value of the different setting parameters. In the [Supplementary Material](#), correlations and regressions on how the setting parameters were related to MEQ and CEQ experiences per tradition can be found.

Results

Participants

All participants that were included in the study had consumed ayahuasca within the last 6 months. The study included 47% males

and 53% females. Eleven percent were between 18–23 years old, 19% aged 24–30, 30% aged 31–40, 34% aged 41–60, and 6% > 60 years old. Two percent of the participants completed basic education, 16% middle school and the majority followed some type of higher education (82%). Eight percent of the respondents were first time ayahuasca users, 10% drank less than five times, 13% drank between 5–20 times, 20% between 20–100 times, and 50% drank over 100 times ayahuasca (majority of those were members of the Santo Daime church or UDV). Of the 3,070 participants, 1,041 were categorized as (neo)shamanic, 1,413 as UDV, and 296 as SD. [Figure 1](#) displays the average ratings of mystical (MEQ) and challenging (CEQ) experiences reported by participants on the different subscales, across traditions (see [Figure 1](#)).

Setting questionnaire for the ayahuasca experience

Mean scores were calculated for all SQA dimensions for the total group and for each tradition separately (see [Figure 2](#)). Their ratings at the Leadership and Infrastructure dimensions were highest, followed by Social aspects. Firstly, it was examined whether setting characteristics were related to reports of mystical and challenging experiences, as measured with MEQ and CEQ. Correlation analyses between the total MEQ and CEQ scores and setting characteristics indicated that for MEQ, only Leadership correlated positively with MEQ total score ($r = 0.132$, $p < 0.001$). All SQA subscales correlated negatively with the level of self-reported challenging experiences (see [Figure 3](#)). That is, higher endorsement of the importance of all setting elements was associated with fewer self-reported challenges. Correlation between the presence of stimuli and natural elements and self-reported mystical and challenging experiences can be found in the [Supplementary Material](#).

In a second step, using regression analyses, it was investigated whether certain setting elements predicted higher MEQ and CEQ scores. A linear regression analysis was conducted with MEQ total score as dependent variable and the six SQA dimensions as independent variables. Stepwise backward elimination with a criterion of $p < 0.05$ resulted in a model in which “Comfort” and “Leadership” were predictive of MEQ scores. The model accounted for 14% of the variance. A similar procedure was followed for CEQ scores, resulting in the final model with the elements “Social,” “Decoration,” “Comfort,” and “Instructions” being predictive of CEQ ratings, together explaining 41% of the variance of CEQ ratings (see [Tables 1](#) and [2](#)).

The second objective was to see whether setting elements differentially affected MEQ and CEQ ratings in the three ayahuasca using traditions. [Figure 2](#) displays mean scores on the six main setting dimensions per tradition. Although all traditions rated Leadership and Infrastructure as most important setting elements, followed by Social, Instructions, Comfort and

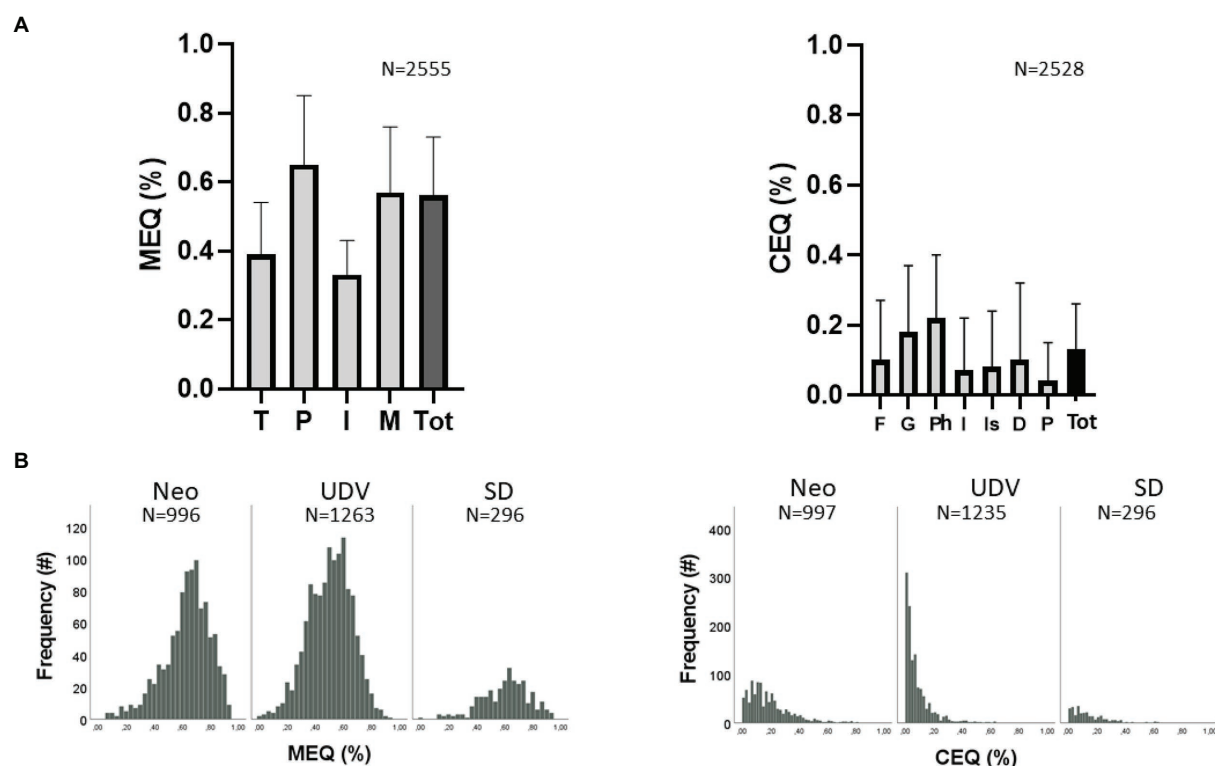


FIGURE 1

Mean (SD) subscale ratings and total scores of the Mystical Experience Questionnaire (MEQ) and Challenging Experience Questionnaire (CEQ) across the three ayahuasca conditions (panel A) and the frequency distribution of the total MEQ and CEQ scores per tradition (panel B). MEQ labels indicate transcendence (T), positive mood (P), ineffability (I), mysticism (M), and total score (Tot). CEQ labels indicate fear (F), grief (G), physical distress (P), insanity (I), isolation (Is), death (D) paranoia (P), and total score (Tot).

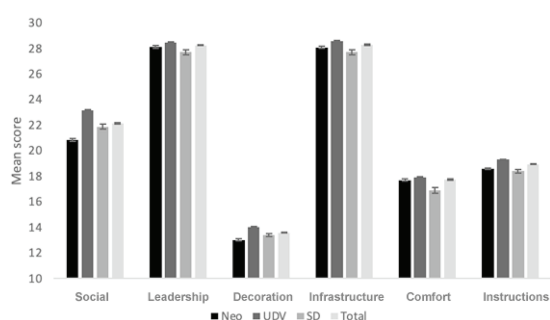


FIGURE 2

Mean Setting Questionnaire for the Ayahuasca Experience (SQAE) ratings. Specified for the entire sample (Total) and by tradition (Neo, UDV, SD). All between tradition p 's < 0.005, except Comfort – Neo vs. UDV, and Instructions – Neo vs. SD.

Decoration (see Figure 2), there were significant differences between traditions. One-way ANOVA showed that ratings at all SQAE dimensions significantly differed between traditions (all F 's > 10.48, all p 's < 0.001). The largest difference between traditions was found for the Social subscale ($F(2, 2,749) = 178.526$, $p < 0.001$) with UDV rating this as more important than neo-shamanic and SD.

Separate correlations were calculated between ratings of the six setting dimensions and MEQ/CEQ ratings per tradition. As can be seen in Table 3, setting dimensions were more positively correlated to MEQ ratings in the neo-shamanic and Santo Daime traditions than in the UDV tradition. For CEQ ratings, in all traditions higher ratings of all setting dimensions were inversely related to CEQ ratings, albeit stronger in the religious traditions than in the neoshamanic groups.

The setting questionnaire also inquired about the presence of secondary elements such as music, noise and activities performed.

Chi square analyses were conducted to see whether the presence of different music elements differed across traditions. Figure 4 gives the percentages of "yes" responses to the presence of different musical elements per tradition. For all elements, chi square tests were significant (all $X^2 > 1.762$, all p 's < 0.001).

Across traditions music elements contributed to the mystical experience with the highest positive correlations existing between MEQ and music in a foreign language ($r = 0.301$, $p < 0.001$), religious music ($r = 0.221$, $p < 0.001$) and *icaros* (South-American traditional ayahuasca singing; $r = 0.314$, $p < 0.001$). When exploring differences between traditions, we found the above pattern for UDV but not for neo-shamanic groups and Santo Daime. That is, for neo-shamanic participants, only *icaros* were positively

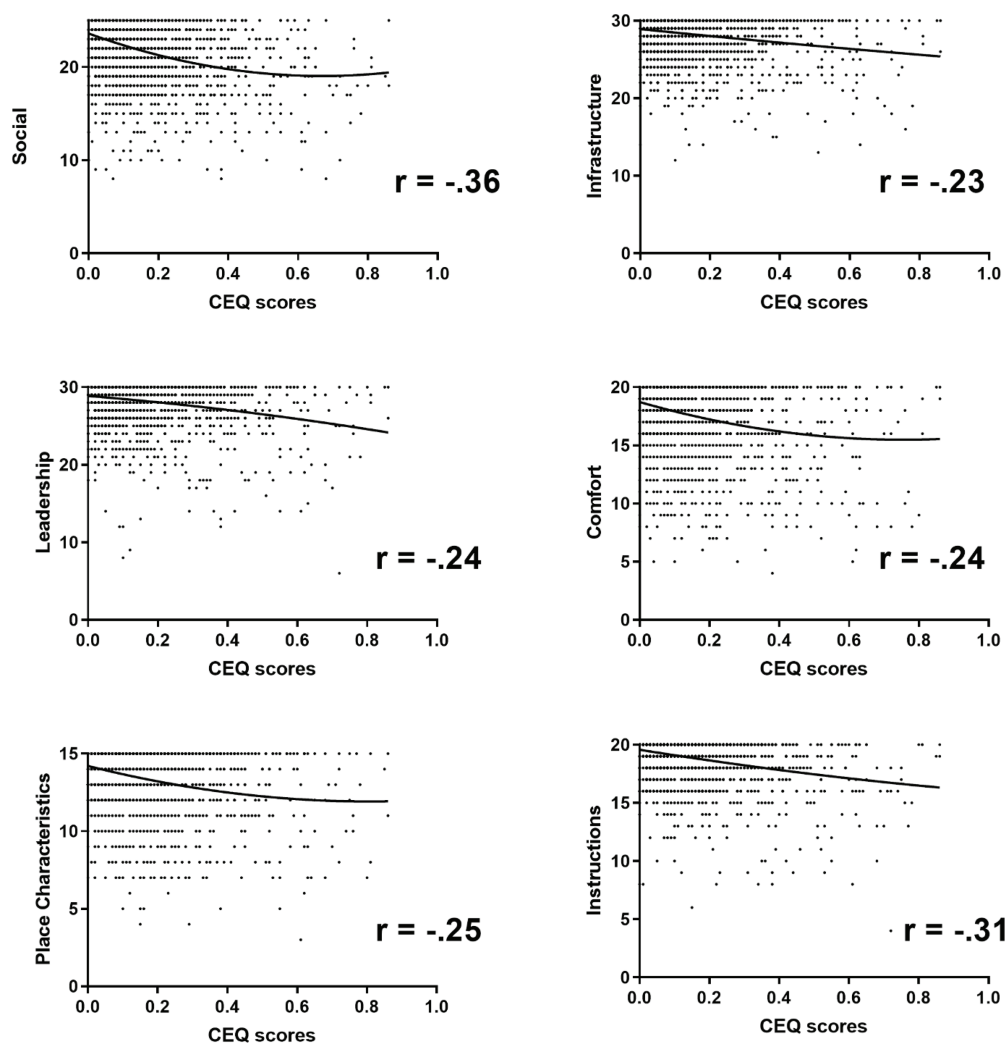


FIGURE 3
Correlations between SQAE scales (Social, Leadership, Decoration, Infrastructure, Comfort, and Instructions) and the CEQ total score.

TABLE 1 Summary of linear regression with Mystical Experience Questionnaire (MEQ) and Challenging Experience Questionnaire (CEQ) as dependent variables and the setting elements (social, leadership, decoration, infrastructure, comfort and instructions) as independent variables.

	<i>B</i>	<i>SE</i>	β	<i>t</i>	<i>p</i>
MEQ					
Comfort	0.002	0.001	0.041	1.960	0.050
Leadership	0.008	0.001	0.118	5.618	<0.001
CEQ					
Social	-0.010	0.001	-0.232	-10.81	<0.001
Decoration	-0.003	0.001	-0.047	-2.61	0.031
Comfort	-0.005	0.001	-0.111	-5.54	<0.001
Instructions	-0.010	0.002	-0.138	-6.34	>0.001

B, regression coefficient; SE, standard error; β , beta.

correlated to MEQ scores ($r=0.101$, $p=0.001$). For Santo Daime only silence was related to mystical experiences ($r=0.149$, $p=0.010$). Only for UDV, the presence of *icaros*/indigenous music obtained a higher correlation with

both mystical and challenging experiences ($r=0.162$, $p<0.001$). It is noteworthy that in the case of the UDV that almost 100% of participants reported the presence of recorded music, a regular feature of UDV sessions. However, less than 50%

TABLE 2 Summary of linear regression by tradition [neo-shamanic, União do Vegetal (UDV) and SD] with MEQ and CEQ as dependent variables and the setting elements (social, leadership, decoration, infrastructure, comfort and instructions) as independent variables.

	<i>B</i>	<i>SE</i>	β	<i>t</i>	<i>p</i>
MEQ neo-shamanic					
Social	0.010	0.002	0.212	6.473	<0.001
Infrastructure	0.008	0.002	0.123	4.032	<0.001
UDV					
Social	0.005	0.002	0.086	2.731	0.006
Leadership	0.007	0.002	0.099	3.129	0.002
SD					
Stability	0.016	0.004	0.226	3.985	<0.001
CEQ neo-shamanic					
Social	−0.005	0.002	−0.115	−3.82	0.001
Leadership	−0.007	0.002	−0.140	−3.95	<0.001
Comfort	−0.005	0.002	−0.102	−3.04	0.002
UDV					
Social	−0.008	−0.001	−0.202	−6.662	<0.001
Decoration	−0.005	−0.002	−0.084	−2.775	0.006
Infrastructure	−0.003	−0.001	−0.062	−2.167	0.030
Comfort	−0.006	−0.001	−0.181	−6.164	<0.001
SD					
Social	−0.013	0.002	−0.329	−5.733	<0.001
Comfort	−0.008	0.002	−0.221	−3.854	<0.001

B, regression coefficient; SE, standard error; β , beta.

TABLE 3 Correlations between the MEQ/CEQ and Setting Questionnaire for the Ayahuasca Experience (SQAE) elements (social, leadership, decoration, infrastructure, comfort and instructions) by tradition.

SQAE subscales	MEQ			CEQ		
	Neo	UDV	SD	Neo	UDV	SD
Social	0.260**	0.133**	0.186*	−0.202**	−0.325**	−0.427**
Leadership	0.192**	0.139**	0.218**	−0.227**	−0.220**	−0.314**
Decoration	0.170**		0.168*	−0.141**	−0.254**	−0.231**
Infrastructure	0.210**		0.124*	−0.187**	−0.208**	−0.312**
Comfort	0.176**			−0.191**	−0.304**	−0.367**
Instructions	0.188**	0.109**	0.226**	−0.293**	−0.205**	−0.311**

* $p < 0.010$ and ** $p < 0.001$.

reported religious music and less than 40% indicated the presence of live music, which probably indicates a flaw in the instrument in detecting the traditional *a cappella* UDV chants, named chamadas (“callings”), which are performed live and a key element in absolutely all UDV sessions. They are not understood and referred to as “music,” and the idea of “singing” does not apply to them (chamadas are “done”; not “sung”). Therefore, it is possible that many UDV members did not classify chamadas in any of the available options. The instrument should be corrected to include these chants in a more explicit way and data should be interpreted with caution.

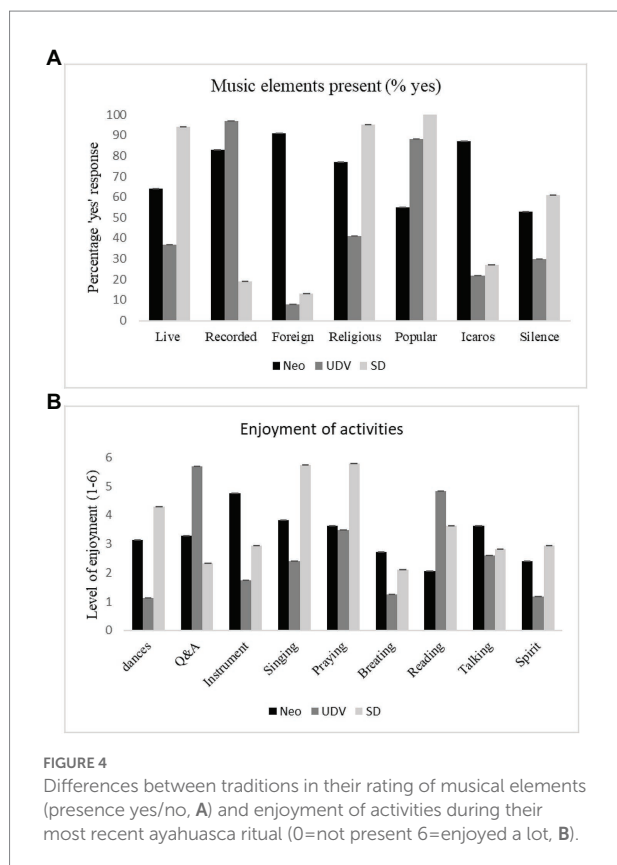
Participants were also asked how much they enjoyed certain activities that were performed during the ceremonies or rituals in which they most recently drank ayahuasca. Figure 4B shows how much an activity was enjoyed in each of the traditions.

Except for “praying” and “talking,” all traditions differed significantly in their enjoyment of the activities (all F 's > 66.52 , all p 's < 0.001).

Only for the neo-shamanic tradition, dancing and praying were positively related to the level of mystical experiences ($r = 0.234$ and $r = 0.268$, respectively), not for the other traditions. In none of the traditions, activities were related to the level of challenging experiences.

Discussion

The present study investigated the association between setting parameters during ayahuasca ceremonies and the occurrence of self-reported mystical and challenging experiences of ayahuasca



users from UDV, Santo Daime and neoshamanic traditions, as well as whether setting ratings differed between the three ayahuasca traditions. Total scores in all SQAE subscales negatively correlated with total scores in the CEQ. Therefore, higher (quality) ratings of setting dimensions during the ceremonies were associated with a lower incidence of challenging experiences. A positive correlation was found between (quality) ratings of setting dimensions and ratings of mystical experience. Regression analyses including all denominations showed that higher ratings of feeling part of the social group (Social dimension), feeling physically comfortable, and at ease with the decorations of the space (Decoration dimension) and having had adequate instructions (Instructions) predicted fewer challenging experiences. Analyses per tradition showed some minor differences between traditions, with UDV having Infrastructure, and neo-shamanic having Leadership as one of their predictors. Adequate Leadership and Comfort were associated with higher self-reported levels of mystical experiences in the regression analyses including all denominations, but analyses per tradition showed discrepancy among traditions, with the Stability dimension being the sole predictor to show in the Santo Daime regression.

The influence of leadership on the occurrence of mystical experiences may be related to the feeling of being guided by a more advanced practitioner, which could increase the level of confidence in the experience. Clinical trials conducted with the use of psychedelics have suggested the importance of having someone with a non-judgmental posture caring for the participant and

guiding their experience (Johnson et al., 2008; Carhart-Harris et al., 2018). Considering the Social dimension, feeling integrated with other participants within the ritual was found to be important for fewer challenging experiences. This may be related to a large part of the sample being composed of members of the UDV and Santo Daime, churches where the sense of community is reinforced (MacRae, 2004; Hartogsohn, 2017) and has also being reported as correlated to positive outcome of psychedelic rituals (Kettner et al., 2021). Similarly, the influence of decoration was also related to the prevention of challenging experiences, as found by Hartogsohn (2017), who cited the importance of space organization for the therapeutic potential with psychedelics. Decorations that conform to spiritual beliefs can also provide a sense of safety and wholeness.

The second objective was to assess whether the setting dimensions were rated differently between the three traditions. Ratings in all setting dimensions differed significantly between all traditions and were most apparent for ratings in the Social Dimension. Ratings in the Social Dimension were highest among UDV members, followed by those of Santo Daime, and lowest among followers of the neo-shamanic tradition. This finding can be explained by differences in social elements among each tradition. Santo Daime and UDV are religions in which their members attend weekly or fortnightly rituals (De Rios and Grob, 2005). Therefore, the social context of these traditions is associated with a strong sense of community. The promotion of other activities within the religion and outside the ritual itself also reinforces the creation of bonds. Apud (2015) and Townsend (2004) highlight the fact that in neo-shamanic settings it is common that motivations of visitors are either driven by curiosity or the need for psychological healing due to existential conflicts, using this as a psychotherapeutic device for specific problems and transformations in their daily lives. Therefore, a stronger focus on the individual experience is observed, independent of others who may be present at the ceremony. Accordingly, its social context relates more to the intention of a new experience, and less to the affiliation with a religious doctrine or community (Apud, 2015).

Infrastructure, Comfort and Decoration ratings were more consistently correlated with the MEQ in the neo-shamanic tradition compared to the religious traditions. In neoshamanic ceremonies participants usually have an individual experience (i.e., laying on their mattress) and there is little group interaction, in comparison with Santo Daime e UDV (Goulart, 2006; Hartogsohn, 2021). This may explain the neoshamanic emphasis on individual experience-oriented elements to induce mystical experiences, such as good site infrastructure and feeling comfortable. Conversely, within a Santo Daime or UDV ritual other factors (i.e., social) were reported to be more important. As shown in Figure 4, the presence of group activities such as singing and praying were rated higher among members of Santo Daime (see also MacRae, 2004), whereas questions and answers and reading were more valued among UDV members.

Regarding other elements in addition to the SQAE factors, music has already been described as an important element of the psychedelic consumption setting (Zinberg, 1984; Barrett

et al., 2018; Carhart-Harris et al., 2018; Hartogsohn, 2021). Analysis of music elements revealed that MEQ ratings were positively correlated with music in foreign languages, religious music and *icaros*, across the three traditions. This association was most apparent in the UDV, whereas in the neo-shamanic tradition and Santo Daime correlations with MEQ were specific to *icaros* and silences, respectively. These differences may be related to the cultural load and meanings attributed to the musical element in each tradition. Regarding the neoshamanic tradition, *icaros* assume a central conducting role (Labate and Cavnar, 2014; Apud, 2015), and may be associated with an expression of visual effects (Labate and Cavnar, 2014). Apud (2015) points out that they can also serve as a psychological support, at times when the experience becomes chaotic. In Santo Daime, the songs (mostly with religious content) are encouraged to be sung by all participants, and acquire a significance that contributes to increase the closeness among them (Hartogsohn, 2021).

Likewise, the ratings of activities performed during the ayahuasca ceremonies significantly differed among the traditions. Only for the neo-shamanic tradition such activities, i.e., dancing and praying, were positively related to the level of mystical experiences, despite dancing and praying being core elements of the various religious traditions (MacRae, 2004; Hartogsohn, 2021). The fact that the participants of Santo Daime and UDV frequently attend rituals might cause these activities to be perceived as commonplace, decreasing their impact on the mystical experience.

The current data also comes with limitations. The majority of the sample consisted of UDV members and visitors of neo-shamanic ceremonies, with members of Santo Daime only comprising about 10% of the entire sample. Ratings of the latter group therefore might be less representative than those obtained from the other traditions. Furthermore, about 50% of the sample had drunk ayahuasca over 100 times, which may have affected their reports of the relevance of the setting parameters, with the perception of adverse effects possibly varying according to the participants' length of experience (Durante et al., 2020).

Finally, correlations obtained in large datasets are easily inflated. Even very low correlations can achieve statistical significance with very large sample sizes, even in the absence of clinical relevance. The risk of overinterpreting the current findings was reduced by thresholding p and r values, however, it cannot be totally excluded.

This study shows that the setting seems to be an important moderator of mystical and challenging experiences during ayahuasca ceremonies, which is in agreement with the studies that reinforce this influence of the setting for the use of ayahuasca (Thomas et al., 2013; Hartogsohn, 2021) and other psychedelic substances (Hartogsohn, 2016; Carhart-Harris et al., 2018; Haijen et al., 2018). Maximizing the quality of the setting in which ayahuasca is consumed may increase the likelihood of a mystical experience and reduce the chance of a challenging experience.

The present findings can be taken into account when designing the rituals and (social) environment of ayahuasca ceremonies, and indicate that the SQAE questionnaire can be employed to monitor the influence of ceremonial settings on the ayahuasca experience.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Comitê de Ética em Pesquisa da Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto – USP CAAE: 64130517.8.0000.5407. The patients/participants provided their written informed consent to participate in this study.

Author contributions

AP, AD, KO, and JR devised the project, designed the study, and developed the theory. AP, AD, and KO performed data analysis. JR verified the analytical methods. All authors provided critical feedback and helped shape the research, analysis, and manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary materials

The Supplementary Materials for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpsyg.2022.857372/full#supplementary-material>

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