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The cumulative social adversity hypothesis of psychosis: Intolerance of uncertainty and aberrant salience mediate the association between humiliation and psychotic-like experiences

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Background: The social defeat hypothesis, here framed as cumulative social adversity (CSA) to avoid disempowering terminology, posits that individuals with long-term experience of an unwanted, subordinate position present an elevated risk of psychosis. It has been observed that humiliation might be the most central component of the CSA hypothesis that increases the risk of psychosis through specific information processing patterns. The present study aimed to further investigate as to whether two cognitive processing patterns, i.e., aberrant salience (AS) and intolerance of uncertainty (IU), play a mediating role in the association between CSA and psychotic-like experiences (PLEs).

Methods: A total of 1308 non-clinical young adults (aged 31.1 ± 5.9 years, 47.9% men) were assessed with self-reports recording the occurrence of PLEs, AS, IU, and cumulative humiliation via computer-assisted web interview

1 Introduction

Psychosis exists on a continuum, with a range of experiences that can be observed even in healthy individuals (1). These subclinical phenomena, observed in healthy individuals, are commonly referred to as psychotic-like experiences (PLEs). They cover perceptual abnormalities and delusion-like experiences that show low severity and impact on general functioning. Their lifetime prevalence has been estimated at 6% and in most individuals they occur as transient experiences (2). Nonetheless, there is evidence that PLEs might precede the onset of psychosis, but might also occur in the context of various mental disorders that do not represent the psychosis spectrum (3, 4). The etiology of PLEs and possible contribution to the development of mental disorders are still unclear.

Several factors have been implicated in the development of PLEs, i.e., psychosocial factors, a history of childhood trauma, and cognitive processing differences (3). Psychosocial factors that might influence psychosis development via dopaminergic disruptions are conceptualized within the social defeat hypothesis (5). Considering the fact that the term “social defeat” might be disempowering towards excluded groups, in this article we propose the term cumulative social adversity hypothesis of schizophrenia (CSA). We aim to retain continuity with the original model developed by Selten (5) highlighting the role of persistent exclusion, marginalisation, and subordination in sensitising dopaminergic pathways, while avoiding language that implies individual weakness. In accordance with the CSA framework, individuals who feel vulnerable in social interactions (6), may be more prone to develop cognitive processing differences (7) and increased levels of anxiety (8) that ultimately lead to the development of PLEs (9). Individuals whose sense of self naturally varies across contexts and who engage with others’ mental states in ways that differ from typical patterns may be more inclined to interpret certain interpersonal situations as humiliating. Such interpretations could, in turn, activate increased threat-detection processes and contribute to the occurrence of PLEs (6). Perhaps more importantly, humiliation can be enhanced by prolonged subordinate social position due to migration, low income, or minority status (10). In our most recent study, we found that cumulative humiliation may be the most central aspect of CSA that is most closely related to the occurrence of PLEs (11).

Intolerance of uncertainty (IU) refers to a negative cognitive response to ambiguity, characterized by the tendency to perceive possibility of a negative event as unacceptable and threatening, regardless of its actual likelihood (12). The construct is grounded in the premise that IU may contribute to the development of anxiety, which can be conceptualized as a complex preparatory response to potential, yet unidentified, threats (13–16). Importantly, uncertainty itself may be experienced as threatening, thereby intensifying anxiety and fostering a false sense of certainty regarding threat presence (12, 17). Although

IU is recognized as a transdiagnostic risk factor for a range of mental disorders (18, 19), it has been most extensively examined in the context of anxiety disorders and depression (12, 14, 19–22, 60). Moreover, evidence suggests that IU is linked to heightened threat generalization and may facilitate early, automatic detection of ambiguous stimuli, accompanied by alterations in cognitive processing (14, 23). Individuals with high IU may be more likely to draw premature conclusions and adopt rigid beliefs when confronted with ambiguous information, potentially increasing the risk of PLEs (24, 25) and exaggerated assignment of salience (26). This is consistent with the established link between enhanced anxiety and PLEs development that often co-occur during the prodromal phase of psychosis (27, 28). In line with this, recent literature identifies IU as a potential transdiagnostic marker for assessing paranoia across clinical and subclinical populations (19). IU and paranoia may interact to exacerbate levels of negative affectivity and depressive symptoms. IU might therefore be one of the key transdiagnostic dimensions that binds and modulates different symptoms across anxiety, depression, and schizophrenia-spectrum conditions (15, 19, 29). Importantly, this raises the question of whether IU modulates the cognitive, somatic, and behavioral processes underlying anxiety, depression, and psychosis. Supporting this possibility, negative affect and worry (core processes closely linked to IU) have been implicated in both the emergence and exacerbation of psychotic symptoms (30, 31). Consistent with this view, a recent meta-analysis reported elevated IU in individuals meeting criteria for an ‘at-risk mental state’ for psychosis, as well as correlations between IU and psychotic symptoms involving delusions and paranoia in both clinical and nonclinical samples (29).

2 Material and methods

2.1 The sample

The study was conducted by means of online surveys. Invitations were sent through the online platform designed for research surveys, maintained by the polling company (Pollster). Recruitment procedures were implemented in June 2024 and the surveys were conducted using computer-assisted web interview CAWI. The inclusion criteria were age between 18 and 40 years and a negative lifetime history of psychiatric treatment. An age restriction has been implemented, as psychotic disorders most often emerge in younger populations (40, 41). Additionally, participants were selected to reflect the sociodemographic characteristics of the Polish population based on data from 2021. Participants were reassessed after 6 months (June 2024). Some findings from the present cohort were published previously (11). The study received approval of the Bioethics Committee at Wrocław Medical University, Wrocław Poland (approval number: 22/2024).

2.2 Assessments

The participants were assessed with respect to the level of humiliation, AS and PLEs (at baseline and after 6 months) as well as IU (after 6 months). To maintain data reliability, several accuracy measures were integrated into the survey process, both during and after its completion. Participants who did not meet the predetermined accuracy standards were excluded from the final dataset. The exclusion criteria were: excessively short survey completion times (below 30% of the median completion time), failure to pass attention checks (i.e., participants were asked to respond to items requesting them to select a specific answer), inconsistent responses to repeated items, and the presence of random or nonsensical character strings in their responses.

2.2.1 Humiliation

We used the Humiliation Inventory to assess the internal experience of humiliation (42). The inventory consists of 32 self-reported items rated between 1 (“not harmed at all”) to 5 (“extremely harmed”). The original version of this questionnaire includes two subscales, i.e., the cumulative humiliation subscale and the fear of humiliation subscale. The first one measures the severity of lifetime humiliating experiences, while the latter one records the level of anticipation and anxiety regarding future humiliating experiences. In our study, we used the first subscale that is based on 12 items (lifetime experiences of humiliation, e.g., “Throughout your life how seriously have you felt harmed by being excluded?... by being cruelly criticized?... discounted?”). The total score ranges between 12 and 60, where higher scores reflect higher levels of humiliation experiences. The Cronbach’s alpha was 0.961 in the present study.

2.2.2 AS

The Aberrant Salience Inventory (ASI) was used to measure the tendency to assign meaning to irrelevant stimuli. The ASI consists of 29 self-report items (e.g., “Do you sometimes notice small details that you have not noticed before that seem important?”, “Do you ever feel the need to make sense of seemingly random situations or occurrences?”). with yes-or-no responses (rated as 1 or 0). It is based on five subscales (increased significance, senses sharpening, impending understanding, heightened emotionality, and heightened cognition) and has good psychometric properties (32). It has been shown that a higher ASI total score is related to a greater risk of psychosis (7, 35). The Cronbach’s alpha for ASI was 0.925 in the present study.

2.2.3 PLEs

We used the Prodromal Questionnaire-16 (PQ-16) to record the presence of PLEs over the preceding month (43). The PQ-16 has been designed to detect psychosis risk states. It consists of 16 true-or-false items that capture various PLEs (e.g., “I often seem to live through events exactly as they happened before (*déjà vu*)”, “I often hear unusual sounds like banging, clicking, hissing, clapping or ringing in my ears”), along with associated distress rated from 0 (lack of distress) to 4 (

stable two-factor structure, representing both anxious and avoidance components of IU (45). In this study, the Cronbach's alpha of the IUS was 0.901.

2.6 Data analysis

The comparisons across continuous variables between participants completing both assessments and those lost to follow-up (here and after referred to as completers and non-completers) were performed using the Mann-Whitney U test (non-normal distribution) or t-tests (normal distribution). Normality of data distribution was assessed using the Kolmogorov-Smirnov test. Differences with respect to categorical variables were tested using the χ^2 test. Bivariate correlations between humiliation, IU, AS, and PLEs were analyzed using the Spearman's rank correlation coefficients due to non-normal distribution. In bivariate tests, results were interpreted as statistically significant in case of $p < 0.05$. After a series of bivariate tests, the PROCESS macro was used to assess serial mediation (model 6, see: Figure 1). The level of baseline humiliation (T1) was included as an independent variable (X) while the level of PLEs at the second wave (T2) was included as an outcome (Y). The levels of IU and AS (T2) were included as mediators (M). The models were analyzed before and after adjustment of covariates that included age, gender, the level of education, monthly income, and depressive symptoms (T1). Results were presented as standardized coefficients (β) with corresponding 95%CI values. Results were considered statistically significant if the 95%CI did not include zero. It was further explored whether mediation was full or partial (46). In mediation analysis, full mediation occurs when the association between an independent variable (X) and an outcome (Y) is entirely accounted for by one or more mediating variables (M), such that the direct effect of X on Y (controlling for M) is statistically non-significant, while the indirect effect via M is statistically significant. Partial mediation occurs when the indirect effect via M is statistically significant but the direct effect remains statistically significant as well, indicating that X influences Y both through the mediator(s) and through other pathways not captured by the model. All analyses were carried out in the SPSS software, version 28.

3 Results

Altogether, 4756 participants were invited to participate in the present study. In this sample, 1098 individuals (23.1%) reported a positive lifetime history of psychiatric treatment and 1417 individuals declined to participate or were non-responsive (29.8%). Therefore, 2241 individuals (30.3 ± 6.3 years, 53.4% females) completed the baseline assessment. At baseline, the participants were most likely to report a higher education level (49.4%), full-time work status (66.7%), and a monthly income equivalent to 750 – 1,500 USD (53.1%). From the initial sample (n = 2241), 1308 participants (58.4%) completed the second-wave

assessment. Non-completers were younger, were more likely to be men (or reported gender identities other than men and women), had lower education levels, and reported unemployment status (see: Supplementary Table 1).

All constructs planned to be tested in a serial mediation model showed statistically significant and positive correlations (Table 1). Results of serial mediation analysis are reported in Table 2. The same effects were found statistically significant in unadjusted and adjusted analyses. After adjustment for covariates, the direct effect of humiliation on PLEs was not statistically significant (adjusted model: $\beta = 0.045$, 95%CI = $-0.001 - 0.090$). However, two indirect paths linking humiliation and PLEs appeared to be statistically significant. The first one led through AS (without a mediating effect of IU, ($\beta = 0.062$, 95%CI = $0.023 - 0.103$). In turn, the second one led through IU and AS($\beta = 0.029$, 95%CI = $0.018 - 0.042$). Importantly, the indirect path with IU as the only mediator was not statistically significant($\beta = 0.003$, 95%CI = $-0.007 - 0.012$). Also, direct effects of IU on PLEs were not statistically significant ($\beta = 0.012$, 95%CI = $-0.033 - 0.056$

TABLE 2 Results of a serial mediation analysis with adjusted covariates and unadjusted mediations.

Effect	Path	Unadjusted analysis			Adjusted analysis*		
		β	95%CI		β	95%CI	
			LLCI	ULCI		LLCI	ULCI
Humiliation → IU	a ₁	0.342	0.291	0.393	0.214	0.156	0.273
Humiliation → AS	a ₂	0.216	0.163	0.269	0.097	0.038	0.157
IU → AS	a ₃	0.264	0.211	0.318	0.211	0.153	0.269
IU → PLEs	b ₁	0.043	0.002	0.084	0.012	–0.033	0.056
AS → PLEs	b ₂	0.680	0.640	0.720	0.643	0.599	0.687
Humiliation → PLEs	c	0.004	–0.004	0.013	0.045	–0.001	0.090
Humiliation → IU → PLEs	a ₁ b ₁	0.015	–0.002	0.028	0.003	–0.007	0.012
Humiliation → AS → PLEs	a ₂ b ₂	0.147	0.107	0.189	0.062	0.023	0.103
Humiliation → IU → AS → PLEs	a ₁ a ₃ b ₂	0.062	0.047	0.079	0.029	0.018	0.042
Total indirect effect	ab	0.223	0.181	0.266	0.094	0.053	0.136

Statistically significant effects refer to those where 95%CI does not include zero. Age, gender, education, monthly income, and baseline depressive symptoms were included as covariates. AS, aberrant salience; IU, intolerance of uncertainty; PLEs, psychotic-like experiences.

relationship between humiliation and PLEs. Hence, the statistically significant indirect effects identified reflect the unique contribution of each mediator, supporting the specificity of IU and AS as distinct psychological pathways. These results are supported by findings from previous studies indicating the association of low social status with heightened awareness of threat and development of psychotic symptoms (6, 47, 48). Low social status is often linked to, and discussed in the context of, the experience of cumulative humiliation

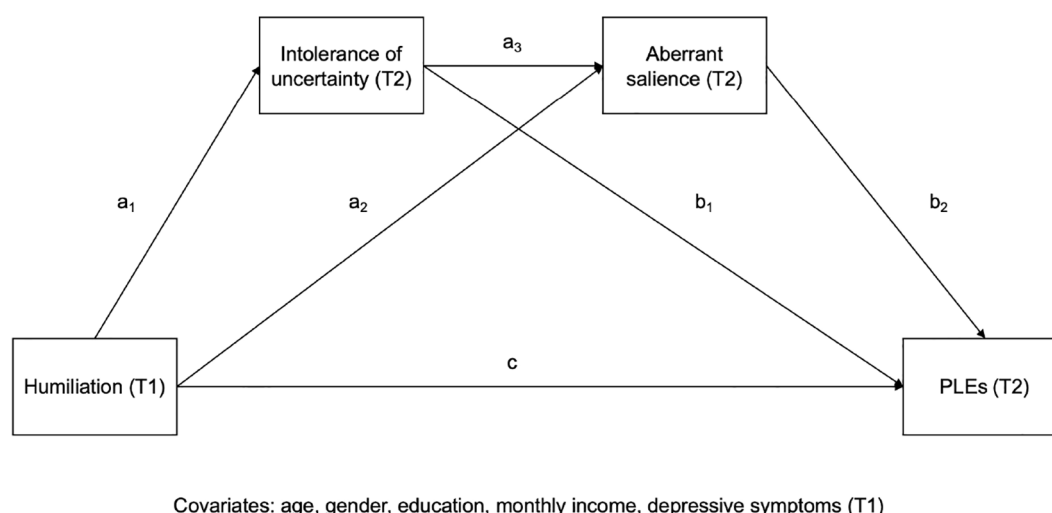


FIGURE 1

The serial mediation model tested in the present study. T1 refers to the first-wave assessment, and T2 represents the second-wave assessment. Paths a_1 – a_3 and b_1 – b_2 represent the indirect effects through the mediators, and c denotes the total (pre-mediation) effect of humiliation on PLEs.

defined as interpretations or judgments that are made early and in response to insufficient evidence (60). Findings from some studies suggest that individuals prone to psychosis also show a specific hasty decision-making style, requiring less information to come to a conclusion compared to healthy controls (55). Importantly, IU has been posited as the phenomenon motivating early termination of data gathering thereby promoting the occurrence of JTC. Our findings warrant the discussion about potential mechanisms explaining the association of humiliation with various cognitive patterns and PLEs.

Finally, existing empirical evidence indicates a relationship between anxiety, depression, and PLEs, demonstrated through mediation analyses (8, 9, 61, 62). This process is commonly referred to as the affective pathway to psychosis (63). Our previous work supported this framework, showing that both depressive symptoms and AS mediated the relationship between humiliation and PLEs (11). In the current study, we considered IU in the context of its established links to anxiety and negative affectivity (12, 64). While our data do not allow firm conclusions about its causal role, the affective implications of IU may offer an additional perspective for understanding how repeated experiences of humiliation could contribute to salience alteration and, in turn, the development of PLEs. The findings of Toh and colleagues (2024) are consistent with this broader view, highlighting the combination of humiliation and anxiety as a potential contributor to PLEs. We suggest that IU could be explored further in future research on affective pathways to PLEs.

Our results suggest that humiliation and AS, and to a lesser extent IU, might be involved in the development of PLEs. This process could potentially lead to the clinical onset of psychosis; however, this line of reasoning requires further investigation. This assumption is based on both theoretical and empirical evidence,

indicating a pathogenetic pathway leading to psychosis via PLEs, AS, and potentially humiliation and IU (3, 11, 28, 65). We consider these factors as causes rather than consequences of early psychosis development. An alternative hypothesis, that early psychotic symptoms increase sensitivity to humiliation, IU and AS, does not account for the presence of IU and AS in individuals without psychosis, including those at familial or environmental risk (27, 29). Moreover, humiliation being externally observable, often occurs before the onset of psychiatric symptoms, particularly during formative developmental periods (e.g. adolescence), making a reverse temporal order less comprehensible (6, 42).

Limitations of the current study should be considered when interpreting the results. The sample was not assessed through clinical interviews to record the presence of underlying psychiatric disorders. Nevertheless, studies indicate that even self-reported PLEs, revealed as false positives after a comprehensive clinical assessment, may still predict the onset of psychosis (

on longitudinal studies with at least three waves or systematic data collection methods that measure the level of humiliation, IU, AS, and PLEs.

Our analysis may provide a more nuanced understanding of how social and cognitive processes interact to contribute to the emergence of PLEs in otherwise healthy individuals. The findings suggest that cognitive processing patterns, such as AS and IU, may serve as key psychological mechanisms through which experiences of humiliation promote the development of PLEs. Specifically, intense feelings of humiliation may prime the perceptual system to detect and attribute heightened significance to ambiguous stimuli, thereby increasing uncertainty and, ultimately, contributing to the occurrence of PLEs. Future studies might therefore consider IU as a novel indicator of the CSA hypothesis, given that IU may enhance the development of AS and, in turn, facilitate the onset of PLEs. Further investigation of the CSA hypothesis could also determine which cognitive processing patterns most strongly reinforce the development of PLEs.

From a clinical perspective, the findings highlight the importance of addressing cognitive processing differences during non-pharmacological interventions, particularly therapeutic approaches that target heightened levels of AS. While reducing AS may remain a primary objective of psychological treatment, our results indicate that targeting IU may also be beneficial, as it could influence AS levels. This holds significance, given that cognitive behavioral therapies commonly employed for anxiety and depression have demonstrated efficacy in mitigating intolerance of uncertainty (64). Moreover, we emphasize the potential value of early psychological interventions aimed at mitigating exposure to prolonged humiliation in order to prevent the emergence of PLEs in vulnerable individuals. Taken together, these findings underscore the potential of combining interventions to enhance treatment efficacy.

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.

Ethics statement

The studies involving humans were approved by Bioethics Committee at Wrocław Medical University, Wrocław Poland (approval number: 22/2024). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

TB: Conceptualization, Writing – original draft, Project administration, Investigation, Writing – review & editing. BM: Formal analysis, Data curation, Writing – review & editing, Software, Methodology, Supervision.

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Conflict of interest

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Supplementary material

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