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Electroconvulsive therapy: from mechanisms to clinical practice

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Electroconvulsive therapy: from mechanisms to clinical practice

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Editorial: Electroconvulsive therapy: from mechanisms to clinical practice

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Editorial on the Research Topic
Electroconvulsive therapy: from mechanisms to clinical practice

Electroconvulsive therapy (ECT) continues to be a mainstay in clinical practice due to its proven effectiveness (1–3), despite its long-standing history of stigma and controversy (4–6). In recent years, alongside technological advancements, clinical attitudes toward ECT have improved significantly (7–10). A cross-sectional survey conducted in Europe reported that early-career psychiatrists generally expressed favorable views toward ECT and a strong interest in expanding their knowledge of the procedure. Access to ECT training during psychiatry residency was associated with a greater likelihood of endorsing its safety and effectiveness, thus reinforcing the importance of continuing education and research in this area (11).

This Research Topic brings together 11 articles that cover a wide range of topics relevant to modern ECT practice. These contributions integrate insights into ECT's mechanisms of action, clinical optimization, and the perspectives of patients, caregivers, and clinicians. By combining recent advances in neurobiological and neuroimmune research with ongoing efforts to improve clinical practice, this Research Topic highlights the dynamic bench-to-bedside trajectory of modern ECT practice.

João et al. conducted a comprehensive review of 26 studies investigating potential biomarkers related to the immune-inflammatory, structural, and cellular mechanisms underlying ECT's therapeutic effects. Their findings provide valuable evidence of reductions in inflammatory markers, increased hippocampal neurogenesis, enhanced BDNF expression, and long-term cellular reprogramming following treatment. This helps to close the gap in our understanding of ECT's efficacy.

Ruiz et al. presented a narrative review focusing on ECT in treatment-resistant depression (TRD). Their analysis highlights ECT's superior efficacy in severe depression episodes, particularly life-threatening conditions where rapid symptom relief is essential, compared with other interventions known to have efficacy in TRD, such as ketamine or

transcranial magnetic stimulation. The review also sheds light on the ECT's impact on neurotransmitter systems, neurogenesis, brain networks, and the immune system, which serve as potential pathways through which ECT exerts its antidepressant effects. The authors emphasize the need for larger, longitudinal, and standardized studies to help us understand the predictors of ECT response and its underlying mechanisms.

Zhang et al. performed a retrospective analysis of the medical records of 895 patients who underwent ECT over the course of 10 months, investigating the incidence and risk factors for a fever episode within 24 hours post-treatment. The authors found that 11.6% of patients developed a fever within 24 hours after treatment, with risk factors including male sex, younger age, being treated in a closed psychiatric ward, and receiving etomidate. These results underline the importance of vigilant temperature monitoring after ECT, especially in high-risk groups.

Wang et al. conducted a retrospective study on the efficacy of ECT in patients diagnosed with schizophrenia, together with factors predicting response. Their study included 237 inpatients in China who had received ECT between January 2023 and December 2024. Their results revealed an overall ECT response rate of 70.46%. Positive predictors of treatment response included first-episode schizophrenia, higher baseline positive symptom scores, and longer EEG seizure duration, while older age and more prolonged illness duration were negative predictors. These findings emphasize the value of ECT in the early treatment of psychosis and the need for personalized ECT treatment protocols.

Bobo et al. conducted a scoping review of 82 studies evaluating ECT for perinatal depression, including its safety and efficacy. Their findings show the rapid alleviation of depressive, psychotic, and catatonic symptoms, with adverse effects typically mild and transient. However, this study also underscores the need for more research in this population, as data on fetal and neonatal safety remain limited.

Li et al. examined trends in ECT use in a psychiatric hospital in China over five years (2015-2020). Of the 22,120 inpatients admitted during this period, 10% received ECT. Emergency department referral, unstable vital signs, and severe impairment in daily functioning were independent predictors of ECT use, highlighting its role in cases requiring rapid symptom relief. This study also observed a decline in ECT utilization, from 13.2% in 2015 to 5.7% in 2020, a trend consistent with global trends.

Patel et al. reported the case of a 35-year-old female patient with TRD and an implanted sacral neurostimulator for an overactive bladder, who safely received three sessions of ECT. At the same time, her device was placed in magnetic resonance imaging mode to prevent electrical interference. This case showed that ECT can be an effective and safe treatment option, emphasizing the importance of a thorough assessment and an individualized treatment plan in patients with neurostimulators. The case highlights the need for specific protocols for safely administering ECT in patients with implanted electronic devices.

Pinchuk et al. described two cases of patients who developed status epilepticus after ECT, which resolved through restimulation. These reports support the view that ECT has anticonvulsant properties and underscore the need to develop clear clinical protocols for restimulation in cases where conventional interventions, such as propofol or lorazepam, fail to stop prolonged seizures.

Zhou et al. explored the knowledge of, attitude toward, and willingness to undergo ECT among Chinese patients diagnosed with bipolar disorder through a questionnaire-based survey. Although knowledge levels were low and attitudes toward ECT were negative, patients expressed a surprisingly high willingness to undergo the treatment. These findings highlight the importance of clinician-led education to improve knowledge of and acceptance of ECT.

Geerts et al. conducted semi-structured clinical interviews with nine significant others of patients who received ECT to investigate caregivers' perspectives and experiences. Participants described the emotional burden of supporting patients with severe mental illness, and said that a sense of hope accompanied the decision to commence ECT. However, they also expressed apprehension regarding potential side effects and a high sense of responsibility. Psychiatrists were identified as pivotal in fostering trust and providing accurate information. Given the crucial role of significant others in treatment decision-making and patient adherence, this study highlights the importance of clear communication from psychiatrists, efforts to counter stigma, and the provision of experience-based information to support both patients and their families.

Hosseni et al. examined the training experiences, knowledge of, and attitudes toward ECT among trainees and early-career psychiatrists in Iran via an online survey. Their findings showed a high availability of ECT centers in Iran, generally positive attitudes, and a strong interest in further ECT training. This study emphasizes the importance of exposure to and education in ECT in shaping positive professional views.

In conclusion, this Research Topic demonstrates the enduring significance of ECT in contemporary psychiatry by showcasing advances in its application while incorporating the perspectives of patients and caregivers. Together, these studies provide a comprehensive and contemporary appraisal of modern ECT practice.

Author contributions

CȚ: Writing – original draft, Writing – review & editing. LA: Writing – review & editing. MP: Writing – review & editing. JQ: Writing – review & editing. MJ: Writing – review & editing.

Conflict of interest

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The perspective and experiences of significant others on electroconvulsive therapy

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Introduction: Electroconvulsive therapy (ECT) is an essential but often controversial treatment in psychiatry. While existing research focuses on patient outcomes, the perspectives of significant others (SOs) remain underexplored. They play, nevertheless, a crucial role in decision-making, treatment adherence, and post-treatment evaluation. To better understand their perceptions, challenges, and support needs, this study aims to explore the lived experiences of SOs and ECT.

Methods: A qualitative phenomenological approach was employed using semi-structured interviews with nine SOs of patients who underwent ECT. Thematic analysis was conducted using Braun and Clarke's framework, and data were analyzed using the NVivo software.

Results: Before ECT, SOs experienced a significant emotional burden, describing their lives as unlivable due to the patients' severe illness. The decision to start ECT was marked by feelings of responsibility and fear but also driven by hope. During ECT, SOs closely monitored treatment effects and side effects, balancing improvements against challenges such as memory loss and fatigue. The psychiatrist played a central role in shaping perceptions and instilling hope. During the maintenance phase, SOs faced logistical challenges and stigma but aimed to integrate ECT into daily life while supporting patient autonomy.

Conclusion: This study highlights the complex role of SOs in ECT. Unlike previous studies that have focused on caregiver burden, it emphasizes the role

of hope in decision-making and treatment adherence. SOs value transparent communication from psychiatrists and seek structured support systems to navigate practical and emotional challenges. Stigma remains a significant barrier to open discussion and social integration.

KEYWORDS

electroconvulsive therapy, significant others, decision-making, hope, stigma, perspective, experiences

Introduction

Electroconvulsive therapy (ECT) is an essential treatment in psychiatry (1). Despite its importance, it remains a controversial and sometimes misunderstood treatment (2, 3). Fears surrounding the use of electrical impulses on the brain, negative representations in movies and games, and the primitive practices of the past have contributed to uncertainty that extends beyond that of the majority of other therapies (4–6). When ECT is proposed, patients and their significant others (SOs) often voice their fears. The term "significant other" is used in this study to include individuals who have a meaningful personal relationship with the patient, regardless of legal or caregiving obligations. In existing research, terms such as "carer" and "caregiver" are commonly used. While some SOs appreciate this label as they recognize their supportive role in the patient's care and adherence to treatment, others reject them, as they may imply a formalized caregiving role that does not align with their personal relationship, as it may create division between the caregiver and the person receiving care (7). Because patients eligible for ECT are often severely ill and may have limited capacity to give informed consent, SOs play a crucial role in the decision-making process. A recent review found that SOs generally have positive attitudes toward ECT and report high levels of satisfaction with treatment (8). However, many SOs express a need for more comprehensive information regarding side effects, prognosis, and long-term impact. The majority of studies of SO perspectives have relied on quantitative measures such as surveys, limiting the depth of understanding of their experiences (8). A qualitative exploration could enhance the role of ECT practitioners in guiding both patients and their SOs through the decision-making process, which not only is crucial at the start of the treatment but also requires ongoing assessment throughout the ECT treatment. As maintenance ECT (M-ECT) is increasingly recognized as a vital strategy to mitigate the high risk of relapse (9–12), the decision to continue or discontinue treatment becomes an ongoing concern for both patients and SOs. Despite this, little is known about how SOs perceive their role in these decisions and how they evaluate the benefits and risks of ECT over time. This study aimed to explore the lived experiences of SOs during the period of ECT. The secondary objectives were to identify the support needs of SOs and to assess the role of psychiatrists in shaping their perspectives throughout the treatment process.

Methods

Study design

To gain insight into the lived experiences and perceptions of SOs on ECT, a qualitative phenomenological approach was used (13). Semi-structured interviews were conducted with SOs, and the data were analyzed thematically using the framework developed by Braun and Clarke (14). The COnsolidated criteria for REporting Qualitative research (COREQ) checklist was utilized to ensure comprehensive and transparent reporting of the findings.

Setting

Patients were recruited from the ECT unit of a large general hospital. This unit treats in- and outpatients with ECT, along with referrals from other general and psychiatric hospitals in the area. Both acute ECT and maintenance ECT were provided.

Sampling and participants

To capture a broad range of experiences and perceptions, purposive sampling was employed. Participants were selected to ensure diversity in demographic characteristics (e.g., gender and age) and treatment-related factors (e.g., number of ECT sessions and phase of ECT). Although this study did not aim to compare perceptions between acute ECT and M-ECT, it included SOs from both groups. Patients were provided with an information letter about the study and were invited to personally nominate SOs to participate. SOs who expressed interest were contacted by telephone, and the study was explained in detail. Informed consent was obtained before conducting interviews. Notably, all approached patients and their SOs agreed to participate.

Participants were eligible if they were Dutch-speaking adults identified by patients as their primary SOs and had had experience with ECT within the past year.

Data collection

From September 2022 to June 2023, SOs participated in a single interview one-on-one with an SA, an advanced practice nurse in mental health. Interviews were conducted based on the preference of the participants, at their home (n = 5) or in a meeting room in the hospital (n = 4), to make them feel at ease and to be relevant to their daily lives (15, 16). There was no relationship between the participants and the researcher prior to the interview, and participants knew the researcher's occupation and affiliation.

Each interview began with an open-ended question to introduce the focus without directing it toward a specific theme. The opening question was, "I understand that you are a significant other for someone who is/was treated with ECT. Can you describe how you experience(d) that?" Follow-up questions had the purpose of gaining a deeper understanding of what the participants were bringing to the interview. They were formulated as, e.g., "Can you tell me something more about it, can you give an example, what did that mean for you?" All interviews were audio-recorded and transcribed verbatim. The average duration of the interviews was 120 minutes. Nine participants were included. The mean age was 68.5 years, and the mean number of ECT sessions was 78. The respondent characteristics are listed in Table 1.

TABLE 1 Characteristics of relatives.

Female respondents	Total n = 9 n = 5
Age SO	
Age 18–35	1 (11.1%)
Age 36–55	0
Age 46–55	0
Age 56–65	2 (22.2%)
Age 66–75	3 (33.3%)
Age 76–87	3 (33.3%)
Diagnosis of patient	
Difficult to treat depression	3 (33.3%)
Psychotic depression	5 (55.6%)
Catatonia	1 (11.1%)
Relation to patient	
Parent	3 (33.3%)
Partner	3 (33.3%)
Friend	1 (11.1%)
Child	1 (11.1%)
Cohabiting with patient	6 (66.7%)
Timing of interview to last ECT in days	
<7	3 (33.3%)
7–14	4 (44.4%)
14–21	2 (22.2%)
ECT course phase	
Maintenance ECT	6 (77.8%)
Continuation ECT	1 (11.1%)
During acute course	1 (11.1%)
After acute course	1 (11.1%)
Number of ECT sessions	
0–10	1 (11.1%)
10–20	1 (11.1%)
20–50	4 (44.4%)
>50	3 (33.3%)

SO, significant other; ECT, electroconvulsive therapy; d, days.

Analysis

The research team consisted of an advanced practice nurse (SA) experienced inpsychiatric care, a psychiatrist (PG) experienced in ECT and geriatric psychiatry, a professor and PhD nurse (SV) experienced in mental health and qualitative research methods, a psychiatrist experienced in ECT (NVDV), and an associate professor and psychiatrist (GL) experienced in systemic psychotherapy, liaison psychiatry, and qualitative research collaborated. The diversity in backgrounds broadened and deepened the analyses (17). SA conducted the interviews. The interviews were critically revised by SV to avoid biased, influencing, or closed questions and lack of exploratory and in-depth questions. The first analysis of the data was conducted by SA, PG, and SV. They read and reread the interviews independently. This enabled them to immerse themselves in the data and to identify similarities, differences, and patterns. Discussions and reflections formed the basis for the coding. In the next step, the SA coded the transcripts in the NVivo11 software. Critical reflections on the coding were discussed with PG and SV, code categories were created, and themes were conceptualized. The researchers contextualized the findings, weaved together the analytical narrative, and added data extracts to inform their findings. The findings were then discussed with the other authors (GL and NVDV). Based on their questions and critical appraisal, the analyses were broadened and deepened. Data saturation was reached for all reported themes.

Ethics

The study was approved by the ethics committee of AZ Groeninge, Kortrijk. All participants provided signed informed consent prior to the study. Anonymity and confidentiality were maintained throughout the entire research process. All interviews

were anonymized by removing identifiable details from the transcripts. Data were securely stored and encrypted, ensuring full confidentiality throughout the research process.

Results

Before ECT

"Life is no longer livable"

Throughout the interviews, SOs consistently reported a long trajectory before the first mention of ECT. They described a journey marked by increasingly more disabling symptoms of the patient and a significant impact on daily life. The majority of SOs mentioned psychiatric hospitalizations, psychotherapy, and psychopharmacologic strategies before ECT, which often resulted in temporary or no success. As the illness became central to the SOs' lives, they began to reverberate with the illness. When symptoms improved, they felt the positive aspects and optimism. When the patient's symptoms worsened, they experienced increased stress, negatively impacting their own lives. The SOs appeared to have no control over the illness and, consequently, over their own lives. Their lives appeared to be entirely dictated by the illness, and they expressed a sense of powerlessness over it. During this process, they adjusted their expectations about life and what they wanted from it. They pushed boundaries, sought solutions, and tried to adapt.

> "I started working part-time so that I can continue to combine caregiving with a job. Although it is financially very difficult and I don't know how we will cope, there is no other option right now"

Despite intensive treatment and therapy, the illness kept demanding more. It took a central place in the life of the patient and the SO. It gradually made their lives unrecognizably different than before.

> "We become isolated, can't meet with friends anymore and even can't see the children in the weekends or go for a bike ride together as we did for so many years."

By the time ECT was considered, SOs indicated that life no longer felt livable. It became a matter of survival, with daily struggles to support the patient to accomplish even the most basic tasks. Essential activities like getting up, dressing, and even eating required special effort from the SOs. Social contacts were absent, and SOs often did not find the time and possibility to fulfill their basic needs. Activities such as eating, taking a shower, and going to the supermarket have to be planned and must be done in a rush.

> "She doesn't accomplish anything anymore, whereas she used to be a vibrant woman, managing the household, having a responsible job. Now, having the children around is already too much."

The SOs' energy was depleted, and the limit of what is livable was reached. SOs described it as "life is not life anymore". In this context, they indicated that the decision to start ECT is not really a choice. It appears to be the only possibility to get out of an unbearable situation that keeps worsening, and there appears to be no alternative.

The weight of responsibility and the perspective of hope in the decision to start ECT

In comparison to medication or psychotherapy, SOs saw ECT as a more radical treatment. The effect of electricity on the brain appeared to be more dangerous to them than the effect of chemical products.

> "You have the image in your head of someone shaking and having a kind of epileptic insult. A pill is just a pill. You take it and … finished."

ECT is a treatment that SOs did not have in mind when they first heard of it. Several SOs indicated that when ECT was introduced as a possible treatment, it induced much uncertainty and anxious feelings. SOs regarded ECT as an old and rather inhumane therapy, and some SOs were surprised that it was still being used. Since ECT was not really known to the SOs, they had many questions about the procedure.

When giving consent for ECT, SOs reported feeling fully responsible for the decision, as patients were sometimes unable to provide consent themselves due to their illness. SOs indicated that it was even difficult to have a conversation with the patient about (starting) ECT. SOs who were legally required to provide formal consent and whose loved ones were able to consent indicated that this feeling of responsibility put a burden on their shoulders and induced fear. Because of the responsibility they felt, support for this decision was often sought from another family member or friend.

> "Imagine if something were to go wrong; I did make the decision for my mom."

The psychiatrist and his/her role in decision-making and trust

SOs all indicated that the psychiatrist is pivotal in the process that they go through, especially in the process of decision-making. Information regarding ECT, more specifically on the effects and the side effects, is important, and the psychiatrist is the first and most important source to provide this information. While brochures, internet resources, and explanations from nurses and other staff provide helpful knowledge about the treatment and practical aspects, SOs perceived the psychiatrist as the person who has answers to their

most important and pressing questions and concerns. A psychiatrist who demonstrates interest in understanding the patient's specific situation, acknowledges the unique needs, and expresses genuine concern fosters a strong sense of trust in SOs. This trust reassures SOs that the patient is receiving individualized care and is not merely one of many being treated. SOs emphasized that confidence in the psychiatrist alleviated fear and uncertainty, making the decision to proceed with ECT more manageable. A question that SOs often (wanted to) ask was what the psychiatrist would decide if it was, e.g., his/her mother, partner, or brother. If the psychiatrist answered that he/she would decide to start the treatment, SOs felt strengthened in their decision to start ECT. When a psychiatrist stated that starting ECT was a good decision, it relieved the SOs of the burden of responsibility.

The psychiatrist and his/her role in instilling hope and shaping perspectives

By receiving information about ECT and its effects, hope is induced in SOs. When the psychiatrist shared his/her experience with ECT and its effects on other patients, this reassured them and introduced hope. Afterward, they mainly remembered positive remarks from the received information. Concerning the effect of ECT, words such as significant, substantial, successful, and improvement were remembered by the SOs. Side effects and the knowledge that ECT is not always successful were addressed and considered important. However, in weighing their decision, SOs gave less weight to the possible side effects, as hope for a life that is more livable was more prominent and necessary to make the decision for ECT.

> "After I asked, the psychiatrist said that he would decide to start ECT for his partner. I was really sure then, that ECT was ok and the only option to get out of the misery."

> "The psychiatrist has seen good effects of ECT and saw patients as my wife who couldn't accomplish anything anymore and who recovered to function normally again. Although I am rather careful, hearing this from someone who knows and who has seen the recovery in many patients, gives hope. It gives you the courage to try it and to go on enduring and hope that ECT will bring relief."

> "How will the future be? I don't know. We hope for ECT to bring change. It can't remain as it is now."

During ECT

Monitoring and balancing effects and side effects

During ECT, SOs closely monitored the progress and changes in the patient. In the beginning, SOs mentioned that they did not expect radical change. They looked for small progress and anticipated improvements in the patient's ability to function. SOs stated that change in real-life situations was important to them. Small changes make a big difference. Having more interactions and seeing the patient become more independent are the first signs of progress.

> "When I asked him what he wanted to eat, he answered. He didn't do that before (ECT). Yesterday we looked at a television show and I commented on something. I was surprised because he reacted."

> "She put on her clothes last week. Didn't wear her pyjamas all day."

> "When his friend visited, he (the patient) seemed to have a conversation with him. It was already a long time ago that that was possible."

For SOs, changes in interactions, communication, and self-care were the first and most important indicators of the effect of ECT. They did not expect radical transformation but rather assessed progress by comparing small changes to the patient's prior life, the life before the illness. Recovery, in their view, was marked by the patient "becoming his/her former self again".

> "When I arrived with my parents, mother (the patient) was cleaning the windows. Having a clean house and especially clean windows has always been very important to her. The disease made her indifferent to a clean house and seeing her cleaning the windows when I arrived, gave me the feeling that I had my mother back. It made me cry from relief, joy and tristesse for what she must have gone through (cries)."

SOs monitored effects and side effects almost constantly. As for side effects, they stated that they wanted to make sure ECT did not make the situation worse in the short term and that they also did not want to risk (brain) damage in the future. Memory loss is the side effect they monitored most closely. The side effect that was seen as most hindering in daily life was fatigue and the need for sleep after ECT.

> "After ECT she sleeps for three days. She disappears in the bedroom. That is not good. It takes a week before she recovers a bit and then the next ECT is coming. This is no progress, on the contrary. If it stays like this, we will not go on with it (ECT)."

The effects and side effects are balanced. As long as the benefits outweigh the discomfort caused by the side effects, SOs perceived ECT as a valuable therapy. They actively encouraged and supported

the patient in continuing ECT while also addressing practical and organizational challenges to ensure treatment adherence. The positive changes, consistently described as "the patient returning his/her old self again", justify the significant efforts required to adjust daily life around ECT sessions.

As the patients showed improvement, SOs increasingly prioritized the patients' own assessment and evaluation of the treatment. If patients were able to express discomfort and side effects of ECT, SOs followed and respected their judgment about whether to continue ECT. SOs refrained from pressuring them to proceed with ECT if they did not want to go on with it. Data indicate that SOs initially took on the responsibility of making decisions until the patients could express what they wanted. From that point on, SOs shifted from making decisions to advocating for the patients' wishes. At that stage, they no longer assumed responsibility for the continuation or cessation of ECT but instead supported the patients in their own decisions.

> "He says the ECT does something with him. He cannot say what exactly, but it does not feel good. He also complains of memory loss and that frightens him. He wants to stop ECT. Eventually it is he who must undergo the treatment every time. I can point out the positive effects, but I cannot decide what is bearable and good for him."

ECT as part of daily life

When confronted with maintenance ECT, SOs started integrating it into their daily routines. Recurrent ECT sessions require a feasible organization and practical arrangements that do not unnecessarily interfere with their core responsibilities and roles. SOs sought to establish a new routine and needed help from (mental) health professionals to adapt ECT into a life that could be considered "normal" again. Professionals who are willing to consider the needs of SOs in planning ECT, who facilitate the hospital stay during ECT, or who help find solutions for practical issues, such as transportation, timing of ECT, and food, are highly valued.

> "As it is a long drive to bring my wife to the hospital for treatment, I cannot go to work the day of ECT. I have a busy job and can't afford to stay home or work less. But if I can stay in a private hospital room where I can quietly work on my laptop while my wife gets ECT or recovers from it, I can do my job and stay with my wife at the same time. Some nurses really think of my needs and arrange a private room, others don't and then it costs me a lot of energy to argue and find other solutions. I know my week will be a mess then."

> "ECT was always on a day that I had to work and I wasn't allowed to change my work schedule. That was a real problem because in the long run I wouldn't be able to keep my job. I also couldn't find anyone else to accompany my son. When talking to the nurse about it, she arranged ECT-sessions on another day. That was such a relief and resolved a lot of my problems and worries for the future."

The challenge of disclosure: overcoming stigma and rebuilding social connections

Beyond logistical and practical arrangements, integrating ECT into daily life also requires navigating social disclosure and talking about it with people in their environment. SOs reported avoiding discussions about ECT, even with close family members, both due to the patient's condition and because of concerns about stigma. While they acknowledged that not talking about it could lead to social isolation, they felt reluctant to do so. Disclosure of ECT is perceived as a difficult but necessary hurdle to take in restoring social connections. When they did discuss ECT with family and friends, they frequently encountered misinformation and a lack of knowledge about ECT. As a result, SOs often felt the need to defend the decision to initiate ECT and reassure others that it is a legitimate treatment. They recognized the same fears and uncertainties in others they had experienced. It cost them energy to explain everything, but discussing their experiences fostered a renewed sense of connection and support in their social circles.

Discussion

This study provides an in-depth exploration of the perspectives and experiences of SOs involved in ECT and highlights the importance of their involvement in ensuring successful treatment.

Much of the existing literature focuses on the concept of caregiver burden, recognizing that chronic mental health conditions place significant emotional, psychological, social, and financial strains on both patients and their informal caregivers (18, 19). While this study acknowledges the burden, it goes further by illustrating the specific challenges that SOs encounter in the context of ECT. Our findings align with prior qualitative research on the experiences of relatives of individuals with depression, particularly regarding emotional distress and interruptions to relationships (20). However, ECT introduces additional complexities as it is a particularly impactful treatment. Previous qualitative studies have reported similar distress and anguish because of the illness among families of ECT patients (21, 22). The notion of ECT as a "last resort" is mentioned along with patients expressing a sense of "blind trust" in the psychiatrist during the decision-making process toward ECT (21). However, our findings show that SOs actively engage in decision-making, seeking guidance, involvement, and reassurance from the psychiatrist—not just to make the decision but also to cope with its weight. Hope emerged as a central theme driving the decision to start and pursue ECT. While Sethi and Williams (22) described hope as a factor in families' responses to ECT, they did not explicitly link it to the decision-making process.

Our findings suggest that hope is crucial not only for initiating treatment but also for sustaining it. Previous studies on chronic illness have emphasized the role of hope in engaging with challenging treatments, such as cancer therapies (Snyder et al., 2002). In the context of ECT, SOs derive hope from the information provided by the psychiatrist, reinforcing the need for clinicians to communicate effectively and instill a realistic sense of optimism.

Hope can thus serve as both a therapeutic target and an integral part of informed consent, influencing adherence to therapy. Ensuring that SOs receive adequate, clear, and transparent information about ECT can strengthen their ability to balance risks and benefits, ultimately improving treatment adherence. Beyond the provision of information, clinicians may consider actively fostering hope and incorporating tailored interventions that support hope and optimism into the care of ECT patients and their SOs.

During the course of ECT, SOs closely monitor the real-life impact of ECT treatment. Unlike formalized assessments or rating scales that measure change over short periods of time, SOs evaluate progress in the broader context of the patient's pre-illness functioning (23). This discrepancy between subjective and clinical assessments underscores the need for clinicians to recognize the limitations of rating scales and to incorporate not only the patient's but also the SO's perspectives in evaluating treatment outcomes.

A significant proportion of the sample was SOs of patients undergoing M-ECT. Existing literature underscores the essential role of M-ECT in sustaining remission and preventing relapse (11, 12). However, our study reveals that while SOs acknowledge the benefits of M-ECT, they also face logistical and emotional challenges in sustaining long-term adherence. Practical support from ECT clinics, such as accommodating schedules and providing adequate facilities, is crucial. These considerations, while seemingly peripheral, impact the overall experience and adherence of SOs to ECT.

Additionally, stigma remains a substantial burden for SOs; even within their own families, SOs report encountering skepticism and misinformation. This underscores the need for targeted informational programs by ECT clinics that extend beyond the patient–clinician relationship to SOs and their broader network. One potential intervention to mitigate stigma and strengthen social support is the organization of network-focused meetings, similar to those implemented in other medical contexts, such as adolescent and young adult cancer care (24). These meetings are organized for a patient and his/her SO. Meaningful people from their network are invited to the hospital to address concerns and receive validated information from healthcare professionals, ultimately fostering a supportive environment for both patients and their SOs.

Limitations

This study has some limitations. It was monocentric, conducted in one supra-regional hospital. Although the hospital treats patients from different regions, psychiatrists, and other hospitals, and although the themes are not explicitly or exclusively linked to the hospital or psychiatrists' practice, there may be bias or lack of diversity. This possibly reduced the transferability of the findings. To capture diverse perspectives, we included SOs of patients who had just started ECT along with those receiving M-ECT. However, since all interviews were conducted post-ECT, there is a potential for recall bias, and the timing of the interviews may have influenced the responses. Interviews conducted shortly after the acute phase may have reflected more distress, while later interviews may have been shaped by perceived improvement. While these factors introduce variability, the consistency of themes across participants suggests that the risk of systematic bias was limited. There were no SOs of patients who dropped out, refused, or did not start ECT. This could emphasize the more positive perceptions and themes. A more heterogeneous selection of SOs, e.g., from patients who dropped out or did not start ECT, would be desirable to gain broader insight. Additionally, there was only one participant under the age of 56. Young SOs were underrepresented in this study, raising the question of whether the process differs for younger individuals. Additionally, the sample primarily consisted of SOs of patients with affective disorders and no other psychiatric disorders, such as schizophrenia. As this is a qualitative and explorative study, it is not possible to compare experiences between groups or analyze covariates such as phase of ECT, illness severity, duration of illness, or relation to the patient.

Implications for practice

The findings of this study highlight five important key areas where clinical practice can be improved to better support SOs throughout the ECT treatment.

Encouraging a nuanced approach to shared decision-making

SOs often experience a heavy burden and responsibility in making treatment decisions. This study highlights the importance of a balanced and supportive approach in which clinicians actively assist and guide SOs, ensuring that they do not feel solely responsible. At the same time, SOs play a critical role in evaluating treatment outcomes. Their perspective and real-world observations provide valuable insights that extend beyond standardized assessment tools.

Providing tailored and experience-based information to foster hope and perspective

SOs rely on psychiatrists not only for medical facts but also for personalized, experience-driven guidance that addresses their specific concerns. While supplementary materials such as brochures, videos, and testimonials can help, they cannot replace a psychiatrist's tailored explanation that fosters trust, reduces uncertainty, and supports informed decision-making. Beyond factual knowledge, the way psychiatrists communicate information—highlighting realistic hope and treatment potential—plays a crucial role in how SOs perceive and engage with ECT. Ensuring that SOs receive clear, transparent, and empathetic communication can strengthen their confidence in treatment decisions, ultimately improving adherence and emotional resilience.

Facilitating practical solutions

Logistical challenges, such as scheduling and transportation, can affect the continuation of maintenance ECT. Instead of one-size-fits-all solutions, providing tailored practical support that meets the specific needs of SOs can make a meaningful difference in ensuring treatment adherence.

Developing strategies to destigmatize ECT and psychiatric illnesses

To combat the stigma surrounding ECT and psychiatric illnesses, targeted initiatives could be implemented. These may include organizing network meetings and multi-family meetings and increasing public engagement through media and community outreach efforts.

Recommendations for future research

Future research could focus on exploring the perceptions of young SOs or SOs of patients who did not start or dropped out of ECT. Their perceptions and the dynamics between them and the patient could give valuable insights. The study highlighted specific perspectives on the role of the psychiatrist. Further research can elaborate on the key components of this role. Studying the function of hope before and throughout the process of ECT, mental illness, and recovery can help to understand and guide SOs and patients. Research on the role of SOs in assessing the effects and side effects of ECT and in defining (intermediate) goals and outcomes could be valuable to complement clinical evaluation (instruments). In this study, the focus was on the perspectives of SOs. It may also be relevant to explore how patients, psychiatrists, and other mental healthcare professionals perceive and experience ECT and how interpersonal dynamics and boundaries influence the decisions course of the treatment.

Conclusion

This study gives additional insight into the perspectives of SOs of patients before, during, and after ECT. Despite experiencing strain on multiple levels, SOs seek information, understanding, and hope before the initiation of ECT. They express a desire to be involved in evaluating the treatment and encounter various practical challenges during maintenance therapy. Our findings highlight the necessity of an integrated and holistic approach to ECT care, one that actively includes SOs as key stakeholders in the treatment process.

Data availability statement

The datasets presented in this article are not readily available because the Dataset was anonymised qualitative data from interviews. Requests to access the datasets should be directed to pieter-jan.geerts@azgroeninge.be.

Ethics statement

The studies involving humans were approved by the Ethical Board Az Groeninge, Kortrijk, Belgium. 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

P-JG: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. SA: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Software, Writing – review & editing. NV: Validation, Writing – review & editing. CB: Writing – review & editing. GL: Conceptualization, Methodology, Supervision, Validation, Writing – review & editing. SV: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Writing – original draft, Writing – review & editing.

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Knowledge, attitudes, and experiences of ECT among psychiatric trainees and early career psychiatrists in Iran

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Objective: This study aimed to examine the experiences of psychiatric trainees and early career psychiatrists in Iran with Electroconvulsive Therapy (ECT).

Methods: A cross-sectional survey, employing a 36-item questionnaire was conducted in Iran from March to November 2023. The survey targeted psychiatric trainees and early career psychiatrists, assessing ECT availability, training experiences, knowledge and attitudes.

Results: 173 responses were received. The majority of respondents were female (79.2%) and had experience in inpatient settings. About 63.0% reported ECT availability in their institutions, with 89.0% confirming the presence of specialised ECT centers within 100 km. Training in ECT was widely reported (96.5%), with 77.4% administering ECT to 10 or more patients during psychiatry training. However, only 55.5% were familiar with national ECT guidelines, and even fewer knew about international recommendations. Attitudes toward ECT were largely positive, with 86.2% agreeing on its effectiveness and 77.5% willing to recommend it to patients. ECT services were less frequently available in institutions where ECPs were employed compared to institutions where trainees were undergoing their psychiatry training. Confidence in ECT knowledge varied, with 52.6% feeling confident in their understanding, and 75.7% expressed interest in additional training.

Conclusions: The study highlights a gap between ECT training and confidence among Iranian psychiatrists. Positive attitudes toward ECT and a high level of interest in further training underscore the need for enhanced educational programs and the standardisation of guidelines. Addressing stigma and policy gaps is crucial for improving ECT access and utilisation.

KEYWORDS

ECT, electroconvulsive therapy, attitudes, experiences, knowledge, early career psychiatrists, psychiatric trainees

Introduction

Electroconvulsive Therapy (ECT) is an effective treatment for severe psychiatric conditions, including major depressive disorder, bipolar disorder (in manic, depressive, or mixed episodes), psychotic disorders, postpartum mental disorders, and catatonia (1, 2). ECT is primarily used in two contexts: when psychiatric disorders are resistant to initial treatments (e.g. medication and psychotherapy); and in urgent or life-threatening situations, such as acute suicidality, with minimal contraindications (3–6).

ECT involves applying an electrical pulse to the scalp, inducing a seizure that typically lasts 15 to 70 seconds (7). Potential risks include complications related to general anesthesia, and oral injuries, while common side effects include post-treatment sedation, headache, nausea, muscle pain, and temporary memory loss (8). In case of memory loss, emotional and personal memories are typically preserved (9).

ECT has shown success in addressing neuroplasticity impairments by rewiring the brain, and increasing gray matter volume (10). Despite scientific support for its use, with response rates of 70% to 80% in treatment-resistant depression, ECT remains underutilised, raising concerns given the prevalence and impact of depression (6, 7). ECT is also associated with a low mortality rate in adults, approximately 2.1 per 100,000 treatments, which is lower than the mortality rate for general surgery under anesthesia (3.4 per 100,000) (11).

The introduction of modified ECT techniques in the 1950s, incorporating anesthesia, muscle relaxants, oxygenation, and monitoring, significantly improved safety and reduced side effects, making significant progress in treatment practices (7, 12). ECT can be used across diverse populations, including in pregnant women, adolescents, and the elderly to mitigate medication-related side effects (13, 14).

However, misconceptions about ECT persist, often rooted in its historical associations with inhumane practices, media portrayals and anti-psychiatry narratives, which contribute to its underuse. Patients frequently fear ECT, believing it to be violent, painful, or likely to cause memory loss or personality changes – perceptions reinforced by films and television (1). Despite efforts by professional organisations, such as the American Psychiatric Association (APA) and the Royal College of Psychiatrists (15) to provide accurate information, negative media portrayals continue to depict ECT as barbaric and cruel (16). Research conducted has refuted claims of long-term adverse effects on memory or intelligence (5, 17, 18). Nevertheless, stigma remains a significant issue, leading to social rejection, avoidance, or discrimination against those who have undergone ECT (19).

The attitudes of mental health professionals, particularly those in training, play a crucial role in shaping clinical practice (12). A German survey identified several factors associated with positive attitudes towards ECT, including professional status (physicians being more optimistic than nursing staff), feeling well-informed, and having contact with patients undergoing ECT (20). Research indicates that psychiatrists with greater knowledge and experience in ECT tend to have more positive attitudes toward its use. In the United States of America (USA), psychiatrists who referred or administered ECT expressed more positive feelings, and perceived a greater impact when involved with the treatment (21). Similarly, in South Africa, a positive relationship was observed between mental health professionals' knowledge of ECT and their attitudes towards its use, suggesting that enhancing knowledge could improve attitudes towards the treatment (7). Physicians and healthcare professionals are essential in promoting the acceptability of ECT by educating patients and their families (19), as those who receive information from their doctors tend to have fewer fears and misconceptions (6).

In Iran, psychiatric trainees and early career psychiatrists (ECPs) face significant challenges, including the demanding nature of healthcare work, income dissatisfaction, political instability, economic sanctions, and social insecurity (22). In Iran, psychiatry training is available at over 20 medical universities, with medical doctors entering a four-year psychiatric training residency programme after a national entrance exam. Following residency, they must pass a board exam and complete a 2–5-year compulsory service as general psychiatrists before engaging in private practice (23, 24).

In Iran, ECT training is mandatory and psychiatry trainees are required to perform 100 ECT procedures before graduation, including 30 observations, 30 supervised administrations, and 40 unsupervised administrations. However, little is known in Iran on the extent that ECT is used or professionals' attitudes towards it.

This study aims to explore the context of ECT in Iran, including the availability of ECT centers, usage patterns, general attitudes towards ECT, and the accessibility of ECT educational resources.

Methods

Study design

This cross-sectional survey used a 36-item self-report questionnaire, administered anonymously and voluntarily.

Data collection

The questionnaire was distributed across Iran from March to November 2023, targeting both psychiatric trainees and ECPs, defined as psychiatrists within their first five years after completing their psychiatry training. The questionnaire was disseminated via email and social media, targeting trainees from nationally recognised institutions and ECPs affiliated with the Early Career Psychiatrists Committee of the Iranian Psychiatric Association. The sample size was determined based on the available population of psychiatrists in Iran, aiming for a 20% response rate, employing a non-random, convenience sampling method.

Instruments

Originally developed in English for an international survey (25), the questionnaire was translated into Persian by a bilingual author. The back-translation method was employed, followed by face validity assessment with input from six experts in psychiatry and psychology. Content validity was confirmed with a Cronbach's alpha of 0.88.

The questionnaire comprised 36 questions covering: i) sociodemographic data of participants, ii) availability of ECT, ECT training experiences, and ECT guidelines within the national legal framework, and iii) attitudes towards, knowledge of, and personal interest in ECT, including viewpoints of its relevance, efficacy, safety, recommendation to patients, and associated negative perceptions. Participants were also queried about risks, contraindications, long-term harms, use in pregnant women, and their confidence in their own knowledge.

Data analysis

Data was analysed using IBM SPSS Statistics (v. 27.0). Descriptive statistics were used to report frequencies and percentages for categorical variables. Associations between professional experience and questionnaire responses were examined using chi-square test. Odds ratios with confidence intervals were calculated for key variables (e.g., ECT availability); however, no multivariate adjustments for potential confounders were performed due to the exploratory, descriptive nature of this study. A Kruskal-Wallis test was conducted to compare confidence levels in ECT knowledge across different training types (including clinical rotations, courses/workshops, or other training formats).

Results

Sociodemographics

This online questionnaire was distributed to 760 psychiatrists in Iran, yielding 173 respondents (22% response rate). The sample comprised ECPs (N=89, 51.4%) and psychiatric trainees (N=84, 48.6%). The majority were female (n=137, 79.2%), married (n = 113, 65.3%), and without children (n=113, 65.3%). Over half (N=103, 59.5%) worked in inpatient psychiatric wards. Trainees were also significantly more involved in inpatient settings, whereas ECPs were more commonly working in day clinics (Table 1).

The availability of ECT, ECT training experiences, and ECT guidelines within the national legal framework

Regarding ECT availability, 109 respondents (63.0%) reported its presence in their workplace, while only 19 (11.0%) indicated the absence of a specialized ECT center within 100 km of their work institution. The vast majority (n=155, 98.8%) were confident in the use of anesthesia during ECT administration. ECT was performed in both inpatient and outpatient settings within their institutions (n=135, 78%) and nationally (n=155, 89.6%) (Table 2).

With respect to ECT training experiences, 167 respondents (96.5%) confirmed the availability of ECT training during their psychiatry training. Nearly all (n=172, 99.4%) had observed ECT administration, with 156 individuals (90.2%) noting supervised administration, and 130 (75.1%) actively performing ECT themselves independently without supervision during their training. Various training methods were reported during psychiatry training, including clinical rotations (n=48, 27.7%), courses/workshops (n=52, 30.1%), and other forms of training (n=73, 42.2%). A total of 134 respondents (77.4%) had administered ECT to 10 or more patients during their training.

Regarding national and international ECT guidelines, 96 respondents (55.5%) were familiar with national ECT treatment guidelines, whereas only 37 respondents (21.4%) were aware of international treatment recommendations. Among those aware of international guidelines, specified resources included Kaplan and Sadock's Comprehensive Textbook of Psychiatry (26), Kaplan and Sadock's Synopsis of Psychiatry (27), and the State of Queensland (Queensland Health) Guideline for the Administration of Electroconvulsive Therapy (2018). Nearly all respondents (n=172, 99.4%) highlighted the requirement for patients or their caretakers to sign informed consent for ECT in the country.

A significant difference was observed between psychiatric trainees and ECPs regarding the availability of ECT in their institutions (χ^2= 78.25, df = 1, p<0.001). ECPs were significantly

TABLE 1 Comprehensively outlines the sociodemographic data of the participants based on the two groups of ECPs and psychiatric trainees.

Socio-demographic variables		Count (percentage)			
		Total	Psychiatric trainee	ECP	
Response rate		173 (100%)	84 (48.6%)	89 (51.4%)	P-value
Sex	Male	36 (20.8%)	13 (15.5%)	23 (25.8%)	0.093
	Female	137 (79.2%)	71 (84.5%)	66 (74.2%)	
Marital status	Sigle	36 (20.8%)	24 (28.6%)	12 (13.5%)	0.067
	Married	113 (65.3%)	48 (57.1%)	65 (73%)	
	In a relationship	16 (9.2%)	9 (10.7%)	7 (7.9%)	
	Separated	8 (4.7%)	3 (3.6%)	5 (5.6%)	
Children	Yes	60 (34.7%)	20 (23.8%)	40 (44.9%)	0.004
	No	113 (65.3%)	64 (76.2%)	49 (55.1%)	
Workplace	Inpatient mental health center	103 (59.5%)	77 (91.7%)	26 (29.2%)	< 0.001
	Outpatient mental health center	16 (9.2%)	2 (2.4%)	14 (15.7%)	
	Day clinic	34 (19.7%)	3 (3.6%)	31 (34.8%)	
	Private practice	10 (11%)	1 (1.2%)	18 (20.2%)	
	Research center	1 (0.6%)	1 (1.2%)	0	
City	Tehran	94 (54.3%)	46 (54.8%)	48 (53.9%)	0.039
	Shiraz	54 (31.2%)	24 (28.6%)	30 (33.7%)	
	Esfahan	16 (9.2%)	7 (8.3%)	9 (10.1%)	
	Mashhad	6 (3.5%)	6 (7.1%)	0	
	Mazandaran	1 (0.6%)	1 (1.2%)	0	
	Kerman	1 (0.6%)	0	1 (1.1%)	
	Ahvaz	1 (0.6%)	0	1 (1.1%)	

more likely than trainees to report the absence of ECT availability in their workplaces, with an odds ratio of 58.82 (CI: 17.08-202.48). No significant correlations were observed between professional experience and other Yes/No responses.

The attitudes towards, knowledge about, and personal interest in training in ECT

Attitudes

The majority of respondents (n=156, 86.2%) either strongly agreed or agreed that *"ECT represents an effective treatment option"*, with a few (n=15, 8.7%) being neutral, and fewer (n=2, 1.2%) disagreeing.

Similarly, the majority (n=149, 86.1%) agreed or strongly agreed that *"ECT is lifesaving for some patients who are at risk"*, whilst some (n=18, 10.4%) were neutral, and only a few (n=6, 3.5%) disagreed.

Regarding ECT safety, over three quarters agreed (n=91, 52.6%) or strongly agreed (n = 46, 26.6%) that *"ECT is a safe treatment choice"*, while some (n=24, 13.9%) held a neutral opinion, and a few (n=12, 6.9%) disagreed.

The majority of respondents agreed (n=92, 53.2%) or strongly agreed (n=42, 24.3%) with *"Recommending ECT to their patients"*, whilst some (n=27, 15.6%), remained neutral, and fewer (n=12, 6.9%) disagreed.

Most (n=49, 28.4%) disagreed or strongly disagreed (n=101, 58.4%) that *"ECT is outdated"* whilst some (n=21, 12.1%) were neutral, and only a few (n=2, 1.2%) agreed.

Half of the participants (n=88, 50.9%) strongly disagreed, and nearly a third (n=53, 30.6%) disagreed that *"ECT is a cruel treatment"*, whilst some (n=22, 12.7%) were neutral, but a few agreed (n=8, 4.6%), or strongly agreed (n=2, 1.2%).

The majority (n=152, 87.9%) were not in agreement that *"ECT as a form of control or punishment"* with most strongly disagreeing (n=102, 59%) and the rest disagreeing (n=50, 28.9%). Neutral views were held by some (n=12, 6.9%), with a few agreeing (n=8, 4.6%) or strongly agreeing (n=1, 0.6%) (Figure 1).

Knowledge

Most respondents either agreed (n=91, 52.5%) or strongly agreed (n=67, 38.7%) that *"ECT can be used on pregnant women"*,

TABLE 2 Distribution of ECT availability, training experiences, and knowledge about guidelines among psychiatric trainees and early career psychiatrists (ECPs).

		N (%)
Availability of ECT specialized centers		
Is ECT available in your institution?	Yes	109 (63.0%)
	No	64 (37.0%)
Is ECT provided on an inpatient or outpatient basis in your institution?	Inpatient procedure only	33 (19.1%)
	Outpatient procedure only	5 (2.9%)
	Both	135 (78%)
Is an ECT specialized center within 100 km from your workplace?	Yes	154 (89.0%)
	No	19 (11.0%)
Is ECT provided with anesthesiology in your country?	Yes	171 (98.8%)
	No	2 (1.2%)
Is ECT provided on an inpatient or outpatient basis in your country?	Inpatient procedure only	14 (8.2%)
	Outpatient procedure only	3 (1.7%)
	Both	155 (89.6%)
Experience with ECT during training		
During your psychiatry training, was ECT training available?	Yes	167 (96.5%)
	No	6 (3.5%)
What form of ECT training was available during your psychiatry training?	Courses or workshops	52 (30.1%)
	Clinical rotation	48 (27.7%)
	Other forms	73 (42.2%)
Have you witnessed ECT being administered during your training?	Yes	172 (99.4%)
	No	1 (0.6%)
Have you administered ECT with supervision during your training?	Yes	156 (90.2%)
	No	17 (9.8%)
Have you administered ECT without supervision during your training?	Yes	130 (75.1%)
	No	43 (24.9%)
How many patients have you administered ECT to during your training?	1-2	4 (2.3%)
	3-5	10 (5.8%)
	6-9	25 (14.5%)
	More than 10	134 (77.4%)
Knowledge about ECT guidelines and national legal framework		
Are you aware of national treatment guidelines on ECT in your country?	Yes	96 (55.5%)
	No	77 (44.5)
Do patients or carers need to sign an informed consent for ECT in your country?	Yes	172 (99.4%)
	No	1 (0.6%)
Are you aware of international treatment guidelines on ECT?	Yes	37 (21.4%)
	No	136 (78.6%)

with only a few (n=8, 4.6%) neutral, disagreeing (n=5, 2.9%) or strongly disagreeing (n=2, 1.2%).

When asked whether they believe *'ECT is associated with long-term side effects,'* most respondents disagreed (n=96, 55.5%) or strongly disagreed (n=21, 12.1%), while some remained neutral (n=34, 19.7%), agreed (n=19, 11%), or strongly agreed (n=3, 1.7%).

Almost three quarters of participants (n=133, 76.9%) were not in agreement that *"The harmful effects of ECT could manifest months or even years after treatment"*, of which most (n=96, 55.5%) disagreed or strongly disagreed (n=37, 21.4%); some remained neutral (n=23, 13.3%), agreed (n=13, 7.5%), or strongly agreed (n=4, 2.3%).

Almost half of the respondents agreed (n=83, 48%) with *"Having confidence in their knowledge about ECT"*, and some (n=8, 4.6%) strongly agreed. Nearly a third were neutral (n=63, 36.4%); some disagreed (n=15, 8.7%), or strongly disagreed (n=4, 2.3%).

Regarding the belief that "*ECT has many risks and contraindications*" the majority (n=108, 62.4%) disagreed, some strongly disagreed (n=15, 8.7%), were neutral (n=25, 14.5%), agreed (n=21, 12.1%) or strongly agreed (n=4, 2.3%) (Figures 1, 2).

Interest in training

The majority agreed (n=85, 49.1%) or strongly agreed (n=46, 26.6%) to have an *"Interest in receiving training in ECT"*, approximately one-third (n = 30, 17.3%) were neutral, with a few disagreeing (n=10, 5.8%) or strongly disagreeing (n=2, 1.2%).

Comparison

Regarding "The attitudes toward, knowledge about, and personal interest in training in ECT", a significant difference was found in the "Confidence in their knowledge about ECT" ($p = 0.016$), with ECPs exhibiting higher confidence in their knowledge, and fewer disagreements. Additionally, participants who completed courses and workshops reported significantly higher confidence in their knowledge compared to those who underwent other training types (Kruskal-Wallis test, $p = 0.012$). The chi-square tests did not reveal any other significant differences between ECPs and psychiatric trainees for the other questions.

Discussion

Key findings

ECPs were significantly more likely than trainees to report the absence of ECT services at their workplaces. Several reported receiving training, observing, and administering ECT during their psychiatry training. However, familiarity with national and international guidelines was relatively low.

Overall, respondents held positive attitudes towards ECT, considering it an effective, lifesaving, and safe treatment, while rejecting the notion of it being outdated, cruel, or a form of control or punishment. Generally, respondents demonstrated a clear

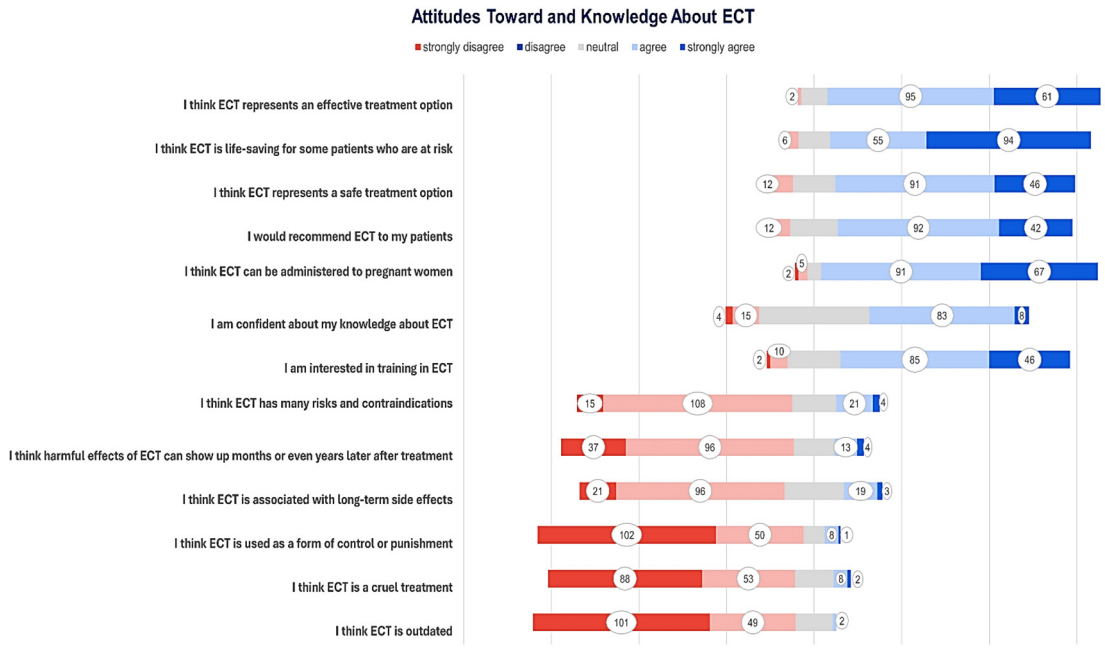

FIGURE 1
Attitudes and knowledge about ECT among respondents, displayed from strongly disagree to strongly agree.

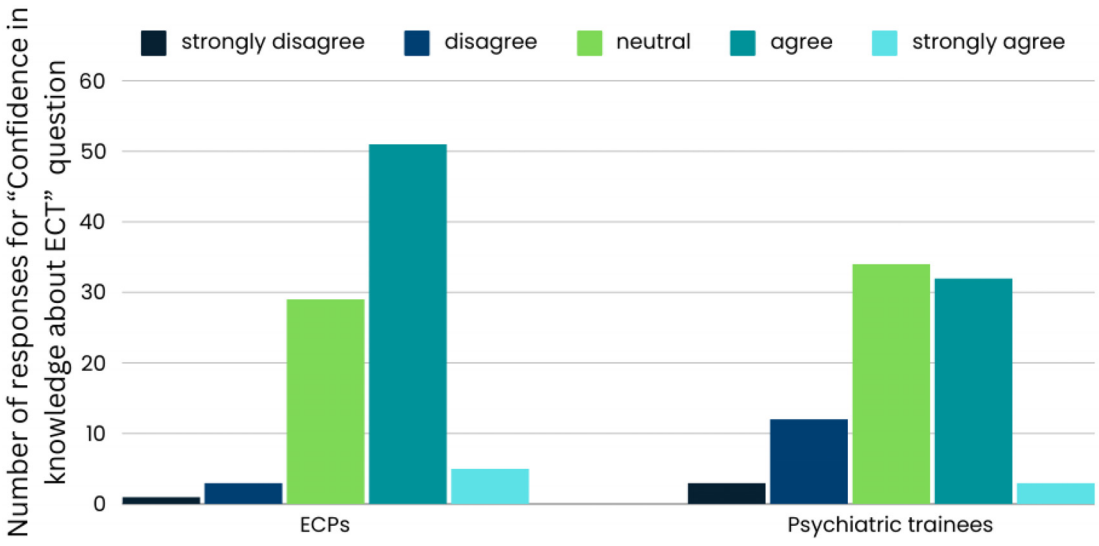

FIGURE 2
Confidence in ECT knowledge among early career psychiatrists and psychiatric trainees.

understanding of ECT, recognising its applicability to pregnant women and dismissing concerns about long-term side effects. Most participants expressed interest in ECT training. Whilst we distinguished between current trainees and ECPs to capture the transition from supervised residency to independent practice, this was reflected by ECPs' significantly higher confidence in ECT knowledge and a higher likelihood of reporting the absence of ECT services in their institutions.

Strengths and limitations

This study is the first to investigate the attitudes and knowledge of psychiatric trainees and ECPs in Iran regarding ECT. Strengths include its focus on the use of a questionnaire adapted from validated instruments, supported by a robust methodological framework. However, it has some limitations. Firstly, the low response rate (22%) and small sample size limit generalisability of

the findings. Secondly, the use of self-report data may be subject to reporting bias, and the voluntary nature of the survey may lead to non-response bias. Thirdly, the recruitment strategy, predominantly via online distribution in a setting of variable internet connectivity, raises concerns about selection bias. The gender imbalance (79.2% female) may also affect findings. While this reflects the demographic distribution in psychiatric training in Iran (23, 24), response bias cannot be ruled out. Moreover, geographical limitations and cross-sectional design restrict both the general applicability and the ability to conduct chronological analysis. Additionally, the 36-item questionnaire may not cover all relevant aspects, and potential cultural barriers could affect the accuracy of responses. Finally, the anonymity of the survey precluded follow-up clarifications, leaving some responses open to misinterpretation.

Comparison with other literature

Availability of ECT

Access to ECT varies significantly worldwide (3). For example, in Canada, approximately 84% of the population has convenient geographic access to ECT services (28). In Thailand, a 2022 survey revealed that 34 hospitals now offer ECT, indicating an increase from previous studies (29). In Slovenia, ECT is completely banned, although it is the only European country where this happens, according to a 2023 review (30).

In our study, most respondents acknowledged the availability of ECT services, though ECPs were more likely to report its absence in their institutions. Trainees, often based in inpatient settings or university-affiliated hospitals where typically ECT services are offered, had greater exposure compared to ECPs, who often worked in day clinics or outpatient settings with less access to ECT. This discrepancy may stem from institutional policies or regional resource variations, with some institutions lacking the necessary equipment or staff for ECT or prioritising other treatments.

In Iran, the use of the modified ECT (including anesthetics, muscle relaxants, oxygenation, and monitoring) is mandatory. However, the high cost of muscle relaxants and anesthetic drugs, along with a shortage of skilled anesthetists and restrictions in the health insurance system, limit the wide use of modified ECT (16).

ECT training

In 2001, the APA's Task Force on ECT recommended that psychiatry trainees receive at least 4 hours of didactic instruction and participate in at least 10 ECT treatment procedures. However, a 2010 survey of 91 US training programs found that few met these standards: most provided less than 4 hours of lectures, and 37% indicated trainees participated in 10 or fewer ECT treatments (31, 32). In contrast, several trainees in our study reported receiving ECT training, both didactic and hands-on, with 77.4% administering ECT to 10 or more patients during their psychiatry training. Experienced clinicians also showed higher confidence in their knowledge. Similarly, a 2018 quantitative survey in Scotland found that nearly 90% of psychiatry trainees felt their ECT training was sufficient, with senior trainees rating their knowledge higher. A study conducted across Europe also revealed that ECT training is associated with a more favorable perception of its safety and efficacy among ECPs (25). This highlights strong support for ECT training and its effectiveness in building trainees' confidence (33).

Educational resources such as videos could enhance the educational process. In France, psychiatrists and psychiatric trainees completed a questionnaire before and after watching a short educational video on ECT, which resulted in positive changes in their ECT practice (3). In Norway an interventional study developed a Virtual Reality (VR) based ECT training program, involving physicians, simulation experts, and VR developers, which received positive feedback from collaborators (32). Shifting focus from lectures to psychiatry clerkships, where trainees can observe the positive effects of ECT (33) and closely monitor patients until remission would be valuable steps (34).

ECT training is more accessible in Iran, where 96.5% of respondents reported having access, compared to 54.5% in a European survey across 30 countries (35). While countries like the UK, Portugal, Germany, and Spain offered more frequent training, access was notably lower in Romania, Greece, Albania, Latvia, and Italy.

National and international guidelines

Our study found that awareness of both national and international ECT guidelines was not particularly high. A 2016 survey in Italy revealed the absence of national ECT guidelines, with only 2 out of 20 regions having local standards, despite repeated government requests for national policies (34). Conversely, a 2009 survey in the Netherlands showed that 75% of institutions adhered to 14 out of 16 clinical guideline criteria, indicating high compliance with international requirements (36). Similarly, a 2012 questionnaire in Canada found that 84% of centers closely followed existing standards (37).

Globally, documents such as the APA Task Force Report, the ECT Recommendations for Health Authorities of British Columbia, and standards developed by bodies like the Royal College of Psychiatrists and the National Institute of Care and Excellence (NICE) form the foundation for ECT quality assurance. The ECT Accreditation Scheme (ECTAS) (38) is also designed to help ECT facilities in the United Kingdom and Ireland raise their standards of care. While there is no globally accepted guideline for ECT administration, these frameworks provide useful insights into ensuring ECT quality and adapting to changes in management over time (32).

Attitude toward and knowledge about ECT

Generally, respondents in this survey displayed positive attitudes and a thorough knowledge of ECT. Similarly, a 2015 study in Germany found that psychiatrists across various settings, including those supervising ECT therapy in hospitals, those in hospitals without ECT facilities, and those in private practice, all had a positive perception of ECT (4). Psychiatrists in Poland also exhibited more positive attitudes compared to some other Eastern

European nations (39). A survey conducted in Saudi Arabia among psychiatrists and family physicians (including trainees), showed that psychiatrists had a much clearer understanding and approach to ECT compared to family physicians, suggesting a link between knowledge and attitude regarding this treatment (9). This is consistent with findings from a United Kingdom (UK) survey, where psychiatrists had the most positive attitudes and highest level of knowledge, ahead of nurses, social workers, and psychologists (14).

The finding that a small yet notable proportion of respondents perceive ECT as cruel, a form of control or punishment, and outdated is concerning. Earlier research (1) indicates that bad experiences with outdated ECT practices, when procedures were performed without adequate anesthesia and muscle relaxation, may continue to shape negative perceptions among some clinicians. Additionally, cultural attitudes and media portrayals have been shown to influence beliefs about ECT, further contributing to skepticism regarding its use (40). Interestingly, a 2011 U.S. survey revealed psychiatrists who were less knowledgeable about ECT viewed the treatment rather negatively and were less likely to refer patients (6). Among Russian psychiatrists, familiarity with ECT was more limited, and many expressed doubts about its efficacy (41). Likewise, a 2004 study among Hungarian psychiatrists revealed that 32% would decline ECT even if experiencing a psychotic depressive state. Notably, these negative perceptions were more prevalent among psychiatrists working in outpatient care settings (42).

Impact of the findings on practice, policies and research

Enhancement of ECT training

Although most respondents had receiving ECT training during psychiatry training, only just over half felt confident in their knowledge. Those who attended courses and workshops reported significantly higher confidence compared to those who underwent other types of training (Kruskal-Wallis test, $p = 0.012$). The gap between training and confidence suggests that current training programs might not be comprehensive or practical enough. Given that 75.7% of respondents expressed interest in receiving further ECT training, future research should assess how ECT training ranks compared to other psychiatric training needs.The Iranian curriculum for psychiatry education has been revised to incorporate focused educational programs aligned with textbooks used in the US and UK, while continuously striving to integrate Iranian cultural issues and eastern psychiatric treatment modalities (23).

Addressing stigma and misconceptions

Despite the generally positive view within the psychiatric community in our study, some respondents regard ECT as a cruel treatment (5.8%) or believe it may be used for control or punishment (5.2%). Previous studies have identified fear and stigma as the most significant obstacles to ECT treatment access (6, 19). Since patients are likely to be less fearful of ECT and hold fewer misconceptions after receiving information from their physician (6), continuous education and awareness, both among medical professionals and the general public, become a high priority. Mental health activists should also urge cinema and the media to portray mental health conditions honestly and respectfully, in order to combat misconceptions that hinder the social inclusion of people with these conditions (43).

Standardisation of ECT guidelines

Our study revealed that respondents were not highly familiar with national and international ECT treatment guidelines. Given the evolving nature of ECT practices, it would be beneficial to ensure that national guidelines are reviewed and updated regularly to reflect current best practice, and disseminated amongst practitioners. Guidelines ensure a uniform approach to pretreatment assessment, premedication strategies, and the technical aspects of ECT administration (4).

Policy recommendations

Our findings indicate that ECPs were more likely than trainees to report a lack of ECT availability in their institutions. While our study did not directly assess the need for ECT expansion, the observed differences in access suggest that further exploration of institutional barriers to ECT implementation may be warranted. Additionally, dedicated funding is necessary to maintain ECT as a viable treatment option in clinical practice.

Future research directions

Future research should assess the long-term outcomes for patients who undergo ECT in Iran. Future research should explore whether male trainees engage differently in surveys or hold distinct perspectives on ECT. Additionally, evaluating the impact of enhanced or intervention-based training programs on clinical practice will help determine how such programs influence ECT administration. Another important area of research involves exploring the attitudes and knowledge of other healthcare professionals and the general population about ECT. Investigating the barriers to ECT utilization and the factors influencing ECT referrals could also help support broader implementation of this treatment.

Conclusions

This study found that ECT training during psychiatry training in Iran varies, and ECT is generally available across the country. Psychiatrists are actively involved in both observing and administering ECT, and they mostly hold positive views about its effectiveness. While confidence in personal knowledge varies, there is notable interest in further training. These findings emphasize the

importance of continuous education to enhance understanding and utilisation of ECT among psychiatric trainees and ECPs in Iran.

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 humans were approved by Iran University of Medical Sciences. 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

SH: Formal Analysis, Investigation, Writing – original draft. MS: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing – review & editing. FG: Data curation, Investigation, Writing – review & editing. MB: Data curation, Investigation, Writing – review & editing. SA: Data curation, Investigation, Writing – review & editing. AN: Data curation, Investigation, Writing – review & editing. MM: Data curation, Investigation, Writing – review & editing. CT: Conceptualization, Methodology, Writing – review & editing. MPdC: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing.

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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.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

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Restimulation could stop status epilepticus after electroconvulsive therapy: 2 case reports

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Background: Electroconvulsive therapy (ECT) is an effective treatment for severe depression, mania, psychosis and catatonia. While seizures are considered essential for the therapeutic effect of ECT, it concurrently has an anticonvulsant effect which plays a role in its mechanism of action. This property has also prompted the use of ECT in managing status epilepticus (SE).

Case Presentation: We report two distinct cases of prolonged seizures during ECT that persisted for more than 5 min despite administration of propofol and lorazepam, ultimately meeting criteria for status epilepticus (SE). The first case involved an 80-year old woman with severe psychotic depression starting ECT, while the second case involved a 30-year old man receiving maintenance ECT for difficult-to-treat schizophrenic psychosis. In both cases, SE was promptly terminated by restimulation, defined as an additional stimulus delivered within the same ECT session. After epilepsy and intracranial pathology were ruled out, ECT was safely resumed in both patients after switching from etomidate to propofol induction.

Conclusion: Status epilepticus after ECT can be resolved by restimulation when standard interventions are unsuccessful, thereby avoiding potential neurological complications. We provide an overview of the mechanism and current clinical evidence supporting this strategy, and propose an amended clinical practice protocol for SE after ECT.

KEYWORDS

electroconvulsive therapy, status epilepticus, prolonged seizure, mechanism, complication, anticonvulsant hypothesis, restimulation

1 Introduction

Electroconvulsive therapy (ECT) is an effective treatment for difficult-to-treat depression, particularly in older patients and when psychotic features are present (1). It is also a second-line treatment for clozapine-resistant psychosis (2). While there is an abundance of evidence for the efficacy and safety of ECT (3), the mechanism of action remains unresolved. ECT was developed in 1938 as a safe way to elicit a seizure, as it was believed that seizures counteracted psychosis (4). The three currently most accepted hypotheses still stem from the assumption that seizures are directly involved in the therapeutic effect of ECT. The generalized seizure hypothesis posits that the therapeutic effect of ECT is dependent on the elicitation of generalized seizures (5), while the combined anatomical-ictal hypothesis suggests that therapeutic effect is driven by seizure activity in the limbic system which induces neurotrophic effects through brain derived neurotrophic factor (BDNF) (6, 7). The anticonvulsant hypothesis suggests that the therapeutic effect of ECT originates from an increased inhibitory GABA-ergic neurotransmission, as the seizure threshold often rises during a course of ECT (8, 9). This phenomenon has facilitated the use of ECT in status epilepticus (SE) (10). Status epilepticus is defined by the International League Against Epilepsy (ILAE) as a generalized seizure lasting more than 5 min, which is considered a practical time point for initiating treatment, or more than 30 min, beyond which significant risk of long-term neuronal injury and functional deficits arise (11).

Prolonged seizures after ECT are seizures of >180 seconds occurring in 1-2% of ECT courses (12) and are typically managed by intravenous anesthesia or benzodiazepines (13). However, in rare cases these interventions are ineffective leading to SE (14). Tardive seizures after ECT, meaning seizure activity after termination of the therapeutic seizure, can also occur (15). Managing SE poses significant clinical challenges. Evidence guiding interventions is limited and entails general intensive care, antiepileptic drugs and treatment of underlying pathology (11, 16). We illustrate the paradoxical relationship between seizure and ECT by presenting two cases where SE following ECT was promptly managed by restimulation.

2 Case presentation

2.1 Case A

2.1.1 Patient information

Ms. A, an 80-year-old woman, was admitted for severe depression with psychotic features. She had no prior psychiatric or neurological history, and no known family history of depression or epilepsy. She had a history of breast cancer with bone metastasis diagnosed in the previous year. She had been treated with escitalopram 15 mg and mirtazapine 15 mg for three months before admission without any clinical improvement. Further medication consisted of letrozole 2.5 mg.

2.1.2 Clinical findings and diagnostic assessment

The patient exhibited depressed mood, anhedonia, cognitive impairment, and psychotic features such as nihilistic delusions and paranoid behavior. Her Montgomery-Åsberg Depression Rating Scale (MADRS) (17) score was 40/60, and her CORE score was 15, suggestive of a melancholic depression (18). Upon admission, olanzapine 5 mg was added to the regimen which showed no effect after the first week. Given the severity of her symptoms, ECT was advised and started after informed consent by proxy was granted by the patient's family. Pre-ECT evaluations, including EKG and laboratory tests, were unremarkable.

2.1.3 Therapeutic intervention

Right unilateral ECT twice a week was started using a square-wave, brief-pulse, constant-current device (MECTA SR1-5000Q; Lake Oswego, Oregon). Figure 1a shows a timeline of the index ECT. Anesthesia consisted of etomidate 12 mg, succinylcholine 35 mg and 100% oxygen. The seizure threshold was established by empirical titration (see Table 1). The second titration step resulted in a threshold seizure, followed by a therapeutic stimulus at 6 times seizure threshold. The following seizure exceeded 2 min on electroencephalogram (EEG). Per hospital protocol (see Table 2a), propofol 60 mg was administered, followed by lorazepam 2 mg at 4 min and an additional 2 mg at 6 min. Despite these interventions, EEG showed sustained spike and wave activity consistent with SE

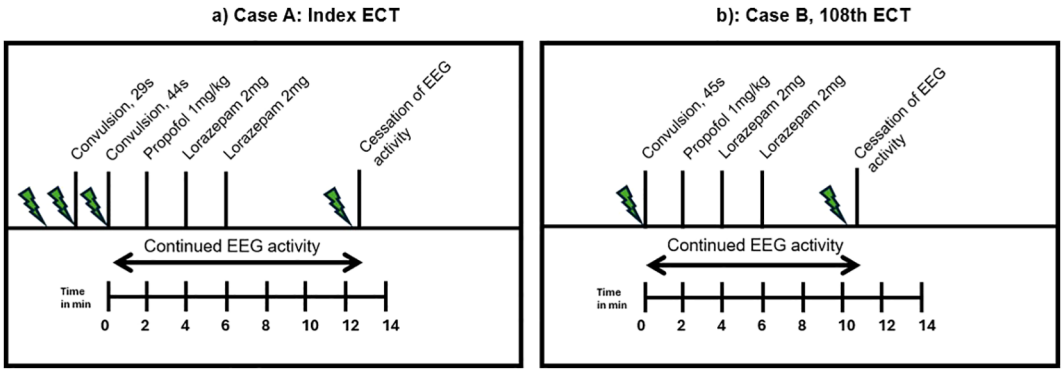

FIGURE 1
(a) Case A, Index ECT. **(b)** Case B, 108th ECT.

TABLE 1 Stimulus parameters for Case A and B.

Stimulus Nr.	Stimulus type	Electrode position	Pulsewidth	Pulse frequency	Train	Charge
Case A						
1	Titration	RUL	0.5ms	20Hz	1.75s	28mC
2	Titration	RUL	0.5ms	20Hz	3.25s	52mC
3	Therapeutic	RUL	0.5ms	50Hz	8s	320mC
4	Termination	RUL	0.5ms	50Hz	8s	320mC
Case B						
1	Therapeutic	BT	0.5ms	20Hz	3.75	60mC
2	Termination	BT	0.5ms	20Hz	3.75	60mC

RUL, Right unilateral electrode position; BT, Bitemporal electrode position.

(Figure 2). The clinical team decided to administer another stimulus using the same parameters applied 15 min after the first. After restimulation, EEG monitoring showed immediate cessation of seizure activity, followed by postictal suppression.

2.1.4 Follow-up and outcomes

Post-ECT, Ms. A was closely monitored and her vital signs and neurological status remained stable. A neurologist (EB) evaluated the patient, and subsequent 24-channel EEG showed no epileptic activity. A CT ruled out intracranial pathology, including breast cancer metastasis. After weighing risks and benefits with the patient's family, ECT was resumed using propofol for induction. The patient tolerated subsequent sessions without complications. After 8 sessions her MADRS score decreased to 4 and CORE score to 0, indicating remission. She was discharged with maintenance ECT and continued to do well at follow-up after 6 months.

TABLE 2 Protocol to manage prolonged seizures after ECT.

a. Current protocol at University Psychiatric Center KU Leuven	
Duration of convulsion	Action
1 min 30 seconds	Prepare propofol 1 mg/kg
2 min	Administer propofol 1 mg/kg
4 min	Administer lorazepam 2 mg
6 min	Administer lorazepam 2 mg
b. Proposed amendment based on current report	
10–15 min	Consider restimulation
15 min	Transfer to expert acute neurological care
Follow up:	· 24h in-hospital monitoring · Neurological consult with 24-channel EEG to rule out epilepsy · Consider intracranial imaging to rule out intracranial pathology · Consider stopping medication that lowers seizure threshold · Switch to propofol induction if ECT would be resumed

2.1.5 Patient perspective

Ms. A recalls little about her depressive symptoms and often wonders what she was doing in the months before her hospitalization. She felt well-informed about side effects before and during treatment. As she was unconscious during the status epilepticus and still severely depressed afterward, she has limited recollection of discussions about the events. Her son, who was also informed, felt he received adequate explanations regarding what happened. Both Ms. A and her family emphasize that they mainly remember the rapid and complete remission of depression after ECT sessions. They also emphasized the importance of the kindness and warmth of the ECT team as a key aspect of her care. At the time of writing maintenance ECT was discontinued and Ms. A remains in remission.

2.2 Case B

2.2.1 Patient information

Mr. B was a 30-year old male diagnosed with schizophrenia, showing first symptoms of disorganization and paranoid delusion at 17 with severe impact on his functioning. Before admission, he was treated with Amisulpride 400 mg, olanzapine 10 mg and paliperidone long acting injection 150 mg with little improvement in functioning, which lead to the diagnosis of difficult-to-treat schizophrenia. Physically he was diagnosed with Juvenile Polyposis Syndrome at 11, for which he received a total colectomy. His current admission started several years before the event for non-suicidal self-injurious behavior and catatonia.

2.2.2 Clinical findings and diagnostic assessment

On admission, Mr. B showed mannerisms, stereotypical behaviors, autonomic instability, perseverations and non-suicidal self-injurious behavior, particularly severe scratching, leading to diagnosis of schizophrenia with catatonia. A CT brain and extensive blood work showed no abnormalities, inferring no organic

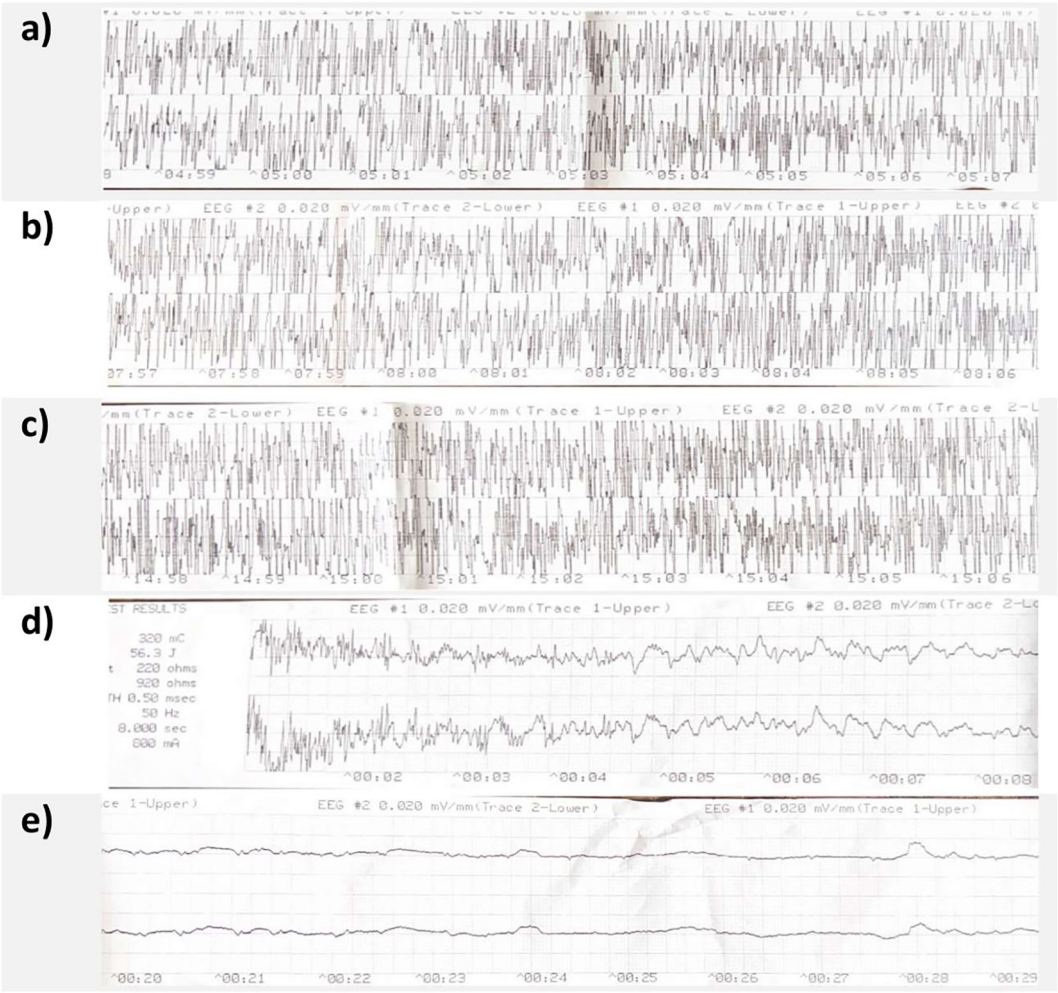

FIGURE 2
Case A's MECTA 2-channel EEG. Panel (**a–c**) show continued spike and wave activity at 5 min, 8 min and 15 min respectively. Panel **(d)** shows restimulation at 15 min with termination of clear spike and wave activity, panel **(e)** shows clear postictal suppression 20 seconds after restimulation.

etiologies of catatonia. Alongside clorazepate 15 mg 3x/day, clozapine 200 mg was initiated and initially provided partial improvement. However, residual stereotypical behaviors and scratching persisted. Clozapine was eventually discontinued because of recurrent gastrointestinal obstruction, which was considered a side effect aggravated by Juvenile Polyposis Syndrome and colectomy. After multidisciplinary discussion and pre-ECT evaluations, ECT was advised and informed consent by proxy was obtained from his family.

2.2.3 Therapeutic intervention

Bitemporal ECT for catatonia in schizophrenia was started with good effect on catatonic symptoms and non-suicidal self-injury. The reduction in symptoms led to an improvement of activities of daily living on the ward. Reduction to biweekly ECT led to an increase in catatonic symptoms, after which weekly ECT was continued. Aside from clorazepate 15 mg 3x/day, he was on aripiprazole 15 mg and clotiapine 20 mg 3x/day. Furthermore he received lorazepam 2.5 mg as needed. ECT was continued with important clinical improvement for 107 sessions. During his weekly maintenance ECT treatment, the patient had a prolonged seizure on session 100 necessitating propofol with successful termination of the seizure.

On the 108th ECT session, he received 16 mg etomidate and 50 mg succinylcholine for induction. Figure 1b shows a timeline of this ECT session. Therapeutic stimulus was given with the same parameters as previous stimulations (see Table 1), and motor convulsions terminated at 45 seconds. He showed epileptic activity on EEG for more than 2 min, after which the same protocol as above was followed (see also Table 2a). EEG showed continued epileptic activity after 8 min. The clinical team decided to administer 8 mg etomidate and 50 mg succinylcholine and stimulate the patient 10 min 43s after the first stimulation with the same dose as the therapeutic stimulus. A 25-second convulsion ensued, after which EEG monitoring showed immediate cessation of seizure activity and postictal suppression.

2.2.4 Follow-up and outcomes

The patient was closely monitored for 24 hours and received a neurological follow up consultation with 24-channel EEG which showed no epileptic activity. After careful consideration, imaging was not performed since there was no indication that the patient had any structural brain abnormality. Discharge of residential hospitalization was already being planned in the time leading up to this event, but was only possible due to continued improvement with weekly ECT. Therefore weekly ECT was resumed with propofol induction. After no prolonged seizures or other complications were reported in the next month, the patient was discharged from residential hospitalization, while continuing weekly maintenance ECT.

2.2.5 Patient perspective

Communicating with Mr. B remained challenging even after symptom improvement with ECT, making it difficult to fully understand his personal experience of the treatment. However, given the severity of his symptoms, it was evident that he endured significant suffering. As he had no recollection of the SE, he expressed no concern about its implications. His father was more worried about potential cognitive side effects of ECT than the prolonged seizures.

With continued maintenance ECT sessions, Mr. B showed noticeable improvement in paranoid delusions, stereotypical behaviors, excessive scratching, and disorganization, allowing for better engagement in activities of daily living. One month after the SE, he was discharged from the hospital after several years of inpatient care and transitioned to a psychiatric care home. However, he continues to experience disorganization and is still receiving maintenance ECT at the time of writing.

3 Discussion

3.1 Mechanism

The anticonvulsant effects of ECT have long been recognized, giving rise to the anticonvulsant hypothesis of its mechanism of action. This hypothesis states that increased inhibitory GABA-ergic neurotransmission is necessary for the therapeutic effect of ECT (8, 9). As genetic deficits of GABA-ergic metabolism lead to epileptic syndromes and many GABA-agonists are anticonvulsants, we know that GABA plays a central role in seizures. Furthermore, GABA might stimulate neuroplasticity (19). During the course of ECT, seizure duration decreases while seizure threshold increases (20), which could be due to increased levels of GABA, GABA-receptor activity and GABA-ergic interneurons (21–24) and may be linked to neuroplastic effects of ECT (20). Postictal suppression, seen at the end of an ECT-induced seizure on EEG, could be the expression of an increased postictal inhibitory process and appears to be a useful predictor of clinical outcome of depression (25, 26).

The anticonvulsant hypothesis has provided a theoretical basis for the use of ECT as a treatment for SE. A recent scoping review describes 28 patients with refractory or super-refractory SE that received ECT, all of which resulted in SE resolution, with clinical improvement reported in 20 patients (10). ECT is classified at a GRADE D/Oxford level 4 evidence for treatment of SE (10, 27) and is mentioned in 5 clinical practice guidelines as alternative therapy for specific cases of refractory and super refractory SE (28). The limited evidence supporting these clinical recommendations highlights the relevance of our report.

3.2 Current findings and clinical practice

The cases described in our study demonstrate that administering an additional ECT stimulus can effectively terminate SE when conventional treatments fail. This approach is theoretically grounded in the anticonvulsive hypothesis and in clinical evidence showing that ECT is an effective treatment for refractory SE. Although propofol induction prevented prolonged seizures in subsequent ECT sessions and is usually sufficient to terminate prolonged seizures, it was ineffective in these two cases. Similarly, the ensuing doses of lorazepam were insufficient. The temporal relationship between the stimulus and the swift cessation of the seizure reinforces this hypothesis. Additionally, this approach was validated in two patients. It should be noted that in case B, we used etomidate in preparation for the terminating stimulus instead of propofol. Although this strengthens the hypothesis that the seizure stopped because of the stimulus and not due to additional anesthesia, propofol bears preference due to its stronger anticonvulsive properties (29).

Our cases can be considered both a prolonged seizure and SE, explaining why terminology in literature of abnormal seizures after ECT is heterogenous. We consider all prolonged or tardive seizures with >5 min of generalized seizure activity, or all partial and absence seizures >10 min as status epilepticus, based on the ILAE classification (11). In a search of the literature we found 35 cases of status epilepticus after ECT meeting these criteria (14, 30–63) (see Supplementary Materials for search method). Only two of these describe restimulation to terminate SE. Hazimeh et al. (28) describe a convulsion starting 11 min after ECT which was initially managed with midazolam and propofol. When convulsions resumed and propofol had no effect, the convulsion ceased after the second stimulus. However, more convulsions followed after 5 min and SE was not resolved by this intervention. Goh et al. (37) describe a prolonged seizure of more than 12 min, constituting SE, which was terminated completely by a second stimulus. In these two cases described in the literature, the eliciting stimulus was the seizure threshold, and both terminating stimuli used were six times seizure threshold equivalent to a therapeutic stimulus. Conversely, in our cases the eliciting stimulus was therapeutic and both terminating stimuli were of the same dose, suggesting the dose of the terminating stimulus is not a critical factor in the mechanism of seizure termination. It has indeed been shown that seizure duration decreases between the first and second treatment, while the relationship between stimulus dosage and seizure duration is less

straightforward (64). It is also known that an effective ECT session results in an immediate and substantial surge of GABA (22). The finding that the second stimulus is more effective than the administered medication could be explained by the electrical stimulus provoking an excitatory wave immediately followed by a massive outpouring of GABA and other inhibitory neurotransmitters (19). However, if the eliciting stimulus dose is the seizure threshold, we would recommend restimulating with a therapeutic stimulus.

Prolonged seizure, SE, and tardive seizures after ECT share risk factors that lower seizure threshold, which should be considered and mitigated following an abnormal seizure after ECT:

- Medication: clozapine (59), lithium (65), bupropion, antibiotics, theophylline (15).

  Seizure risk may increase after recent tapering of antiepileptics or benzodiazepines (15).
- ECT delivery: first sessions (15), multiple monitored ECT (30).
- Anesthesia: etomidate (29), hyperventilation, anesthetic-ECT time interval (66).
- Patient specific factors: younger age (65), women (67), height (64), intracranial pathology like brain metastasis (42), although ECT can remain safe in these patients (68).

Based on these findings, we propose amendments to the protocol used to manage prolonged seizure after ECT (See Table 2b). We suggest considering restimulation after all other treatments have failed. All 4 available reports restimulated 10–15 min after the eliciting stimulus, and it should be considered before 30 min of SE as risk of neurological complications is significant by this time (11). Additionally, we suggest minimizing risk factors for prolonged seizures like intracranial pathology and medication before considering resumption of ECT. Finally, we propose to resume ECT using propofol induction as this raises the seizure threshold (29). Further research is necessary to bolster the evidence for these recommendations, although we report that both of our patients were able to continue ECT without further complications and with important clinical benefit.

3.3 Limitations

Aside from publication bias and possible overinterpretation which are limitations inherent to case series (69), a limitation of our report is that we do not have 24-channel EEG data of the events themselves as patients in our center are monitored through the MECTA 2-channel EEG during ECT. Difficulty in diagnosing SE, particularly non-convulsive SE, has been noted in previous reports, as EEG slowing after ECT is a physiological phenomenon (70–72). Additionally, while ECT has been safely used in SE, our report is not able to offer a comparative analysis of the tolerance of this intervention. However, we offer suggestions on how to manage follow-up.

3.4 Conclusion and implications

This report suggests that status epilepticus after ECT can be safely treated by restimulation, avoiding a longer seizure and potential severe neurological complications. Our report describes the theoretical foundations and acknowledges two previous reports with this finding, leading us to believe this strategy is warranted if this rare complication arises. After risk factors were determined, anesthesia was switched to propofol and both patients resumed ECT without complications. Further research would have to validate this strategy which might offer a safe and effective way to address SE when other treatments fail.

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.

Ethics statement

The studies involving humans were approved by EC Research UZ/KU Leuven and EC UPC KU Leuven. 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. 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

MP: Conceptualization, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing. KH: Supervision, Writing – review & editing. PS: Supervision, Writing – review & editing. EB: Writing – review & editing. FB: Conceptualization, Writing – original draft, Writing – review & editing.

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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.

Generative AI statement

The author(s) declare that Generative AI was used in the creation of this manuscript. The authors used AI-assisted proofreading (ChatGPT, OpenAI) only for English language optimalisation of the manuscript. All content was reviewed and approved by the authors.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2025.1576374/full#supplementary-material

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Trend of electroconvulsive therapy use and its relationships with clinical characteristics from a large psychiatric center in China

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Background: Recent studies on electroconvulsive therapy (ECT) have reported inconsistent frequencies of ECT use in various countries. Therefore, this study aimed to investigate the trends of ECT use in a large psychiatric center in China over 6 consecutive years.

Methods: A total of 22,120 inpatients, aged 18–59 years, admitted during the period 2015–2020 to a large grade-A tertiary psychiatric center in Beijing were enrolled in this retrospective study. Demographic and clinical data including vital signs; daily living abilities(ADL); emergency referrals; psychiatric and physical prescriptions were collected from an electronic medical records system.

Results: In all, 2,213 (10.0%) inpatients received ECT, with an average number of sessions of 10.3 ± 6.6. There were no significant differences between the ECT and non-ECT groups in terms of educational level, marital status, length of hospital stay, and blood pressure. After using the propensity score matching (PSM) method, Multiple logistic regression analysis revealed that ECT use was independently associated with married/cohabitating (OR = 1.21, 95% CI: 1.03-1.43); few hospitalizations (OR = 0.96, 95% CI: 0.93-0.99); unemployed (OR = 1.43, 95% CI: 1.16-1.76); emergency referral (OR = 1.62, 95% CI: 1.36-1.93); increased use of antipsychotics (OR = 2.63, 95% CI: 1.88-3.68), mood stabilizers (OR = 1.30, 95% CI: 1.01-1.67), antidepressants (OR = 1.40, 95% CI: 1.13-1.73), and trihexyphenidyl (OR = 1.30, 95% CI: 1.05-1.50); reduced use of hypoglycemic drugs (OR = 0.64, 95% CI: 0.45-0.83); fast heart rate (OR = 1.01, 95% CI: 1.01-1.02); and severe impairments in ADL. Compared with that in 2015 (13.2%), ECT use decreased annually from 2016 (12.4%) to 2019 (9.6%), especially in 2020 (5.7%), given the impact of the COVID-19 pandemic in China.

Conclusions: The ECT usage and year-by-year decrease in ECT use in this study were consistent with the recent trends in other regions. Patients with the married/cohabitating, unemployed, and emergency-referral, unstable vital signs, more severe disability received ECT for quick alleviation of their conditions.

KEYWORDS

electroconvulsive therapy, inpatients, China, daily living abilities, clinical characteristic

Introduction

Electroconvulsive therapy (ECT) is considered a highly effective nonpharmacological intervention for patients with severe psychiatric disorders (1). With the rapid development of psychiatry, there is a growing body of evidence indicating that comprehensive treatment patterns, including medication, psychotherapy, physical therapy, and social rehabilitation therapy, are currently the main clinical strategies. ECT plays a crucial role in the acute phase of several serious mental illnesses (2), and its role is incomparable to the roles of medication and psychological therapy (3).

ECT has been used clinically for nearly 90 years since it was first demonstrated in Rome in 1938. The basic mechanism of ECT is the application of a brief electric current to the patient's scalp to induce a generalized seizure that, in turn, alleviates severe psychiatric symptoms (4). As the findings of Leiknes and colleagues' 2012 review (5), Regenold and colleagues' 2022 survey (6), the ECT performed today has remained roughly the same as that in the past decade since the early 20th century. ECT is considered a strict therapeutic strategy for patients with a high risk of suicide, impulsiveness, aggressive tendencies, and resistance to pharmacotherapy (7, 8).

Information on the patterns of ECT use across countries has been inconsistent (5, 9). There had been sustained declining use of ECT in the United States from 1993 to 2009 (10). In contrast, a large survey found that 30% of the patients with mood disorders in southern China received ECT – while the rate is lower than that reported in Beijing (33.6% in 2007 and 61.8% in 2013), it is far higher than the rates reported in European countries and the United States (11, 12). However, with the popularization of ECT usage in mental disease and stigmatization of ECT, it is necessary to update the information on the use of ECT in China in the recent 5 years or even longer (5).

This study retrospectively investigated the ECT use and the correlated demographic and clinical factors by examining data from a large psychiatric hospital in China for a period of 1 January 2015 to 31 December 2020.

Methods

Subjects and ECT setting

The study was conducted at Beijing Huilongguan Hospital, Huilongguan Clinical Medical School, Peking University, China. This center has 1369 beds and is one of the largest grade-A tertiary psychiatric hospitals in Beijing and even in China. In this hospital, ECT is primarily administered to inpatients. For adult patients, the ECT course usually comprises 6–12 sessions under general anesthesia, over 2–3 weeks (13). The anesthesia and muscle relaxation is induced with propofol (1–1.5 mg/kg) accompanied by succinylcholine (0.3–0.7 mg/kg) and oxygenation. The intensity of ECT is based on two-thirds of the patient's age (14).

ECT is delivered via the electrodes of a MECTA spectrum M5000Q stimulator (MECTA Corp, Tualatin, Oregon, USA) that are placed on the bilateral temporal lobes. The following ECT parameters are used: maximum charge delivered, 504 mC; output current, 0.9 A; frequency, 10 to 70 Hz; pulse width, 1.0 ms; maximum stimulus duration, 8 s (15). After each ECT session, the patient is transferred to the recovery room for close monitoring.

Collection of demographic and clinical characteristics

The information of all patients aged 18–59 years who were receiving adult psychiatric services was retrieved from the electronic medical record system (EMRS). The following inpatient data were collected: basic demographic and clinical characteristics including the diagnoses, psychiatric and physical (non-psychiatric) prescriptions, emergency referrals, vital signs, and ADL performance.

Psychiatric diagnoses were divided into four categories: schizophrenia or other psychotic disorders (SZ), bipolar disorders (BD), major depressive disorders (MDD), and others. The diagnosis was confirmed by two experienced psychiatrists according to the diagnostic criteria of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). If a patient had more than one diagnosis, only the primary diagnosis was used.

Vital signs, including systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate, was considered one of the crucial indicators for indirectly assessing the stability of physical conditions. Unstable physical conditions can also have an negative impact on mental illnesses, such as the blood pressure variability increasing the risk of anxiety (16). These indicators were recorded and calculated as the average of measurements before each ECT using a unified electronic sphygmomanometer. The accuracy of an electronic sphygmomanometer is usually verified every 6 months.

Generally, the blood pressure and heart rate in the right upper limb is measured while the patient is seated.

ADL performance, an important outcome evaluated in this study, was assessed using the Barthel ADL Index at admission and discharge (17). The ADL index includes 10 items (feeding, transfer, personal hygiene, toilet use, bathing, walking, going up and down stairs, dressing, stool, and urination). ADL ability was classified as follows according to the ADL score (range: 0–100): ADL self-care (100), mild ADL disability (65–95), moderate ADL disability (45–60) and severe ADL disability (0–40). Low scores indicate impairments in ADL (18). Cronbach's alpha for ADL was 0.94 (19).

The authors (X.X.G and J.H.T.) and a technician responsible for EMRS collected the data and established the study database. The study design was approved by the Ethics Committee of Beijing Huilongguan Hospital.

Statistical analysis

All data were analyzed using SPSS software (version 22.0; SPSS Inc., Chicago, IL, USA). Basic demographic and clinical characteristics between the ECT and non-ECT groups were compared using the chi-square test for categorical variables and the Mann–Whitney U test for continuous non-normally distributed variables, as appropriate. To reduce bias and confounding variables, propensity score matching (PSM) analysis was conducted on participants based on gender and age, with matching pairs on 1:1. SPSS software was used to calculate conditional logistic regression between the paired data. The odds ratio (OR) and 95% confidence interval (CI) for each variable were calculated. Finally, the trends and use rate in ECT among the four disease types from 2015 to 2020 were analyzed separately. The level of significance was set at 0.05 (two-tailed).

Results

The data of 22,120 patients who were hospitalized during the study period and met the study criteria were analyzed. The mean age was 41.8 ± 12.7 years, the length of current hospital stay was 71.8 ± 68.2 days, and the number of hospitalizations was 7.4 ± 7.9; 57.1% of the sample consisted of men; 59.5%, 14.7%, 12.6%, and 13.2% had a primary diagnosis of SZ, BD, MDD, and other, respectively. The most frequently prescribed medication class was antipsychotics (89.6%), followed by trihexyphenidyl (30.7%), antidepressants (25.8%), mood stabilizers (21.9%), and cognitive-enhancing drug (0.4%). Commonly prescribed drugs for physical diseases included lipid-lowering drugs (24.0%), hypoglycemic drugs (11.6%), and anti-hypertensive drugs (11.1%).

Table 1 outlines the demographic and clinical characteristics of the study sample and the results of the comparative analyses between the ECT and non-ECT groups. Of these, 2213 individuals (10.0%) underwent ECT. The corresponding proportions were 17.8% for BD, 17.8% for MDD, 8.2% for SZ, and 2.1% for other diagnoses (P<0.001). There were significant differences in all demographic and clinical characteristics, except education, marital status, nationality, religion, current hospital stay, and DBP and SBP before ECT between the two groups (Table 1).

After the PSM based on gender and age and matching pairs on 1:1, Supplementary Table 1 outlines the demographic and clinical characteristics of the paired sample (2213 patients in each group). Compared with the comparison results of the previously unmatched group, there were differences in gender, age, marital status, use of antihypertensive drugs, use of lipid-lowering drugs, and ADL total at discharge among the paired samples, while other results were generally consistent.

Conditional logistic regression analysis showed that married/cohabitating, unemployed, emergency admissions were significantly associated with the use of ECT (OR_1 = 1.21, 95% CI_1: 1.03-1.43) (OR_2 = 1.43, 95% CI_2: 1.16-1.76) (OR_3 = 1.62, 95% CI_3: 1.36-1.93). The use of antipsychotics, mood stablilizers, antidepressants and trihexyphenidyl were also significantly associated with the use of ECT (OR_1 = 2.63, 95% CI_1: 1.88-3.68) (OR_2 = 1.30, 95% CI_2: 1.01-1.67) (OR_3 = 1.40, 95% CI_3: 1.13-1.73) (OR_4 = 1.30, 95% CI_4: 1.05-1.50). Patients with mild, moderate and severe ADL disability had 1.56 times (95% CI: 1.36-1.79), 5.95 times (95% CI: 4.51-7.85), 10.14 times (95% CI: 4.15-24.80) higher risk of using ECT compared to the ADL self-living individuals. Patients with diagnosing schizophrenia, bipolar disorder and major depression had 5.62 times (95% CI: 3.97-7.94), 7.55 times (95% CI: 4.86-11.73), 8.99 times (95% CI: 14.00-21.84) higher risk of using ECT compared to the individuals with other diagnosis. The use of hypoglycemic drugs (OR = 0.64, 95% CI: 0.45-0.83), hospitalizations (OR = 0.96, 95% CI: 0.93-0.99) were negatively associated with the use of ECT. The effect of heart rate was relatively small but still statistically significant (OR = 1.01, 95% CI: 1.01-1.02) (Figure 1).

In addition, compared to ECT use on 2015, ECT use decreased significantly from 2016 to 2020. In 2020, when all aspects of life were negatively affected by the COVID-19 pandemic in China, the number of patients receiving ECT treatment was the lowest (Figure 2).

Discussion

This observational study found that 10.0% of 22,120 inpatients in Beijing's largest Grade A tertiary psychiatric hospital between 2016 and 2020 received ECT. We analyzed the largest single center ECT data in China in the past eight years. In contrast to previous studies, our research included detailed basic demographic and clinical characteristics as well as analyzed the vital signs and ADL ability of inpatients. Finally, we found that the receipt of ECT was independently associated with Married/cohabitating; few hospitalizations; unemployed; emergency referral; reduced use of hypoglycemic drugs; fast heart rate; severe ADL disability; and primary diagnoses of BD, MDD, and SCH.

We found that 10% of the inpatients received ECT, and this rate is slightly lower than that reported at a Chinese psychiatric hospital outside the Beijing area (17.8%) (12). Moreover, another study conducted in the Beijing area reported an ECT rate of 57.7% (11),

TABLE 1 Demographic and characteristics of the study sample.

Characteristics	The whole sample(n=22120)		Non-ECT group (n=19907)		ECT group (n=2213)		Statistics		
	N	%	N	%	N	%	X^2	Df	*P*
Male, N(%)	12629	57.1	11818	59.4	811	36.6	419.6	1	<0.001
Education(Undergraduate)	11510	52.0	10411	52.3	1099	49.7	3.5	1	0.61
Married/cohabitating	11163	50.5	10053	50.5	1110	50.2	0.04	1	0.85
Han nationality	21597	97.6	19432	97.6	2165	97.8	0.4	1	0.52
Religion(No religious belief)	20892	94.4	18812	94.5	2080	94.0	0.5	1	0.45
Local resident	13985	63.2	13039	65.5	946	42.7	443.4	1	<0.001
Employed	18556	83.9	16791	84.3	1765	79.8	31.1	1	<0.001
Emergency in hospital	4240	19.2	3438	17.3	802	36.2	462.6	1	<0.001
Primary psychiatric diagnosis							654.5	3	<0.001
Schizophrenia-spectrum disorders	13155	59.5	12077	60.7	1078	48.7			
Bipolar disorder	3259	14.7	2680	13.5	579	26.2			
Major depression	2779	12.6	2285	11.5	494	22.3			
Others	2927	13.2	2865	14.4	62	2.8			
Psychiatric drugs									
Use of antipsychotics	19818	89.6	17758	89.2	2060	93.1	32.2	1	<0.001
Use of mood stabilizers	4844	21.9	4152	20.9	692	31.3	126.3	1	<0.001
Use of antidepressants	5710	25.8	4850	24.4	860	38.9	218.6	1	<0.001
Use of cognitive-enhancing drug	88	0.4	86	0.4	2	0.1	5.9	1	0.019
Use of trihexyphenidyl	6796	30.7	5938	29.8	858	38.8	74.8	1	<0.001
Physical disease drugs									
Use of antihypertensive drugs	2248	11.1	2289	11.5	159	7.2	37.7	1	<0.001
Use of lipid-lowering drugs	5306	24.0	4881	24.5	425	19.2	30.9	1	<0.001
Use of hypoglycemic drugs	2576	11.6	2482	12.5	94	4.2	130.8	1	<0.001
Year							127.8	5	<0.001
2015	3376	15.3	2931	14.7	445	20.1			
2016	3570	16.1	3128	15.7	442	20.0			
2017	3926	17.7	3537	17.8	389	17.6			
2018	4163	18.8	3788	19.0	375	16.9			
2019	4106	18.6	3713	18.7	393	17.8			
2020	2979	13.5	2810	14.1	169	7.6			
	M	SD	M	SD	M	SD	*Z*		*P*
Age	41.8	12.7	42.5	12.6	35.7	12.2	-23.8		<0.001
Current hospital stay (days)	71.8	68.2	72.4	69.1	66.5	59.7	-0.8		0.45
No. of hospitalizations	7.4	9.7	7.9	9.9	2.6	3.3	-30.3		<0.001
Heart rate (/min)	81.2	12.4	81.0	12.5	83.0	12.1	-9.5		<0.001
SBP before ECT course (mmHg)	117.7	12.9	117.8	12.8	117.4	13.9	-0.8		0.41
DBP before ECT course (mmHg)	76.0	8.6	76.0	8.5	76.0	9.4	-0.2		0.89

(Continued)

TABLE 1 Continued

Characteristics	The whole sample(n=22120)		Non-ECT group (n=19907)		ECT group (n=2213)		Statistics		
	N	%	N	%	N	%	X^2	Df	*P*
	M	SD	M	SD	M	SD	*Z*		*P*
ADL total at admission	91.6	10.6	92.2	10.1	87.2	13.1	-20.1		<0.001
ADL total at discharge	96.1	8.2	96.0	8.2	96.9	7.6	-8.5		<0.001
Changes in ADL total	4.2	8.4	3.8	7.5	9.7	12.3	-30.4		<0.001
No. Sessions of ECT					10.3	6.6			
The intensity of ECT (J)					27.7	15.2			
Seizure duration (s)					49.2	23.1			

SBP, systolic blood pressure; DBP, diastolic blood pressure; ADL, daily living abilities.

and the frequency of ECT use in our study was closer to that reported in foreign countries: 1.2–7.4% in the USA, 13.6% in Japan, 13.8% in India, and 6% in Denmark (10, 20–25). This difference in the rates between China and these countries can be attributed to an inconsistent understanding of ECT indications among different hospitals. In addition, our treatment principle of focusing on early prevention of mental illness and reducing the possibility of severe mental diseases requiring ECT may also explain some of these differences. Of note, the annual decline in ECT use in our study was roughly consistent with the global trends (10, 26). In particular, the lowest uptake of ECT was reported in 2020 – when the COVID-19 pandemic impacted ECT services worldwide. During the COVID-19 period, several realistic factors limited the use of ECT, such as: the ECT operation room needing longer time for disinfection (about twice the usual time), patients without the cold symptoms (not considered as a source of viral infection), manpower shortage (many doctors were appointed to service nucleic acid testing), and patients restricted in their own wards (to reduce virus transmission) (27, 28).

ECT is commonly assumed to be a primary (first-line) treatment with strict indications, referring to the clinical guidelines of five authoritative psychiatric associations (American Psychiatric Association, Canadian Network for Mood and Anxiety Treatments, The Royal Australian and New Zealand College of Psychiatrists, The Royal College of Psychiatrists, and World Federation of Societies of Biological Psychiatry) (29–33). In China, patients with high suicide/aggressive behavior risk, food/fluid refusal, stupor, and extreme lack of cooperation or treatment resistance are given priority for ECT (34). Similar to our findings, ECT is used more frequently for BD or MDD inpatients (35). According to authoritative reviews and international guidelines, ECT can also be used to relieve symptoms of treatment-resistant schizophrenia; however, attention should be paid to its benefits and side effects.

From the initial results, we speculate that younger and female patients were more likely to receive ECT, which is consistent with other results (12), Demographically, there was a predominance of female patients of 53.4% in our results, 51% in Japan (36), 56% in Pakistan (37), 60% in Saudi Arabia (38), 71% in Australia (39), 57.7%-60.1% in Sweden (40, 41), 61.0% in Poland (42) and 57% in Norway (43). Our analysis of sex distribution in affective disorders showed that there were a higher proportion of female, up to 62%. We realize that the higher proportion of female in ECT is a global trend, especially in Western countries where ECT originated (44). This may be related to factors such as the higher prevalence of mental disorders among women, their susceptibility to hormones and environmental variability (45). On the contrary, in several African regions (29%-46%) (46, 47) and other Asian countries [28% in Katmandu (48); 39% in India (49)], the proportion of women in ECT is relatively low. This the specific reasons maybe need further investigations. However, from another perspective, the above different results are not inconsistent and may be related to bias and confounding factors. Therefore, we further conducted PSM analysis based on gender and age, with matching pairs on 1:1.

After PSM analysis, the figure clearly shows that the use of ECT was independently associated with fewer hospitalizations, confirming earlier results that ECT may reduce readmission rates through satisfactory treatment outcomes (50). Our analysis showed that the status of being married was associated with the use of ECT. One possible explanation is that being married was associated with family members recognizing of faster disease relief through the use of ECT (51). We speculate that unemployment may be an aspect of impaired social functioning in patients with mental illness. This suggested that the disease may be more severe and patients may be more likely to choose ECT to get quickly improvement and restore their health (52).

Notably, this is the first retrospective study to explore the relationship between the use of ECT and severity (including assessment of emergency, vital signs, and physical prescriptions). The results showed that more than one-third of the patients in the ECT group were referred from emergency departments. Emergency hospitalization may provide a fast and effective therapeutic opportunity for patients at risk, including receiving ECT services. In previous studies, the heart rate was associated with disease severity and urgency (53, 54). In addition, the different result of hypoglycemic drugs in Figure 1 maybe need further research to verify the differences (55).

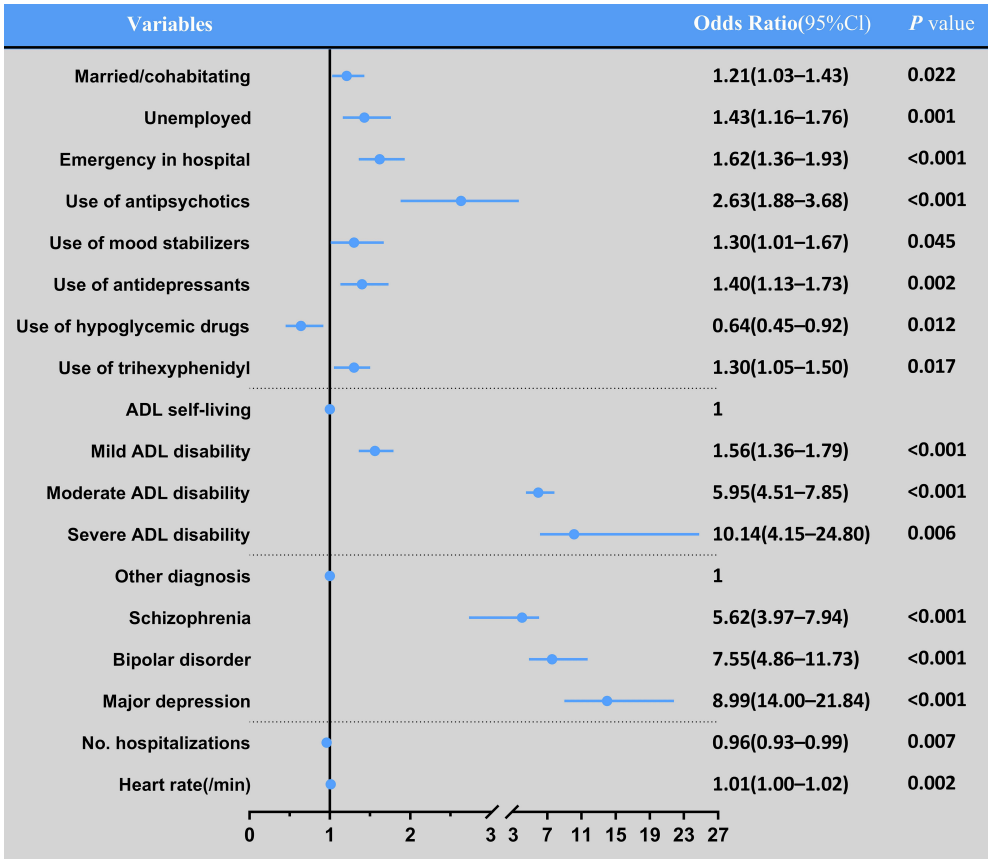

FIGURE 1
Independent contributors to ECT (multiple logistic regression analysis).

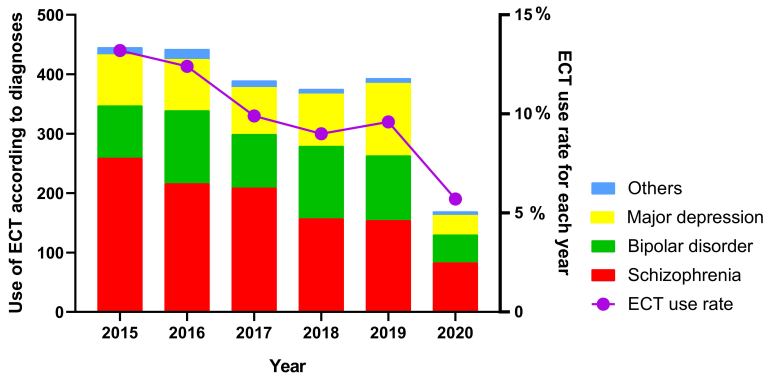

FIGURE 2
Use of ECT according to diagnoses and ECT use rate by year.

Diminished ADL is often regarded as a characteristic feature of severe mental disorders (56), such as the incapacity of individuals with profound depression or impulsivity to effectively accomplish certain activities in their daily lives (57). Consistent with our viewpoint, another study found the patients with ECT had worse ADL score compared to those without ECT. As shown in our results, the degree of ADL disability at admission is a positive factor for predicting acceptance of ECT treatment (58). Previous studies have shown that psychiatric patients in the acute phase have varying degrees of impairment in the self-care and daily life (59). During the rehabilitation period, except for severe organic psychiatric disorders, the impaired daily living abilities will get recovery for most patients (60). This is as observed in Table 1 of this article.

Limitations

This study had several limitations. First, the results of this retrospective study should be considered with caution owing to methodological limitations. Second, the data were collected from a single center, and the findings are not entirely applicable to other regions of China. Third, although our study included relevant variables such as non-psychiatric prescriptions and vital signs, evaluation data on the severity of psychiatric symptoms were still lacking. Finally, some specific indications like catatonia were not been extracted, and might be classified as special symptoms of a disease, not been independently diagnosed. Nevertheless, we analyzed a large dataset covering 6 consecutive years to determine the pattern of ECT use and the factors correlated with ECT usage from a large psychiatric center in China over the last years.

Conclusion

In conclusion, this study found that the usage rate and yearly decreasing trend in ECT use in the largest tertiary psychiatric center in Beijing were roughly consistent with the recent trends in other regions. ECT use was associated with married/cohabitating; unemployed; few hospitalizations; emergency referral; increased use of antipsychotics, mood stabilizers, antidepressants; reduced use of hypoglycemic drugs; fast heart rate; and severe ADL disability. Given the variations in previous research findings, it is crucial for clinical psychiatrists to adopt a scientific approach and the evidence based practice when establishing ECT protocols that adhere to the ECT utilization standards.

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 humans were approved by The Ethics Committee of Beijing Huilongguan Hospital. 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

WL: Data curation, Funding acquisition, Writing – original draft. NH: Data curation, Funding acquisition, Investigation, Writing – review & editing. XG: Data curation, Funding acquisition, Investigation, Writing – review & editing. YSo: Data curation, Formal Analysis, Methodology, Writing – review & editing. RZ: Investigation, Validation, Writing – review & editing. SS:. JS(first author): Data curation, Investigation, Writing – review & editing. JT: Data curation, Formal Analysis, Writing – review & editing. YSh: Data curation, Formal Analysis, Writing – review & editing. YY: Data curation, Investigation, Supervision, Writing – review & editing. KY: Data curation, Validation, Writing – review & editing, Methodology. YC: Data curation, Formal Analysis, Investigation, Writing – review & editing. JS(second author): Data curation, Funding acquisition, Investigation, Writing – review & editing.

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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.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2025.1508044/full#supplementary-material

SUPPLEMENTARY TABLE 1
Demographic and characteristics of the two groups by propensity score matching (PSM).

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Knowledge, attitudes, and willingness of bipolar disorder patients toward electroconvulsive therapy: a cross-sectional study

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Objective: This research aims to explore the levels of knowledge, attitudes, and willingness (KAW) of patients with bipolar disorder (BD) regarding electroconvulsive therapy (ECT).

Methods: A cross-sectional survey was conducted in Nanjing from April 10 to November 3, 2024, using a validated questionnaire [Cronbach's $\alpha = 0.936$, Kaiser–Meyer–Olkin (KMO) = 0.917]. Participants completed structured items assessing knowledge, attitudes, and willingness toward ECT. Data analysis involved descriptive statistics, non-parametric tests, Spearman correlation, multivariate logistic regression, and structural equation modeling (SEM).

Results: The study successfully enrolled 479 participants. Of these, 282 participants (58.87%) were female. One hundred and sixty seven respondents (34.86%) had previously undergone ECT. The mean knowledge, attitude, and willingness scores were 5.57 ± 4.84 (possible range: 0–16), 29.08 ± 6.21 (possible range: 9–45), and 21.49 ± 5.14 (possible range: 6–30), respectively. SEM analysis showed that electroconvulsive therapy ($\beta = -0.377$, $P = 0.014$), years of BD ($\beta = 0.196$, $P = 0.014$) had direct effects on knowledge. Knowledge ($\beta = 0.526$, $P = 0.023$) directly affected attitude. Meanwhile, electroconvulsive therapy ($\beta = -0.198$, $P = 0.013$) and years of BD ($\beta = 0.103$, $P = 0.016$) indirectly affected attitude. Knowledge ($\beta = 0.107$, $P = 0.018$), attitude ($\beta = 0.674$, $P = 0.009$), and gender ($\beta = 0.104$, $P = 0.020$) directly affected willingness. Knowledge ($\beta = 0.355$, $P = 0.011$), electroconvulsive therapy ($\beta = -0.174$, $P = 0.015$), and years of BD ($\beta = 0.090$, $P = 0.020$) indirectly affected willingness.

Conclusion: The study found that bipolar disorder patients generally lack knowledge and hold negative attitudes but demonstrate a relatively high willingness to accept ECT treatment. Targeted educational programs are recommended to improve understanding, shift attitudes, and enhance acceptance of this treatment in clinical willingness.

KEYWORDS

knowledge, attitudes, and willingness, bipolar disorder, modified electroconvulsive therapy, health education, cross-sectional study

Introduction

Bipolar disorder (BD) is a severe and chronic psychiatric condition characterized by recurrent mood episodes, including depressive episodes, manic or hypomanic episodes, mixed states, and inter-episodic periods of remission (1). Epidemiological studies estimate the lifetime prevalence of bipolar I disorder at ∼1.06% and bipolar II disorder at 1.57% (2). Among these, depressive episodes are more commonly reported than manic episodes and are associated with a greater burden of disease (3, 4). Studies indicate that ∼55.2% of patients experience a relapse within 2 years (5). Even during remission, patients often exhibit cognitive impairments, which significantly affect their daily functioning (6). While negative attitudes toward electroconvulsive therapy (ECT) are well-documented globally, regional variations in healthcare systems, cultural contexts, and treatment accessibility necessitate location-specific investigations. This study's focus on a Chinese metropolitan setting provides valuable insights into how local factors influence treatment perceptions and acceptance. Previous studies have predominantly been conducted in Western healthcare contexts, leaving a significant knowledge gap in understanding ECT attitudes within Asian healthcare systems, particularly in China's rapidly evolving mental health landscape. This regional perspective is crucial for developing culturally appropriate interventions to improve treatment acceptance and outcomes. Furthermore, BD is associated with increased suicide risk, higher rates of comorbidities, and accelerated physiological aging, all contributing to a markedly reduced life expectancy (7, 8).

Electroconvulsive therapy (ECT) which has been in use since the 1930s (9, 10). Advances in electrode placement have also been instrumental in optimizing outcomes, transitioning from bilateral to unilateral stimulation, typically on the right side (right unilateral, RUL). Additionally, the use of ultra-brief or brief square-wave pulse currents with individualized dosing strategies has been shown to minimize cognitive side effects (11–14).

While negative attitudes toward ECT are well-documented globally, regional variations in healthcare systems, cultural contexts, and treatment accessibility necessitate location-specific investigations (15). Previous studies have predominantly been conducted in Western healthcare contexts, leaving a significant knowledge gap in understanding ECT attitudes within Asian healthcare systems, particularly in China's rapidly evolving mental health landscape (16). The efficacy of ECT in treating bipolar disorder has been well-documented, particularly in cases of treatment-resistant depression, mania, and mixed states (17, 18). Clinical evidence suggests that significant symptom improvement, defined as a reduction of at least 50%, can be achieved within 2–3 weeks (approximately six sessions) of treatment (18). Moreover, studies have demonstrated that patients receiving ECT exhibit significantly lower all-cause mortality and suicide rates within 1 year post-discharge (19). Consequently, ECT is now recognized as a recommended therapeutic option in clinical guidelines for the management of bipolar disorder (20–23). It is important to note that ECT is not considered a first-line or second-line treatment for bipolar disorder. Rather, it is specifically reserved for severe cases such as treatment-resistant depression, severe manic episodes, and severe psychotic depression episodes (24, 25). The treatment can be administered either as acute intervention or maintenance therapy, with different protocols and considerations for each approach. In acute treatment, ECT is typically administered 2–3 times per week for 6–12 treatments, while maintenance ECT follows a more individualized schedule based on patient response and relapse prevention needs (26, 27).

The knowledge, attitudes, and willingness (KAW) model plays a pivotal role in understanding health-related behaviors and is frequently employed alongside KAW questionnaires to assess individuals' knowledge, attitudes, and willingness within healthcare contexts (28, 29). This theoretical framework posits a sequential relationship wherein knowledge positively influences attitudes, which subsequently shape willingness (30). As a cornerstone of health literacy, the KAW model also evaluates the acceptance and demand for specific healthcare interventions among target populations (28).

Despite its proven safety and efficacy, ECT remains underutilized in clinical willingness, largely due to persistent concerns among patients and the public. Common fears include apprehension about the procedure itself and potential memory impairments, both of which contribute to a reluctance to undergo this treatment (2, 31, 32). Such reservations are often rooted in a lack of understanding of the underlying mechanisms of ECT (32, 33).

Given these challenges, this study aims to investigate the KAW of patients with bipolar disorder to undergo ECT, thereby addressing gaps in understanding and potentially alleviating concerns surrounding its application.

Materials and methods

Study design and participants

This cross-sectional study was conducted in Nanjing from April 10, 2024, to November 3, 2024, involving patients diagnosed with bipolar disorder. Inclusion criteria: (1) had a diagnosis with bipolar disorder based on the International Classification of Diseases, 10th Revision, as confirmed by a physician qualified at the attending level or higher; (2) had sufficient cognitive ability and language skills to understand the questionnaire and communicate with the research team, as determined by a brief clinical interview; and (3) had provided informed consent voluntarily. Exclusion criteria: (1) the presence of comorbid psychiatric disorders; (2) severe visual or auditory impairments that would prevent understanding written or verbal instructions, even with corrective devices; and (3) inability to complete the questionnaire independently or with minimal assistance, based on a pre-survey evaluation by trained investigators. Ethical approval was obtained from the Clinical Research Management Committee of Nanjing Brain Hospital, and informed consent was secured from all participants prior to participation. Participants were recruited through convenience sampling from both outpatient clinics and inpatient wards at the Brain Hospital Affiliated to Nanjing Medical University. This sampling approach was chosen due to its feasibility and accessibility to the target population within our hospital setting. Participants were recruited through convenience sampling from both outpatient

clinics and inpatient wards at the Brain Hospital Affiliated to Nanjing Medical University. This sampling approach was chosen due to its feasibility and accessibility to the target population within our hospital setting.

Sample size calculation

We determined our sample size based on the well-established 5–10 events per variable (EPV) principle commonly used in survey research. Our questionnaire consisted of 24 structured questions (variables), which according to this principle would require a sample size of 120–240 participants (24 variables × 5 EPV = 120; 24 variables × 10 EPV = 240).

Questionnaire introduction

The pilot study yielded 51 responses, of which 44 were deemed valid for analysis. The overall internal consistency of the questionnaire, as measured by Cronbach's α coefficient, was 0.889, with subscale coefficients of 0.930 for the knowledge dimension, 0.762 for the attitude dimension, and 0.881 for the willingness dimension. Additionally, the Kaiser–Meyer–Olkin (KMO) value for the pilot study was 0.955, reflecting excellent sampling adequacy. In the main study, a total of 479 valid questionnaires were collected. The overall Cronbach's α coefficient was 0.936, and the KMO value was 0.917, further demonstrating the questionnaire's strong reliability and construct validity. These metrics confirmed the robustness of the instrument for evaluating the targeted dimensions.

The knowledge, attitudes, and willingness (KAW) questionnaire was developed based on extensive literature review and expert consultation. The knowledge dimension assessed participants' understanding of ECT mechanisms, procedures, and effects through eight items covering two aspects: basic knowledge of ECT procedures and understanding of potential benefits and risks. The attitude dimension contained nine items evaluating emotional and cognitive responses toward ECT, including concerns about side effects, social stigma, and treatment efficacy. The willingness dimension comprised seven items measuring behavioral intentions and readiness to accept ECT treatment, considering both personal acceptance and compliance with medical recommendations. The finalized Chinese-language questionnaire consisted of four sections: (1) sociodemographic and clinical characteristics (including age, gender, residence, education level, employment status, monthly household income, marital status, duration of bipolar disorder, family history of mental health issues, history of electroconvulsive therapy, and type of medical insurance), (2) knowledge dimension, (3) attitude dimension, and (4) willingness dimension. The knowledge dimension comprised eight questions addressing two aspects of awareness. For the knowledge dimension, responses were scored as follows: "very familiar/correct" = 2 points, "heard of it/partially correct" = 1 point, and "unclear/incorrect" = 0 points. Higher scores indicated better understanding of ECT. For the attitude dimension, items were rated on a 5-point Likert scale from "very positive" (5 points) to "very negative" (1 point), with higher scores reflecting more positive attitudes. The willingness dimension used a similar 5-point scale from "strongly agree" (5 points) to "strongly disagree" (1 point), where higher scores indicated greater willingness to accept ECT. The attitude dimension included nine items rated on a five-point Likert scale, with options ranging from "very positive" (5 points) to "very negative" (1 point), yielding possible scores between 9 and 45. The willingness dimension consisted of seven items, six of which were scored on a similar five-point Likert scale from "strongly agree" (5 points) to "strongly disagree" (1 point), with total scores ranging from 6 to 30. Following established criteria from previous studies (15, 34, 35), scores exceeding 70% of the maximum possible score were categorized as indicative of adequate knowledge (>11.2 points), positive attitude (>31.5 points), or proactive willingness (>21 points). This categorization has been validated in similar healthcare assessment studies (36). In our sample, 272 participants (56.8%) scored above the willingness cutoff point of 21, while 207 participants (43.2%) scored at or below this threshold.

A combination of online and offline methods was employed for data collection. Paper-based questionnaires were distributed during outpatient clinic visits, while online surveys were administered through the Wenjuanxing platform. For participants who encountered difficulties in self-completion, trained members of the research team conducted face-to-face interviews to facilitate data collection. For the paper-based surveys, all investigators underwent standardized training to ensure adherence to the study protocol. This training included detailed guidelines on questionnaire distribution, as well as clarification of principles and precautions to ensure consistency in data collection. Two investigators were assigned to oversee data collection, ensuring its accuracy.

For the online component, a QR code linked to the electronic questionnaire was distributed through the "Mind Home" QQ group and displayed on ward bulletin boards. Participants accessed the survey using WeChat by scanning the QR code. To maintain data integrity, the system restricted submissions to one per IP address, and prompts alerted participants to address any unanswered items before submission. Entries with inconsistent or unreasonable responses were excluded. Nurses provided assistance to participants with online surveys as needed.

Data quality control was a key focus throughout the study. Investigators monitored the backend data in real time, and a double-entry method was utilized to ensure accuracy during data transcription. This multi-faceted approach addressed the diverse needs and capabilities of the participants.

Statistical methods

Data analysis was performed using SPSS 27.0 (IBM Corp., Armonk, NY, USA) for statistical tests and AMOS 26.0 for structural equation modeling (SEM). Continuous variables were presented as means and standard deviations (SD), while categorical variables, including responses to specific questionnaire items, were expressed as frequencies and percentages. The statistical significance threshold was set at a two-sided P-value of <0.05.

Group comparisons of knowledge, attitude, and willingness scores across demographic characteristics were conducted using non-parametric tests, as the KAW scores did not follow a normal distribution. For comparisons between two independent groups, the Mann–Whitney *U* test was applied, while the Kruskal–Wallis *H* test was used for comparisons among three or more groups. Spearman's rank correlation coefficient was employed to assess the relationships among the three dimensions of KAW, given the ordinal nature of the data. Independent risk factors associated with the willingness dimension were identified through multivariate logistic regression analysis. This method enabled the evaluation of the influence of knowledge and attitudes, alongside key demographic and clinical variables, on the likelihood of engaging in proactive health willingness. The model results were presented as odds ratios (ORs) with corresponding 95% confidence intervals (CIs). To explore the interrelationships among knowledge, attitudes, and willingness, structural equation modeling (SEM) was conducted. SEM allowed for the simultaneous examination of direct and indirect effects within the hypothesized KAW framework Model fit was evaluated using established indices, including the root mean square error of approximation (RMSEA), comparative fit index (CFI), Tucker–Lewis index (TLI), and incremental fit index (IFI). Models with RMSEA $\leq$ 0.08 and CFI, TLI, and IFI values $\geq$0.90 were considered acceptable.

Results

Demographic characteristics

Initially, a total of 589 samples were collected for this study. Samples with the following conditions were excluded, specifically: (1) 24 cases with a missing baseline information (one case who did not fill in the gender; six cases who did not fill in the age; one case who did not fill in the current work status; one case who did not fill in the marital status; two cases who did not fill in the diagnosed years; 10 cases who did not fill in the family history; two cases who did not fill in the electroconvulsive treatment status; and one case who did not fill in the type of medical insurance); (2) 56 cases whose age was <18 years; and (3) 27 cases with missing responses and three cases with abnormal responses to the KAW dimension; the final valid questionnaire was 479 cases.

Of the 479 participants, 282 (58.87%) were female, 247 (51.57%) were no more than 34 years old, 257 (53.65%) lived in urban areas, 143 (29.85%) had a Bachelor Degree or above, 315 (65.76%) were unemployed, 259 (54.07%) were single, 171 (35.7%) had been diagnosed with bipolar disorder for more than 3 years, 167 (34.86%) had received ECT. Significant differences in knowledge scores were found among participants with different demographic and clinical characteristics. Specifically, younger participants ($\leq$34 years) had higher knowledge scores than older participants (6.19 $\pm$ 5.03 vs. 4.92 $\pm$ 4.56, $P = 0.005$). Urban residents scored higher than those in suburban and rural areas (6.09 $\pm$ 4.78 vs. 4.61 $\pm$ 5.05 and 5.14 $\pm$ 4.78, respectively, $P = 0.005$). Educational attainment was positively associated with knowledge scores, with the highest observed among those holding an associate degree (6.56 $\pm$ 5.68, $P = 0.021$). Participants with a longer duration of bipolar disorder (>3 years) had significantly higher scores (7.29 $\pm$ 5.24) than those with 1–3 years (4.80 $\pm$ 4.67) or <1 year of illness (4.50 $\pm$ 4.10; $P < 0.001$). Prior experience with ECT was also linked to markedly higher knowledge scores (8.77 $\pm$ 5.44) compared to those without such experience (3.66 $\pm$ 3.35; $P < 0.001$). Additionally, knowledge scores varied by type of medical insurance ($P = 0.048$), with participants holding commercial health insurance scoring highest (7.20 $\pm$ 4.89). Differences in attitude scores were more likely to be found among those with different family history of emotional disorders or other mental health issues ($P = 0.044$) and electroconvulsive therapy status ($P < 0.001$). Differences in willingness scores were more likely to be found among those with different gender ($P = 0.026$), monthly household income per capita ($P = 0.045$), family history of emotional disorders or other mental health issues ($P = 0.024$), and electroconvulsive therapy status ($P < 0.001$; Table 1).

Knowledge, attitude, and willingness dimensions

The mean knowledge, attitude, and willingness scores were 5.57 $\pm$ 4.84 (possible range: 0–16), 29.08 $\pm$ 6.21 (possible range: 9–45), and 21.49 $\pm$ 5.14 (possible range: 6–30), respectively. Based on the established criteria where scores exceeding 70% of the maximum possible score indicate adequate knowledge (>11.2 points), positive attitude (>31.5 points), or proactive willingness (>21 points), our findings reveal that patients generally demonstrated insufficient knowledge (mean score represents only 34.8% of the maximum possible score) and predominantly negative attitudes (mean score represents 64.6% of the maximum possible score) toward ECT. However, the willingness score (mean score represents 71.6% of the maximum possible score) exceeded the threshold for proactive willingness, with 272 participants (56.8%) scoring above the cutoff point of 21. The distribution of knowledge dimensions showed that the three questions with the highest number of participants choosing the "Unclear" option were "ECT may cause transient side effects such as elevated blood pressure or arrhythmias." (K6) with 57.83%, "ECT requires a sustained treatment cycle to significantly alleviate symptoms of bipolar disorder." (K8) with 56.78%, and "ECT may have positive effects on the brain and activate neuroplasticity." (K3) with 50.52%. Responses to the attitude dimension showed that 16.08% strongly concerned and 41.75% concerned about social prejudice and misunderstandings related to ECT (A3), 25.05% strongly agreed and 33.4% agreed that Negative opinions from family and friends would make them resist accepting ECT (A4), and 34.86% strongly worried and 36.74% worried about the potential risks and side effects of ECT (A6). Overall, the responses to the attitude dimension indicate predominantly negative or concerned perspectives toward ECT, with a majority of participants expressing concerns about social prejudice (57.83%), negative family opinions (58.45%), and potential risks and side effects (71.6%). Across all nine attitude items, the average proportion of participants expressing negative or concerned responses was 53.7%, compared to 24.8% expressing positive or unconcerned responses, further supporting the conclusion that patients generally hold negative attitudes toward ECT. Responses to the willingness dimension showed

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TABLE 1 Demographic characteristics.

Variables	*N* (%)	Knowledge, mean ± SD	*P*-value	Attitude, mean ± SD	*P*-value	Willingness, mean ± SD	*P*-value
N = 479		5.57 ± 4.84		29.08 ± 6.21		21.49 ± 5.14	
Gender			0.943		0.958		**0.026**
Male	197 (41.13)	5.85 ± 5.39		29.08 ± 7.02		20.89 ± 5.21	
Female	282 (58.87)	5.38 ± 4.42		29.07 ± 5.59		21.91 ± 5.05	
Age			**0.005**		0.539		0.277
≤34 years old	247 (51.57)	6.19 ± 5.03		29.23 ± 6.29		21.83 ± 5.05	
>34 years old	232 (48.43)	4.92 ± 4.56		28.91 ± 6.14		21.13 ± 5.22	
Residence			**0.005**		0.349		0.892
Rural	155 (32.36)	5.14 ± 4.78		29.64 ± 5.60		21.81 ± 4.25	
Urban	257 (53.65)	6.09 ± 4.78		28.75 ± 6.44		21.24 ± 5.73	
Suburban	67 (13.99)	4.61 ± 5.05		29.01 ± 6.69		21.72 ± 4.59	
Education			**0.021**		0.954		0.579
Middle school or below	118 (24.63)	4.57 ± 4.69		28.84 ± 6.39		20.97 ± 4.90	
High school/technical school	125 (26.1)	5.70 ± 4.52		29.16 ± 5.67		21.51 ± 4.71	
Associate degree	93 (19.42)	6.56 ± 5.68		29.54 ± 6.28		21.88 ± 5.41	
Bachelor's degree or above	143 (29.85)	5.66 ± 4.54		28.90 ± 6.52		21.65 ± 5.52	
Employment status			0.917		0.608		0.291
Employed	164 (34.24)	5.45 ± 4.66		28.86 ± 5.65		21.88 ± 4.80	
Unemployed	315 (65.76)	5.64 ± 4.95		29.19 ± 6.49		21.29 ± 5.30	
Monthly household income per capita			0.207		0.228		**0.045**
<5,000	172 (35.91)	5.15 ± 4.64		28.89 ± 5.80		21.50 ± 4.82	
5,000–10,000	186 (38.83)	6.03 ± 4.97		29.66 ± 6.06		22.10 ± 4.95	
>10,000	121 (25.26)	5.47 ± 4.91		28.45 ± 6.95		20.55 ± 5.74	
Marital status			0.055		0.480		0.245
Single	259 (54.07)	5.93 ± 4.88		29.24 ± 6.37		21.77 ± 5.17	
Married	220 (45.93)	5.15 ± 4.77		28.88 ± 6.03		21.16 ± 5.09	
Duration of bipolar disorder			**<0.001**		0.822		0.366
<1 year	184 (38.41)	4.50 ± 4.10		28.78 ± 5.79		21.95 ± 4.75	
1–3 years	124 (25.89)	4.80 ± 4.67		29.12 ± 4.69		21.62 ± 4.60	
>3 years	171 (35.7)	7.29 ± 5.24		29.36 ± 7.51		20.91 ± 5.84	
Family history of emotional disorders or other mental health issues			0.221		**0.044**		**0.024**
Yes	139 (29.02)	6.05 ± 4.99		29.77 ± 6.08		22.24 ± 5.04	
No	340 (70.98)	5.38 ± 4.78		28.79 ± 6.26		21.19 ± 5.15	
Undergone electroconvulsive therapy			**<0.001**		**<0.001**		**<0.001**
Traditional electroconvulsive therapy	16 (3.34)	6.63 ± 5.19		29.50 ± 2.99		22.44 ± 5.97	
ECT	167 (34.86)	8.77 ± 5.44		32.48 ± 6.22		24.14 ± 4.25	
No	256 (53.44)	3.66 ± 3.35		26.72 ± 5.53		19.57 ± 4.88	
Don't remember	40 (8.35)	4.08 ± 2.76		29.78 ± 4.36		22.40 ± 4.65	

(Continued)

TABLE 1 (Continued)

Variables	*N* (%)	Knowledge, mean ± SD	*P*-value	Attitude, mean ± SD	*P*-value	Willingness, mean ± SD	*P*-value
Type of medical insurance			**0.048**		0.208		0.595
Only social health insurance	384 (80.17)	5.58 ± 4.86		29.42 ± 6.37		21.54 ± 5.22	
Only commercial health insurance	15 (3.13)	7.20 ± 4.89		27.67 ± 3.50		22.27 ± 5.30	
Both social and commercial health insurance	40 (8.35)	6.18 ± 4.35		27.80 ± 3.98		21.98 ± 3.86	
No insurance	40 (8.35)	4.33 ± 5.01		27.60 ± 6.96		20.28 ± 5.38	

Bold values indicate $P < 0.05$.

TABLE 2 Correlation analysis.

Dimensions	Knowledge	Attitude	Willingness
Knowledge	1		
Attitude	0.470 ($P < 0.001$)	1	
Willingness	0.452 ($P < 0.001$)	0.746 ($P < 0.001$)	1

that 16.08% disagreed and 7.31% strongly disagreed that they would actively consult doctors for information and advice about ECT (P2), 15.24% disagreed and 7.31% strongly disagreed that they would willing to consider ECT under the recommendation of healthcare professionals (P6), and 13.78% disagreed and 5.85% strongly disagreed that they would willing to participate in more ECT-related awareness and educational activities (P3; Supplementary Table S1).

Correlations between KAW

Spearman correlation analysis indicated significant positive correlations between knowledge and attitude ($r = 0.470$, $P < 0.001$), as well as willingness ($r = 0.452$, $P < 0.001$). Meanwhile, there was also correlation between attitude and willingness ($r = 0.746$, $P < 0.001$; Table 2).

Univariate and multivariate logistic regression analysis

Multivariate logistic regression showed that knowledge (OR = 1.087, 95% CI: 1.017–1.161, $P = 0.014$), attitude (OR = 1.333, 95% CI: 1.252–1.420, $P < 0.001$), being male (OR = 0.593, 95% CI: 0.355–0.990, $P = 0.046$), and undergone ECT (OR = 1.840, 95% CI: 1.013–3.344, $P = 0.045$) were independently associated with willingness (Table 3).

Interactions between KAW

The SEM demonstrate a highly favorable model fit indices (GFI value: 0.960, RFI value: 0.843, IFI value: 0.917, and TLI value: 0.861), suggesting a well-fitting model (Supplementary Table S2). SEM analysis showed that electroconvulsive therapy ($\beta = -0.377$, $P = 0.014$), years of BD ($\beta = 0.196$, $P = 0.014$) had direct effects on knowledge. Knowledge ($\beta = 0.526$, $P = 0.023$) directly affected attitude. Meanwhile, electroconvulsive therapy ($\beta = -0.198$, $P = 0.013$) and years of BD ($\beta = 0.103$, $P = 0.016$) indirectly affected attitude. Knowledge ($\beta = 0.107$, $P = 0.018$), attitude ($\beta = 0.674$, $P = 0.009$), and gender ($\beta = 0.104$, $P = 0.020$) directly affected willingness. Knowledge ($\beta = 0.355$, $P = 0.011$), electroconvulsive therapy ($\beta = -0.174$, $P = 0.015$), and years of BD ($\beta = 0.090$, $P = 0.020$) indirectly affected willingness (Table 4 and Figure 1).

Discussion

The study reveals that patients with bipolar disorder exhibit a significant gap in knowledge and generally hold negative attitudes toward ECT, although their willingness to undergo ECT is relatively high. Clinicians should focus on enhancing educational interventions that address misconceptions and provide comprehensive information about ECT, potentially increasing patient acceptance and adherence to recommended treatment protocols.

The results highlight critical challenges in patient understanding and perception of ECT, which are consistent with broader trends observed in mental health care. Previous research has indicated that misinformation and stigma surrounding electroconvulsive therapy often lead to apprehension and reluctance among patients, even when they recognize its potential effectiveness (37, 38). Similarly, our study found that knowledge deficits and misconceptions about the procedure are prevalent, reflecting a systemic issue in the dissemination of accurate and comprehensive information about ECT. This aligns with studies showing that inadequate patient education contributes to negative treatment attitudes, which can subsequently hinder adherence and therapeutic outcomes (39, 40).

The relationships among knowledge, attitudes, and willingness underscore the complexity of these challenges. Positive correlations between knowledge and attitude, as well as knowledge and willingness, emphasize the critical role of education in shaping patient perceptions. Path analysis further supports this relationship, demonstrating that knowledge directly influences attitudes and indirectly impacts willingness through improved attitudes.

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TABLE 3 Univariate and multivariate logistic regression analysis on willingness.

Variables	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Knowledge	1.225 (1.165–1.288)	**<0.001**	1.087 (1.017–1.161)	**0.014**
Attitude	1.361 (1.285–1.442)	**<0.001**	1.333 (1.252–1.420)	**<0.001**
Gender				
Male	0.683 (0.473–0.986)	**0.042**	0.593 (0.355–0.990)	**0.046**
Female	Ref		Ref	
Age				
≤34 years old	1.175 (0.818–1.688)	0.382		
>34 years old	Ref			
Residence				
Rural	Ref			
Urban	0.887 (0.592–1.328)	0.559		
Suburban	0.749 (0.421–1.333)	0.326		
Education				
Middle school or below	Ref			
High school/technical school	1.354 (0.813–2.254)	0.244		
Associate degree	1.264 (0.730–2.189)	0.404		
Bachelor's degree or above	1.048 (0.642–1.708)	0.852		
Employment status				
Employed	1.403 (0.954–2.063)	0.085		
Unemployed	Ref			
Monthly household income per capita				
<5,000	Ref			
5,000–10,000	1.407 (0.921–2.148)	0.114		
>10,000	0.771 (0.484–1.229)	0.275		
Marital status				
Single	Ref			
Married	0.874 (0.608–1.256)	0.467		
Duration of bipolar disorder				
<1 year	Ref			
1–3 years	0.986 (0.622–1.562)	0.951		
>3 years	0.920 (0.604–1.400)	0.697		
Family history of emotional disorders or other mental health issues				
Yes	1.463 (0.975–2.195)	0.066		
No	Ref			
Undergone electroconvulsive therapy				
Traditional electroconvulsive therapy	1.370 (0.499–3.766)	0.541	0.511 (0.166–1.576)	0.243
ECT	5.565 (3.532–8.767)	**<0.001**	1.840 (1.013–3.344)	**0.045**
No	Ref		Ref	
Don't remember	1.675 (0.857–3.275)	0.132	0.760 (0.341–1.692)	0.501
Type of medical insurance				
Only social health insurance	1.201 (0.625–2.306)	0.583		

(Continued)

TABLE 3 (Continued)

Variables	Univariate logistic regression		Multivariate logistic regression	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Only commercial health insurance	1.034 (0.315–3.396)	0.956		
Both social and commercial health insurance	1.357 (0.559–3.292)	0.499		
No insurance	Ref			

Bold values indicate $P < 0.05$.

TABLE 4 SEM analysis.

Model paths	Standardized total effects		Standardized direct effects		Standardized indirect effects	
	β (95% CI)	*P*-value	β (95% CI)	*P*-value	β (95% CI)	*P*-value
Electroconvulsive therapy → Knowledge	−0.377 (−0.447 to −0.311)	0.014	−0.377 (−0.447 to −0.311)	0.014		
Years of BD → Knowledge	0.196 (0.120–0.264)	0.014	0.196 (0.120–0.264)	0.014		
Electroconvulsive therapy → Attitude	−0.198 (−0.249 to −0.149)	0.013			−0.198 (−0.249 to −0.149)	0.013
Years of BD → Attitude	0.103 (0.058–0.148)	0.016			0.103 (0.058–0.148)	0.016
Knowledge → Attitude	0.526 (0.452–0.581)	0.023	0.526 (0.452–0.581)	0.023		
Electroconvulsive therapy → Willingness	−0.174 (−0.225 to −0.127)	0.015			−0.174 (−0.225 to −0.127)	0.015
Years of BD → Willingness	0.090 (0.050–0.125)	0.020			0.090 (0.050–0.125)	0.020
Knowledge → Willingness	0.462 (0.381–0.525)	0.023	0.107 (0.023–0.180)	0.018	0.355 (0.296–0.412)	0.011
Gender → Willingness	0.104 (0.030–0.159)	0.020	0.104 (0.030–0.159)	0.020		
Attitude → Willingness	0.674 (0.613–0.725)	0.009	0.674 (0.613–0.725)	0.009		

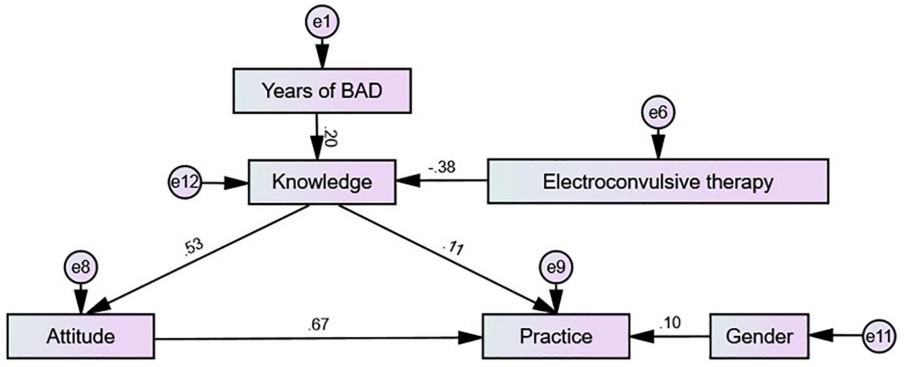

FIGURE 1
SEM analysis.

These findings are consistent with prior studies suggesting that patients with a better understanding of treatment options are more likely to perceive them positively and express willingness to engage in care (41, 42). However, the negative association between previous exposure to electroconvulsive therapy and attitudes highlights a paradox: while firsthand experience improves knowledge, it does not always translate to positive attitudes, potentially due to inadequate communication about the procedure's benefits and side effects during treatment (15, 36).

The influence of demographic and clinical factors further contextualizes these findings within broader health disparities. Younger patients, urban residents, and those with higher educational attainment were more likely to exhibit better knowledge and more positive attitudes. These patterns align with studies suggesting that access to educational resources and

health literacy significantly impact patient understanding and perceptions of treatment options (43, 44). Moreover, patients who had previously undergone ECT showed higher levels of knowledge and willingness, indicating that direct exposure can demystify the procedure and reduce fear. However, concerns about social stigma, misinformation, and side effects remain barriers to acceptance, as reflected in both attitude dimensions and broader studies on mental health interventions (45, 46). The relatively limited impact of family history on attitudes in our study contrasts with findings from other research, where familial understanding of mental health treatments has been shown to positively influence perceptions (47, 48).

Knowledge dimension reveals a nuanced picture of patient awareness. Many participants demonstrated limited understanding of critical aspects of ECT, such as its role in neuroplasticity or the necessity of sustained treatment cycles. These findings mirror broader patterns in mental health care, where technical aspects of interventions are often poorly communicated to patients (49, 50). Socio-cultural factors and disparities in resource availability likely exacerbate these challenges. For instance, patients in rural or suburban areas exhibited lower levels of knowledge compared to their urban counterparts, reflecting systemic inequities in healthcare infrastructure and educational outreach. These patterns are consistent with studies highlighting the impact of geographic and socio-economic factors on access to mental health care and patient education (51, 52). Concerns about social stigma and potential side effects were particularly pronounced, underscoring the importance of addressing these misconceptions to improve acceptance of ECT.

These findings call for a multi-dimensional approach to improving patient understanding and acceptance of ECT. At a systemic level, healthcare organizations must prioritize equitable access to mental health education and resources, particularly in underprivileged and rural areas. Establishing integrated mental health education programs within community health centers could help bridge these gaps by providing targeted outreach and personalized education tailored to the needs of diverse populations. Specific efforts should include visual and interactive educational tools, such as videos and workshops, to enhance understanding of complex procedures like ECT (53, 54). These interventions should not only focus on the technical aspects of the treatment but also address common misconceptions and fears, using evidence-based communication strategies to improve patient confidence.

Healthcare professionals play a crucial role in this process and require adequate training to effectively communicate the benefits and risks of ECT. Incorporating ECT-specific modules into continuing medical education programs could enhance providers' ability to address patient concerns and build trust. Furthermore, leveraging patient testimonials and real-life case studies could serve as powerful tools for reducing stigma and fostering acceptance, as studies have shown that relatable narratives can significantly influence attitudes toward mental health treatments (35, 55). To support sustained improvements, it is essential to establish feedback mechanisms within healthcare systems to monitor the effectiveness of these initiatives and adapt them based on patient and provider input.

In addition to systemic and educational strategies, targeted policy changes are needed to address the structural factors contributing to disparities in ECT knowledge and attitudes. Policies that incentivize mental health education and awareness campaigns, particularly in underserved areas, could help reduce geographic and socio-economic inequities. Collaborative efforts between healthcare providers, policymakers, and community leaders are critical to ensuring that these initiatives are both culturally sensitive and contextually appropriate. For example, involving local mental health advocates in program design and implementation could enhance their relevance and effectiveness (56, 57).

This study has several limitations that should be considered when interpreting the findings. First, the cross-sectional design precludes any causal inferences regarding the relationships between knowledge, attitudes, and willingness related to ECT. Second, the use of self-reported questionnaires may introduce response biases, such as social desirability or recall bias, potentially affecting the accuracy of the data. Third, potential sampling bias may exist as participants were recruited through convenience sampling from a single hospital, which might not fully represent the entire bipolar disorder population. Fourth, although our questionnaire showed good reliability and validity in the pilot study, further validation with larger and more diverse populations would strengthen its psychometric properties. Fifth, as the study was conducted in a single city, the generalizability of the results to broader populations with bipolar disorder may be limited, necessitating further research in diverse geographic and cultural settings.

Conclusion

In conclusion, patients with bipolar disorder demonstrated insufficient knowledge and predominantly negative attitudes toward ECT, despite showing a relatively high willingness to consider it as a treatment option. Tailored educational programs and counseling interventions that focus on improving patient understanding of ECT are essential to address misconceptions, enhance positive attitudes, and support informed decision-making, ultimately fostering greater acceptance and appropriate utilization of this therapeutic approach.

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 Ethics Committee of the Affiliated Brain Hospital of Nanjing Medical University (2024-KY008-01). 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

LZ: Investigation, Methodology, Resources, Validation, Writing – original draft, Writing – review & editing. XQ: Formal analysis, Methodology, Resources, Software, Writing – original draft, Writing – review & editing. LX: Formal analysis, Resources, Software, Supervision, Writing – original draft, Writing – review & editing. XD: Data curation, Project administration, Software, Visualization, Writing – original draft, Writing – review & editing. KW: Data curation, Investigation, Project administration, Supervision, Writing – original draft, Writing – review & editing. KL: Formal analysis, Investigation, Resources, Software, Writing – original draft, Writing – review & editing. YZ: Formal analysis, Methodology, Resources, Supervision, Writing – original draft, Writing – review & editing.

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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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Analysis of clinical characteristics and influencing factors of fever after electroconvulsive therapy: a retrospective study from the Chinese population

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Background: Although well-established as a first-line treatment for psychiatric disorders, electroconvulsive therapy (ECT) carries risks of adverse effects, including fever. The purpose of this study was to elucidate the incidence, clinical characteristics, and risk factors related to fever after ECT.

Methods: We retrospectively analyzed medical records of patients receiving ECT at the Second Affiliated Hospital of Xinxiang Medical University (April 2019–January 2020). Patients were subsequently divided into two groups: a fever group, in which the body temperature was ≥ 38°C; and a non-fever group, in which the body temperature was <38°C.

Results: A total of 895 patients underwent 7801 units of ECT treatment. Fever was analyzed at the patient and treatment unit level. At the patient level, 104 out of 895 patients (11.6%) experienced at least one fever within 24 hours after ECT, Compared with the non-fever group, the fever group showed statistically significant differences in age, gender, types of psychiatric ward (closed or open), and anesthetic type (all $P < 0.05$) but not in the total number of ECT units or diagnoses, Logistic regression analysis identified the risk variables for fever as younger age (≤ 29), closed psychiatric ward, etomidate administration, and being male; and at the treatment units level, among the 7,801 ECT units, fever occurred in 129 units (1.7%), with a median maximum temperature of 38.5 (38.0–40.3)°C. Following ECT, 55.8% (72/129) of the fever unit temperatures returned to normal body temperature as assessed by clinical observation or cooling measures, whereas 44.2% (57/129) required cooling combined with antibiotics. Compared to baseline, the fever units had higher white blood cell and neutrophil counts ($P < 0.001$) but lower lymphocyte counts ($P < 0.001$). In 79.8% (103/129) of the units, the fever was observed during the first 5–8 hours after the ECT treatment was completed, with 94.6% (122/129) of the units

returning to normal body temperature within 24 hours of treatment. Only 5.4% (7/129) of the units opted to discontinue ECT treatment due to fever.
Conclusion: We found that fever after ECT requires attention in clinical practice. Although the direct impact of fever after ECT treatment is limited, given its potential risks, it is advised to focus on strengthening the temperature monitoring of high-risk groups.

KEYWORDS
electroconvulsive therapy (ECT), fever, mental disorders, risk factors, incidence

1 Introduction

Electroconvulsive therapy (ECT) is a method for treating severe mental disorders, which works by inducing a therapeutic seizure through a safe electrical stimulation of the brain. While pharmacotherapy remains the most frequently employed treatment for mental disorders, ECT is nevertheless recognized as a first-line therapeutic option in specific clinical scenarios (1), particularly in patients with depression accompanied by psychotic, suicidal, or treatment-resistant features (2). Indeed, in many cases, ECT can more effectively improve depressive symptoms compared to medication (3).

Modern ECT is performed under conditions of general anesthesia, muscle relaxants, and oxygen inhalation, and is usually well tolerated, although adverse reactions may still occur after treatment. Headaches and muscle pain are common adverse reactions after treatment, although the symptoms are usually mild (4). In addition, the incidence of nausea after treatment is also relatively high, which may be related to headaches and anesthetics (5). The most concerning side effect after ECT is cognitive function impairment, with common types including immediate postoperative confusion, attention and executive function issues, anterograde amnesia, and retrograde amnesia (6). Additionally, 1%–2% of patients may experience prolonged seizures (>180 s) (7), which increases the risk of consciousness impairment and memory decline.

The adverse reactions after ECT treatment have drawn significant attention, In clinical practice, we have observed that some patients experience fever after ECT; however, the number of studies is limited to a few case reports (8–10) and small retrospective studies (11). Overall, the reported incidence of fever after ECT varies significantly, ranging from 5.3% to 54.2% (12–16). Regarding the clinical features of fever, the degree and duration after ECT have been examined in several studies (13, 14). However, treatment measures and effects of fever after ECT and the impact of fever on ECT treatment course, among other clinical features, have not been reported. Additionally, literature shows inconsistent results in terms of the risk factors for developing fever after ECT (14, 16).

Considering that fever after ECT can cause subjective discomfort for patients and reduce treatment compliance, we believe that previous studies (11–16) have inadequately described the clinical characteristics of fever after ECT. Specifically, these studies have reported widely varying incidence rates and conflicting evidence on anesthetic-related risk factors. This gap necessitates further research. Here, we investigated the incidence, clinical characteristics, and risk factors of fever after ECT in Chinese psychiatric patients.

2 Methods

2.1 Study population

A retrospective study examined the medical records of patients underwent ECT treatment at the Second Affiliated Hospital of Xinxiang Medical University (Xinxiang, China) from April 2019 to January 2020. The demographic characteristics, clinical features, and anesthetic agents of all patients undergoing ECT were collected through the hospital's electronic medical chart system. The study was approved by the hospital's ethics committee (No. XYEFYLL-2023-30), and due to the retrospective design, no informed consent was required.

The inclusion criteria: 1) inpatients diagnosed with major mental disorders (ICD-10); and 2) received ECT treatment. Exclusion criteria: 1) fevers were due to infections (bacterial, COVID-19), other physical diseases, or medication; and 2) incomplete medical record; and 3) due to medication.

2.2 Study design

All enrolled patients were divided into a fever group and non-fever group based on whether they experienced fever within 24 h after ECT treatment course. As fever did not occur after every ECT session, we defined each individual ECT session as a 'unit' for analysis. In this study, we defined fever as an axillary temperature ≥ 38.0°C (17, 18). The fever group included patients with a temperature ≥ 38.0°C within 24 h after any ECT units.

A total of 998 patients underwent ECT treatment between April 2019 and January 2020, of which 103 patients were ultimately

excluded. The reasons for exclusion were 92 with incomplete data, four with drug allergies, six with pulmonary infections after fever, and one with infection. Ultimately, 895 patients were included in the study, as shown in Figure 1. The original 998 patients and the 895 included patients were evenly matched in terms of age, gender, and other clinical variables (including inpatient area and incidence of fever), suggesting that missing data did not affect the final results.

2.3 Prevalence of fever after ECT

The incidence of fever after ECT was calculated by dividing the number of patients who developed fever by the total number of enrolled patients; similarly, the incidence of fever per unit was determined by dividing the number of fever cases by the total number of units in the study. Considering that the physical development of adolescents is ongoing, the temperature regulation mechanisms of such patients are different from those of adults. Therefore, we specifically focused on the incidence of fever in adolescent patients after ECT.

2.4 ECT procedure and related parameters

Each patient underwent a comprehensive assessment and preparation prior to ECT, including blood routine tests, biochemistry tests, electrocardiogram, electroencephalogram, and chest computerized tomography. Patients received oxygen supplementation until spontaneous breathing resumed. Before anesthesia, 0.5–1.0 mg atropine was administered intravenously (IV). The anesthesiologist selected etomidate (0.15–0.30 mg/kg) or propofol (1.0–2.0 mg/kg) for anesthesia. Following loss of consciousness, 0.50–1.25 mg/kg succinylcholine was administered IV for muscle relaxation. Standard bi-temporal ECT was performed using the MECTA Spectrum 5000Q device (MECTA Corporation, Tualatin, OR, USA). The electrical parameters were as follows: pulse width 0.25 ms, frequency 60 Hz, duration 2 s, and current 0.9 A. In this study, an age-related method (%charge = patient's age; 100% = 504 initial treatment charge dose) was used to estimate the initial treatment charge dose (19). Each ECT session was conducted three times a week, during the hours between 06:30 a.m. and 10:30 a.m. During the treatment, heart rate, blood oxygen saturation, and respiration were monitored.

2.5 Statistical analysis

Statistical analysis was performed using SPSSv26.0 (IBM Corp., Armonk, NY, USA). Categorical data are presented as numbers (%), and continuous data are presented as mean ± standard deviation. Continuous variables were analyzed using t-tests (normally distributed) or Mann-Whitney U tests (non-normal), while categorical variables used χ^2 tests with results expressed as n (%). Variables showing intergroup differences underwent multivariate logistic regression to evaluate fever incidence impact. Statistical significance was defined as two-tailed $P < 0.05$.

3 Results

3.1 The incidence of fever after ECT

A total of 895 patients underwent 7801 units of ECT treatment. Fever was assessed using two distinct levels. At the patient level, 104 out of 895 patients (11.6%) experienced at least one fever within 24 hours after ECT. At the treatment unit level, among the 7,801 ECT units, fever occurred in 129 units (1.7%). We specifically focused on fever occurrence among adolescent patients (13–18 years old) after

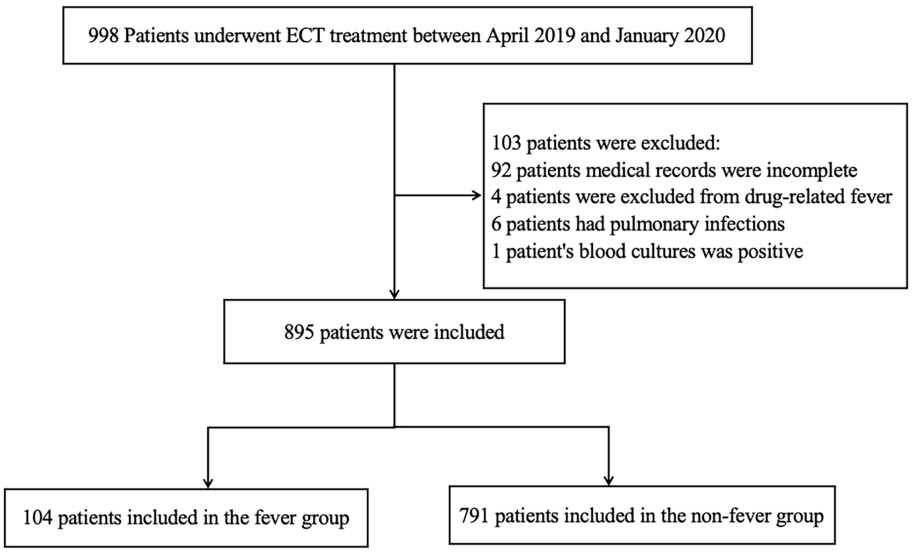

FIGURE 1
Flowchart of the study on fever after ECT treatment.

ECT and found that among patients under 18 years old, 26.1% (18/69, 95% CI: 14.4%–38.3%) experienced fever after ECT, while only 10.4% (86/826, 95% CI: 8.6%–12.9%) of patients aged 18 and older experienced fever after ECT ($P < 0.001$).

3.2 Clinical characteristics of patients between the fever group and non-fever group

Table 1 presents the clinical characteristics of 895 patients receiving ECT. The median age of patients in the fever and non-fever groups was statistically different [24 (range: 14–54) vs 29 (range: 13–77); $P< 0.05$]. Fever incidence differed significantly by setting: 12.4% (97/780; 95% CI: 10.3%–14.9%) in closed wards versus 6.1% (7/115; 95% CI: 2.8%–12.3%) in open wards ($P < 0.05$). Gender differences were significant, with males showing a higher incidence (18.3% [65/356; 95% CI: 14.5%–22.6%]) than females (7.2% [39/539; 95% CI: 5.3%–9.7%]; $P < 0.05$). Anesthetic agent usage significantly affected outcomes: etomidate-associated fever (12.5%, 101/811; 95% CI: 10.3%–15.0%) exceeded propofol-associated cases (3.6%, 3/84; 95% CI: 1.2%–10.1%; $P < 0.05$). However no significant differences existed in total ECT treatments or diagnoses.

3.3 Comparison demographic and clinical characteristics between fever and non-fever Units

The specific details of the 129 fever units after ECT treatment are shown in Table 2. The median age was 23 years (14–54 years). Overall, 62.8% (81/129) of the fever units were male, 92.2% (119/129) came from closed wards, and 97.7% (126/129) were anesthetized using etomidate injection. A total of 792 units were anesthetized using propofol injection, three of which experienced fever.

3.4 Clinical characteristics of the fever units

3.4.1 Frequency and temperature profile

The clinical characteristics of the fever units are shown in Table 3. Fever occurred once in 86 fever units (66.7%), twice in 14 (10.9%), three times in one (0.8%), and four times in three (2.3%), which resulted in a mean number of episodes per unit (N = 104) of 1.24 ± 0.62.

3.4.2 Temperature profile

The median peak body temperature across the fever units was 38.5°C (range: 38.0–40.3°C). The temperature distribution of the fever units was as follows: 71.3% (92/129) measured 38.0–38.9°C, 28.5% (35/129) 39.0–39.9°C, and 1.6% (2/129) ≥ 40.0°C.

3.4.3 Temporal pattern

Overall, fever occurred in 31% of the fever units (40/129) after the first treatment session, with most cases (79.8%, 103/129) emerging within 5–8 hours after treatment, while in 10.9% (14/129) and 9.3% (13/129) of fever units the fever occurred within 1–4 and 9–24 hours, respectively.

3.4.4 Recovery trajectory

All fever units achieved normothermia within 72 hours after treatment, predominantly via clinical observation/cooling (55.8%, 72/129) or antibiotics (44.2%, 57/129). Recovery to normothermia occurred in 94.6% (122/129) of fever units within 24 hours after treatment, whereas in 4.7% (6/129) and 0.8% (1/129) fever units, it occurred within 24–48 and 48–72 hours, respectively. No significant difference was found between the 24 hour-recovery rate between antibiotic-treated (96.5% [55/57], 95% CI: 88.1%–99.0%) and non-antibiotic patients (93.1% [67/72], 95% CI: 84.8%–97.0%; P = 0.463, RR = 1.04, 95% CI:0.95–1.13).

3.4.5 Treatment continuation

Following fever, 88.4% (114/129) of units continued ECT treatments as usual, whereas 6.2% (8/129) and 5.4% (7/129) either extended treatment intervals or discontinued therapy, respectively.

3.4.6 Inflammatory dynamics

Among 129 the fever units, 98 underwent paired pre/post-ECT blood tests. Results indicated a significantly increased white blood cell (11.78 ± 3.62 vs baseline 6.81 ± 6.09 × 10^9/L; $P < 0.001$, $t = 13.461$) and neutrophil count (9.72 ± 3.47 vs 4.28 ± 1.94 × 10^9/L; $P < 0.001$, $t = 14.673$), with a significant reduction in lymphocytes (1.38 ± 0.47 vs 1.89 ± 0.63 × 10^9/L; $P < 0.001$, $t = -7.548$). Complete hematologic shifts are detailed in Table 4.

3.5 Analysis of risk factors for fever after ECT

Logistic regression analysis was performed with collinearity diagnostics to confirm all variance inflation factor values < 5. The Hosmer-Lemeshow test indicated an adequate model fit ($\chi^2 = 2.383$, df = 5, $P = 0.794$). Age (OR = 0.435, $P < 0.001$), gender (OR = 0.386, $P < 0.001$), inpatient ward type (OR = 2.802, $P = 0.016$), and anesthetic agent (OR = 3.856, $P = 0.026$) were significantly associated with fever. The total ECT sessions and diagnosis showed no independent correlation. Detailed results are shown in Table 5.

4 Discussion

To the best of our knowledge, this study includes the largest sample size (n = 895) investigating the incidence of fever after ECT. The findings demonstrate that fever is common, with an elevated risk among males, adolescents, patients in closed psychiatric wards,

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TABLE 1 Demographic and clinical characteristics between patients in the fever group and non-fever group, (n = 895).

Variables	Fever group (n = 104)	Non-fever group (n = 791)	Statistics	P value
Median age (years), [range]	24 (14–54)	29 (13–77)	z = −5.257	**<0.0001***
Age (years), n (%)			χ^2 = 16.203	**<0.0001***
≦29	74 (71.2%)	397 (50.2%)		
>29	30 (28.8%)	394 (49.8%)		
Age (years), n (%)			χ2 = 15.236	**<0.0001***
<18	18 (26.1%)	86 (10.4%)		
≧18	51 (73.9%)	730 (89.6%)		
Gender, n (%)			χ^2 = 25.365	**<0.0001***
Male	65 (62.5%)	291 (36.8%)		
Female	39 (37.5%)	500 (63.2%)		
Total number of ECT units for the same patient, [mean (± SD)]	9.14 (3.58)	8.67 (3.04)	χ^2 = 2.271	0.132
Diagnosis, n (%)			χ^2 = 2.747	0.432
Schizophrenia	60 (57.7%)	480 (60.7%)		
Depression	15 (14.4%)	120 (15.2%)		
Bipolar disorder	18 (17.3%)	92 (11.6%)		
Other mental disorders	11 (10.6%)	99 (12.5%)		
Inpatient area, n (%)				
Open ward	7 (6.7%)	108 (13.7%)	χ^2 = 4.06	**0.044***
Closed ward	97 (93.3%)	683 (86.3%)		
Anesthetic, n (%)			χ^2 = 5.847	**0.016***
Etomidate	101 (97.1%)	710 (89.8%)		
Propofol	3 (2.9%)	81 (10.2%)		

*Statistical significance at two-tailed $P < 0.05$.
Bold values indicate p<0.05.

TABLE 2 Comparison demographic and clinical characteristics between fever units and non-fever units (n = 7801).

Variables	Fever units (n = 129)	Non-fever units (n = 7672)	Stats	P value
Median age (years), [range]	23 (14–54)	29 (13–77)	z = −5.987	**<0.0001***
Gender, n (%)			χ^2 = 25.728	**<0.0001***
Male	81 (62.8%)	3118 (40.6%)		
Female	48 (71.2%)	4554 (59.4%)		
Inpatient area, n (%)				
Open ward	10 (7.8%)	828 (10.8%)	χ^2 = 1.223	**0.269**
Closed ward	119 (92.2%)	6844 (89.2%)		
Anesthetic, n (%)			χ^2 = 8.790	**0.003***
Etomidate	126 (97.7%)	6884 (89.7%)		
Propofol	3 (2.3%)	788 (10.3%)		

*Statistical significance at two-tailed $P < 0.05$.
Bold values indicate p<0.05.

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TABLE 3 Clinical characteristics of fever units after ECT treatment (n = 129).

Variables	Categories	Frequency (n)	Percentage (%)
Fever unit for the same patient	1	86	66.7
	2	14	10.9
	3	1	0.8
	4	3	2.3
Degree of fever	38.0°C ≦ T < 39.0°C	92	71.3
	39.0°C ≦ T < 40.0°C	37	28.5
	40.0°C ≦ T	2	0.02
Fever occurred after first ECT unit	Yes	40	31
	No	89	69
Fever period after ECT	1-4 h	14	10.9
	5-8 h	103	79.8
	9-24 h	12	9.3
Treatment measures	Clinical observation or cooling	72	55.8
	Cooling and antibiotic treatment	57	44.2
Duration of fever	t ≦ 24 h	122	94.6
	24 h < t ≦ 48 h	6	4.7
	48 h < t ≦ 72 h	1	0.8
Effects on the ECT	Continue treatment	114	88.4
	Prolonged treatment interval	8	6.2
	Stop treatment	7	5.2

T, temperature; t, time; h, hour.

and those given etomidate as an anesthetic. We speculate that the elevated risk among males may be associated with two mechanisms: (1) increased heat production from larger skeletal muscle mass during ECT-induced contractions; and (2) sex-based immune modulation–testosterone-mediated suppression versus estrogen-enhanced responses in females (20). Minors and adolescents also showed an increased likelihood of fever, which is likely attributed to underdeveloped thermoregulatory mechanisms relative to adults (21).The association between closed psychiatric wards and fever, the first identified in the Chinese population, may arise from shared living conditions with poor air circulation that heightens exposure to respiratory pathogens, which is compounded by severe mental illnesses and reduced self-care capacities.

In agreement with previous findings (14), we found that, compared with propofol, etomidate usage during ECT was associated with an increased risk of fever. This increased risk may involve the adrenal suppression and prolonged seizure activity that are associated with etomidate. Specifically, etomidate is known to work on the hypothalamus to inhibit the secretion of adrenal cortical hormones (22), whereas not such effects are associated with propofol (23, 24). Indeed, a single IV dose of etomidate was found to significantly reduce cortisol levels and increase those of adrenocorticotropic hormone (25, 26). Notably, significant adrenal suppression was found to last for 6 to 8 hours after IV etomidate (23, 26, 27), but resolved within 12 to 24 hours (23, 28, 29). Additionally, adrenal insufficiency is known to be one cause of unexplained fever (30). Our findings indicated that the onset of fever occurred within 5–8 hours after ECT in 79.8% of the fever units, which coincided with the alterations observed during the cortisol suppression found in previous studies. In addition, studies

TABLE 4 Blood routine of 98 fever units before and after ECT.

Variables	Pre-ECT	After ECT	Statistics	Df	P value
WBC count, $\times10^9$/L	6.81 (2.09)	11.78 (3.62)	t = 13.461	97	**<0.0001***
NEUT count, $\times10^9$/L	4.28 (1.94)	9.72 (3.47)	t = 14.673	97	**<0.0001***
LYMPH count, $\times10^9$/L	1.89 (0.63)	1.38 (0.48)	t = −7.548	97	**<0.0001***

*Statistical significance at two-tailed $P < 0.05$.
Bold values indicate p<0.05.

TABLE 5 Multivariable logistic regression analysis of factors associated with fever after ECT treatment (n = 895).

Variables	VIF	OR	95% CI	*P* values
Age	1.050	0.435	0.273–0.692	<0.001*
Gender	1.046	0.386	0.250–0.597	<0.001*
Diagnosis	1.027	1.605	0.702–3.670	0.262
Type of inpatient ward	1.045	2.802	1.213–6.457	0.016*
Anesthetic	1.011	3.856	1.176–12.641	0.026*
Total number of ECT units	1.060	1.059	0.678–1.655	0.801

OR, adjusted odds ratio; CI, confidence interval; *statistical significance at two-tailed $P < 0.05$; VIF, variance inflation factor.

have indicated that etomidate is linked to longer seizure activity than propofol (31, 32), and this generalized epileptic activity can raise body temperature (33). The length of seizures is also significant predictor of fever after ECT (11). Therefore, since etomidate is associated with longer seizure activity, it may have contributed to an increase in body temperature and resultant fever.

Our research further indicated that fever after ECT most commonly occurred during the afternoon of the day that the treatment was completed. Overall, the fevers were mild to moderate and transitory, with body temperature returning to normal within 24 hours. These clinical characteristics may explain why fever after ECT has often been overlooked. Therefore, we recommend monitoring for fever on the day of treatment completion, especially during the afternoon hours. If fever occurs after initial treatment, subsequent ECT treatments may induce fever.

Fever is usually seen as a sign of infection or systemic inflammation and can indicate serious or life-threatening diseases. We found that not all fevers after ECT were indicative of infection. Specifically, more than half of patient temperatures returned to normal body temperature through clinical observation or cooling measures. Interestingly, cooling combined with antimicrobial treatments was as effective as cooling or observation alone. Regardless, most patients' temperatures returned to normal body temperature within 24 hour after fever onset. Given that the ECT treatment frequency in the current study was 2–3 times per week, fever did not impact the overall treatment course, and 94.6% (122/129) of fever units chose to continue or extend treatment interval, while only 5.4% (7/129) opted to discontinue ECT after experiencing fever. The 94.6% continuation rate after ECT shows that transient fever seldom requires changes to treatment protocols. This clinically significant finding suggests that in cases of fever without evidence of infection, prioritizing observation or physical cooling may be necessary. If the drop in body temperature is minimal, consider administering antibiotics, as this may help reduce unnecessary antibiotic use, which occurred in 44.2% of fever units, potentially lowering healthcare costs.

It is worth noting that this study has several limitations. First, due the retrospective study design, complete blood counts, C-reactive protein levels, and chest computed tomography scans were not performed after each fever occurrence; thus it is impossible to determine if the fevers were caused by infection. Second, the selection of etomidate and propofol was not completely randomized and the cohort size using propofol as an anesthetic was relatively small, which may have led to selection bias. However, we treated each ECT session as an independent unit to compare the fever rates after using two anesthetics; therefore this limitation did not affect the finding that etomidate administration was more likely to cause fever after ECT than propofol. Third, fever may be related to factors such as anesthesia time and duration of seizures. We did not measure adrenocorticotropic hormone or cortisol levels, nor did we compare the seizure time between etomidate and propofol. These factors represent important limitations of our research, and future studies should directly investigate the relationship between fever and neuroendocrine changes after ECT, as well as the relationship between seizure time and fever. Fourth, this study did not analyze the use of antipsychotic medications. Indeed, reports have shown that antipsychotic drugs can affect body temperature, with fluphenazine, olanzapine, and risperidone potentially lowering the axillary temperature in patients with psychosis (34), which we believe may lead to an underestimation of the incidence of fever after ECT. Finally, fevers have been associated with concomitant medications, comorbidities, body-mass index, hydration status, smoking, position of the electrodes, and other clinical factors parameters not addressed in the study. In the future, we will conduct prospective randomized controlled studies of fever after ECT.

5 Conclusions

This study found that fever after ECT requires attention in clinical practice. Although the direct impact of fever on the ECT treatment is relatively limited, given its potential risks, it is necessary to focus on strengthening the temperature monitoring of high-risk groups. To further clarify the relevant mechanisms and clinical significance, prospective studies should be conducted to further explore the occurrence mechanism of fever and its specific impact on treatment outcomes.

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 authors.

Ethics statement

Ethical approval was obtained from the Ethics Committee of the Second Affiliated Hospital of Xinxiang Medical University, Henan, PR China (No. XYEFYLL-2023-30). The studies were conducted in accordance with the local legislation and institutional requirements. The human samples used in this study were acquired from a by-product of routine care or industry. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

M-mZ: Conceptualization, Investigation, Writing – original draft, Writing – review & editing. RX: Conceptualization, Writing – review & editing, Data curation, Formal analysis, Methodology. JW: Methodology, Investigation, Resources, Writing – review & editing. CW: Investigation, Methodology, Project administration, Writing – review & editing. HR: Project administration, Supervision, Writing – review & editing. ZZ: Supervision, Writing – review & editing, Conceptualization, Investigation, Methodology. JL: Conceptualization, Writing – review & editing, Funding acquisition, Writing – original draft.

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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.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Publisher's note

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New insights into the mechanisms of electroconvulsive therapy in treatment-resistant depression

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Electroconvulsive therapy (ECT) remains one of the most effective interventions for treatment-resistant depression (TRD), particularly in cases involving severe symptomatology, suicidality, or psychotic features. Despite advancements aimed at enhancing the safety and cognitive tolerability of ECT, concerns about cognitive side effects continue to limit its broader acceptance. A deeper understanding of the mechanisms underlying ECT is therefore critical for refining its use and maximizing clinical outcomes. Through a narrative review of recent literature, this paper synthesizes current evidence comparing the efficacy of ECT, ketamine, and repetitive transcranial magnetic stimulation (rTMS) in the treatment of TRD. Then, the review delves into the neurobiological mechanisms through which ECT exerts its therapeutic effects, including modulation of neurotransmitter systems, enhancement of neurogenesis, changes in brain network connectivity, immune response regulation, neurotrophic signaling, and epigenetic alterations. These mechanistic insights may inform the identification of biomarkers predictive of treatment response. Moving forward, future research guided by interaction mechanisms hypotheses could provide more insights into alternative neuromodulation techniques, optimize ECT procedures, and improve patient-specific treatment approaches to enhance therapeutic benefits while minimizing adverse effects.

KEYWORDS

electroconvulsive therapy, major depressive disorder, treatment-resistant depression, interventional psychiatry, neuromodulation

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Introduction

Treatment-resistant depression (TRD) represents a subtype of major depressive disorder (MDD) characterized by an inadequate response to standard antidepressant treatments. While various definitions and staging models exist, a commonly accepted criterion proposed by the U.S. Food and Drug Administration (FDA) is the failure to achieve a satisfactory response after at least two adequate trials of different antidepressant medications (1). This lack of consensus on a precise definition reflects the complexity of TRD and underscores the need for individualized treatment approaches. TRD remains a significant clinical challenge, affecting approximately 30-40% of individuals with MDD. These patients experience extended periods of illness while struggling with disabling symptoms such as hopelessness, anhedonia, and cognitive dysfunction. Additionally, the chronic nature of their condition increases their risk for a wide range of psychiatric and somatic comorbidities, such as chronic suicidality, anxiety disorders, substance abuse, and cardiovascular disease (2).

Introduced in the 1930s, ECT emerged as a groundbreaking intervention for severe psychiatric conditions. Its application in treating depression, particularly in cases resistant to other treatments, has been well-documented. A study from the 1940s reported that 80% of patients receiving ECT experienced symptomatic improvement, compared to 50% in the control group. Additionally, the average length of hospitalization for the ECT group was significantly shorter, underscoring its efficacy in managing severe depression (3). In modern clinical practice, ECT remains a highly effective treatment for TRD and is considered a first-line treatment for severely depressed patients who require a fast response because of a high suicide or homicide risk, extreme agitation, life-threatening inanition, psychosis, or stupor (4). Beyond its established use for severe TRD, bipolar disorder, schizophrenia, and catatonia, electroconvulsive therapy (ECT) is also being investigated for a broader range of psychiatric and neuropsychiatric conditions. These include post-traumatic stress disorder (PTSD), Parkinson's disease with psychiatric symptoms, neuropsychiatric complications associated with COVID-19, and perinatal psychiatric disorders, where pharmacologic treatments may pose risks (5). Additionally, ECT is increasingly being applied in acute medical scenarios where a rapid therapeutic response is essential. For medically unstable patients suffering from severe somatic comorbidities, such as dehydration, malnutrition, or profound weight loss, ECT can facilitate urgent clinical stabilization. Emerging evidence also supports its efficacy in managing intractable delirium, particularly in intensive care settings, and in select cases of refractory or super-refractory status epilepticus, where standard treatments have proven ineffective and ECT has been associated with clinical improvement (6, 7).

Although ECT is highly effective in the rapid treatment of various psychiatric disorders and symptoms, it continues to be an underutilized and stigmatized intervention (8), mainly due to its cognitive side effects, such as anterograde and retrograde amnesia. However, ongoing research continues to shed light on its mechanisms of action and develop strategies to mitigate adverse effects, reinforcing its role as a vital option in treating TRD (9). Moreover, recent advancements in ECT techniques have significantly enhanced both its safety and therapeutic efficacy. Innovations in dosing parameters, electrode placement strategies, and the integration of augmenting agents have been meticulously designed to optimize clinical outcomes while minimizing adverse effects. These refinements emphasize the evolving role of ECT in contemporary psychiatric practice, broadening its applicability while ensuring greater precision and safety in treatment delivery.

This review aims to synthesize recent findings on the effectiveness and biological mechanisms of ECT in treating TRD. It includes a discussion of studies that compare ECT with ketamine and repetitive transcranial magnetic stimulation (rTMS), focusing on differences in clinical outcomes. Furthermore, we highlight emerging insights into the neurobiological mechanisms underlying ECT's antidepressant effects, emphasizing pathways implicated in its therapeutic action. By integrating these findings, this review offers a comprehensive overview of the current state of ECT research and outlines promising directions for optimizing its clinical utility in TRD.

Review methodology

This narrative review was conducted using a targeted literature search conducted across multiple databases, including PubMed, PsycINFO, and Scopus. The strategy utilized combinations of terms such as "electroconvulsive therapy," "ECT," treatment-resistant depression," "mechanisms," "efficacy," "neuroplasticity," "cognitive effects," "biomarkers,", "rTMS," and "ketamine," In addition to database searches, we performed manual screening of relevant articles from ECT-specific and interventional psychiatry journals, including The Journal of ECT, Brain Stimulation, and Neuropsychopharmacology.

We prioritized peer-reviewed English language publications, including systematic reviews, meta-analyses, randomized controlled trials (RCTs), mechanistic studies, and high-impact narrative reviews. Studies were included if they addressed the clinical efficacy, biological mechanisms, or safety profile of ECT in TRD or related neuropsychiatric conditions.

Exclusion criteria included non-peer-reviewed content, case reports with unclear methodology, or studies focused exclusively on other disorders without relevance to TRD or ECT. This methodology aimed to synthesize foundational and emerging findings while capturing the comparative landscape between ECT, rTMS, and ketamine. The final selection includes over 80 references, representing a balance of clinical and mechanistic perspectives to guide future research and practice.

Comparative efficacy of ECT

Electroconvulsive therapy (ECT), ketamine, and rTMS are among the most effective treatments for individuals with TRD, each offering distinct clinical advantages (Table 1). ECT remains

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TABLE 1 Comparison of neuromodulation treatments for TRD.

Treatment	Pros	Cons
Electroconvulsive Therapy (ECT)	• Most effective for severe TRD, especially with psychotic features or suicidality. • Particularly effective in older adults, with higher response and remission rates in late-life depression • Rapid symptom relief, often within days. • High remission rates compared to other treatments. • Long-standing clinical use with well-established efficacy.	• Cognitive side effects, especially memory loss (more common with bilateral ECT). • Requires anesthesia and muscle relaxants, increasing medical risks. • Stigma and fear surrounding treatment.
Ketamine	• Fast-acting antidepressant effects (within hours to days). • Fewer cognitive side effects than ECT. • Non-invasive, no need for anesthesia. • May reduce suicidal ideation quickly, making it useful for crisis intervention. • Can be used in outpatient settings.	• Effects are short-lived, requiring maintenance doses or additional therapy. • High cost and limited insurance coverage. • Risk of dissociation, hallucinations, and blood pressure spikes during administration. • Long-term safety and efficacy remain under investigation. • Potential for misuse or dependence with repeated use.
Repetitive Transcranial Magnetic Stimulation (rTMS)	• Non-invasive and generally well-tolerated. • No anesthesia or systemic medications required. • Minimal cognitive side effects. • Suitable for patients who are not candidates for ECT or ketamine.	• Less effective than ECT, particularly in severe TRD. • Slower onset of symptom relief (weeks to months compared to days with ketamine or ECT). • Requires daily sessions over 4–6 weeks. • Variable response rates; not all patients benefit. • Less effective for psychotic or highly severe depression.

the gold standard, particularly for patients with severe symptoms, suicidality, or psychotic features, or late-life depression, where its efficacy is consistently supported by meta-analyses and geriatric trials. Moreover, older adults often respond more robustly to ECT than younger populations, likely reflecting age-related neurobiological differences and the distinct clinical characteristics of late-life depression (10, 11). However, its broader use is limited by the need for anesthesia and the risk of cognitive side effects, as well as associated costs. Moreover, ECT's requirement for general anesthesia and muscle relaxation imposes procedural constraints and hospital burdens. In particular, it affects patients with complex medical conditions. Individuals with cardiovascular conditions, such as recent myocardial infarction, unstable coronary artery disease, congestive heart failure, or arrhythmias, as well as those with pulmonary comorbidities (e.g., COPD or OSA). These patients require extensive pre-anesthetic evaluation, which may lead to delays or disqualification from treatment (12). rTMS, on the other hand, offers a non-invasive alternative that targets specific brain regions through magnetic pulses, without the need for anesthesia and with generally good tolerability. Ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist, has gained recognition for its rapid antidepressant effects, more favorable cognitive profile, and ease of administration. This section examines current evidence comparing ECT, ketamine, and rTMS in the treatment of TRD, focusing on onset of therapeutic effects, cognitive outcomes, and durability of response.

A growing body of literature comparing ECT and ketamine for TRD underscores the effectiveness of both interventions. However, they exhibit notable differences in the speed of onset, cognitive effects, and patient outcomes preference. Basso et al. (13), conducted an open-label clinical trial demonstrating that, while both treatments were equally effective, ketamine exerted a more rapid antidepressant effect and improved neurocognitive functions. In contrast, ECT was associated with a mild decline in cognitive performance. In line with this, Ghasemi et al. (14), found that ketamine led to a significantly faster reduction in depressive symptoms within 24 hours compared to ECT. However, its efficacy became comparable to ECT after multiple treatments. A study by Kheirabadi et al. (15), further supported these findings, showing no statistically significant difference in antidepressant efficacy between ECT and ketamine. However, cognitive performance was slightly better in the ketamine group. The KetECT, a multicenter randomized controlled study, added another layer to this evolving comparison, showing that ECT had superior remission rates (62.6% vs. 46.3% for ketamine) (16). The ELEKT-D trial, a multicenter randomized controlled study, found that ketamine was noninferior to ECT in reducing depressive symptoms, with response rates of 55.4% for ketamine and 41.2% for ECT (17). In a *post hoc* secondary analysis, the authors found that patients with the highest severity appeared to benefit more quickly from ECT, potentially due to its robust neurobiological impact. However, ketamine demonstrated higher overall response rates and was especially effective among outpatients with nonpsychotic depression who experienced moderate to severe symptoms of depression (18). A recent meta-analysis encompassing six randomized controlled trials found that both treatments significantly reduced depressive symptoms, with no substantial difference in overall efficacy between the two modalities. Ketamine demonstrated superior memory function improvement compared to ECT. In terms of adverse events, ketamine was associated with significantly higher rates of dissociative symptoms, blurred vision, and dizziness, while demonstrating a lower incidence of muscle pain (19).

Comparative studies have also shown differences in efficacy between rTMS and ECT. In a meta-analysis by Ren et al. (2014), ECT had a higher response rate than high-frequency rTMS (HF-rTMS) for major depression, with response rates of 52.9% for ECT versus 38.3% for HF-rTMS. Similarly, Micallef-Trigona (20) found that ECT was more effective than rTMS, with a significant reduction in HDRS scores in the ECT group. However, rTMS still showed a

notable antidepressant effect, suggesting its potential as a viable alternative, especially for patients who may not tolerate ECT. On the other hand, Cano et al. (21), showed that both right unilateral (RUL) ECT versus left dorsolateral prefrontal cortex (lDLPFC) rTMS significantly reduced depressive symptoms in patients with TRD, with QIDS scores decreasing by 30.40% and 36.13%, respectively. Despite higher baseline severity in the ECT group, there was no significant difference in clinical response between the two treatment modalities. A retrospective cohort study showed that ECT exerted a significantly stronger antidepressant effect than rTMS in terms of MADRS-S score reduction, response rate, remission rate, and clinically meaningful change (22). Kaster and Blumberger (23) emphasized the role of rTMS in sequential treatment models, noting that while less effective than ECT, it remains a viable step before ECT for patients seeking non-invasive options. A recent meta-analysis comparing ECT, rTMS, and ketamine in adolescents with TRD confirmed that while ECT remains the most effective, it is often avoided due to stigma and accessibility issues (24). Similarly, a systematic review of RCTs found that ECT is superior to both ketamine and rTMS in overall efficacy. However, ketamine offers faster symptom relief, making it useful in acute interventions (25). Despite these findings, more research is needed to better characterize patient-level predictors of treatment response, which could help guide the selection of optimal treatment modalities based on individual clinical profiles.

ECT, ketamine, and rTMS are three principal interventions for TRD, each characterized by distinct advantages and limitations. ECT has historically been regarded as the most efficacious treatment, particularly for individuals with severe depression, psychotic symptoms, suicidality, or late-life depression. Its well-established effectiveness in older adults should be especially noted, as this population often shows greater clinical response and tolerability (10, 11). However, concerns regarding its associated cognitive impairment, societal stigma, and restricted accessibility have contributed to a decline in its utilization. Ketamine has emerged as a promising alternative due to its rapid antidepressant effects, a more favorable cognitive side effect profile, and its comparatively less invasive administration. rTMS, a non-invasive neuromodulation technique, represents another viable therapeutic option, offering a favorable safety profile but exhibiting more variable efficacy across patient populations (Table 2).

Cognitive outcomes

Concerns about cognitive side effects are a significant barrier to the wider acceptance of ECT, despite its effectiveness in treating TRD (26). While early reports highlighted cognitive risks, accumulating evidence indicates that many of these effects are time-limited and, in some cases, reversible. Studies indicate that impairments in attention, executive function, and processing speed typically persist for a brief duration. Most studies find a return to baseline or improvement within weeks to three months after treatment, suggesting that these improvements likely result from both the effects of ECT on the brain and the relief of depressive symptoms (27–29). A large-scale longitudinal study utilizing data from 1,498 patients in the Swedish National Quality Register for ECT found that 25.2% of individuals reported subjective memory worsening six months after treatment. Notably, the strongest predictor of long-term cognitive complaints was residual depressive symptoms, as measured by MADRS-S scores, rather than ECT technical variables such as electrode placement, pulse width, or number of sessions. These findings suggest that patients' perception of cognitive impairment may reflect unresolved mood symptoms more than the direct neurobiological effects of ECT and highlight the importance of achieving and maintaining full remission (30). Xu et al. (31), demonstrated that ECT is effective in treating young adults with TRD and highlighted the heterogeneous nature of cognitive outcomes during treatment. While global cognition, verbal fluency, and working memory generally remained stable or showed improvement, delayed verbal recall exhibited a transient decline that typically resolved after treatment. Importantly, cognitive impairments were more pronounced among individuals with older age, lower educational attainment, and pre-existing cognitive deficits. A quasi-experimental study examining the timing of autobiographical memory retrieval relative to ECT initiation found that patients who completed the Autobiographical Memory Interview within 24 hours before their first session showed a decline in memory performance post-treatment, whereas those who completed it more than 24 hours in advance demonstrated improvement. These results support the hypothesis that ECT can interfere with the reconsolidation of reactivated memories, a process during which recalled memories become temporarily labile and susceptible to disruption (32).

A recent consensus guideline, developed by a committee of clinical and academic experts from Australia and New Zealand, emphasizes that while most cognitive domains return to baseline or improve shortly after treatment, autobiographical memory loss may endure in a subset of individuals and can be distressing and functionally impairing. Factors influencing cognitive risk include older age, pre-existing brain vulnerability, concurrent lithium use, and extended or bilateral treatment protocols. Although the mean group data suggest recovery, individual-level analyses reveal that some patients may experience significant impairments that are masked by group averages (33).

Collectively, these findings suggest that while most cognitive effects of ECT are transient and may even improve over time, persistent autobiographical memory loss remains a significant concern for a subset of patients. Importantly, perceived cognitive deficits appear to be shaped by both neurobiological and psychological factors, including symptom resolution and timing of memory activation. Future work should focus on refining cognitive monitoring strategies, elucidating individual risk profiles, and exploring behavioral or procedural adjustments to minimize adverse cognitive outcomes without compromising therapeutic efficacy.

TABLE 2 Summary of comparative studies evaluating the antidepressant efficacy of ECT and ketamine or rTMS in TRD.

Study	Design	Sample size	Mainfindings	Limitations
Basso et al. (13),	Naturalistic, non-randomized, comparative study	50 patients	Ketamine and ECT were similarly effective; ketamine acted faster and improved attention and executive function. ECT led to minor cognitive decline.	Non-randomized; Concurrent medication use; No placebo group.
Ghasemi et al. (14),	Randomized, blinded comparison	18 patients	Ketamine showed faster antidepressant effects than ECT within 24h and throughout the second treatment. Similar efficacy by the end (1 week).	Small sample; Titration method was used for ECT; Thiopental as anesthetic (anticonvulsant properties); Short treatment and follow-up period; Did not record seizure durations.
Kheirabadi et al. (15),	Randomized controlled trial	32 patients	No significant difference in HDRS outcomes between ketamine and ECT. Cognitive state was more favorable (not significant) in the ketamine group.	Small sample size; Limited generalizability; No blinding reported.
Ekstrand et al. (16),	Randomized, open-label, non-inferiority trial	186 inpatients	ECT had higher remission rates than ketamine (63% vs 46%, p=0.026). Relapse rates were similar at 12 months. Persistent amnesia was more common with ECT.	No placebo group; Open-label; hospitalized patients only; limited data on long-term cognitive effects.
Anand et al. (17),	Open-label, randomized noninferiority trial	403 randomized (365 treated)	Ketamine was noninferior to ECT in response rates (55.4% vs 41.2%). ECT appeared to be associated with a decrease in memory recall after 3 weeks of treatment, with gradual recovery during follow-up.	Open-label design; Short initial treatment phase; Long-term safety and durability unclear.
Jha et al. (18),	Secondary analysis of an open-label noninferiority randomized clinical trial	365 patients	Ketamine had greater effect in moderately to severely depressed outpatients. ECT was more effective early in very severe or inpatient cases, but effects equalized by week 3.	Secondary analysis; Results not prespecified; Nonblinded; No formal cognitive assessment.
Cano et al. (21),	Prospective, non-randomized observational study.	32 patients	Did not observe a significant difference in clinical response between patients treated with RUL ECT and rTMS (30.40% vs 36.13% change in QIDS score)	Small sample size; Non-randomized; Concomitant medications not controlled; Use of self-report (QIDS) over clinician-rated scales for primary clinical outcomes.
Strandberg et al. (22),	Register-based cohort study	138 patients	ECT was more effective than rTMS (MADRS-S reduction: 15.0 vs 5.6; Response rates: 38% vs 15%). ECT superiority was consistent across age and severity subgroups.	Observational study design; Non-randomized; No formal cognitive assessment.

Mechanistic insights

Neurotransmitter modulation by ECT

The classical monoamine neurotransmitter theory of depression, which posits that a depletion of serotonin, norepinephrine, and dopamine plays a key role in the pathophysiology of the disorder, has historically influenced our understanding of antidepressant mechanisms. Evidence suggests that ECT enhances the neurotransmission of these monoamines.

Post-mortem and *in vivo* imaging studies suggest that ECT increases the availability of serotonin in synaptic clefts by enhancing the function of serotonin transporters (5-HTT) and increasing serotonin receptor sensitivity (34). Hoekstra et al. (35), found an increase in the plasma levels of tryptophan at approximately 24 h post-ECT only in those patients who responded to the treatment, while another study showed total plasma tryptophan levels remained elevated between 2 and 24 hours following ECT, but these alterations were reversible within 48 hours (36). Moreover, studies indicate that serotonin receptor 5-HT_{1A} postsynaptic density is decreased following ECT in depressed patients (37). However, other studies have found that 5-HT_{1A} postsynaptic receptors become more sensitive to serotonin after ECT treatment (38). A significant decrease in brain 5-HT_2 receptors has also been observed in patients with depression following ECT, mirroring the effects seen with antidepressant medications (38, 39). A pilot study examined how patients undergoing ECT altered the loudness dependency of auditory evoked potentials (LDAEP), a proposed indicator of central serotonergic activity. The results indicated that changes in LDAEP measurements after treatment demonstrated that ECT influences serotonergic activity (40). The differential effects of ECT on various serotonin receptor subtypes highlight the nuanced way in which ECT interacts with the serotonergic system, potentially differing from the more direct actions of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs).

ECT has also been shown to influence dopaminergic neurotransmission, which is closely linked to motivation and reward processing. Masuoka et al. (41), showed that ECT can decrease striatal dopamine transporter binding, leading to increased dopamine availability in the synaptic cleft. Preclinical studies using animal models of depression suggest that ECT enhances dopamine release in the nucleus accumbens and striatum, potentially reversing anhedonia, a core symptom of depression (42, 43). Functional imaging studies further support this, demonstrating increased dopaminergic activity in reward-related brain circuits post-ECT (44). These changes might help reduce the psychomotor slowness and anhedonia that are frequently seen in depressed people (45).

Beyond monoaminergic changes, ECT significantly impacts the balance between excitatory and inhibitory neurotransmission, particularly through GABAergic and glutamatergic systems. ECT exhibits anticonvulsant properties, leading to a decrease in neural metabolic activity over the course of treatment (46). Repeated seizures induced by ECT result in reduced seizure duration and increased intracortical inhibition, which has been correlated with clinical improvement (47, 48). Bajbouj et al. (47), showed that ECT enhances the activity of inhibitory circuits in the motor cortex, as evidenced by increased intracortical inhibition and cortical silent period duration. Moreover, studies have shown that ECT responders tend to have higher GABA levels at baseline and after a course of ECT when compared to non-responders (49). Moreover, ECT has been found to increase levels of GABA in the anterior cingulate cortex, a region implicated in emotional regulation (49). A proposed neurophysiological theory suggests that mood stability is enhanced by increasing the activity of GABAergic neurons that regulate neurocircuits, attributed to the rise in the seizure threshold caused by the repeated electrically-induced seizures.

The glutamatergic system has also garnered increasing attention for its role in depression and the effects of ECT. Evidence from proton magnetic resonance spectroscopy (^{1}H-MRS) studies indicates that individuals with MDD exhibit reduced glutamate levels and glutamate/glutamine (Glx) in the anterior cingulate cortex (ACC), a region implicated in mood regulation. Notably, these alterations appear to normalize following successful ECT, correlating with clinical improvement (50–52). Similarly, Njau et al. (53), found that, at baseline, patients had lower Glx levels in the subgenual ACC (sgACC) and higher levels in the left hippocampus compared to healthy controls. After ECT, Glx levels increased in the sgACC and decreased in the hippocampus, with these neurochemical changes correlating with mood improvement. Pfleiderer et al. (54), also observed significantly reduced Glx levels in the left cingulum of depressed patients relative to controls. In patients who responded to ECT, Glx levels normalized and no longer differed from those of healthy individuals, a pattern not observed in non-responders. Supporting these findings, Ermis et al. (55), reported in a longitudinal study that ECT remitters had higher baseline ACC Glx than non-remitters. Notably, after ECT, ACC Glx levels decreased in remitters but increased in non-remitters. Collectively, these studies indicate that severe depression is characterized by regional Glx deficits or dysregulation and support the "anticonvulsant hypothesis" of ECT, which proposes that ECT reverses the GABA/glutamate imbalance underlying the hyperexcitatory state in MDD through glutamate receptor modulation (e.g., NMDA receptors) (56).

It is important to note that these neurotransmitter systems do not function in isolation but rather interact in a complex and interconnected manner. The therapeutic effects of ECT likely arise from a synergistic modulation of these systems, leading to a more balanced neurochemical environment in the brain. The observed changes in neurotransmitter levels and receptor sensitivity following ECT may contribute to the neuroplastic and neuroanatomical changes seen with the treatment, suggesting a cascade of effects that ultimately lead to symptom alleviation.

Impact of ECT on neurogenesis, brain network connectivity and function

Preclinical and clinical studies indicate that ECT treatment leads to an increase in the count of hippocampal granule cells. Madsen et al. (57), found that ECT induces a more pronounced neurogenic effect compared to traditional pharmacological antidepressants, exhibiting a faster onset of action. Nordanskog et al. (58), showed an increase in hippocampal volumes following ECT using a 3-Tesla MRI scanner. Subsequent longitudinal MRI studies and meta-analyses confirmed increases in hippocampal and amygdala volumes after ECT (59–61).

In a study using longitudinal MRI and neuropsychological testing in two distinct clinical populations (MDD and schizophrenia-spectrum disorders), greater hippocampal volume increases were consistently associated with poorer post-ECT cognitive performance, despite differences in diagnostic profile, electrode placement, and treatment parameters. Notably, the study investigated 42 cortical and subcortical regions and demonstrated that the cognitive outcomes were specifically related to the hippocampus (62). Another study focusing on subjective memory outcomes found that increases in the volume of hippocampal subregions (the right and left dentate gyrus) were associated with greater self-reported memory impairment, particularly in autobiographical recall. Conversely, by the 6-month follow-up, reductions in dentate gyrus volume compared to pre-ECT assessments were observed, and these reductions correlated with improvements in objective cognitive performance (63). These findings highlight a potential paradox: while hippocampal enlargement may reflect a form of treatment-induced neuroplasticity, it may also contribute to cognitive side effects.

Mechanistically, ECT is known to upregulate neurotrophic factors and stimulate neurogenesis within the dentate gyrus, contributing to synaptic remodeling and circuit reorganization. However, the rapid onset and magnitude of observed volume changes suggest that neurogenesis alone cannot fully account for these effects. Corroborating this hypothesis, a study using high-field MRI in mice found that electroconvulsive stimulation induced dose-dependent increases in hippocampal volume. Notably, these

volumetric changes persisted even in mice where neurogenesis was ablated through X-ray irradiation, implying that other neuroplastic processes, such as increased synaptic density, contribute to the observed structural alterations (64). While some studies hypothesized that the volumetric changes are a result of the hemodynamic and metabolic shifts that occur during seizures, potentially leading to vasogenic or cytotoxic edema, several studies have found no evidence of increased T2 signal intensity or alterations in diffusivity after ECT, suggesting that edema may not play a central role in the observed structural changes (58, 65, 66). Seizure-induced neuroinflammation remains a plausible contributor, potentially facilitating aberrant neurogenesis and transient blood-brain barrier disruption, which may further explain associated cognitive side effects.

Beyond hippocampal changes, large-scale analyses, such as those from the Global ECT-MRI Research Collaboration (GEMRIC), demonstrated that ECT-induced brain volume changes extend beyond the hippocampus, affecting multiple brain regions, with the most significant changes occurring in the hippocampus and amygdala (67, 68). The magnitude of these volumetric changes was found to be dose-dependent and influenced by the electrical field and induced seizures (69). Moreover, several studies have shown that volume increase was most pronounced in the dentate gyrus, a region associated with neurogenesis, aligning with the neuroplasticity hypothesis (70–72). A recent neuroimaging study by Cano et al. (21),, using structural MRI, found that only ECT caused notable increases in gray matter volume, in the right striatum, pallidum, medial temporal lobe (including the amygdala and hippocampus), anterior insula, anterior midbrain (substantia nigra/ventral tegmental area), and subgenual anterior cingulate cortex. In contrast, no significant structural changes occurred after rTMS, even though both groups showed similar improvements in depressive symptoms. Importantly, these volume changes did not relate to the level of symptom reduction. The findings support the idea that ECT leads to large-scale structural changes in the brain through neuroinflammatory or cellular remodeling processes.

Diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI) studies provide valuable insights into the microstructural effects of ECT on brain tissue, complementing volumetric findings. In white matter, early reports suggested that ECT enhances fiber integrity, as reflected by increased fractional anisotropy (FA) in regions such as the anterior cingulum and frontal tracts; however, more recent findings have revealed increases in mean diffusivity (MD) and radial diffusivity (RD), which may indicate transient extracellular fluid shifts or blood–brain barrier permeability rather than lasting improvements in white matter organization. Gray matter DWI studies have more consistently reported reductions in MD within the hippocampus and amygdala following ECT, potentially reflecting increased cellular complexity (73). Multisite studies further clarify these effects. Repple et al. (74), found ECT-specific increases in MD in right-hemispheric white matter tracts, with baseline white matter integrity (higher FA, lower MD/RD) predicting greater clinical response. Similarly, Belge et al. (75), reported increases in FA, MD, and axial diffusivity (AD) across several white matter pathways post-ECT, notably in cortico-spinal and fronto-occipital tracts. Although diffusion changes were not directly associated with symptom improvement, both studies suggest that baseline microstructural differences may help identify individuals more likely to benefit from ECT, reinforcing the role of ECT in modulating neural circuits implicated in emotion regulation and neuroplasticity.

Besides these structural modifications, ECT also causes functional changes in the connectivity of the brain network. An overactive default mode network (DMN), especially in the medial prefrontal cortex, is closely associated with ruminative thinking, which is a prevalent disorder associated with depression (76). According to fMRI studies, ECT decreases DMN hyperconnectivity, which is linked to symptom alleviation (77). Additionally, ECT improves stress management and emotional processing by increasing connections between the prefrontal cortex and limbic regions like the hippocampus and amygdala (78). Pang et al. (79), showed that clinical improvement was associated with improved connections within the DMN and between the DMN and the central executive network following ECT. Furthermore, Sun et al. (80), revealed that ECT changed the brain's local and global information-processing processes, and the increase in network metrics was associated with clinical remission. A study using resting-state electroencephalography (RS-EEG) showed that ECT significantly changed the network's topology, indicating a restructuring of functional connections that might be the basis for its antidepressant effects (81). Thus, it is believed that these modifications in functional connectivity contribute to the strong and rapid antidepressant effects of ETC (82, 83).

In summary, ECT causes significant structural and functional changes in the brain, especially in hippocampal circuits, through a complex interplay of neurogenesis, synaptic plasticity, and inflammatory signaling. While these changes contribute to its therapeutic efficacy, they may also explain the temporary cognitive side effects observed in some patients, as they may transiently disrupt pre-existing memory circuits (84). Such effects are commonly observed in the early post-treatment phase, and are typically time-limited, with most patients recovering cognitive function over the weeks to months following treatment (27). These findings underscore the importance of balancing therapeutic efficacy with individualized cognitive risk assessment, particularly in patients with baseline memory vulnerabilities.

The role of neurotrophic factors

A significant body of evidence indicates that ECT plays a role in upregulating neurotrophic factors. Preclinical and clinical studies have reported that ECT leads to a significant increase in peripheral Brain-Derived Neurotrophic Factor (BDNF) concentrations (85, 86). A meta-analysis indicated that ECT elevates plasma BDNF levels, but not in serum, although this increase was not consistently associated with clinical improvement in depressive symptoms (87). Another study observed that serum BDNF levels increased following ECT, irrespective of its effectiveness, suggesting a direct effect of ECT on BDNF expression (88). More recently, a study

showed that BDNF in plasma was significantly lower in TRD patients compared to HCs at baseline but increased following ECT. More importantly, the authors found a potential positive dose-response relationship between doublecortin (DCX) levels in neuron-derived extracellular vesicles (NDEVs) and plasma BDNF, suggesting that neurogenesis and neuroplasticity may be interconnected (89). However, some findings on the changes in BDNF and the response to ECT are controversial, with studies reporting no influence of ECT on serum or plasma BDNF levels during or after ECT series (90–92).

Emerging research also highlights the role of vascular endothelial growth factor (VEGF) in the mechanism of ECT. Preclinical studies have shown that ECT increases VEGF levels in the hippocampus region of the brain (93). Clinical studies have also reported increased VEGF levels in the serum and plasma of patients with TRD following ECT (94, 95). Additionally, reduced VEGF levels have been associated with a poor response to ECT, suggesting that this neurotrophin may serve as a predictive biomarker for treatment outcomes (93, 96).

In summary, the increased neurotrophic factor levels following ECT might be associated with the structural and functional brain changes associated with successful treatment. The emerging role of VEGF in the mechanism of ECT, particularly its potential to promote neurogenesis and interact with BDNF, suggests a more complex interplay of neurotrophic factors than initially considered.

Inflammatory aspects of ECT

ECT has been shown to influence the immune system, with both acute and long-term effects that may contribute to its therapeutic efficacy. Several studies have documented an immediate immune response following ECT, characterized by transient increases in pro-inflammatory cytokines. For example, interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) levels have been observed to rise shortly after ECT sessions (97). This acute inflammatory response is thought to be part of the body's physiological reaction to the induced seizure and stress associated with ECT. The elevation in cytokine levels, however, is typically short-lived, returning to baseline within hours to days (98).

While the acute phase of ECT elicits a temporary pro-inflammatory response, long-term effects suggest an overall anti-inflammatory outcome. Chronic inflammation has been linked to depressive disorders, with elevated levels of inflammatory markers such as C-reactive protein (CRP), IL-1β, and TNF-α correlating with symptom severity. Research indicates that repeated ECT sessions contribute to a sustained decrease in inflammatory markers, suggesting an immunoregulatory role (99). Patients who experience symptom relief post-ECT often exhibit reductions in CRP and IL-6 levels, supporting the hypothesis that ECT's antidepressant effects may be partially mediated through immune modulation (100)

Emerging studies suggest that baseline inflammatory marker levels may predict an individual's response to ECT. Du et al. (101), observed that the ECT group exhibited higher levels of pro-inflammatory biomarkers (IL-1β and IL-6) and lower levels of the anti-inflammatory biomarker (IL-10) at baseline. The authors also found a substantial decrease in IL-1β and IL-6 and an increase in IL-10 levels post-ECT. Moreover, participants who responded to the treatment showed a significant decline in HAMD-17 scores, accentuating ECT's therapeutic potential. Hough et al. (102), found that ECT induces an initial rise in IL-6 and CRP, followed by a post-treatment decline. While these changes did not predict overall depression severity improvements, higher post-treatment IL-6 correlated with better affective and cognitive outcomes, while CRP reductions linked to neurovegetative symptom relief.

In addition to systemic immune responses, ECT has been shown to influence neuroimmune function, particularly through microglial activation. Microglia, the resident immune cells of the brain, play a crucial role in neuroinflammation and neuroplasticity. Studies suggest that ECT may initially activate microglia but later promote an anti-inflammatory state, reducing neuroinflammation associated with psychiatric disorders (103). Studies have also demonstrated that ECT induced the proliferation of NG2-expressing glial cells in the adult rat hippocampus and amygdala (104, 105).

Together, these studies suggest that ECT's antidepressant effects may involve resetting immune balance, marked by a predictable transition from a transient pro-inflammatory spike to longer-term anti-inflammatory effects. Importantly, the acute increases in inflammatory markers, such as IL-6 and TNF-α, may not be harmful or indicative of adverse outcomes. Rather, they might reflect a normal physiological response to induced seizure activity and may be necessary for initiating downstream neurotrophic and immunoregulatory processes. These early immune shifts are thought to facilitate neuroplasticity and emotional regulation, ultimately contributing to symptom improvement (106). Monitoring both acute and longer-term inflammatory trajectories may offer valuable clinical insights: while short-term elevations are expected and adaptive, sustained reductions in inflammatory tone may underlie durable antidepressant effects. Additionally, tracking post-ECT inflammatory profiles may help identify treatment responders and inform relapse risk, offering a potential avenue for early intervention and individualized care. Despite these promising implications, further research is needed to validate these biomarkers for clinical application and to better understand the mechanistic role of inflammation in mediating ECT outcomes.

Genetic and epigenetic modifications

Studies have shown that ECT affects DNA methylation patterns, which are essential in neurotrophic signaling, and upregulates genes linked to neuroplasticity and synaptic function. The antidepressant benefits of ECT may be maintained by these molecular changes after the initial post-treatment phase (107). Additionally, a methylome-wide analysis identifies differentially methylated CpG sites annotated in *TNKS* associated with ECT binary response and one differentially methylated CpG site annotated in *FKBP5* associated with continuous response (108). Furthermore (109), found numerous differentially methylated positions and regions

(DMPs and DMRs) in genes linked to inflammatory and immune processes, supporting the inflammatory theory of MDD pathogenesis and suggesting a potential role for epigenetic modification in the therapeutic effects of ECT.

A recent study that integrated neuroimaging with transcriptomic gene expression analyses in patients with MDD undergoing ECT revealed a correlation between increased gray matter volume and higher expression levels of MDD risk genes, including CNR1, HTR1A, MAOA, PDE1A, and SST. It also identified ECT-related genes such as BDNF, DRD2, APOE, P2RX7, and TBC1D14 (80). On the other hand, Moschny et al. (110), found no global DNA methylation differences between measured time points (before and after the first and last ECT session) or between ECT responders and non-responders.

These mixed findings highlight the preliminary and heterogeneous nature of epigenetic research in ECT. While some studies point to promising epigenetic signatures associated with treatment response, others report minimal or inconsistent changes, underscoring the need for larger longitudinal and standardized studies to clarify the clinical utility of epigenetic biomarkers in ECT.

Limitations and future directions

Although mechanistic studies of ECT have advanced our understanding of its biological effects, the current body of evidence is still limited by methodological inconsistencies, underpowered study designs, and substantial patient heterogeneity. These challenges limit the reproducibility and clinical applicability of findings, underscoring the need for more rigorous and standardized research approaches.

Evidence on the impact of ECT on neuroplasticity, inflammation, neurotransmitter systems, and epigenetic regulation remains mixed. Contradictory results across studies, particularly those examining biomarkers such as BDNF, inflammatory cytokines, and methylation signatures, reflect wide variability in sampling techniques, timing of assessments, assay sensitivity, and storage conditions. Similarly, neuroimaging studies frequently differ in modality, analysis pipelines, and regions of interest, contributing to inconsistent reports of hippocampal and network-level changes. These inconsistencies make it difficult to draw firm conclusions and underscore the need for methodological harmonization across studies.

One of the most persistent limitations in the current literature is small sample size. Many mechanistic studies of ECT are conducted with limited cohorts, which reduces statistical power and increases the likelihood of spurious findings. This issue is further exacerbated by heterogeneity in ECT administration protocols, including differences in electrode placement, stimulus intensity, session number, anesthesia protocol, and maintenance strategies. Without standardized treatment and assessment protocols, comparing results across studies or synthesizing them in meta-analyses remains a challenging task.

Patient heterogeneity adds another layer of complexity. TRD encompasses a diverse range of clinical presentations influenced by subtype (e.g., melancholic vs. atypical), age, sex, comorbid medical or psychiatric conditions, medication history, and genetic background. Yet many studies fail to stratify or control for these variables. In particular, the high prevalence of co-occurring disorders such as PTSD and personality disorders can influence treatment response and mechanistic signatures, but are often overlooked in study design. Without accounting for such variation, findings may reflect group averages that obscure clinically meaningful subgroup effects.

Addressing these limitations will require coordinated efforts to standardize research methodology, including ECT protocols, biomarker collection procedures, and cognitive assessments. Multi-site collaborations are needed to increase sample sizes, enhance

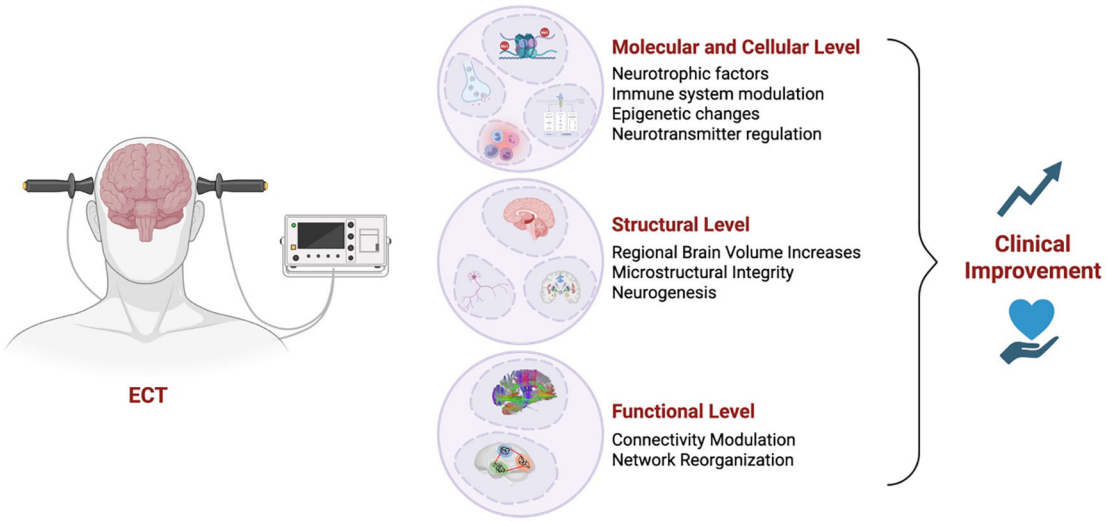

FIGURE 1
Mechanisms underlying electroconvulsive therapy (ECT)-induced clinical improvement. Schematic illustration summarizing the multilevel mechanisms through which electroconvulsive therapy (ECT) may lead to clinical improvement in individuals with treatment-resistant depression. At the molecular and cellular level, ECT enhances neurotrophic factor expression, modulates immune responses, induces epigenetic modifications, and regulates neurotransmitter systems. At the structural level, ECT has been associated with regional brain volume increases, improved microstructural integrity, and adult neurogenesis, particularly in the hippocampus. Finally, ECT influences functional connectivity and brain network organization. Together, these converging effects contribute to clinical improvement in depressive symptoms.

generalizability, and facilitate replication across diverse populations. Future research should incorporate stratified analyses based on clinical subtypes and comorbidity profiles and move toward integrative, systems-level approaches that combine neuroimaging, molecular, and clinical data. Multi-omics studies will be particularly valuable in identifying converging biological pathways predictive of treatment response. Advanced neuroimaging techniques, including functional MRI and DTI, offer valuable tools for tracking treatment-related brain changes and may aid in identifying biomarkers of response and recovery.

In addition to mechanistic investigations, future work must also prioritize long-term outcomes, particularly in relapse prevention. Although ECT is highly effective acutely, relapse rates remain high, often exceeding 50% within the first-year post-treatment, yet many studies offer limited follow-up. Maintenance strategies involving adjunctive treatments, such as rTMS or ketamine, represent promising avenues for sustaining response and minimizing cognitive burden. For instance, using rTMS as a priming intervention before ECT or ketamine as a post-ECT maintenance therapy may enhance the durability of the effect and mitigate side effects, though these approaches require systematic evaluation. Standardized neuropsychological assessments should also be consistently integrated into these trials to better characterize the cognitive effects of ECT and optimize treatment parameters accordingly. Ultimately, aligning mechanistic research with emerging precision psychiatry models will be essential for tailoring interventions, improving prognosis, and reducing relapse in this complex and high-risk population.

Conclusion

The findings reviewed in this paper highlight the continued efficacy of ECT in TRD, while shedding light on its mechanistic underpinnings and potential avenues for refinement. Comparative analyses highlight ECT's superiority in severe cases, particularly when rapid symptom relief is necessary, while alternative treatments, such as ketamine, offer advantages in tolerability and cognitive preservation. Mechanistic insights reveal that ECT may exert its antidepressant effects through the regulation of neurotransmitters, neurogenesis, modulation of brain networks, and neuroimmune modulation, suggesting potential biomarkers for treatment response (Figure 1). These insights collectively emphasize the potential of integrating mechanistic understanding with technological advancements, such as fMRI-guided electrode placement and biomarker-driven treatment personalization, to enhance the therapeutic precision of ECT and mitigate its adverse effects. Future research should focus on refining individualized treatment protocols, leveraging neurobiological markers for predicting response, and addressing the stigma surrounding ECT to maximize its accessibility and clinical impact in TRD.

Author contributions

AR: Writing – original draft, Conceptualization. AH: Resources, Writing – original draft, Data curation. WB: Writing – review & editing. EL: Writing – review & editing. GS: Writing – review & editing, Supervision, Conceptualization, Funding acquisition. JQ: Funding acquisition, Writing – review & editing, Supervision, Conceptualization.

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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.

Correction note

A correction has been made to this article. Details can be found at: 10.3389/fpsyt.2025.1700480.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

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Electroconvulsive therapy in a patient with an implanted sacral neurostimulator: a case report on safe administration and short-term outcomes

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We present a case of a 35-year-old patient with treatment-resistant depression and an implanted sacral neurostimulator for overactive bladder (OAB). The patient experienced an exacerbation of depression with suicidal ideation and failed multiple medication trials. Due to her significant history of adverse medication reactions and the severity of her condition, electroconvulsive therapy (ECT) was selected as a treatment option despite concerns about the safety of administering ECT with a sacral neurostimulator. To minimize potential risks, the device was placed in Magnetic Resonance Imaging (MRI) mode during each ECT session, successfully avoiding electrical interference. She underwent three ECT sessions, which resulted in significant improvement in depressive symptoms and resolution of suicidal ideation without adverse effects on the device's integrity or OAB symptoms. This case highlights the feasibility and safety of ECT in patients with implanted sacral neurostimulators, emphasizing the importance of precautionary measures and individualized patient assessment. Further research is needed to explore the long-term effects of ECT on such devices and their impact on OAB.

KEYWORDS

electroconvulsive therapy (ECT), overactive bladder (OAB), implanted medical devices (IMD), safety, case report, depression, adult, treatment outcomes

Introduction

Electroconvulsive therapy (ECT) is a well-established treatment for severe and treatment-resistant depression (TRD), with open-label remission rates around 48% for non-psychotic cases, significantly surpassing those achieved through pharmacologic augmentation strategies (1). Despite its efficacy, ECT is often withheld in patients with

implanted electronic medical devices due to theoretical concerns about induced currents, tissue heating, or device malfunction. One such device is the sacral neuromodulator system InterStim X®, increasingly used to manage refractory overactive bladder (OAB) and urinary urge incontinence when behavioral modifications and pharmacotherapy have failed (2, 3). With over 300,000 implants globally (4) and device longevity frequently exceeding a decade, evaluating the safety implications of administering ECT to patients with implanted sacral neurostimulators is of growing clinical relevance (5).

Although electromagnetic modeling suggests potential risks from ECT currents coupling with distant leads, empirical evidence from other neurostimulators, such as deep-brain, spinal cord, and cardiac stimulators, suggests that the risk is negligible when stimulation is suspended and leads are anatomically distant (6–11). However, only one prior case has specifically examined ECT in a patient with a sacral neuromodulator (11), leaving clinicians with limited guidance. This case report addresses that gap by describing the successful administration of bitemporal ECT in a woman with chronic InterStim X® therapy, treated for TRD and acute suicidality. We emphasize the practical peri-procedural precautions that supported safe treatment delivery, underscoring the feasibility of ECT in patients with implanted sacral neurostimulation systems.

Case presentation

The patient is a female in her mid-30s with a long-standing history of recurrent major depressive disorder (MDD), generalized anxiety disorder (GAD), ADHD, and PTSD. At the time of presentation, she had been admitted due to increased symptom severity and active suicidal ideation. Her medical history includes a traumatic brain injury requiring ICU admission and resulting in a coma; obesity managed with prior bariatric surgery; recurrent cystitis; and overactive bladder (OAB) previously treated with botulinum toxin and currently managed with an implanted neuromodulation device. She lives independently and serves as the primary caretaker of a minor. No relevant family psychiatric history was reported.

She was first diagnosed with MDD in her adolescence following a suicide attempt and has since received psychiatric care for over a decade, including individual therapy, psychotropic medications, and neuromodulation therapies. She reports approximately 20 prior psychiatric hospitalizations due to symptom exacerbation, and has a previous history of two suicide attempts. Over the years, she has tried over 25 psychotropic agents across multiple classes. Many were discontinued due to side effects (e.g., TCAs, SSRIs, mood stabilizers, atypical antipsychotics), while others failed to achieve sustained symptom relief despite adequate dosing and duration according to the American Psychiatric Association Guidelines (12). She also attempted transcranial magnetic stimulation (TMS) therapy at an external facility but discontinued after 24 sessions due to a perceived lack of benefit. Detailed protocol parameters and outcome measures were unavailable at the time of evaluation. A summary of her clinical timeline can be found in Figure 1.

During her initial evaluation at our facility, the clinical team reviewed her extensive medication history, prior augmentation strategies, and limited access to detailed external records. Given her history, past suicidal attempts, and current severity, she was considered a candidate for ECT and admitted for inpatient care.

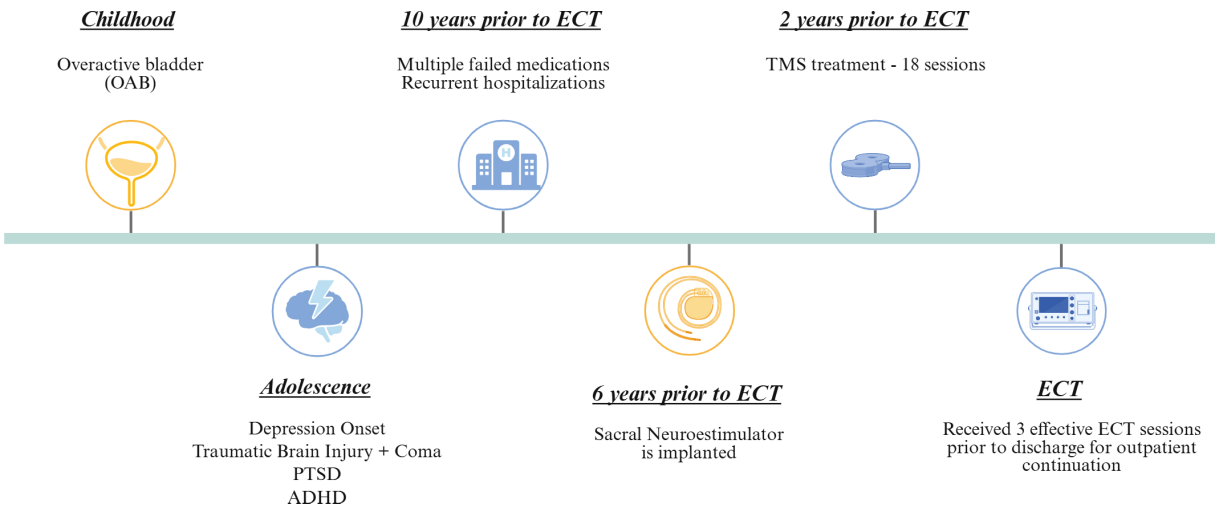

FIGURE 1
Clinical timeline summarizing the patient's psychiatric and neuromodulation history. The patient's clinical course is shown chronologically, beginning in childhood with overactive bladder (OAB), followed by psychiatric symptom onset and comorbidities in adolescence, including depression, traumatic brain injury with coma, PTSD, and ADHD. Over the subsequent decade, the patient experienced multiple medication failures and hospitalizations. A sacral neurostimulator was implanted 6 years prior to electroconvulsive therapy (ECT), and transcranial magnetic stimulation (TMS) was trialed 2 years prior to ECT. The patient ultimately received a successful course of ECT with three effective inpatient sessions prior to discharge for outpatient continuation. Created in BioRender. Carbajal Tamez, M. (2025) https://BioRender.com/2umw1qi.

On physical examination, she was alert and oriented, with normal vital signs and no focal neurological deficits. Mental status examination revealed depressed mood, passive suicidal ideation, intact insight and judgment, and no evidence of psychosis or cognitive impairment. Her admission medication regimen included lurasidone, haloperidol, gabapentin, alprazolam, and eszopiclone. The patient refused changes to her medications during hospitalization, citing prior poor tolerability and perceived ineffectiveness; the treatment team respected her autonomy and maintained the regimen. To preserve patient anonymity, treatment details are summarized in Table 1 by drug class without specific dosages or dates, along with a response summary.

During hospitalization, diagnostic evaluation included repeat physical and psychiatric examinations, confirming passive suicidal ideation without psychosis, routine laboratory testing, and medical clearance for ECT. Psychiatric symptom severity was regularly monitored using the Patient-Health Questionnaire (PHQ-9) alongside daily psychiatric evaluations and nursing assessments. The patient also actively participated in milieu therapy, psychoeducational sessions, and substance abuse counseling. A diagnostic challenge was the limited availability of detailed prior treatment records, necessitating reliance on patient report and clinical judgment for treatment planning.

A key consideration in procedure planning was her implanted sacral neurostimulation device (InterStim X, Medtronic), placed six years prior for OAB management. According to product documentation (13), the safety of ECT in patients with this device is unestablished due to the theoretical risks of induced electrical currents causing device malfunction or tissue damage. However, given the anatomical distance between the ECT electrodes and the implanted device (Figure 2), the risk was assessed as minimal. To further mitigate potential risks, the device was set to Magnetic Resonance Imaging (MRI) mode—suspending stimulation—before each ECT session and reactivated afterward to restore programmed settings. The plan was reviewed with the patient, who consented to proceed with a low-dose ECT regimen incorporating these precautions.

The patient underwent three ECT sessions every other day using a Mecta Σigma ECT machine. Anesthesia was induced with propofol, and muscle relaxation was achieved with succinylcholine. Bitemporal electrode placement was selected. Seizure threshold was established during the first session using the following parameters: pulse width of 0.5 ms, frequency 20 Hz, duration 4.5 seconds, current 800 mA, energy 12.7 Joules, and charge 72 mC. The second session charge was increased to 1.5 times the initial seizure threshold, reaching 96 mC (energy of 16.9 Joules while keeping all other parameters constant. This same configuration was maintained for the third session. Figure 2 summarizes the ECT protocol employed.

The patient experienced a significant improvement following the first ECT session, with her suicidal ideation resolving completely. Her pre-treatment Patient Health Questionnaire - 9 score of 4 decreased to 2 by the third session. At discharge, she reported substantial symptom relief, denied any ongoing suicidal thoughts, and was stable on daily psychiatric and nursing evaluations. The patient was subsequently discharged to continue ECT as an outpatient at a frequency of three sessions per week.

No adverse effects were observed from ECT at the time of discharge. The patient's OAB symptom diary and urinary frequency chart showed no changes from baseline. One month post-intervention, and during her outpatient treatment, the patient attended a previously scheduled surgical device revision with her urologist and a Medtronic representative, who confirmed device integrity, remaining battery life (6–12 months), and unchanged stimulation parameters.

Discussion

To our knowledge, empirical reports describing the administration of electroconvulsive therapy (ECT) in patients with an implanted sacral neuromodulation device (such as the Medtronic InterStim system) remain rare in the published literature. This case report highlights the safe and effective administration of electroconvulsive therapy (ECT) in a patient with an implanted sacral neurostimulator. Our findings align with previous research (6–11), including the case reported by Hiremani RM (11), demonstrating that ECT can be safely administered in patients with implanted devices such as sacral neurostimulators, deep brain stimulators, cardiac pacemakers, and spinal cord stimulators. These devices, despite their complex functionalities, do not necessarily contraindicate ECT and might be able to

TABLE 1 Summary of prior pharmacologic and interventional treatments.

Strategy	Examples	Reason for discontinuation	Response summary
SSRIs, SNRIs	Citalopram, Sertraline, Venlafaxine	Anxiety worsening, side effects	Ineffective/poorly tolerated
TCAs	Amitriptyline, Doxepin	Side effects	Early discontinuation
Atypical Antipsychotics	Quetiapine, Olanzapine, Paliperidone	Side effects or partial response	Partial benefit (Ongoing)
Mood stabilizers	Valproate, Lamotrigine, Lithium	Inadequate response	Augmentation trials, partial benefit
Anxiolytics	Clonazepam, Lorazepam, Alprazolam	Partial relief	Partial benefit (Ongoing)
Hypnotics	Zolpidem, Eszopiclone	Varied tolerability	Limited utility
Interventional Strategies	TMS	18 sessions	Ineffective

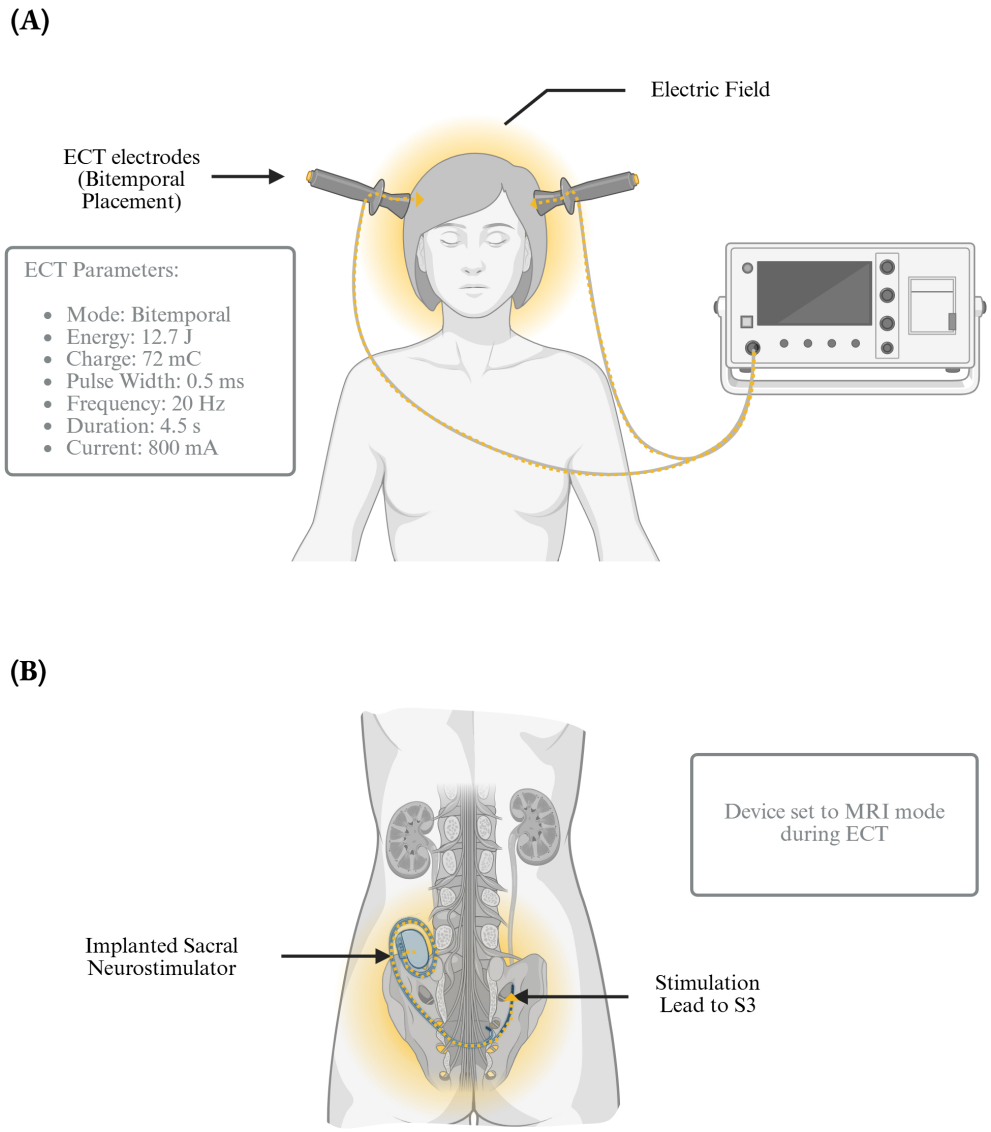

FIGURE 2
Electroconvulsive therapy administration in a patient with an implanted sacral neurostimulator. **(A)** Frontal view of bitemporal ECT administration, showing electrode placement, electric field distribution, and stimulation parameters including mode, energy, charge, pulse width, frequency, duration, and current. **(B)** Posterior view of the patient depicting an implanted sacral neurostimulator with a lead targeting the S3 nerve root. During ECT, the device was placed in MRI mode to minimize potential interference or adverse effects. Created with BioRender.com. Carbajal Tamez, M. (2025). https://BioRender.com/20tyitk.

withstand the electrical demands of this procedure, provided that appropriate precautions are taken.

The risk of lead heating during ECT is proportional to pulse width, current density, and tissue conductivity. Prior bench testing of DBS hardware exposed to ECT-like pulses produced < 1 °C temperature change at worst-case parameters. Sacral leads are shorter, lie in high-resistance soft tissue, and—when the generator is disabled—form an open circuit, further minimizing current flow. MRI-mode on the InterStim X® additionally deactivates telemetry, preventing spurious resets.

In this case, precautions were taken by putting the patient's InterStim device in MRI mode before each ECT session, which turned off the stimulation and minimized the risk of potential electrical interference. This strategy, coupled with careful patient monitoring, allowed us to successfully conduct three sessions without any adverse outcomes related to the stimulator. Notably, our case contributes to the limited literature on this topic by providing additional evidence supporting the compatibility of ECT with sacral neurostimulation devices. Aligning with previous research documented in > 30 DBS recipients (6), cardiac pacemakers (7), cochlear implants (8), and spinal stimulators (9). Across these series, no permanent hardware damage or stimulation-related injury has been recorded, supporting a class-effect of low risk when stimulation is suspended.

While our report demonstrates the short-term safety of ECT in a patient with an implanted sacral neurostimulator, it is essential to acknowledge that the primary limitation of this report includes its single-case nature and the observation of exclusively short-term safety. Long-term effects on device integrity remain unexplored. Additionally, the effect of ECT on OAB symptoms has not been comprehensively studied, and objective urodynamic data were unavailable.

Future directions

Prospective registries are needed to quantify long-term device longevity, lead integrity, and bladder outcomes after repeated ECT exposures. Integration of impedance logging into routine post-ECT follow-up could provide objective safety metrics. In the interim, shared decision-making that balances psychiatric urgency against theoretical device risks remains essential.

Patient perspective

The patient shared that receiving ECT was initially a source of anxiety, particularly due to the presence of her implanted sacral neurostimulator. However, she reported significant relief after treatment, expressing appreciation for the careful planning and collaborative communication from the care team regarding her device safety, and felt reassured throughout the process.

Conclusion

In conclusion, this case reinforces existing evidence that with thoughtful multidisciplinary planning, ECT can be safely administered to patients with implanted devices, including sacral neurostimulators. It also emphasizes the importance of individualized patient assessment and meticulous precautionary measures when implementing ECT in such cases. Further research is essential to expand our understanding of both the long-term device safety and the broader implications of ECT on coexisting conditions like OAB.

Learning points

- Safe Administration of ECT in Patients with Implanted Devices: With appropriate precautions, such as placing the device in MRI mode, ECT can be safely administered in patients with implanted sacral neurostimulators without compromising device integrity or functionality.
- Importance of Individualized Patient Assessment: Comprehensive assessment and tailored treatment plans are critical when managing patients with complex medical histories and implanted devices to minimize risks and optimize outcomes.
- Short-term Safety Demonstrated; Long-term Effects Unknown: While short-term outcomes were positive in this case, further research is needed to explore the long-term impact of ECT on implanted neurostimulators and associated conditions like OAB.
- Potential Neural Modulation Implications: ECT may potentially influence symptoms related to coexisting conditions such as OAB, warranting additional study into its broader therapeutic effects beyond primary psychiatric indications.

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

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article. Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

Author contributions

JP: Writing – original draft, Data curation, Conceptualization, Methodology. MC: Writing – original draft, Writing – review & editing, Conceptualization, Visualization. CA: Writing – original draft, Data curation, Investigation, Resources. WB: Supervision, Resources, Investigation, Writing – review & editing. EL: Conceptualization, Supervision, Resources, Investigation, Writing – original draft. JQ: Supervision, Resources, Investigation, Writing – review & editing.

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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 material

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Modified electroconvulsive therapy for perinatal depression: scoping review

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Background: Modified electroconvulsive therapy (mECT), the administration of ECT under general anesthesia with muscular relaxation, is indicated for perinatal depression complicated by high severity, psychosis, catatonia, or resistance to conventional therapeutics; however, knowledge gaps remain regarding its effectiveness and safety in depressed patients and its fetal/neonatal risk profile.

Materials and methods: We conducted a scoping review of the literature describing the effectiveness and safety (maternal, fetal, and neonatal) of mECT for perinatal depression. Online databases were searched (inception to December 31, 2024) to identify clinical trials, observational studies, case series, and case reports that were topically relevant. Information on key methodological details, clinical characteristics, interventions, and outcomes from each report was extracted by all investigators working in pairs, using an electronic abstraction form.

Results: A total of 82 reports (with information on >1,300 pregnancies/deliveries) were included, consisting mainly of case reports (n=57) and case series (n=14), with the remaining citations being non-randomized or retrospective studies. The reviewed reports collectively described a broad spectrum of effectiveness and safety outcomes associated with predominantly acute mECT across multiple forms of perinatal depression, multiple trimesters of pregnancy, and the postpartum. mECT conferred rapid benefit for depressive, psychotic, and catatonic symptoms in severely depressed perinatal patients when effectiveness outcomes were described. The most frequent adverse events were generally mild and transient. However, cases of placental abruption (n=1), premature delivery (n=21), congenital malformations (n=6), and stillbirth (n=4) were also reported across the reviewed reports. Due to limited information, causal links between mECT and many adverse events were difficult to establish and inferences about differential effectiveness and safety between important patient subgroups or variations in mECT technique could not be drawn.

Conclusion: mECT appears to be an effective acute phase treatment for severely ill perinatally depressed patients. Although the maternal safety profile of mECT appears reassuring, the available data are far from comprehensive. Moreover, fetal and neonatal safety risks are even less-well-characterized. mECT should be regarded as an important therapeutic option for severe cases of perinatal depression. Informed consent practices should reflect the knowledge gaps highlighted in this review in addition to the well-known side-effects of mECT and the substantial adverse consequences of untreated or undertreated maternal depression.

Systematic Review Registration: This project was registered on Open Science Forum, 10.17605/OSF.IO/KB67J.

KEYWORDS

perinatal depression, peripartum depression, postpartum depression, prenatal depression, electroconvulsive therapy, non-invasive brain stimulation

1 Introduction

Depression is among the most common complications in the perinatal period, spanning pregnancy through the first postpartum year. A 2005 systematic review estimated prevalence rates of 8.5%-11% for antenatal depression and 6.5%-12.9% for postpartum depression (PPD) in the U.S., including cases of unipolar major depression and minor depression (1). Other reviews have documented even higher average prevalence rates of 17% for antenatal depression and 13% for PPD (2). Beyond high prevalence, the public health importance of perinatal depression is highlighted by its association with increased maternal, neonatal, and early childhood morbidity (including negative effects on language, motor, and emotional development), poor obstetric outcomes, economic loss, and early maternal mortality including death by suicide (3–6). Indeed, perinatal depression presents across a broad severity spectrum, ranging from mild symptoms to behavioral emergencies requiring psychiatric hospitalization (7, 8).

In non-perinatal patients, modified electroconvulsive therapy (ECT), the administration of ECT under general anesthesia with muscular relaxation, is a high-priority treatment for refractory unipolar or bipolar depression, psychosis, refractory catatonias, and other psychiatric conditions for which the customary lag times to therapeutic benefit with conventional antidepressive treatments would be unacceptable, including cases with high suicide risk, evidence of medical or nutritional compromise, and others (9, 10). mECT is also indicated for perinatal depression complicated by high severity, psychosis, catatonia, or resistance to conventional approaches (11).

Previous reviews on the effectiveness and safety of mECT during the perinatal period have broadly supported the utility of mECT for severe perinatal depression but have arrived at mixed conclusions regarding the interpretation of obstetric and fetal/neonatal risks (12–20). And with relatively few exceptions (11), adaptations to standard mECT technique for perinatal patients were often not summarized. We thus conducted a scoping review to provide an updated survey of the published literature on mECT for perinatal unipolar or bipolar depression and to identify important but underdeveloped areas in need of further study.

2 Materials and methods

2.1 Search strategy

We conducted a scoping review of the literature regarding mECT for perinatal depression, guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) (21). A comprehensive literature search was conducted on December 31, 2024, by a research librarian (RR), in collaboration with the investigative team, using nine databases and registries (see Supplementary Table S1 and Appendix). The reference sections of reviewed papers and selected systematic and meta-analytic reviews were also be used to locate potentially relevant papers. The search strategy facilitated the retrieval of both published and grey literature references.

2.2 Inclusion and exclusion criteria

We selected relevant reports of the effects of mECT for human perinatal depression, published in English, based on the following population/problem, intervention, comparators/controls, and outcome(s) (PICO) elements:

- Population/problem: Perinatal depression was defined as clinically significant depression occurring during pregnancy and/or within the 12 months following the date of delivery. We included papers with unipolar or bipolar depressed patients, any subtype or severity level, with or without psychotic features. Perinatal catatonia or psychosis cases

were considered if a mood disorder diagnosis was specified as an underlying cause, presumed or established. Cases where an underlying mood disorder diagnosis was unspecified could still be included if there was enough detail to suggest the presence of an acute episode of depression, based on agreement between two independent reviewers. Although we did not specify an age range, the inclusion of reproductive-aged persons was presumed given our focus on perinatal depression.

- Intervention: We required the use of mECT as a treatment intervention (with or without co-interventions), using any stimulus parameters or electrode placement montages. Reports describing acute-, continuation-, or maintenance-phase mECT treatments were included.
- Comparators/controls: We included both controlled and non-controlled studies. For controlled research, we did not define acceptable or non-acceptable comparator groups or conditions, as adequate control group design for randomized trials of ECT for depression is debated (22, 23).
- Efficacy or Effectiveness Outcome(s): Efficacy/effectiveness outcomes included acute-phase reduction (improvement) in the severity of depressive symptoms, acute-phase categorical treatment outcome (e.g., remission/full response, partial response, non-response, etc.), duration of clinical response, and maintenance phase effectiveness (e.g., time to relapse, recurrence, or loss of remission or response).
- Safety/Tolerability Outcome(s): Safety/tolerability outcomes included acceptability of mECT as an acute or maintenance treatment (estimated using all-cause dropout rates), cognitive effects based on neuropsychological tests or bedside measures, non-cognitive adverse maternal effects and obstetric safety endpoints (e.g., acute hyper or hypotension, placental abruption, uterine contractions, preterm labor or premature rupture of membranes, difficulty with airway management, aspiration, etc.), and fetal, neonatal, and childhood developmental complications (e.g., intrauterine fetal demise, fetal growth restriction, changes in fetal heart rate, congenital malformations, respiratory depression, low Apgar scores at birth, developmental delay, etc.).

2.3 Study selection

After excluding duplicate articles, five investigators (WVB, OM, KMM, AML, HKB) worked in pairs to screen the titles and abstracts to exclude irrelevant papers. The remaining articles were then subjected to full-text review by six investigators (WVB, OM, KMM, EES, AML, HKB) who worked in pairs to exclude reports that failed to meet inclusion/exclusion criteria. Discrepancies at each step were resolved by discussion and consensus.

2.4 Data extraction and analysis

Data extraction was performed by all investigators, who worked independently in pairs, using a standard electronic extraction form. Disagreements were resolved via discussion and consensus. When necessary, an additional team member with specific domain expertise served a tie-breaking role. In accordance with PRISMA reporting guidelines for scoping reviews (PRISMA-ScR) (21), methodological quality and risk of bias assessments were not reported.

The following information was extracted from the individual studies (see Supplementary Table S2): (1) Study characteristics including publication year, authors, study design/report type, and treatment setting; (2) Subject/enrollee details including mood disorder diagnoses, mECT indication(s), definitions of treatment resistance (if applicable), maternal age, multiple gestation status, obstetric and general medical morbidities, pre-ECT medications, and use of assisted reproductive technology; (3) Treatment details including ECT electrode placement, pulse width, frequency of mECT administration, and ECT dose; (4) Anesthesia technique including anesthetic induction agent(s), pharmacological adjuncts to anesthesia, and airway management approach; (5) Adaptations to standard mECT technique including maternal and fetal surveillance methods; and (6) Effectiveness and safety measures and outcomes. Selected characteristics were summarized as proportions and were presented in table or graphical form.

3 Results

3.1 Format and design characteristics of the included reports

A total of 2,424 citations were identified from the initial literature searches across 14 registers and databases. After removing duplicates, 1,643 records underwent title/abstract screening, 146 of which were subjected to full-text review to determine eligibility for inclusion. On full text review, one case was found in both a published abstract and a published single case report, the former of which was excluded. We also included one of two full-length reports that described the same case. The remaining 82 reports (published between 1974 and 2024) met inclusion/exclusion criteria (Figure 1).

As shown in Figure 2A, 73 reports were published as full-length reports, while the remaining reports were published as abstracts (n=8) or other formats (n=1). Most reviewed citations were from case reports (n=57) and case series (n=14), with the remaining citations being from retrospective cohort, non-randomized prospective studies, or other designs. Sample sizes ranged from single case reports (n=1) to 793 individuals. Most of the included reports were from North America, followed by Europe, Western Pacific, and South-East Asian regions (Figure 2B).

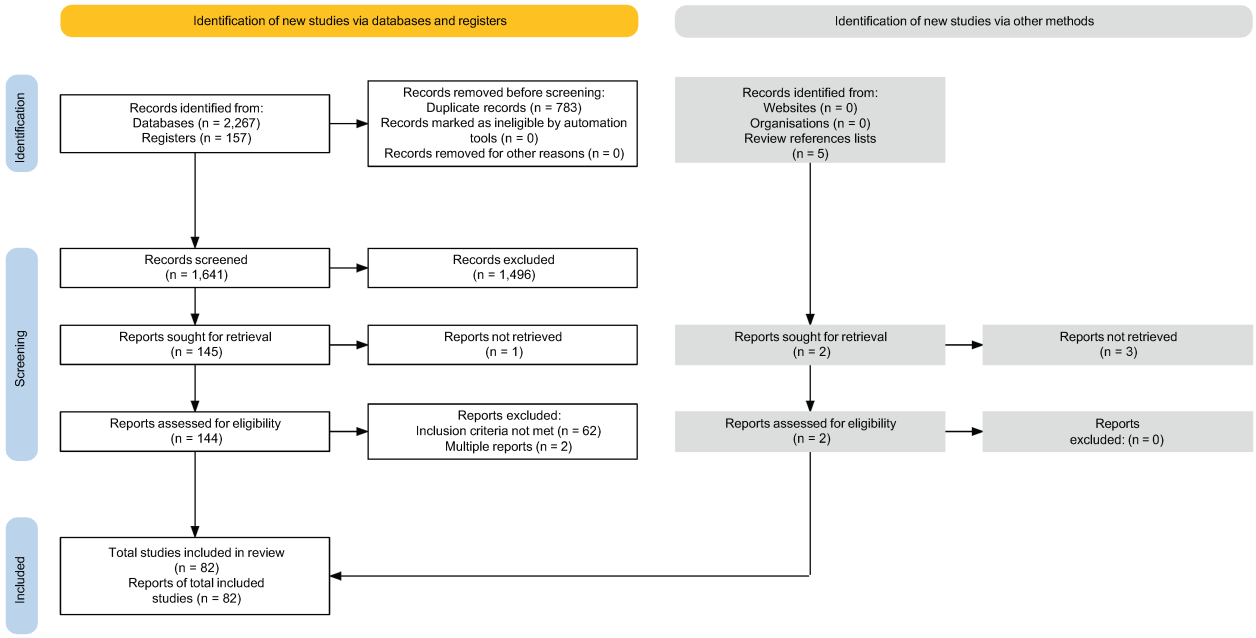

FIGURE 1
PRISMA flow diagram.

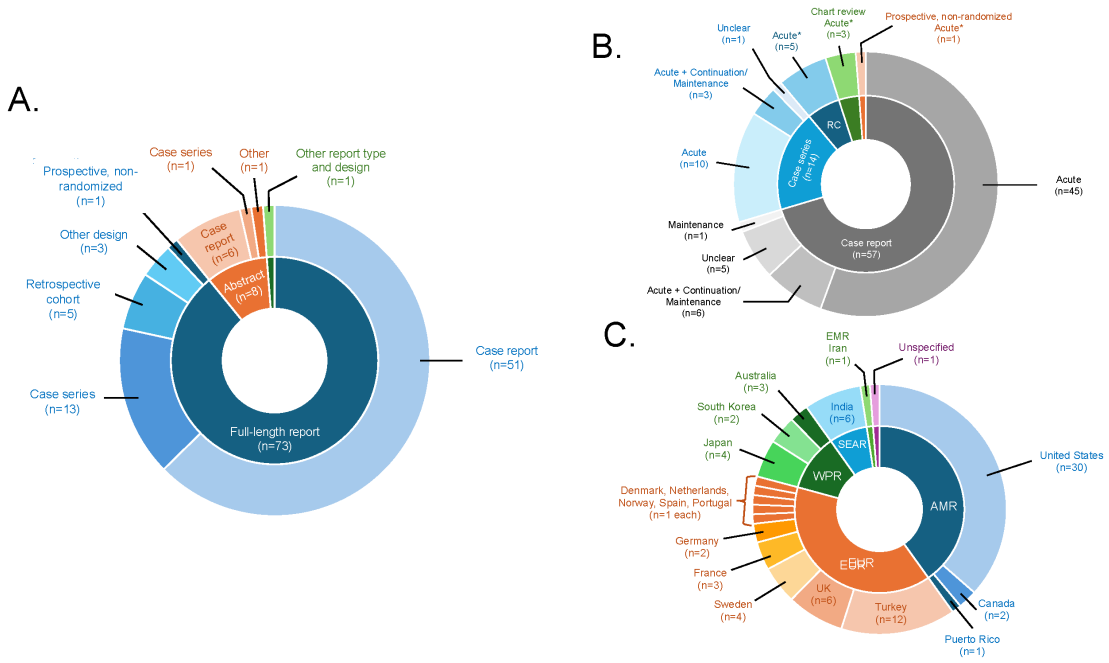

FIGURE 2
Graphical summary of reviewed studies. **(A)** displays the information on study or report design according to publication status (full-length report, conference abstract, other). **(B)** displays the information on phase(s) of modified ECT (mECT) treatment, by study or report design (including case reports, case series, chart review studies, prospective/non-randomized studies, and retrospective cohort studies [RC], absent one first-person account of postpartum mECT treatment and one qualitative mECT study). **(C)** displays the information on the countries in which individual studies or reports were conducted by World Health Organization region (including the Americas [AMR], the Eastern Mediterranean Region [EMR], the European Region [EUR], the South-East Asia Region [SEAR], and the Western Pacific Region [WPR]).

3.2 Age and clinical characteristics of mECT-treated patients

Mean or median ages from case series and observational studies ranged from 23.0 to 37.0 years. The age range of individual cases was 16.5 to 48 years. As shown in Tables 1 and 2, several reports included mixed samples of patients with severe mood disorders, psychotic disorders, unspecified postpartum psychoses, or unspecified catatonia. The most common perinatal mood disorder diagnoses were unspecified nonpsychotic unipolar depression (36 reports), unspecified psychotic unipolar depression (17 reports), nonpsychotic unipolar or bipolar major depression (12 reports each), unspecified bipolar disorder (11 reports), and unspecified unipolar depression with catatonic symptoms or bipolar mixed episodes with severe depression or suicidality (6 reports each).

As shown in Figure 2C, most reviewed papers described acute-phase mECT while just 10 reports described continuation- or maintenance-phase treatment, with or without an acute phase (37, 39, 46, 50, 73, 76, 79, 81, 86, 97). The most common indication(s) for mECT, when specified, were treatment resistance (n=31) followed by psychotic symptoms/features (n=21) and high suicide risk (n=21). Indications for mECT were unspecified in 14 reports. Nearly all the 30 reports that addressed treatment-resistant depression defined treatment resistance as poor response to prior treatments (n=29), including one TMS-resistant case (51). One report identified intolerance of medications as the principal indication for mECT (35). Fourteen reports described mECT for catatonia, including 3 reports that explicitly identified benzodiazepine-resistant catatonia as the intended indication (67, 72, 95). ECT was the preferred treatment or treatment because of pregnancy in 10 reports (34, 37, 39, 52, 54–56, 66, 70, 97).

In terms of obstetric information, most reports described mECT in the setting of pregnancy (n=64) while 23 reports included cases of postnatal mECT delivery, with or without a prenatal treatment phase. When gestational information was provided, nearly all such reports involved singleton pregnancies/deliveries, whereas 2 reports included twin pregnancies/deliveries (69, 97). The pre-ECT use of *in vitro* fertilization was reported in one case (89).

General medical comorbidity was often not reported. For example, of the 9 observational studies, two provided information on the frequency of diabetes and one provided details on the frequency of underweight, overweight, and obesity based on BMI ranges (24, 26, 32). Only limited information on comorbid conditions was available from individual case reports and small case series. However, 15 such reports documented comorbid conditions including obesity, non-gestational hypertension, gestational and non-gestational diabetes, hyperthyroidism, chronic musculoskeletal pain syndromes, migraine headache, congenital neurological diseases, and others. Acute injuries (skeletal fractures) and intentional poisonings (acetaminophen toxicity) related to suicide attempts were described in three reports (13, 50, 61), while anorexia, weight loss, or other conditions related to nutritional compromise in severely depressed patients were documented five reports (45, 49, 62, 70, 99).

Medications taken on or around the time of ECT administration was more thoroughly documented than medical comorbidities. Summary data on the frequency of concurrently prescribed antidepressants, mood stabilizers, antipsychotic drugs, or benzodiazepines were provided for six of nine observational studies. Forty-nine of the 73 individual case reports and small case series included information on individual drugs falling within these same broad categories. In 8 reports, only past failed medication trials were reported (35, 60, 67, 69, 70, 75, 86, 103). The discontinuation of psychotropic medications during or in anticipation of pregnancy or the absence of psychotropic medications at the time of ECT was specified in 6 reports (44, 46, 47, 54, 66, 89).

3.3 ECT treatment characteristics

Of the 56 reports where electrode placement was clearly described, the most common types of ECT electrode placement were bitemporal (34 reports) and right unilateral (12 reports) using a brief pulse width. The use of right unilateral ultrabrief pulse ECT was described in 3 reports (35, 68, 82) and bifrontal ECT was described in 9 reports (13, 28, 30, 31, 41, 49, 66, 77, 81). The number of weekly sessions of acute ECT was often not provided in the reviewed reports. When the number of weekly sessions was specified, thrice-weekly ECT sessions were most described (25, 51, 52, 65, 68, 71, 78, 88, 89), although twice-weekly ECT sessions were also reported (49, 80). Information on ECT stimulus parameters in conjunction with electrode placement was provided in only 27 reports. For summary dose metrics, stimulus train energy values ranged from 29.6 J - 43.6 J, 124.7 mC - 436 mC, or 10% - 75% of maximal charge. Individual ECT dose elements from 23 individual reports included current amplitudes (170 V or 500–842 mA), pulse widths (0.5 msec - 1.6 msec), pulse or pulse-pair frequencies (20 Hz - 90 Hz or 125 pulses/sec), and stimulus train durations (1 sec - 8 sec). Seizure threshold titration or determination was mentioned in 6 reports; however, the exact parameters at each step were not specified (25, 26, 34, 68, 79, 80, 90).

3.4 Anesthesia technique

The most common anesthetic induction agents in the reviewed papers were propofol (21 reports), thiopental (16 reports), and methohexital (14 reports). One report described the use of ketamine augmentation of propofol anesthesia for ECT in the setting of third trimester pregnancy in hopes of enhancing antidepressive efficacy (78). Among the 9 observational studies, only one provided complete information on the anesthetic (thiopental 3–4 mg/kg) and neuromuscular blocking agent (succinylcholine 0.5-0.75 mg/kg) with doses (25). From case reports and small case series, 26 included complete information on anesthetic and neuromuscular blocking agents. Specifically reported anesthetic drugs (with dose ranges in total mg administered or mg/kg infused) included methohexital (50–170 mg or 1 mg/kg), propofol (140 mg or 1

TABLE 1 Characteristics of observational and retrospective studies of modified electroconvulsive therapy (mECT) for perinatal depression.

Reference	Country/ Data source	Study design (n)	Exposure group(s)	Main endpoint(s)	Confounding management	Main effective-ness results	Main safety/tolerability results
Arinson et al. (24)	Sweden/ Population-based registries	Retrospective cohort (n=793)[a]	Main exposure group, ECT for psych-iatric disorder during pregnancy (pregnant ECT group) Control group, other pregnancies from the pregnant ECT group that did not involve ECT treatment (non-ECT additional pregnancy group) Control group, severe prenatal psychiatric disorders requiring hospitalization who did not receive ECT (non-ECT pregnant inpatient group)	Response (CGI-I scores of 1 or 2[b]) within 7 days of finishing index ECT series) Adverse events (premature births, 5-minute Apgar score <7, Cesarean delivery, post-delivery SGA or LGA delivery, congenital malformations, etc.)	Propensity score matching on age, parity, concurrent psychotropic medications, comorbid anxiety disorder, preeclampsia, diabetes	Response rates were similar for the pregnant ECT group and 216 non-pregnant women who received ECT (74% vs 65%, OR 1.61 [95% CI 0.79, 3.27]).	Rates of most reported AE's were similar between the main exposure group and the two control groups.[c] Premature delivery: Significantly higher risk in main exposure group than non-ECT pregnant inpatient group (14.4% vs 9.0%, OR 2.33 [1.15, 4.73]) but not the non-ECT additional pregnancy group (10.9%; OR 2.16 [0.75, 6.22]). Low 5-minute Apgar score: Significantly higher risk in main exposure group than non-ECT pregnant inpatient group (9.3% vs 2.1%, OR 3.68 [1.58, 8.55]) but not the non-ECT additional pregnancy group (2.2%, OR 2.53 [0.59, 10.90]). Stillbirths reported in two (2.1%) pregnancies in the main exposure group, and in one pregnancy each in the control groups.
Babu et al. (25)	India/ Consecutively hospitalized subjects	Prospective non-randomized (n=78)[d]	ECT for PPP No ECT for PPP	CPRS and BFCRS scores Hospital LOS Selected maternal AE's from ECT	All comparisons were unadjusted	CPRS and BFCRS scores were not specified. CPRS scores were described as significantly decreased from baseline at discharge in each group, with no significant between-group difference. Duration of admission was lower in ECT group (19 vs 23 days), with no significant between-group difference	Most common AE's with ECT were antero-grade amnesia (n=6 [17.6%]) and prolonged seizures (n=4 [11.7%]). Fifteen women who receive ECT were admitted with their infants, 10 of whom con-tinued to breast-feed their infants without AE's.
Hauge et al. (26)	Denmark/ Population-based registries	Retrospective cohort (n=91)[e]	ECT for incident postpartum mood or psychotic disorders[e]	Description of acute and post-acute treatment Risk of hospital readmission after 6 months	Not applicable	Acute phase response to ECT was not described. 28 (30.8%) of 91 cohort members were readmitted (median time to readmission was 16 days [IQR 7, 51]). ECT-specific results were not reported.	Safety outcomes were not reported.
Haxton et al. (27)	UK/Scottish ECT Accreditation Network database	Retrospective cohort (n=35)[f]	Postnatal ECT while hospital-ized on mother-baby unit ECT in hospital-ized non-perinatal women	Reduction (improvement) in MADRS scores between baseline and after ECT	Matching (1:2) on age (within 5 years) and initial MADRS score (within 5 points)	Trend towards greater reduction in mean MADRS scores with ECT in the postnatal group than in the non-perinatal group (Δ = -10.1, p=0.06).	Safety outcomes were not reported.
Raghuraman et al. (28)	India/ Hospital records	Retrospective chart review (n = 31)[g]	BT ECT for "severe mental illness" during the perinatal period	Reduction (improvement) in EPDS and CGI-S scores	All analyses unadjusted	Significantly lower post-treatment EPDS score with BF than BT (trend level difference for CGI-S score)	Headache reported with BT ECT (1 patient), "cognitive difficulties" reported with BF ECT (1 patient).

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TABLE 1 Continued

Reference	Country/ Data source	Study design (n)	Exposure group(s)	Main endpoint(s)	Confounding management	Main effective-ness results	Main safety/tolerability results
			BF ECT for similar indications				
Reed et al. (29)	UK/Hospital-based ECT register	Retrospective chart review (n=114)[h]	ECT received for "puerperal psychosis" while admitted to mother-baby unit Inpatients <45 years of age who received ECT for "non-puerperal psychosis"	Ratings of clinical recovery ranging from 0 (no improve-ment or worsen-ing) to 3 (asymp-tomatic)	Multiple regression models (with stepwise covariate selection)	In analyses restricted to patients with depression, there were significantly higher (better) clinical recovery scores in the puerperal ECT group, both at the end of ECT and 1 month after ECT.	Safety outcomes were not reported.
Ronnqvist et al. (30)	Sweden/ Population-based registers	Retrospective cohort (n=360)[i]	ECT received for PPD and/or PPP ECT received for non-postpartum indication	Relapse (defined as rehospitalization for psychiatric reasons or suicide) after 6 months, 1 year, and 2 years	Multivariable Cox regression models	Relapse rates were lower in the postpartum group at 6 months (28% vs 39%), 1 year (31% vs 50%), and 2 years (40% vs 55%). The risk of relapse was significantly lower in the postpartum group in univariable analyses (p=0.001) and was nearly so in multivariable analyses (p=0.051).[i]	Safety outcomes were not reported.
Rundgren et al. (31)	Sweden/ Population-based registers	Retrospective cohort (n=370)[j]	ECT received for PPD and/or PPP ECT received for non-postpartum indication	Response (CGI-I score of 1 or 2)[b] within 1 week after ECT treat-ment Remission (post-treatment CGI-S score of 1 or 2)	Matching of comparator group on age, diagnosis, prior antidepressant medication, and CGI-S score before ECT; statistical adjustment of logistic regression models	Significantly higher response rate (87.0% vs 73.5%) and remission rate (45.4% vs 29.9%) in the postpartum group.	Safety outcomes were not reported.
Saluja et al. (32)	Australia/ Hospital records	Retrospective chart review (n=74)[k]	Descriptive study of treatments re-ceived on a mother-baby unit	Medications used and ECT treatments provided at 3 time points (on admission, half-way through admission, and at discharge)	Not applicable	Not applicable. Eight of 57 women with depression received ECT during their hospitalizations. All were trialed on ADs during admission prior to ECT.	Safety outcomes were not reported for any inter-vention, including ECT.

Key: AD, antidepressant medication; BFCRS, Bush-Francis Catatonia Rating Scale; BF, bifrontal ECT; BT, bitemporal ECT; CGI-I, Clinical Global Impression improvement subscale; CGI-S, Clinical Global Impression Scale severity subscale; CPRS, Comprehensive Psychopathological Rating Scale; ECT, electroconvulsive therapy; EPDS, Edinburgh Postnatal Depression Scale; IQR, inter-quartile range; LGA, large for gestational age; LOS, length of stay; MADRS, Montgomery-Asberg Depression Rating Scale; mECT, modified electroconvulsive therapy; PPD, postpartum depression; PPP, postpartum psychosis; SGA, small for gestational age; UK, United Kingdom.

[a]A total of 793 cases from population-based registers were described. There were 97 pregnancies in which ECT was administered, 54 of which had non-missing CGI-I values. The 97 ECT pregnancies were propensity score (PS)-matched to 388 pregnancies occurring in women who were psychiatrically hospitalized but received no ECT. The 54 ECT-treated pregnancy cases (with complete CGI-I data) were PS-matched to 216 non-pregnant cases (women) who also received ECT. [b]Response was defined based on CGI-I score of 1 (very much improved) or 2 (much improved) within 7 days after finishing the index series of ECT treatments. [c]None of the reported preterm births or other severe pregnancy outcomes occurred in close time proximity to ECT, weakening causal links between ECT and these outcomes. [d]The study sample consisted of 78 consecutively hospitalized women with PPP, 34 of whom received ECT. Twenty-four women were diagnosed with depression, 32 were diagnosed with mania, and 22 were diagnosed with a "non-affective psychosis." [e]The cohort consisted of 91 women with evidence of new-onset (newly diagnosed) postpartum mood or psychotic disorder identified in population-based registers (39 with depression, 17 with a bipolar spectrum disorder/manic episode, and 35 with a psychotic disorder). Seventeen (18.7%) of 91 cohort members received ECT. [f]A total of 12 patients received ECT for postnatal unipolar depression (8 patients), bipolar depression (2 patients), bipolar mixed episode (1 patient), or no specified diagnosis (1 patient). Controls consisted of 24 women matched 2:1 with postnatal ECT subjects on age and pre-ECT MADRS scores. [g]Results were presented as a conference abstract. Thirty-one patients received ECT (BT in 18 patients, BF in 13 patients), 4 during the prenatal period and 27 during the postpartum period. The mixed sample included 3 patients with unspecified depression, 14 with bipolar disorder, 4 with postpartum psychosis, 6 with "acute transient psychosis," and 4 with "psychosis NOS." [h]The cohort consisted of 58 women in the puerperal ECT group (42 diagnosed with a "depressive illness") and 56 women in the non-puerperal ECT group (33 diagnosed with a "depressive illness"). [i]The cohort consisted of 180 women with PPD/PPP who received ECT within 6 months following delivery and an equal number of controls who received ECT but for a non-postpartum psychiatric condition. [j]The cohort consisted of 185 women with PPD/PPP who received ECT within 6 months following delivery and an equal number of matched controls who received ECT for non-postpartum depression/ psychosis. [k]The cohort consisted of 74 patients admitted to a mother-baby unit, 57 with depression, 8 of whom received ECT.

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TABLE 2 Characteristics of case reports and case series describing modified electroconvulsive therapy (mECT) for perinatal depression.

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
Bak et al. (33)	Turkey	Mixed sample, 4 cases total Prenatal depression, n=1 Prenatal BP, n=2 Prenatal "atypical psychosis", n=1	Mean gestational age 23 weeks, individual level data unspecified	ECT electrode placement unspecified; mean of 10 ECT applications (individual level data unspecified)	Not reported.	No maternal complications.	No complications in newborns. Normal development through first 1 month of life.
Balki et al. (34)	Canada	Prenatal BP-D, suicidal ideation, n=1	Second trimester	Acute RUL ECT, three stimuli given during session 1 owing to inadequate seizure activity	Not reported.	SE after third stimulus requiring high-dose BZD, thiopental, propofol, and DPHD, ICU transfer, and prolonged MV	Fetal death followed by spontaneous vaginal delivery
Ballone et al. (35)[a]	Unspecified	PPD, n=1	8 weeks postpartum	Acute RUL/UB ECT, 15 treatments, delivered in an ambulatory setting to permit breastfeeding	Conference abstract, outcomes unspecified	Not applicable.	Conference abstract, outcomes unspecified
Bergink et al. (36)[a]	Netherlands	Postpartum BP, n=7	Postpartum week (s) unspecified	Acute ECT, lead placement and frequency of treatments unspecified	Remission in one patient who received ECT owing to poor response to pharmacotherapy	Not applicable	Conference abstract, outcomes unspecified
Bulut et al. (37)	Turkey	Prenatal MDD, n=3 Prenatal MDD, psychotic features, n=3 Prenatal BP, n=5 Other prenatal depression, n=1	First trimester, n=6 Second trimester, n=3 Third trimester, n=3	Acute BT ECT treatments (all 12 cases), range 3–20 treatments Maintenance BT ECT (2 cases, one with MDD), 3 treatments each	Mean CGI score for all 12 cases reduced from 6.0 (baseline) to 2.6 (end of ECT sessions). Diagnosis-specific results were not provided.	One pregnancy was terminated early. Remaining pregnancies were un-complicated. Diagnosis-specific results were not provided.	One neonate with pes ekinovarus deformity. The remaining 10 new-borns were described as healthy after delivery.
Bhatia et al. (38)	USA	Prenatal MDD, n=1 (Case 1) Other prenatal depression, n=1 (Case 2)	Third trimester, n=2	Case 1 – Acute BT ECT, 3x/week, 6 treatments total Case 2 – Acute BT ECT, 5 treatments total	Case 1 – improvement after 6 treatments, remission at 6-month contact. Case 2 – improvement after 5 treatments, remission at 6-month contact.	Case 1 – transient mild uterine contractions Case 2 – transient uterine contractions, preterm labor on post-ECT day 7 (31 weeks EGA)	Case 1 – delivery of healthy infant at 39 weeks EGA. Case 2 – premature delivery of otherwise healthy infant at 35 weeks EGA, unspecified reason for delivery.
Bozkurt et al. (39)	Turkey	Prenatal psychotic depression, n=1	Second trimester, n=1	Acute BT ECT, 3x/week, 10 treatments Maintenance BT ECT, once monthly, 3 treatments (until 31 weeks EGA)	Remission, as evidence by reduced (improved) HAM-D score from baseline (33) through the 10th treatment (7).	Pelvic pain after the 8th and 9th treatment.	Delivery of healthy infant at 38 weeks EGA.

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
Brown et al. (40)	USA	Prenatal psychotic depression, n=1	Second trimester, n=1	ECT electrode placement unspecified, 8 treatments	Not reported.	Patient required the use of a supraglottic airway owing to difficult ETI, and completed 8 ECT treatments without apparent adverse events.	Not reported.
Bulbul et al. (41)[b]	Turkey	Mixed sample, 33 cases total Prenatal MDD, n=19 Prenatal BD[c], n=12 Schizophrenia, n=2	Multiple trimesters of pregnancy[b]	Acute ECT, electrode placement and treatment frequency unspecified	16 (84.2%) of 19 patients with MDD had a decrease (improvement) in CGI-S scores to ≤ 2 (borderline ill or not ill) 11 (91.7%) of 12 patients with BP[c] had a decrease in CGI-S scores to ≤ 2	Diagnosis-specific information was not available. Three patients had transient uterine contractions during ECT requiring no specific intervention.	Diagnosis-specific information was not available. There was one stillbirth (cause not determined) and once case each of congenital hip dysplasia and SVT after myocarditis.
Bulbul et al. (42)[d]	Turkey	Mixed sample, 68 cases total Prenatal unipolar depression, n=43 Prenatal BP, n=20 (5 with BP-D, 5 with BP-MX, and 10 with BP-M)	First trimester, n=17 (unipolar depression), n=5 (BP) Second trimester, n=22 (unipolar depression), n=9 (BP) Third trimester, n=4 (unipolar depression), n=6 (BP)	ECT electrode placement and treatment frequency unspecified	Remission (HAM-D <7 or CGI-S ≤ 2) in 93% of patients with unipolar depression. Phase-specific information on treatment response was unavailable for patients with BP.	Outcomes unspecified apart from no cases of preterm delivery among 26 women with unipolar depression for whom birth information was available.	No medical problems reported in 30 infants born to mothers with unipolar depression for whom birth information was available. Of 17 infants born to mothers with BP, 16 were normal and 1 had a cardiac disease that healed with treatment.
Chase et al. (43)	USA	Perinatal MDD, psychotic features, n=1	Postpartum week (s) unspecified	Acute BT ECT, 16 treatments	Partial response after 5 treatments, remission after 16 treatments	Not reported.	Not reported.
Choi et al. (44)	S. Korea	Perinatal depression, n=1	Approximately 12 weeks postpartum	Acute BT ECT, stopped after one treatment	Not reported.	ECT stopped owing to treatment-emergent T6 vertebral fracture.[e]	Not reported.
(45)	UK	PPD, n=1[f]	Postpartum week (s) unspecified	Acute ECT, electrode placement unspecified, 6 treatments	Full response after 6 treatments	Not applicable.	Not reported.
DeAsis et al. (46)	USA	Prenatal BP-D, passive suicidal ideation, n=1	Second trimester, n=1	Acute RUL ECT, 10 treatments Continuation RUL ECT, 4 treatments	Remission	Prolonged seizure after 2nd treatment with no recurrence after switching anesthesia induction agent to propofol.	FHR deceleration after 2nd treatment, but non subsequently. Delivery of healthy full-term infant.

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
DeBattista et al. (47)	USA	Prenatal MDD, n=1	First trimester, n=1	Acute BT ECT, 5 treatments	Remission (HAM-D score improved from 31 at baseline to 7 following the 5th treatment)	No significant maternal adverse events.	FHR deceleration after 4th and 5th treatments, each followed by rapid return to baseline. Delivery of healthy infant at 38 weeks EGA.
Dorn et al. (103)	USA	Prenatal BP-D, psychotic features, n=1	First trimester, n=1	Acute BT ECT, 9 treatments	Remission after 9 treatments	No significant maternal adverse events, though "mildly hypomanic" symptoms were described.[g]	No significant fetal or neonatal adverse events.
Echevarria Moreno et al. (48)	Spain	Psychotic depression, n=1	First trimester, n=1	Acute BT ECT, 9 treatments	Remission	Moderate memory loss for the time period around the acute ECT series. "Minimal" vaginal bleeding after the 2nd treatment and "profuse" vaginal bleeding after the 3rd treatment.	Miscarriage after the 3rd treatment.
Erturk et al. (49)	Turkey	Prenatal depression with suicidal ideation, n=1	Second trimester, n=1	Acute BF ECT, 2x/week, 10 treatments	Remission	Not reported.	Delivery of healthy infant at 38 weeks EGA by cesarean section.
Forray & Ostroff (50)	USA	Mixed sample, 5 cases total PPD, psychotic features, n=2 PPP (bipolar I disorder), n=1 Postpartum BP-MX, n=1 Postpartum mood disorder, NOS, n=1	3 weeks to 11 months postpartum	Acute BT ECT, 6 to 9 treatments Continuation BT ECT, 4 to 11 treatments	Case 1 (postpartum mood disorder NOS) – Significant improvement by 3rd treatment and eventual remission.[h] Case 2 (PPP, bipolar I disorder) – "marked response" by 2nd treatment and eventual remission.[h] Case 3 (PPD with psychotic features) – significant improvement by 5th treatment with eventual remission.[h] Case 4 (BP-MX) – Significant improvement by 3rd treatment and eventual remission.[h] Case 5 (PPD with psychotic features) – significant improvement by 2nd treatment with eventual remission.[h]	Transient memory disturbance in 3 of 5 cases.	Not reported.
Gahr et al. (51)	Germany	Prenatal depression, suicidal ideation,	First trimester, n=1	Acute RUL ECT, 13 treatments	Remission (reduction in baseline BDI score [56] before ECT to 4 [1 week after final ECT treatment])	No apparent maternal complications during the acute ECT series.	No fetal trauma based on sonographic data.

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
		resistant to medication and L-DLPFC TMS, n=1				Unimpaired gestation at 24 weeks EGA (2 months after final ECT treatment).	
Gannon et al. (52)	USA	Prenatal BP-D, passive suicidal ideation, n=1	Third trimester, n=1	Acute BT ECT, 7 treatments	Remission noted after delivery	Prolonged seizure, transient uterine contractions (first treatment only), nausea, mild headaches, transient urinary retention. Hypomanic symptoms[i] while receiving ECT and taking sertraline and lurasidone, necessitating discontinuation of sertraline and increasing the dose of lurasidone.	Delivery of healthy infant at 38 weeks EGA.
Gonzales et al. (53)	USA	Depression with catatonia, n=1	Second trimester and in early postpartum, n=1[j]	Acute RUL ECT during the second trimester, 10 treatments Acute ECT during the early postpartum, electrode placement unspecified, 12 treatments	"Notable improvement" in mood and catatonic symptoms after 10 treatments initiated in the second trimester. Improvement in depressive symptoms with residual impoverished speech after 12 treatments (response plateaued after the 10^{th} treatment) given in the postpartum.	Not reported.	Delivery of healthy infant at 40^{+1} weeks.
Gressier et al. (13)	France	PPD, suicidal ideation, n=1	Approximately 12 weeks postpartum	Acute BT ECT, 29 treatments total	Remission, with improvement in HAM-D, QIDS-C, and EPDS scores from baseline (32, 28, and 23) to the end of ECT (3, 2, and 3). No depressive relapse at 6 month follow-up.	Not reported.	Not reported.
Griffiths et al. (54)	USA	Prenatal MDD, suicidal ideation, n=1	Second trimester, n=1	Acute BT ECT, 11 treatments total	Initial series of 6 ECT treatments (given between 23 and 26 weeks EGA) were provided "with good results." Hospital admission was required at 28 weeks EGA, where 5 additional ECT treatments were provided over 3 weeks.	No abnormalities in VS, SaO_2, or uterine activity	No abnormalities in FHR. Delivery of healthy infant at 40 weeks.
Grover et al. (55)[k]	India	Mixed sample, 13 cases total. PPD, n=3	For PPD and BP-D cases, 2 to 21 weeks postpartum.[k]	Acute ECT, electrode placement unspecified, 5 to	Remission for all PPD and BP-D cases based on post-ECT HAM-D score ≤ 7.	Body aches, memory disturbances	All babies were breastfed during the postpartum without observed or reported adverse effects.

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
		PPD, psychotic features, n=4 Postpartum BP-D, n=1 Postpartum manic episode, n=2 Schizophrenia, n=2 "Acute and transient" psychotic disorder, n=1		12 treatments for PPD and BP-D cases.			
Grover et al. (56)[l]	India	Mixed sample, 10 cases total. PPD, n=6 Postpartum manic episode, n=1 "Acute and transient" psychotic disorder, n=2 Organic psychosis, n=1	Mean duration of episode(s) at the time of ECT con-sideration was 3.8 months. Diagnosis-specific results were not provided.	Acute BT ECT, mean number of effective ECT treatments (all cases) was 6.7 (range 2 to 12). Diagnosis-specific results were not provided.	9 or 10 patients had at least a partial response to ECT ("overall improvement >50%"). Diagnosis-specific results were not provided.	"No immediate complications" during the ECT procedure. Two patients developed "delayed complications" (delirium, seizures).	Not reported.
Grover et al. (57)[m]	India	Mixed sample, 5 cases total. Prenatal depression, suicidal ideation, n=2 Manic episode, n=1 Schizophrenia, n=2	Second trimester, n=2	Acute BT ECT, 6 treatments were provided in both prenatal depression cases.	Remission in one prenatal depression case (78.6% reduction in HAMD score), partial response in the other prenatal depression case (65.7% reduction in HAMD score).	No ECT-related complications in either prenatal depression case.	Delivery of healthy infant (both prenatal depression cases). One delivery was by cesarean section at 35 weeks owing to PIH. The other was by NSVD at 38 weeks EGA.
Guillet et al. (58)	France	Prenatal depression, suicidal ideation, in patient with dopamine-responsive dystonia, n=1	Unspecified	Acute ECT, electrode placement unspecified, 13 acute treatments followed by consolidation treatments occurring once every 2 months.	"Clear improvement" in mood symptoms, dyskinesia, and dystonia after 13th treatment	Not reported.	Not reported.

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
Gunduz et al. (59)[a]	Turkey	Prenatal MDD with psychotic features, n=1	Third trimester, n=1	ECT electrode placement unspecified, 4 acute treatments.	Not reported.	Transient uterine contractions that increased in intensity after each ECT treatment despite tocolytic therapy.	FHR fluctuations on continuous fetal monitoring (90 bpm to 140 bpm), each lasting about 5 minutes before returning to baseline. No delivery outcomes reported.
Herzog et al. (60)	USA	Mixed sample, 13 cases total. PPD, n=5 BP, n=5 Schizophrenia, n=3	Unspecified	Acute ECT was provided for three rapid cycling patients diagnosed with BP. ECT electrode placement was unspecified. Four to 8 treatments were provided in these cases.	"Good response" after 4–8 treatments.	Not reported.	Not reported.
Howe et al. (61)	UK	Psychotic depression, n=1	Third trimester, n=1	Acute BT ECT, 4 treatments	"Rapid and sustained recovery." Was noted as being well after 2 years of follow up.	Not reported.	Not reported.
Isik et al. (62)	Turkey	Psychotic depression, n=1	Second trimester, n=1	Acute ECT, electrode placement unspecified, 6 treatments	Not reported.	TMJ dislocation after 2nd treatment in the setting of a prior TMJ dislocation 4 years previously, leading to switch from plastic bite block to cotton bit block and no further complications.	Not reported.
Iwasaki et al. (63)	Japan	Prenatal depression, n=1	Second trimester, n=1	ECT electrode placement unspecified, 14 treatments	Gradual improvement reported.	Not reported.	Transient FHR decrease with propofol but not thiamylal anesthesia. Delivery of healthy infant. Normal development through first three years of life.
Reveles Jensen et al., (64)	Denmark	PPD, psychotic features, n=1	24 weeks postpartum	Acute BT ECT, 26 treatments	Improved depressive symptoms between admission (HAMD score 21) and hospital discharge (HAMD score 16).	Objectively documented improvement in red-green color-blindness. No other side-effects from ECT occurred.	Not reported.
Kasar et al. (65)	Turkey	Prenatal MDD with psychotic features, n=1	Third trimester, n=1	Acute BT ECT, 4 treatments	"Marked improvement" in depressive symptoms (and reduction in HAMD score from 47 to 15) was noted after the 3rd treatment.	Onset of "birth pain" one day after the 4th treatment.	Premature delivery at 34 weeks, with normal newborn development and normal development over the first 6 months of life.

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
Kisa et al. (66)	Turkey	PPD, n=1	Approximately 8 weeks postpartum	Acute BF ECT, 8 treatments	"Substantial improvement" in depressive symptoms after 8th treatment.	Prolonged seizure terminated with midazolam during the 2nd treatment, thought to be influenced by ciprofloxacin. No prolonged seizures after resuming ECT without ciprofloxacin.	Not reported.
Leite et al. (67)[a]	Portugal	PPD with catatonia, n=1	24 weeks postpartum	Acute ECT, electrode placement and treatment frequency unspecified	Remission of catatonic symptoms, "improvement" of depressive symptoms.	Not reported.	Not reported.
Levy et al. (68)	Australia	Mixed sample, 3 cases total PPD, suicidal ideation, n=1 BP-D, suicidal ideation, n=2	Unspecified	Acute RUL/UB ECT, 3x/week. Case 1–10 treatments. Case 2–20 treatments. Case 3–9 treatments.	Cases 1 and 2 had clinically significant improvement in depressive symptoms (EPDS scores 21–22 at baseline, 2–4 at discharge). Clinical outcome was unclear for Case 3.	Not reported.	Not reported.
Livingston et al. (69)	USA	Prenatal psychotic depression, n=1	Second trimester of twin pregnancy, n=1	Acute ECT, electrode placement unspecified, 8 treatments	After delivery, the patient's psychiatric status deteriorated, requiring "multiple medications and regular ECT."	Spontaneous preterm labor at 35 weeks EGA.	One episode of transient FHR deceleration during the 3rd treatment. Preterm delivery at 35 weeks EGA. Twin A was diagnosed with transposition of the great vessels; however, died of postoperative complications after successful surgical repair. Twin B was diagnosed with anal atresia, a small sacral defect, and coarctation of the aorta.
Maletsky et al. (70)	USA	Mixed sample, 27 cases total. Prenatal MDD, n=7 Prenatal MDD, psychotic features, n=7 Prental MDD, catatonia, n=5 Unspecified catatonia, n=8	One pregnancy case was described in detail. Trimesters of pregnancy unspecified.	One pregnancy case was presented in detail and described two acute BT ECT series, the first occurring 3x/week over two weeks (6 treatments).	All four pregnant patients "showed marked improvement." The case described in detail had a partial acute response and declined continuation ECT. She experienced a relapse at 4 weeks postpartum and "responded fully" to a second series of BT ECT.	Not described.	Delivery of a healthy infant.
Malhotra et al. (71)	India	Mixed sample, 2 cases total. Prenatal depression,	Second trimester, n=2	Acute ECT, electrode placements and treatment frequencies unspecified.	Not reported.	No apparent complications.	Normal real-time US findings (pre- and post-procedure).

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
		suicidal ideation, n=1 Unspecified catatonia, n=1					
Martinez-Sosa et al. (72)	USA	Prenatal depression with catatonia, n=1	First trimester, n=1	Acute BT ECT, 7 treatments	Significant improvement after 4th treatment and eventual resolution of mood and catatonic symptoms.	Premature labor/PPROM at 31 weeks	Normal spontaneous premature delivery at 31 weeks. Infant diagnosed remained hospitalized for first 50 days of life with hyaline membrane disease and prematurity associated apnea, retinopathy, and anemia.
May et al. (73)	USA	PPD, suicidal ideation, n=1	ECT offered during third hospitalization within the 1 year after delivery.	ECT electrode placement unspecified, 7 acute treatments followed by maintenance ECT.	Acute remission based on improvement in MADRS score from 45 to 9. Clinical response sustained while receiving maintenance treatments.	None described during acute ECT. Severe unilateral myalgias after one maintenance ECT treatment, "possibly due to insufficient paralysis."	Not reported.
Morris et al. (74)[n]	Puerto Rico	PPD, suicidal ideation, n=1	Unspecified	Acute ECT, electrode placement and treatment frequency unspecified.	Full response achieved after several exacerbations of depressive symptoms	Headache	Not reported.
Mynors-Wallis et al. (75)	UK	Prenatal depression, catatonia, n=1	Third trimester, n=1	Acute ECT, electrode placement and treatment frequency unspecified.	"Good response."	Not reported.	Not reported.
O'Reardon et al. (76)	USA	Prenatal MDD, suicidal ideation, n=1	Second trimester, n=1	Acute BT-BF ECT, 18 treatments, followed by 13 continuation ECT treatments over 6 months.	Positive response based on 50% improvement in HAM-D scores after 3rd acute treatment. Depressive symptoms eventually remitted. Continuation treatments extended into the postpartum were effective.	Not reported.	Delivery of a healthy infant at 37 weeks by scheduled cesarean section. Normal development through 18th month of life.
Ozgul et al. (77)	Turkey	Prenatal depression, suicidal ideation, n=1	First trimester, n=1	Acute BT ECT, 3x/week, 10 treatments	Not reported.	No significant hemodynamic changes.	Condition of the fetus was evaluated by obstetrician after each treatment, but outcomes were not reported.
Patel et al. (78)	USA	Prenatal MDD, suicidal ideation, n=1	Third trimester, n=1	Acute BT ECT, 3x/week, 8 treatments	Remission.	Transient asymptomatic contractions relieved with IV fluids.	Transient decreases in FHR.
Pesiridou et al. (79)	USA	Prenatal BP-D, borderline personality	Third trimester, n=1	Acute RUL ECT, 6 treatments, followed by continuation ECT	Acute remission of suicidal ideations, "significant decreases" in depressive and anxious symptoms.	Disorientation, confusion, and memory disturbances after increasing stimulus strength	Delivery of healthy newborn at 37 weeks EGA.

(Continued)

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
		disorder, PTSD, SUDs, suicidal ideation, n=1				owing to short seizures.° Painful contractions at 32 weeks EGA following 6th treatment, responsive to tocolytics. Experienced periodic contractions until 37 weeks EGA.	
Pierre et al. (80)	France	Prenatal BP-MX, suicidal ideation, n=1	Second trimester, n=1	Acute BT ECT, 5 treatments	Depression scores (HAMD 25) "entirely improved" after ECT. YMRS scores improved from 26 to 3.	Uterine contractions after 1st treatment.	Normal fetal development on ultrasound scanning. No development of fetal bradycardia.
Pinette et al. (81)	USA	Prenatal MDD, n=1	ECT administered throughout pregnancy	Maintenance ECT was continued into and throughout pregnancy	Good response to maintenance ECT was documented.	Induction of labor owing to pre-eclampsia at 37^{+1} weeks.	Small left cerebellar, bihemispheric deep white matter, and cortical infarcts on CT/MRI.
Rabie et al. (82)	USA	Mixed sample, 5 cases total. Prenatal depression, n=3 (1 with suicidal ideation) Prenatal BP/BP-D, n=2 (1 with suicidal ideation)	Trimesters at ECT initiation unspecified.	Acute RUL ECT administered with continuous FHR monitoring, range 2 to 23 treatments	All patients reported improvement, one with "limited improvement" and another rehospitalized due to depressive relapse.	Headaches, muscle soreness, nausea, fatigue, memory disturbances, transient uterine contractions.	Reassuring FHR tracings before and during ECT (data on 32 of 34 treatments that included continuous FHR monitoring). Transient decelerations noted for 4 treatments, none requiring intervention or additional monitoring. Healthy term deliveries in all 5 cases.
Ratan et al. (83)	UK	Perinatal depression with psychotic features, n=1	Postpartum week (s) unspecified	Acute ECT, electrode placement and frequency of treatment unspecified.	Remission	Not reported.	Not reported.
Ray-Griffith et al. (84)	USA	Mixed sample, 8 cases total Prenatal depression, n=3 Prenatal depression, suicidal ideation, n=2 Prenatal BP-D, n=1 Prenatal BP-MX with suicidal ideation, n=1	Second trimester, n=5 Third trimester, n=3	Acute RUL ECT, 30 treatments total, ranging from 1 to 7 treatments individually.	Remission of suicidality in 5 patients who presented with acute suicidal ideation. "Clinical improvement" of depression for 6 of 8 patients.	Case 5 - ECT discontinued due to treatment-emergent hypomanic symptoms after the 1st treatment at 21^{+2} weeks. PPROM/preterm labor at 30^{+1} weeks. Case 8 – ECT stopped after asymptomatic episode of complete heart block requiring atropine and intensive care observation, deemed secondary to anesthesia with methohexital.	Uncomplicated term deliveries except for Cases 3 and 8 (did not deliver at investigators' institution) and Case 7 (below). Case 7 – infant born with right club foot and right 5th toe displacement, detected on ultrasound before ECT.

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
		Unspecified prenatal mood disorder with suicidal ideation, n=1					
Repke et al. (85)	USA	Prenatal depression with psychotic features, n=1	Second trimester, n=1	Acute ECT, electrode placement unspecified, 5 treatments	Positive response	Reduction in blood pressure, though secondary to low intravascular volume, prevented with pre-hydration during treatments 2-5.	Delivery of healthy infant.
Richardson et al. (86)[a]	UK	Prenatal BP-MX, n=1	Third trimester, n=1	ECT electrode placement unspecified, 8 treatments. ECT resumed on a Q 2 week basis following delivery, then extended to monthly maintenance ECT.	Positive acute response and positive maintenance response at 6 months postpartum.	No maternal complications.	No fetal complications. Delivery at 38 weeks EGA by elective cesarean section.
Rineh et al. (87)	Iran	Prenatal MDD, n=1	Third trimester, n=1	Acute ECT, electrode placement unspecified, 3x/week, 6 treatments.	Significant improvement in depression after 3rd treatment and remission after the 6th treatment.	Intermittent uterine contractions, eventually requiring prophylactic magnesium sulfate	Single transient FHR reduction after 2nd treatment.
Sahan et al. (88)	Turkey	Prenatal depression with psychotic features, catatonia, and urinary bladder overdistension, n=1	First trimester, n=1	Acute ECT, electrode placement unspecified, 3x/week, 7 treatments	Patient was able to urinate after 3rd treatment. Negativism resolved. Discharged from the hospital with full recovery. Experienced relapse during third trimester, managed with pharmacotherapy.	Not reported.	Delivery of healthy infant, with normal development through first year of life.
Salzbrenner et al. (89)	USA	Prenatal BP-D with history of IVF and pre-eclampsia, suicidal ideation, n=1	Third trimester, n=1	Acute BT ECT, electrode placement unspecified, 3x/week, 9 treatments	Positive response, improvement in MADRS score from 32 at baseline to 12 after 8th treatment. Psychiatrically stable at 9 month follow-up.	Hypertensive responses to ECT controlled with IV labetalol initially (switched to remifentanil). ECT had to be stopped owing to cognitive side effects (MMSE 19/30 after 9th treatment; 30/30 at baseline). MMSE scores steadily improved to 30/30 over the following 4 months.	No fetal complications. Delivery of healthy infant at 38 weeks EGA by cesarean section. Normal development through first 9 months of life.

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
Sandal et al. (90)	Turkey	Prenatal depression, n=1	Second trimester, n=1	ECT electrode placement unspecified, 6 treatments	Not reported.	Not reported.	Infant diagnosed with Mobius syndrome, not believed to be caused by ECT.
Sarma et al. (91)	Australia	PPD with suicidal ideation and type 1 Chiari malformation, n=1	8 weeks postpartum	Acute BF ECT, 3x/week, reduced in frequency to 2x/week after 2 weeks, totaling 12 treatments	Remission of suicidal ideation and significant improvement in depressive symptoms (MADRS and EPDS 32 and 23 at baseline, 11 and 4 after ECT). Mild reduction in MoCA scores (from 29 to 25).	Mild headaches, concentration and memory disturbances.	Not reported.
Serim et al. (92)	Turkey	Prenatal depression with psychotic features, n=1	Third trimester, n=1	Acute BT ECT, 3x/week, 10 treatments	"Significant" improvement after 5th treatment. Relapse occurred 2 weeks after 10th acute treatment, eventually responsive to medication only.	Brief uterine contractions after one treatment that was responsive to tocolytic therapy.	Brief (2–3 second) FHR deceleration during one treatment. Delivery of healthy infant at 39 weeks by cesarean section.
Shea et al. (93)	USA	PPD with psychotic features in patient with Turner syndrome, n=1	4 weeks postpartum	Acute BT, 6 treatments	Resolution of infanticidal thoughts, "steady" improvement of depressive/ neurovegetative symptoms.	Not reported.	Not reported.
Sherer et al. (94)	USA	Prenatal depression with psychotic features, n=1	Third trimester, n=1	Acute BT, 7 treatments	Not reported.	Transient uterine contractions (eventually requiring tocolytic therapy), vaginal bleeding, abruptio placentae diagnosed after delivery with unremarkable postoperative course.	Delivery of healthy infant at 37 weeks by cesarean section.
Strain et al. (95)	USA	Diagnosed postpartum depression presenting acutely with psychotic features and catatonia, n=1	5 months postpartum	Acute ECT, electrode placement unspecified, 6 treatments	Positive response to ECT, with early improvement noted after the 1st treatment. Stable at 18 month follow up.	Not reported.	Not reported.
Takubo et al. (96)	Japan	PPD, suicidal ideation, n=1	Postpartum week (s) unspecified	ECT electrode placement and frequency of treatment unspecified.	Partial response.	Not reported.	Not reported.

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mg/kg),

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
Walker et al. (97)	USA	Prenatal depression with psychotic features, n=1	Second trimester of twin pregnancy, n=1	Acute BT ECT, 6 treatments initially, 7 treatments after relapse. Two continuation treatments given once-weekly.	Remission of presenting symptoms after initial acute series, followed by relapse 3 weeks later. This was followed by 7 additional treatments that resulted in remission. Two weekly continuation treatments were given.	Occasional uterine contractions on tocodynamometry	Twin B – nonreactive NST after 2nd treatment with normal contraction stress test and normal subsequent NSTs. Delivery at 35 weeks EGA. Twin A - transposition of the great vessels, death 2 weeks after surgery. Twin B- born with imperforate anus, hemivertebra of the sacral vertebra, atrial septal defect, and coarctation of the aorta.
Watanabe et al. (98)	Japan	Prenatal MDD, suicidal ideation, n=1	Third trimester, n=1	Acute BT ECT, 2x/week, 6 treatments	Partial response (improvement in HAM-D score from 36 to 26) with resolution of suicidal ideation and restoration of appetite.	Uterine contractions from the 3rd treatment onward	Persistent fetal tachycardia (180–200 bpm >30 minutes), presumed secondary to maternal apnea during ECT, with no recurrence after the reinitiation of oxygenation just after electrical stimulus delivery. Delivery of healthy infant at 38 weeks EGA.
Wise et al. (99)	USA	Prenatal depression with psychotic features, n=1	Third trimester, n=1	Acute RUL ECT, 8 treatments	Remission after the initial acute series, with good response to 4 additional treatments to address return of depressive symptoms that occurred twice before delivery.	One brief episode of SVT that required no intervention.	Oxytocin-induced vaginal delivery of healthy infant at 37 weeks EGA, with normal development through first 10 months of life.
Yamada et al. (100)[a]	Japan	Prenatal BP-D, n=1	Third trimester, n=1	ECT electrode placement unspecified, 2-3x/week, 10 treatments	Unspecified improvement in depressive symptoms.	FGR diagnosed by ultrasound, with fetal growth delay starting at 29 weeks EGA, possibly caused by thrombosis of the umbilical vein.	FGR-delivery by emergent cesarean section at 32 weeks.
Yang et al. (101)	S. Korea	Prenatal BP-D with psychotic features, n=1	Third trimester, n=1	Acute ECT, electrode placement unspecified, 7 treatments	Positive response to initial acute series followed by relapse 3 weeks after hospital discharge.	Transient uterine contractions/ possible preterm labor, responsive to tocolytic therapy, with no apparent reoccurrence.	FGR fetus diagnosed before ECT initiation. Premature delivery at 35^{+4} by emergency cesarean section. Infant was diagnosed with hyaline membrane disease and congenital hypertrophic pyloric stenosis.

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TABLE 2 Continued

Reference	Country	Diagnos(es), n cases	Trimester(s) of pregnancy or weeks postpartum	ECT delivery characteristics	Main effective-ness outcomes	Obstetric safety outcomes	Fetal/neonatal or nursing infant safety outcomes
Ying et al. (102)[a]	Unspecified	Prenatal depression, suicidal ideation, n=1	Third trimester, n=1	Acute ECT, electrode placement and frequency of treatments unspecified.	Resolution of depression.	Prolonged neuromuscular blockade that delayed extubation, due to pseudocholinesterase deficiency owing to pregnancy. Rocuronium replacement of succinylcholine allowed completion of ECT series.	Prolonged transient FHR deceleration after 1st treatment.

Key: BP, bipolar spectrum disorder; BP-D, bipolar depression; BP-M, bipolar mania; BP-MX, bipolar mixed episode; BF, bifrontal ECT; BT, bitemporal ECT; BZD, benzodiazepine; CGI, Clinical Global Impression scale; CGI-S, Clinical Global Impression severity subscale; CT, computed tomography scan; DPHD, diphenylhydantoin; EGA, estimated gestational age; EPDS, Edinburgh Postnatal Depression Scale; GFR, fetal growth restriction; FHR, fetal heart rate; IV, intravenous; IVF, *in vitro* fertilization; L-DLPFC, left dorsolateral prefrontal cortex; MADRS, Montgomery Asberg Depression Rating Scale; MDD, major depressive disorder; MMSE, Folstein Mini-Mental Status Examination; MoCA, Montreal Cognitive Assessment; MRI, magnetic resonance imaging scan; MV, mechanical ventilation; NST, non-stress test; NSVD, normal spontaneous vaginal delivery; PIH, pregnancy induced hypertension; PPD, postpartum depression; PPROM, preterm premature rupture of membranes; PTSD, posttraumatic stress disorder; QIDS-C, clinician-rated Quick Inventory of Depressive Symptomatology scale; RUL, right unilateral ECT; RUL/UB, right unilateral ultrabrief pulse ECT; SE, status epilepticus; SUD, substance use disorder; SVT, supraventricular tachycardia; TMS, transcranial magnetic stimulation; UK, United Kingdom; USA, United States of America.

[a]Citation is from a published conference abstract. [b]Case series described ECT in 33 pregnant patients, 19 with MDD, 12 with BP, and 2 with schizophrenia. Among all 33 cases, ECT was performed starting in the first, second, and third trimesters for 13, 15, and 5 patients, respectively. [c]Mood polarity was unspecified. [d]A total of 68 cases were presented, including 43 patients with "unipolar depression," 20 with a bipolar spectrum disorder, 3 with obsessive-compulsive disorder, and 2 with schizophrenia. [e]This 29-year-old patient was subsequently found to have osteoporosis based on a dual-energy X-ray absorptiometry (DEXA) scan z-score of -2.5. [f]This was a single case report of ECT for PPD in a patient who attended a day center program for individuals with learning disabilities. [g]"Mildly hypomanic" symptoms were observed for 1 week after the final (9th) ECT treatment that included being "talkative, with elevated mood." Maintenance ECT was planned. [h]All 5 cases were described as achieving remission of acute symptoms with no subsequent relapses in 4 subjects who received continuation ECT treatments. [i]Hypomanic symptoms included increased energy, increased goal-directed behavior, and "slight" decreased need for sleep after the 4th treatment. There was "mild mood elevation" noted after hospital discharge. Euthymia was documented within 2 weeks following delivery. [j]This patient received an acute inpatient series of RUL ECT for depression with catatonic features while pregnant; however, 2 months after discharge, she was hospitalized with a relapse of depressive and catatonic symptoms. Labor was induced at 40^{+1} weeks. ECT was resumed during the early postpartum. [k]A total of 13 postpartum ECT cases are described consisting of a mixed sample of patients with PPD (7 cases), BP (3 cases total, 1 with BP-D), schizophrenia (2 cases), and "transient psychotic disorder" (1 case). The mean total duration of psychiatric symptoms during the postpartum period in the entire case series was 57.8 days, or 8.3 weeks. [l]Ten postpartum ECT cases are summarized, composing a mixed sample of patients with PPD (6 cases), acute mania (1 case), PPP without underlying diagnosis specified (2 cases), and "organic psychosis" (1 case). [m]Mixed sample included 2 cases of recurrent prenatal depression, 1 case with BP-M, and 2 cases with schizophrenia. [n]This was a first-person account of having undergone ECT for PPD. ° Switching anesthesia induction agent from methohexital to etomidate resulted in enhanced seizure durations.

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thiopental (100–300 mg or 3–4 mg/kg), thiamylal (4 mg/kg), succinylcholine (40–120 mg or 1–2 mg/kg). However, anesthetic doses, neuromuscular blocking drugs, airway management techniques, pharmacological adjuncts to anesthetic induction agents, and modifications of anesthetic technique for perinatal safety were unspecified in most reports. In one case report, methohexital was switched to propofol to shorten seizure length after a prolonged ECT seizure that led to an episode of fetal bradycardia (46). Another case report referenced switching from thiopental to etomidate to increase seizure duration and based on "favorable experiences with the drug in obstetrical patients" (47). A third case report described adjusting the dose of methohexital in response to seizure duration and quality but not perinatal safety reasons (79).

3.5 Adaptations to standard ECT technique

Specific maternal and fetal monitoring procedures to accommodate pregnancy or postpartum status were described in fewer than half of the reviewed reports. Still, as shown in Supplementary Table S3, several adaptations to standard ECT technique were documented in case reports and case series. Twenty-three reports provided details on airway management techniques, including 12 that used endotracheal intubation during second- or third-trimester pregnancies and 10 reports of mask airway. One case report described the use of a supraglottic airway for subsequent ECT treatments due to difficult intubation under direct laryngoscopy during her first treatment at 20 week's gestation (40). When described, maternal monitoring techniques included tocometry/tocodynamometry, ultrasound assessments, obstetrician attendance during the procedure, and ready access to emergent cesarean section capabilities in specific cases (Supplementary Table S3). Additional precautions applied in later stages of pregnancy (after the first trimester) included elevation of the right hip to prevent aortocaval compression, cricoid pressure to reduce the risk of regurgitation and aspiration of stomach contents, pre-hydration/pre-oxygenation, and endotracheal intubation. Fetal heart rate monitoring, non-stress tests/biophysical profiling, and ultrasonography for fetal morphology, fetal heart rate and uterine contractility monitoring were also described (Supplementary Table S3).

3.6 Effectiveness

Main effectiveness results from observational studies and from case series/reports are outlined in Table 1 and Table 2, respectively. Treatment effects were reported as categorical outcomes (e.g, remission, partial response, non-response, hospital readmission, etc.) in 35 (42.7%) reports, as continuous outcomes (absolute or relative change in rating scale scores) in 16 (19.5%) reports, and as narrative descriptions of outcomes ("clear," "full," or "complete" response, unspecified improvement in mood symptoms, etc.) in 17 (20.7%) reports. The most used rating scales were the Hamilton Depression Rating Scale (HAM-D, 12 reports), the Clinical Global Impression scale (-severity [CGI-S] or -improvement [CGI-I] subscales, 8 reports), the Montgomery Asberg Depression Rating Scale (MADRS, 5 reports) (104), the Bush Francis Catatonia Rating Scale (BFCRS, 3 reports) (105), and the Quick Inventory of Depressive Symptomatology (QIDS) (106) and the 9-item Public Health Questionnaire (PHQ-9, 1 report each) (107). Therapeutic outcomes were not assessed in 12 reports. One study each focused only on descriptions of interventions provided on a specialized mother-baby unit (32) and on qualitative outcomes (108).

3.6.1 Observational and chart review studies

3.6.1.1 ECT for perinatal vs non-perinatal mental health disorders

Controlled investigations of acute responses to mECT for perinatal depression collectively involved a variety of comparisons, mainly involving ECT for perinatal mental health conditions vs ECT for non-perinatal mental health disorders. For example, a retrospective cohort study of 793 pregnant patients identified in linked registers, including a population-based ECT registry, documented numerically higher positive response rates (CGI-I scores of 2 [much improved] or 1 [very much improved]) with ECT in patients with a perinatal psychiatric diagnosis than with ECT in non-pregnant patients with a psychiatric diagnosis (74% vs 65%) who were matched on propensity scores (24); however, between-group differences in response rates were not statistically significant. Using the same population-based ECT registry, significantly higher rates of response (using the definition above, assessed within 7 days after receiving ECT, 87.0% vs 73.5%) and remission (CGI-S scores of 2 [borderline ill] or 1 [not ill], 45.4% vs 29.9%) were also observed in patients who received ECT for PPD or postpartum psychosis than patients who received ECT for a non-postpartum indication (31).

In another retrospective cohort study, a population-based ECT database and records from an inpatient mother-baby unit were used to identify a cohort of severely depressed patients with postnatal depression/psychiatric disorders (baseline mean MADRS score 43.1, n=12) and patients who received ECT for non-perinatal psychiatric disorders (baseline mean MADRS score 41.3, n=23) (27). After ECT, the mean reduction in MADRS scores was 10.1 points greater for perinatal depression cases than non-perinatal controls (-30.8 vs. -20.7, p=0.06). At baseline, the proportion of individuals with severe depression (based on MADRS scores) was 83% in both the perinatal ECT group and the non-perinatal ECT group. After ECT, the proportion of severe depression cases was 8% in the perinatal ECT group and 22% in the non-perinatal ECT group.

In a university hospital register-based study, clinical recovery ratings (based on a 4-point Likert scale) were compared between patients who received ECT for puerperal mental health conditions and patients (<45 years of age) who received ECT for non-puerperal mental health conditions (29). Complete records were available for 114 of the 137 patients who received ECT, including 58 patients in the puerperal ECT group and 56 patients in the non-puerperal group. Analyses restricted to patients with depression showed a significantly higher proportion of patients rated as either

"asymptomatic" or having achieved "marked improvement" in the puerperal depressed group than in the non-puerperal depressed group at the end of ECT (66.7% vs 27.3%, p<0.001) and at reassessment one month after ECT (61.9% vs 24.2%, p=0.003).

3.6.1.2 Comparisons of bitemporal and bifrontal ECT

One study retrospectively compared the effects of bitemporal (BT, n=18 patients) and bifrontal (BF, n=13 patients) ECT in a mixed cohort of 31 patients (28). Edinburgh Postnatal Depression Scale (EPDS) and CGI-S scores were compared between groups at hospital discharge. Mean numerical pre- and post-treatment EPDS and CGI-S scores were not provided; however, post-treatment EPDS scores were reported as being significantly lower with BF than BT ECT (p=0.004). CGI-S scores were reported to be lower with BF than BT ECT at the level of statistical trend (p=0.06).

3.6.1.3 ECT vs no ECT

Another study prospectively compared clinical responses in a mixed cohort of 78 patients with postpartum psychosis (24 with depression) who received acute ECT and those with similar indications who did not receive ECT (25). Data were analyzed for the entire cohort, without diagnosis-specific results. Psychopathology was assessed in all 78 patients, 34 of whom received ECT, using the Comprehensive Psychopathological Rating Scale (CPRS) (109). CPRS scores were similar between both groups at baseline (ECT 41.8 vs. no ECT, 39.5) and were similarly improved in each group at the end of follow-up (ECT, 4.5, no ECT, 4.2). Duration of admission was lower in the ECT group (19 days vs 23 days); however, there were no significant between-group differences in therapeutic outcomes or hospital lengths of stay.

3.6.1.4 Relapse and rehospitalization after acute ECT

Other reports focused on relapse rates after an acute response to ECT, with relapse generally defined as rehospitalization for a psychiatric indication. For example, in a retrospective cohort study, rates of relapse (defined as rehospitalization for psychiatric reasons or suicide) were lower for patients who received ECT for PPD or postpartum psychosis (n=180) after 6 months (28% vs 39%), 1 year (31% vs 50%), and 2 years (40% vs 55%), as compared with control patients (n=180) who were <46 years of age and received ECT for a non-postpartum indication (30). The mean time to relapse (621 ± 548 days vs 440 ± 475 days) was numerically higher and the risk of relapse was significantly lower for patients who received ECT for PPD or postpartum psychosis (vs control patients) in unadjusted analyses (HR 0.61 [0.45, 0.83]). Statistical differences in relapse risk were nearly significant after adjusting for education level, unemployment, selected comorbidities, CGI-I score one week after treatment, drug treatment, and prior psychiatric admission history (HR 0.72 [0.52, 1.00]).

In a subsequent population-based study, linked registers were used to identify a mixed cohort of 91 patients with evidence of postpartum mood or psychotic disorders and no prior mood or psychotic disorder diagnoses and no history of ECT prior to giving birth (26). Cohort members were all psychiatrically hospitalized within the 6 weeks following delivery, 43% of whom were diagnosed with unipolar depression, 19% with bipolar disorder, and 38% with an unspecified psychotic disorder. A total of 17 (18.7%) patients received ECT. Rehospitalization (readmission to a psychiatric hospital within 6 months of the index hospital admission discharge date) occurred in 28 (30.8%) of the cohort members after a mean post-discharge interval of 16 days; however, ECT-specific results were not reported, nor were they compared with non-ECT treatment outcomes.

3.6.2 Case reports and case series

As shown in Table 2, all but 11 case reports or case series provided details on therapeutic outcomes of mECT. Most cases focused on acute-phase treatment, while 11 reports described continuation or maintenance ECT outcomes. Positive therapeutic responses to mECT were documented in 60 (84.5%) case reports or case series; however, as noted earlier, there were disparate methods for describing treatment outcome. For instance, positive treatment outcomes were narratively described (without the use of psychopathology measures) as "remission" (11 reports); "complete response," "resolution" of symptoms," or "recovery" (7 reports); "improvement" or "partial response" (20 reports); "good response" or "good results" (3 reports); or "well controlled" after ECT (1 report). Improvements in specific symptoms were narratively described in 2 reports. When psychopathology measures were used in single and double case reports, remission was documented in 6 reports (based on HAM-D score <7, QIDS-C <5, MADRS <6, PHQ-9 ≤4, Beck Depression Inventory <9, or CGI-S <2), response was documented in 1 report (based on a 50% improvement in 24-item HAM-D score), and non-response was documented in 2 reports (<50% improvement in 24- and 17-item HAM-D scores).

Patient follow-up was usually confined to the acute treatment phase, which often ended at hospital discharge. Several reports documented recurrences of psychiatric illness after an initial acute treatment series resulting in rehospitalization, with or without additional acute mECT treatments (54, 70, 82, 88, 92, 97, 101). When timelines were provided, symptom relapses were noted to occur within 2–3 weeks following the final ECT treatment or hospital discharge. The extension of a positive acute phase response with continuation or maintenance treatments was documented in 2 reports (73, 76). In one case, additional mECT treatments were provided to address two depressive recurrences following initial symptomatic remission in a patient who required prolonged hospitalization for high-risk pregnancy (99).

3.7 Adverse maternal, fetal, and neonatal events

3.7.1 Observational and chart review studies

Two observational and one chart review study reported safety or tolerability results in patients who received mECT for perinatal depression (and other indications in mixed cohorts). The largest of the three was a previously reviewed retrospective cohort study that used linked population-based registers to compare response rates in

ECT-treated patients with a perinatal psychiatric diagnosis, non-ECT pregnancies from the same group of ECT-treated patients (non-ECT additional pregnancy group), and psychiatrically ill non-pregnant patients who received ECT (24). Control groups were matched with the main exposure group using propensity scores. Registry data included reports for specific complications including preeclampsia, diabetes, congenital malformations, stillbirth, Apgar scores (at 1-, 5-, and 10 minutes), birthweight, large/small for gestational age (LGA/SGA) status, and other maternal and neonatal complications. Most complications, including fetal malformations, LGA deliveries, and SGA deliveries, were comparable across exposure groups. As shown in Table 1, the risks of premature delivery and low 5-minute Apgar scores (< 7) were significantly higher for the pregnant ECT group than the non-ECT pregnant inpatient group, but not the non-ECT additional pregnancy group. Stillbirths occurred in 2 (2.1%) pregnancies in the pregnant ECT group, 1 (0.3%) pregnancy in the non-ECT pregnant inpatient group, and 1 (1.1%) pregnancy in the non-ECT additional pregnancy group.

A retrospective chart review study of 31 patients who received either BT or BF ECT during the prenatal (4 patients) or postpartum (27 patients) periods was presented as a conference abstract (28). Indications for ECT were described as "severe" cases with clinical diagnoses unspecified bipolar spectrum disorder (n=14), unspecified depression (n=3), unspecified psychotic disorder (n=4), unspecified postpartum psychosis (n=4), and "acute transient psychosis" (n=6). Maternal adverse effects of ECT included headache and cognitive difficulties. Fetal and neonatal safety outcomes, however, were not reported.

Preliminary maternal adverse effects and lactational safety data with ECT were provided in a prospective study 78 hospitalized patients with postpartum psychosis, 34 of whom received ECT (25). Clinical diagnoses assigned to cohort members included unspecified depression (n=24), acute manic episodes (n=32), and "non-affective" psychoses (n=22). The most common maternal adverse effects associated with ECT were memory disturbances (anterograde amnesia) in 6 (17.6%) patients and prolonged seizures in 4 (11.7%) patients, the latter managed with additional doses of sodium thiopental. Fifteen ECT-treated patients were hospitalized with their infants and continued breastfeeding without complications or apparent adverse effects.

3.7.2 Case reports and case series

3.7.2.1 Maternal and obstetric adverse events

As shown in Table 2, several reports documented common adverse effects known to be associated with ECT, including headache, nausea, myalgias, transient arrhythmias, hypertensive responses to ECT, cognitive disturbances, and post-ECT confusion. The most frequently reported perinatal adverse effects in patients were transient uterine contractions (14 reports), nearly all of which were transient (did not progress to preterm labor), although some required tocolytic therapy or prophylaxis. There were 5 reports of preterm labor with preterm deliveries occurring between 30^{+1} and 35^{+4} weeks EGA. Prolonged seizures were described in 4 reports, including one case of status epilepticus requiring aggressive doses of anesthetic medications to achieve seizure control, resulting in severe hypotension, the need for pressor support, and fetal demise (34). Other reported adverse events included pelvic pain, blood pressure reduction (owing to low intravascular volume), fetal growth restriction (presumed secondary to umbilical vein thrombosis), and prolonged neuromuscular blockade from administration of succinylcholine in a patient with pseudocholinesterase deficiency. Eleven reports specified no maternal complication with mECT, while information on adverse effects of mECT was not provided in 19 reports. There was one case of confirmed placental abruption diagnosed after Cesarean delivery at 37 weeks in a 35-year-old patient with severe depression and panic attacks who experienced the onset of regular uterine contractions, subsequent hypertonic-tetanic contractions, and blood pressure elevations followed by transient uterine bleeding during mECT at 34 weeks (94).

3.7.2.2 Fetal/neonatal adverse events

The most frequently reported fetal/neonatal adverse events occurring on or around the time of ECT administration were fetal heart rate decelerations (10 reports), the majority of which were transient and without long-term impact on fetal or delivery outcomes. There were 7 cases of premature deliveries occurring between 31- and 35-weeks' gestation, 5 of which also included preterm labor occurring days (3 reports) to weeks (3 reports) following ECT treatment. In general, numerous risk factors for premature delivery were present including severe mood disorder symptoms (all cases), twin pregnancy (2 cases), infectious disease complication during pregnancy (1 case), substance exposures (1 case), food refusal or weight loss during pregnancy (2 cases), maternal age >35 years (1 case), and threatened abortion in the current pregnancy prior to ECT (1 case). In one case, preterm labor occurred 11 weeks after receiving just a single ECT administration (84). There were 6 reports of congenital malformations. Specific congenital defects included cardiovascular (atrial septal defect, coarctation of the aorta, transposition of the great vessels), musculoskeletal (equinovarus foot deformity, congenital hip dysplasia, hemivertebrae, fifth toe displacement), and gastrointestinal (anal atresia). The two reports documenting adverse events in ECT-treated patients with twin pregnancies involved multiple co-occurring congenital malformations and the neonatal demise of one twin, each, following subsequent surgeries (69, 97). There were two reports of fetal death/stillbirth (one occurring in the setting of severe drug-resistant status epilepticus and another from an undetermined cause) and one report of first trimester miscarriage occurring shortly after a third acute ECT treatment. Direct causal links between ECT and these adverse events were unclear. Normal deliveries or child development outcomes were specified in 21 reports, while no information on these outcomes was provided in 9 reports.

4 Discussion

The current report presents an updated scoping review of the literature describing the broad effectiveness and maternal, fetal, and neonatal safety of mECT for perinatal depression as well as details on mECT technique and technical adaptations that may bear on its safety or effectiveness in that population. We abstracted information from 82 reports that included information on over 1,300 pregnancies or deliveries. Our review was limited to mainly individual cases and case series, which accounted for 85% of the reviewed reports, with only a handful of controlled observational studies. The collected literature described a broad spectrum of effectiveness and safety outcomes with predominantly acute mECT for multiple forms of perinatal depression that presented across multiple trimesters of pregnancy and in the postpartum. As with non-puerperal depression, mECT appears to confer rapid benefit for depressive, psychotic, and catatonic symptoms in severely depressed perinatal patients including those with treatment-resistant illness. Reported adverse events, many with uncertain etiologic links to the procedure itself, are discussed further below.

To our knowledge, there have been 7 systematic reviews of the safety and/or effectiveness of ECT administered during the perinatal period (110, 111 12–15, 17). Most reviews focused on ECT effects during pregnancy and generally supported ECT as a rapidly beneficial alternative to conventional antidepressive medications, particularly for pharmaco-resistant cases or instances in which levels of clinical acuity are so high that therapeutic lag times associated with most antidepressive treatments would be unacceptable. Reports of postpartum mECT were fewer in number (about 25% of included papers in our review) than those addressing prenatal mECT, as was also the case with prior reviews. As such, the conclusions from this literature review, which addresses mECT for mainly the acute treatment of depression in pregnancy and postnatal samples, are broadly consistent with those of prior reviews in terms of efficacy as an acute-phase treatment modality.

Although there appears to be a reasonably consistent signal for rapid, acute phase antidepressive efficacy in perinatally depressed patients, several questions remain. The first pertains to who the reviewed evidence applies to. Although most reviewed papers included clearly defined cases of perinatal unipolar or bipolar depression, many of the reviewed reports (a little more than 25% of the total) involved mixed cohorts of individuals, not all of whom received ECT, with clinical diagnoses outside of unipolar or bipolar major depression. This included all 9 observational studies and 12 case series, with diagnoses ranging from unspecified catatonic syndromes to unspecified postpartum psychoses and diagnosed primary psychotic illnesses. In studies with mixed samples, diagnosis-specific outcomes were often not provided—an important limitation considering that, although ECT has robust broad spectrum efficacy across most mood and psychotic disorders (112, 113), general and obstetric adverse event risks from mECT may be disproportionately increased in patients with primary psychotic disorders due to especially high rates of general medical comorbidity (114); substance use (115); pregnancy and delivery complications (116, 117); smoking, obesity, and other negative lifestyle factors (118, 119); and lower rates of preventive or obstetric care seeking/medical follow-up (120, 121). Additionally, an essential core treatment for patients with chronic psychoses, antipsychotic drugs, may increase the risk of gestational diabetes (122), an independent risk factor for numerous pregnancy and neonatal complications (123). While the inclusion of papers with mixed samples and incomplete or disparate approaches to the reporting of diagnosis-specific outcomes are clear limitations, their inclusion in the paper is consistent with our objective of conducting a scoping literature review.

Following an acute phase response to mECT, the continuation (extension) of antidepressive effects becomes most relevant, given the possibility of depressive symptom relapse once a course of ECT has ended. In a meta-analysis of 32 studies of non-puerperal depressive patients who responded to an acute course of ECT, estimated relapse rates were 37% at 6 months and 51% at one year (124), highlighting the need for continuation and maintenance ECT for a significant number of acutely treated patients. The estimated reduction in relapse risk with maintenance ECT in non-puerperal depressed patients may be substantial, even when compared to pharmacologically treated controls (RR for relapse, 0.8 to 0.5) (125); however, to our knowledge, no such estimates have been established for perinatally depressed patients. Very few reports included in this scoping review provided detailed information on the duration of acute responses and only 9 case reports (39, 46, 50, 73, 76, 79, 81, 86, 97) and one small case series (37) described the delivery of continuation of maintenance ECT. A smaller number of reports described early relapses of severe depressive symptoms after an initial acute ECT series (82, 88, 92, 101), some of which required additional ECT treatment sessions (54, 70, 97, 99). Although the case literature reviewed here and existing literature from non-puerperal samples of depressed patients raises the strong possibility of benefit, the effectiveness of continuation and maintenance mECT for perinatal depression remains understudied, constituting an important and persisting clinical knowledge gap.

For decades, ketamine has been used as an alternative anesthesia induction agent when ECT seizures become too short or too difficult to elicit when using first- and second-line agents such as methohexital, propofol, or etomidate (126). Ketamine is not an anesthetic of choice for mECT owing to the potential for increasing seizure duration and for enhanced hemodynamic responses with associated elevations in intracranial pressure (127). However, ketamine and its S-enantiomer, esketamine, have since become established, rapidly acting antidepressive agents in their own right (128), which has raised interest in the therapeutic potential of ketamine-augmented ECT. Only one of the reviewed reports described the clinical effects of ketamine-augmented ECT for an acutely suicidal depressed patient during pregnancy (78). In this case, remission occurred after 8 treatments. However, time course to remission was not described, and there was no viable means of determining if ketamine augmentation was required to achieve that outcome. As of this writing, the evidence base for non-puerperal

depression does not show an advantage of prioritizing ketamine over other anesthesia induction agents for the purposes of maximizing therapeutic efficacy (129). Furthermore, ketamine is contraindicated in pregnancy given a lack of sufficient reproductive and safety data (130), as well as potential associations of ketamine exposure with neurotoxicity during fetal development in preclinical studies and adverse neurodevelopmental outcomes in neonates with repeated exposure to ketamine anesthesia (131–133). The drug label for esketamine indicates that it is also not recommended during pregnancy owing to insufficient reproductive and neonatal safety data (134). As such, augmentation with ketamine or esketamine for the specific purpose of enhancing the efficacy of mECT or accelerating the time to remission with mECT in depressed pregnant patients cannot be recommended at this time.

Interestingly, eight of the reviewed reports described the indication for ECT as the preferred treatment for the specific context of pregnancy, motivated in some cases by the desire to minimize potentially teratogenic medication exposures and other adverse effects (34, 37, 39, 52, 54–56, 66, 70). However, the safety of ECT in pregnant patients has been the subject of debate. In prior reviews and for most cases in this review, ECT appeared to be relatively well tolerated. Frequently reported maternal and fetal adverse events from both prior reviews and ours included transient fetal arrhythmias/fetal bradycardia, uterine contractions, abdominal or pelvic pain, premature deliveries, placental abruption, threatened abortion, and vaginal bleeding. In most cases where adverse events were reported, a healthy term delivery was the ultimate outcome. On the other hand, only one observational study investigated a limited range of neonatal adverse events associated with ECT during 97 pregnancies (24), reporting 2 cases of stillbirth, 14 cases of premature delivery, and 9 cases of 5-minute Apgar scores <7 (with none in the range of 0-3). Individual case reports and case series also documented a variety of adverse fetal/neonatal outcomes including 2 cases of fetal death/stillbirth (33, 42) and one case of miscarriage (48); 7 cases of premature delivery between 31 and 35^{+4} weeks gestation due to pregnancy induced hypertension (57), preterm labor (65, 69), preterm premature rupture of membranes (72), fetal growth restriction (100), and recurrence of depressive symptoms (101); 6 reports of congenital malformations (37, 41, 69, 84, 97, 101), and one report of confirmed placental abruption (94). However, none of these reports can be considered comprehensive in terms of adverse event surveillance. And in the absence of valid denominator data, adverse events from individual case reports (e.g., congenital malformations) cannot be used to estimate event rates for comparisons against background rates [e.g., 3% background congenital malformations rate (135), even if all reported cases were true cases.

Prior reviews of safety data for ECT during pregnancy have documented similar adverse events in ECT-treated pregnancies but differed in their main conclusions. Four reviews supported the safety of ECT during pregnancy (12, 15, 17, 110, 111). However, two reviews suggested that ECT should be considered only when other treatment options are ineffective or infeasible based on low data quality (16) or high reported frequencies of adverse events in general (29%) and child fatalities in particular (7.1%) (14). The review by Leiknes and colleagues (14) has been criticized for including studies dating back to the early 1940s, decades before modified ECT was standard-of-care practice, and for counting adverse events that were not likely to be related to ECT (19, 136). In our review, only a limited number of papers included sufficient details on confounding factors such as maternal psychiatric and general medical comorbidities, pre-ECT obstetric complications, and medications taken prior to or during index courses of mECT, making it difficult in many instances to draw firm causal links between ECT and reported adverse events (137).

The ethical considerations pertaining to the inclusion of pregnant patients in clinical therapeutics research continue to be debated (138). Therefore, it is highly unlikely that clinical decisions pertaining to the effectiveness and safety of mECT for perinatal depression will be guided by evidence from randomized trials any time soon, especially when taking into account the added complexities of addressing issues of capacity and valid informed consent for research participation in highly-vulnerable patients who may require mECT for severe and often psychotic or catatonic illnesses (139). For the time being, we anticipate increasing use of data from linked national registers, such as the Swedish National Quality Registry for ECT, which includes information on patient diagnoses, symptom severities, ECT indications and treatment characteristics, treatment course, side-effects, concomitant medications, and other data elements (140). Linkages with other registries, including birth registries, enabled the construction of retrospective cohorts that include perinatally depressed patients in two of the larger-scale studies included in this review (24, 30). Similarly, we anticipate that electronic medical records-linkage systems will become increasingly important data sources for future studies of mECT for perinatal depression, especially with the continued development of integrated networks between multiple healthcare institutions and linkages with additional sources of structured and unstructured data, such as vital records and clinical symptom measures (141).

There are several limitations for this review in addition to those outlined above. First, the results of this review are current only through 12/31/2024, when the literature search was conducted. Second, a specific definition of the perinatal period or perinatal onset was seldom provided in the reviewed reports, particularly for the postpartum. Third, even though treatment resistance was a specific indication for mECT in several reports, detailed information was often not available regarding the quality of therapeutic trials preceding ECT, including information on previously used therapeutic interventions, their respective doses or frequencies of use, previous treatment durations, or estimated levels of adherence. When information was provided about pre-ECT treatments, it was often unclear if they were utilized during the current episode of depression, making it difficult to define the levels of therapeutic resistance ECT was being administered for. Fourth, even a relatively brief acute series mECT involves a complex set of

interventions, co-interventions, and procedures that may each act as confounders or effect modifiers for questions related to its overall effectiveness or safety for perinatal depression. Regarding confounding, it was not possible to draw clear conclusions regarding causal links between ECT and several of the reported adverse events, as discussed earlier. Concerning effect modification, it was not possible to assess therapeutic or safety outcomes between subgroups defined by concomitant psychotropic or other types of medications, anesthetic agents, obstetric history, primary psychiatric diagnosis, psychiatric or general medical comorbidity, or ECT electrode placement, although controlled evidence has shown generally comparable response rates for ECT with BT, RUL, and BF lead placements in people with non-puerperal unipolar or bipolar depression (142–144). And finally, post-ECT follow-up periods were generally brief across the reviewed reports; thus, longer-term outcomes were unknown for most individual reports.

5 Conclusions

The current report presents an updated scoping review of the literature describing the broad effectiveness and key safety issues relevant to mECT for perinatal depression. Although registry studies have contributed meaningfully to our understanding of mECT effectiveness and safety in recent years, over 89% of the reviewed literature was still comprised of case reports and case series. No randomized trials were available for review. Although the maternal safety profile of mECT appears reassuring thus far, the available data are far from comprehensive. Fetal and neonatal safety risks are less-well-understood, and lactation information was often not included in reports of postpartum ECT. Therefore, many efficacy and safety questions remain, including for continuation or maintenance mECT and for important patient subgroups discussed in this review. Future reports of mECT for perinatal depression should focus on thoroughly describing treatment parameters, including frequencies of treatment sessions, initial doses and titration methods, and complete information on subsequent stimulation parameters (including changes), as has been recommended by others outside of the perinatal context (145).

Pragmatically, while mECT offers the prospect of rapid antidepressive benefit, patients with lower-acuity or less-impairing depression will not require–or even desire—a therapeutic procedure as intensive as mECT (146). For cases of perinatal depression with severe psychosis, catatonia (malignant and benzodiazepine-resistant catatonia, in particular), suicidality, other direct and serious threats to physical integrity (e.g., nutritional compromise, etc.), and marked treatment resistance, ECT is an indispensable therapeutic option that should not be withheld (11, 147). When these severe indications are absent, but ECT is still a therapeutic preference, the tilting of benefits over risks will usually be far less steep. In such cases, we recommend supportive, measured communication that considers the risks of untreated or undertreated depression, the possibility (though not a guarantee) of rapid benefit from mECT, a relatively reassuring maternal safety profile based on information to date, and potential fetal/neonatal risks–including from relatively rare but potentially severe complications such as prolonged seizures, prolonged uterine contractions, decreased uterine blood flow, and hypoxic damage —and precautions and strategies used to manage those risks. Given the high levels of acuity that are likely to be encountered in perinatally depressed patients being considered for mECT, the capacity for providing valid informed consent will require rigorous evaluation, including an assessment of patients' ability to consider both their own needs and risks as well as those of the fetus or infant (148). Whenever possible, the assessment of ECT suitability and risk stratification should be initially conducted and periodically reviewed by a multidisciplinary team including psychiatry, obstetrics, anesthesiology, and pediatrics.

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

WB: Writing – original draft, Formal analysis, Project administration, Conceptualization, Supervision, Investigation, Writing – review & editing. OM: Investigation, Writing – review & editing. CH: Writing – review & editing, Investigation. RR: Conceptualization, Writing – review & editing, Formal analysis, Writing – original draft. ES: Investigation, Writing – review & editing. AL: Writing – review & editing, Investigation. KM: Writing – review & editing, Investigation. HB: Conceptualization, Writing – review & editing, Investigation.

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Supplementary material

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Immune-inflammatory, neuroplastic, and epigenetic effects of electroconvulsive therapy in mood disorders: an overview of recent studies

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Background: Electroconvulsive therapy (ECT) remains an effective intervention for severe and treatment-resistant mood disorders, particularly major depressive disorder (MDD) and bipolar disorder (BD). While traditionally linked to neurotransmitter modulation, recent research suggests that ECT exerts broader biological effects. Currently, there is a necessity for identifying factors that could support a more accurate selection of individuals, predict their therapeutic response, and help investigate evidence of possible neuroplastic effects of this technique. In this setting, many studies have been published in the last few years, aiming to identify potential biomarkers by understanding immune-inflammatory, structural, and cellular mechanisms and their correlations with clinical outcomes post-ECT.

Methods: We searched PubMed, Embase, Scopus, Web of Science, PsycINFO, and Cochrane Library for studies published between 2020 and 2025. Studies were selected based on their relevance to inflammatory, immune, structural, and cellular mechanisms associated with ECT.

Results: Twenty-six studies were included. The main results reported post-ECT reductions in inflammatory markers, including C-reactive protein, interleukin-6, and tumor necrosis factor-alpha, or suggested a biphasic trajectory, with an initial transient immune activation preceding inflammatory partial resolution. Noteworthy differences were related to age, as younger patients showed more favorable immune adaptability in comparison with older individuals, who demonstrated elongated inflammatory activity. Neuroplastic changes following ECT were observed, including increased hippocampal neurogenesis, enhanced brain-derived neurotrophic factor expression, and structural changes in neuroimaging studies. Novel exploratory research on post-mortem analyses further confirmed the upregulation of neuroplasticity markers without evidence of sustained neuroinflammation. In addition, epigenetic mechanisms, particularly microRNA modulation following ECT, may induce long-term cellular reprogramming, potentially influencing treatment response. Moreover, one recent study suggested that elevated baseline levels of miR-223-3p may be a

predictor of ECT response among treatment-resistant depression patients. Finally, a recent study exploring mitochondrial adaptations found that the interactions between mitochondrial DNA copy number, oxidative stress, and ECT remain inconclusive.

Conclusion: Recent studies have expanded the understanding of ECT's neuroinflammation effects and beyond, adding data on its interactions with immune, neuroplastic, and genetic mechanisms in human samples. Although many gaps still exist, these findings pave the way for further research that may improve outcomes of treatment-resistant mood disorders.

KEYWORDS

electroconvulsive therapy, ECT, neuroinflammation, inflammation, neuroplasticity, genetics, epigenetics

Introduction

Electroconvulsive therapy (ECT) remains one of the most effective interventions for severe and treatment-resistant mood disorders, such as major depressive disorder (MDD) and bipolar disorder (BD) (1, 2). Meta-analytic data show that ECT achieves response and remission rates of 74.2% and 52.3% in MDD and 77.1% and 52.3% BD, respectively (3). While its clinical efficacy has been widely documented, the precise neurobiological mechanisms underlying ECT's therapeutic effects are still under investigation (3, 4). ECT is one of the least understood biological treatments in psychiatry. Historically, ECT was found to act primarily through the modulation of neurotransmitter systems, particularly serotonin, dopamine, and gamma-aminobutyric acid (GABA) (4, 5). However, evidence suggests that its effects extend beyond synaptic neurotransmission, involving immune-inflammatory pathways, neuroplasticity, and genetic/epigenetic modifications (4, 6–8).

Neuroinflammation has been increasingly implicated in mood disorders, with elevated pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) contributing to neuronal dysfunction and treatment resistance (9–11). ECT appears to modulate immune responses. However, research findings on this topic have been inconsistent, and many studies continue to explore how ECT influences inflammatory markers and clinical outcomes (12). Concomitantly, growing evidence suggests that ECT may support brain plasticity by increasing hippocampal volume, reshaping neural connections, and enhancing brain-derived neurotrophic factor (BDNF) expression (13). Recently, genetic and epigenetic changes, including DNA methylation shifts and altered microRNA expression, have been implicated in neural adaptation due to ECT modulation effects (8). Mitochondrial function has also been investigated in this setting, with studies linking ECT response to oxidative stress markers and mitochondrial DNA copy number (mtDNAcn) (12).

Understanding how ECT modulates immune-inflammatory pathways, neuroplasticity, and epigenetic processes is paramount to identifying biomarkers of response, improve patient selection, and guide the development of optimized neuromodulatory interventions. Despite recent advances, critical knowledge gaps persist. Thus, we performed this overview of recent findings of studies integrating ECT's inflammatory, immune, neuroplastic, and genetic effects among individuals with mood disorders.

Methods

We searched PubMed, Embase, Scopus, Web of Science, PsycINFO, and Cochrane Library databases to identify original studies published between January 2020 and April 2025 that investigated the effects of ECT on inflammatory, immune, genetic, and neuroplastic processes in mood disorders. The search strategy included terms and keywords related to "electroconvulsive therapy," "inflammation," "immune response," "neuroplasticity," "genetics," "epigenetics," "mood disorders", "depression", "depressive", and "bipolar disorder". In addition, we manually reviewed the references of all included articles and previous relevant reviews for additional studies.

Studies with human samples and correlating inflammatory parameters, molecular profiling, neuroimaging, post-mortem histopathology, or genetic markers were included. Eligible studies included participants diagnosed with major depressive disorder (MDD) or bipolar disorder (BD), as defined by standardized diagnostic criteria (e.g., DSM-IV, DSM-5, or ICD-10/11) (14–16). Biological measures encompassed inflammatory cytokines (e.g., IL-6, TNF-α, IL-1β, IL-10, CRP), hematological inflammatory indexes (e.g., NLR, PLR, SII), neurotrophic factors (e.g., BDNF), DNA methylation changes, microRNA expression, mtDNAcn, and post-mortem markers of neuroplasticity (e.g., DCX, STMN1) and glial activation (e.g., GFAP, Iba1), as well as structural neuroimaging biomarkers.

No restrictions regarding study design were applied; both observational and interventional studies were eligible. Preprint publications were excluded. Data extraction focused on sample characteristics, study design, primary findings, and clinical correlations. Key details of ECT protocols — including electrode placement, dosing strategies, pulse width, frequency, and total number of sessions — are summarized for each study in Tables 1–3.

Results

A total of 26 studies published between 2020 and 2025 were included, investigating the effects of ECT on immune, inflammatory, and cellular processes in patients with mood disorders (e.g., MDD and BD). Sample sizes varied widely, ranging from small pilot studies to large cohorts. The methodologies included longitudinal biomarker investigations, neuroimaging, molecular analyses, post-mortem histopathology, DNA/small RNA sequencing, and mtDNAcn assessments.

Inflammatory markers and antidepressant response

Studies focused on the impact of ECT on peripheral inflammatory markers, reporting reductions in systemic inflammation following treatment. In a prospective cohort study, Du et al. (2024) analyzed inflammatory biomarkers and depressive symptoms in 38 adolescents with severe MDD (median age [interquartile range]: 15 [14–16]; 81.6% female) compared to 29 healthy-controls (median age [interquartile range]: 15 [14.5–16.5]; 53.8% female). Baseline blood samples (e.g., interleukin-1 beta [IL-1β], interleukin-6 [IL-6], and interleukin-10 [IL-10]) were collected before treatment and after completing 6–8 ECT sessions spanning two weeks. The outcomes showed significant post-ECT decreases in IL-1β and IL-6, and an increase in IL-10. Interestingly, improvements in depressive symptoms (as assessed by the 17-item Hamilton Depression Rating Scale scores [HDRS]) were correlated with reductions in IL-1β ($r = -0.343$, $p = 0.035$) and in IL-6 ($r = -0.403$, $p = 0.012$), suggesting a link between anti-inflammatory and antidepressant effects of ECT in this population (17).

Mindt et al. (2020) examined CSF and plasma levels of 25 cytokines in 12 TRD patients (mean ± SD age: 59 ± 21.9; 58.3% female) undergoing ECT, focusing on central immune modulation. CSF levels of IL-6 and IL-1β showed negative correlations with the number of ECT sessions, suggesting progressive reductions over the treatment course. Moreover, patients who achieved remission exhibited reductions in CSF IL-17, MIP-1α, RANTES, and IL-2R, while IP-10 levels increased to a lesser extent compared to non-remitters. Such findings indicate that ECT may modulate central immune processes beyond peripheral inflammation (18). In addition, Kruse et al. (2020) analyzed serum levels of IL-6 and IL-8 in 40 patients with major depression (mean age ± SD: 41.8 ± 13.7; 55% female) treated with ECT. Their findings revealed sex-specific differences in inflammatory dynamics, with increases in IL-8 associated with symptom improvement in women but not in men. These results suggest that IL-8 may serve as a sex-dependent biomarker for ECT response and support further investigations of gender-specific immune signatures (19). In contrast, Ryan et al. (2022a) found no significant post-treatment changes in a panel of classic inflammatory cytokines. The authors examined plasma concentrations of CRP, IL-6, IL-10, TNF-α, and IL-1β in 86 patients with MDD (mean age ± SD: 55.1 ± 14.65; 61.63% female) and 57 healthy controls (mean age ± SD: 51 ± 12.7; 66.1% male). Although IL-6 and TNF-α were elevated at baseline in depressed individuals, these levels remained unchanged after ECT; no associations were found between cytokine concentrations and clinical or cognitive outcomes. IL-1β was undetectable in most samples. Taken together with other studies, these results illustrate the heterogeneity in ECT's effects on systemic inflammatory markers and depressive symptoms (20).

Inflammation and treatment response in late-life depression

Studies have specifically investigated the immunoinflammatory response to ECT in older adults, aiming to clarify its relationship with treatment efficacy in late-life depression (LLD). Carlier et al. (2021) conducted a prospective cohort study evaluating the inflammatory response to ECT in 99 older adults with depression (mean age ± SD: 72.8 ± 8.3; 66.7% female). Patients received right unilateral ECT with dose titration; non-responders were switched to bilateral ECT after six sessions. Across a median of 11 sessions, small reductions in CRP and IL-6 were observed, although these changes did not reach statistical significance after Bonferroni correction. IL-10 and TNF-α levels remained unchanged. Notably, higher baseline CRP were significantly higher among remitters. Clinically, 77.8% of patients responded (e.g., ≥50% MADRS score reduction), and 66.7% achieved full remission (MADRS < 10) (21).

In a complementary analysis of the same cohort, Loef et al. (2021) investigated how the balance between inflammatory activity and neuroplastic support might influence ECT outcomes. In addition to assessing serum IL-6, TNF-α, and BDNF levels, the authors calculated the IL-6/BDNF and TNF-α/BDNF ratios to represent the relative dominance of immune versus neuroplastic signaling. While no direct associations were found between individual biomarker levels and MADRS scores at any time point, a significant interaction effect was observed: the relationship between BDNF and depressive severity became more negative in the presence of elevated TNF-α levels ($p = 0.020$). Moreover, a higher TNF-α/BDNF ratio was significantly associated with greater symptomatic burden ($p = 0.007$), suggesting that imbalance skewed toward proinflammatory signaling may hinder neuroplastic recovery and ECT effectiveness. Thus, these combined results suggest that ECT outcomes in LLD may be influenced by post-treatment biomarker changes, pre-existing inflammatory burden, and interactions with neuroplastic features (22).

Inflammatory dynamics and cognitive adverse events

Other studies investigated the potential relationship between inflammatory responses and cognitive adverse events of ECT in depression treatment. Tian et al., 2021 conducted a prospective controlled study including 40 patients with first-episode, drug-naive MDD (mean age ± SD: 49.5 ± 7.32; 50% female) and 40 healthy controls matched for age, sex, and education (mean age ± SD: 48.3 ± 6.76; 55% female). Individuals underwent 12 sessions of modified ECT (three per week), initiated alongside a stable antidepressant regimen. Blood samples were collected before and after treatment to assess peripheral levels of NLRP3 inflammasome, interleukin-18 (IL-18), and nuclear factor kappa B (NF-κB). Results showed significant post-ECT increases in all three markers (NLRP3: $p < 0.01$; IL-18: $p < 0.05$; NF-κB: $p < 0.01$). Notably, 70% of the patients experienced cognitive impairment, defined as a score below 50 on the Wechsler Memory Scale–Revised. The elevation of inflammatory markers was significantly associated with lower cognitive scores, suggesting that inflammatory activation, particularly via NLRP3-related pathways, may contribute to cognitive adverse events observed in a subset of persons undergoing ECT (23).

Ryan et al. (2022b) further assessed 62 patients with depression (mean age ± SD: 56.84 ± 15.3; 66.1% female) undergoing bilateral ECT and analyzed neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and systemic immune-inflammation index (SII). While elevated PLR and SII correlated with lower HAMD-24 scores at baseline, higher NLR, PLR, and SII values were significantly associated with prolonged time to reorientation following ECT (24). Focusing on psychomotor aspects, Belge et al. (2021) investigated the relationship between IL-6 and depressive symptoms in a cohort of 62 participants undergoing ECT (mean age ± SD: 58.2 ± 14.8; 77.4% female). Following 8 to 12 bilateral sessions, serum IL-6 levels showed a modest yet statistically significant reduction (median from 0.74 to 0.65 pg/mL; $p = 0.02$). Notably, IL-6 changes correlated specifically with improvements in psychomotor retardation, as measured by a validated scale. Depressive symptoms also improved substantially, with HDRS-17 scores decreasing from 24.6 to 8.7 ($p < 0.0001$) (25).

Additionally, Carlier et al. (2021) examined whether baseline inflammatory markers were associated with cognitive outcomes in a cohort of 97 older adults with unipolar depression undergoing ECT (mean age ± SD: 73.1 ± 8.1; 67% female). Serum CRP, IL-6, IL-10, and TNF-α levels were measured prior to treatment, and Mini-Mental State Examination (MMSE) scores were assessed before, weekly during, and immediately after ECT. Higher baseline TNF-α and IL-10 were significantly associated with lower MMSE scores during treatment, while elevated baseline CRP predicted poorer cognitive performance immediately after ECT. These findings suggest that pre-existing inflammation may predispose older individuals to greater cognitive vulnerability during ECT (26).

Collectively, these studies indicate that peripheral inflammation may correlate with cognitive adverse events of ECT, particularly in older adults. While some markers reflect symptom improvement, others—such as TNF-α, IL-10, and inflammatory ratios—may signal greater cognitive vulnerability.

Hematological and systemic immune indices

In 2025, Kirlioglu Balcioglu et al. published a retrospective cohort study investigating the effects of ECT on inflammatory markers in a sample of 156 patients (mean ± SD age: 36.09 ± 13.99; 58.3% male) diagnosed with psychotic and mood disorders. Their results showed significant post-ECT decreases in CRP, CRP–albumin ratio, NLR, MLR, PLR, and cortisol-to-albumin ratio (CAR). Symptom improvement was also observed, with a reduction in the Brief Psychiatric Rating Scale (BPRS) score from 59.93 ± 10.95 pre-ECT to 21.98 ± 5.71 post-ECT ($p < 0.01$) and a Clinical Global Impression – Severity (CGI-S) score decrease from 6.04 ± 0.68 to 1.23 ± 0.52 ($p < 0.01$) (27).

Similarly, Ali et al. (2024) studied 72 BD patients (median age [range]: 30 [17-57]; 55.6% male) and found post-ECT shifts in complete blood count-derived inflammatory markers, such as platelet distribution width (PDW), which increased from 11.7 ± 2.2 pre-ECT to 12.7 ± 2.6 post-ECT ($p = 0.004$), and red cell distribution width (RDW), which decreased from 14.1 ± 1.1 to 13.6 ± 1.0 ($p < 0.001$). No significant differences were found in platelet count, mean platelet volume, and plateletcrit, showing that ECT did not impair platelet homeostasis despite the other observed hematological changes (28). Ryan et al. (2022b), as previously discussed, also explored whether pre-treatment hematological markers—specifically blood cell-derived ratios such as NLR, PLR, MLR, and the SII—could predict cognitive and mood outcomes following ECT. While no associations with mood improvement were observed, higher baseline values of NLR, PLR, and SII were significantly associated with delayed recovery of orientation (24).

Biphasic inflammatory responses and long-term immune activity

Some studies showed a biphasic trajectory of systemic inflammation following ECT. Hough et al. (2024) examined the levels of peripheral inflammatory markers in 40 patients with treatment-resistant depression (TRD) (mean ± SD age: 41.78 ± 13.73; 55% female) undergoing ECT, compared to 26 healthy controls (mean ± SD age: 40.50 ± 13.42; 65% female). Plasma inflammatory markers were evaluated at three time points: (T1) pre-treatment, (T2) post-second ECT session, and (T3) post-treatment. The study found a transient increase in CRP and IL-6 levels from T1 to T2, followed by a decline from T2 to T3. While IL-6 returned to baseline levels post-treatment, CRP remained elevated compared to pre-treatment values. Notably, no direct correlation was identified between general inflammatory changes and symptom improvement; however, a dynamic interaction between the early/acute inflammatory response and post-treatment inflammation compared to baseline correlated with clinical outcomes. While

there was no direct correlation between inflammatory changes and overall symptom reduction, larger early elevations in IL-6 at T2 were associated with more remarkable improvement in affective and cognitive symptoms among individuals with higher levels of IL-6 post-treatment (T3), while a trend to the opposite was observed in those with lower IL-6 levels after the intervention. A similar trend was observed between CRP levels trajectory and neurovegetative symptoms (29).

In 2025, Gaarden et al. conducted a longitudinal study including 64 elderly patients with treatment-resistant unipolar depression (mean ± SD age: 75.2 ± 6.3; 54.7% female) treated with ECT and 18 non-depressed controls (mean ± SD age: 78.1 ± 4.8; 66.7% female). Blood samples for analysis of 27 immune markers were collected from patients pre, mid, and post-treatment and at 12 weeks of follow-up; for controls, the markers were assessed through identical methods at baseline and at 8 weeks of follow-up. The analysis showed that 47% achieved clinical remission (as classified by a score < 8 on the 17-item HDRS). Although a significant decrease of 19 immune markers was observed from pre- to post-treatment in the patients' intra-group comparisons, higher concentrations of 23 immune markers were observed among patients compared to controls at the follow-up. Moreover, there were no differences in immune markers concentrations between responder and non-responder patients. These results raised questions about whether prolonged inflammatory activity in older populations might influence long-term treatment efficacy or relapse risk (30).

The main characteristics of the studies evaluating peripheral inflammatory and hematological biomarkers in relation to ECT outcomes are shown in Table 1.

Neuroplasticity, neuroimmune processes, and post-mortem findings

Beyond the ECT's impact on inflammation, Han et al., in 2023, also added evidence of neuroplasticity in a prospective cohort study including severe MDD patients divided into 102 ECT-treated (mean ± SD age: 46.3 ± 11.2; 56.86% male) and 102 non-ECT treated (mean ± SD age: 45.8 ± 10.9; 58.82% male). The primary outcome was the change in HDRS scores from baseline to 12 weeks. Both groups showed significant symptom improvement, whereas the reduction in HDRS scores was significantly greater in the ECT group (-19.6 ± 6.4) compared to the non-ECT group (-14.2 ± 7.2, $p < 0.001$). Moreover, 68% of the ECT-treated patients achieved remission (HDRS ≤ 7) compared to 42% in the non-ECT group. Biomarker analysis revealed that BDNF levels decreased in both groups; however, the decline was significantly attenuated in the ECT group (-12.8 ± 4.6 vs. -18.6 ± 5.8, $p < 0.001$), suggesting a neuroprotective effect. Similarly, IL-6 increased in both groups, although with a less pronounced rise in the ECT group (+2.2 ± 0.9 vs. +3.4 ± 1.2, $p < 0.001$). No significant differences were found in cortisol levels between the groups. In addition, quality of life (as assessed by the WHO Quality of Life Brief Version) and cognitive function (evaluated by the Montreal Cognitive Assessment)

TABLE 1 Main features of studies evaluating peripheral inflammatory and hematological biomarkers in the context of ECT response, cognitive adverse events, and symptom clusters.

Study, year	Sample	Study Design	ECT Protocol	Biomarkers Assessed	Key Findings	Clinical Outcomes	Conclusions & Implications
Du et al., 2024 (17)	38 adolescents with severe MDD (median age 15; 81.6% female); 29 healthy-controls (median age 15; 53.8% female)	Prospective cohort study	Bilateral ECT, Thymatron DGx, 6–8 sessions over two weeks	IL-1β, IL-6, IL-10	Post-ECT: IL-1β ↓, IL-6 ↓, IL-10 ↑; IL-1β and IL-6 reductions correlated with HDRS ↓	Significant reduction in HDRS scores post-ECT; IL-1β and IL-6 decreases correlated with symptom improvement.	ECT exerts anti-inflammatory effects in adolescents with severe MDD, potentially contributing to its antidepressant mechanism. Inflammatory marker shifts may serve as predictors of treatment response.
Mindt et al., 2020 (18)	12 patients with TRD (mean age 59.0; 58.3% female)	Prospective cohort study	Right unilateral ECT (Thymatron IV), 2–3x/week, mean of 10.6 ± 5.0 sessions; ketamine anesthesia	25 cytokines (including IL-1β, IL-6, IL-8, IL-17, IL-2R, RANTES, IP-10, MIP-1α, etc.) in CSF and serum	Post-ECT: CSF IL-5 ↑, IL-8 ↑, IP-10 ↑; IL-6 ↓ and IL-1β ↓ correlated with number of sessions; responders/remitters showed IL-17 ↓, MIP-1α ↓, RANTES ↓, IL-2R ↓; IP-10 ↑ was attenuated in remitters.	Significant HDRS reduction (mean from 29.9 to 9.0; $p < 0.001$); 83.3% responded, 41.7% remitted.	ECT alters CNS immune activation; reduction in CSF inflammatory cytokines is associated with antidepressant response. Findings support ECT's impact on central (not only peripheral) inflammation.
Kruse et al., 2020 (19)	40 TRD patients (mean age 41.8; 55% female)	Prospective observational study	Right unilateral ultra-brief pulse ECT (5–6x seizure threshold), switching to bilateral if needed; mean 11.8 sessions	IL-8 (primary), IL-6, IL-10, TNF-α, CRP	Baseline IL-8 ↓ predicted response in females; IL-8 ↑ post-ECT correlated with HAM-D ↓ in females ($\beta = -0.458$; $p = 0.03$); no associations in males; no significant effects for IL-6, IL-10, TNF-α, or CRP.	50% response rate (≥50% HAM-D reduction); no remission data reported.	IL-8 may serve as a sex-specific biomarker of ECT response in females with TRD. Highlights the importance of considering sex-specific neuroinflammatory mechanisms in depression treatment personalization.

(*Continued*)

TABLE 1 Continued

Study, year	Sample	Study Design	ECT Protocol	Biomarkers Assessed	Key Findings	Clinical Outcomes	Conclusions & Implications
Ryan et al., 2022a (20)	86 patients with depression (mean age: 55.1; 61.6% female); 57 healthy controls (mean age: 51; 66.1% male)	Prospective case–control	Bilateral ECT, twice weekly; average of 8 sessions	Plasma CRP, IL-6, IL-10, and TNF-α	Baseline: IL-6 and TNF-α ↑ in patients vs. controls; No significant changes post-ECT.	Significant HAM-D24 score improvement. No correlations between inflammatory markers and cognitive outcomes.	Systemic inflammatory markers did not mediate ECT effects on mood or cognition.
Carlier et al., 2021a (21)	99 older adults with depression (mean age: 72.8; 66.7% female)	Prospective cohort study	Right unilateral ECT with titrated dosing; switch to bilateral after 6 sessions if no response; 2 sessions/week; median of 11 sessions (range 5–18)	Serum CRP, IL-6, IL-10, TNF-α	Post-ECT: CRP ↓ (d = −0.29), IL-6 ↓ (d = −0.13); IL-10 and TNF-α unchanged; higher baseline CRP predicted remission.	66.7% achieved remission (MADRS <10); 77.8% responded (≥50% MADRS reduction).	ECT did not significantly reduce inflammatory markers overall; higher pre-treatment inflammation (e.g., CRP) may predict better clinical response.
Loef et al., 2021 (22)	99 older adults with severe LLD (mean age: 72.8; 66.7% female)	Naturalistic longitudinal study	Right unilateral ECT (Thymatron System IV); switch to bilateral after 6 sessions if no response; 2 sessions/week; mean of 11.8 ± 5.53 sessions	Serum IL-6, TNF-α, BDNF; calculated IL-6/BDNF and TNF-α/BDNF ratios	Post-ECT: TNF-α/BDNF ratio ↑ associated with greater depression severity; higher TNF-α amplified the negative correlation between BDNF and MADRS; IL-6, TNF-α, and BDNF alone not associated.	Significant reduction in MADRS score: 33.6 → 9.6 (T0→T2) post-treatment; 83.9% responded, 71.1% remitted.	The interaction between TNF-α and BDNF may be implicated in the LLD pathophysiology and ECT response; BDNF effects are moderated by TNF-α levels.
Tian et al., 2021 (23)	40 patients with MDD (First-episode, drug-free, mean age 49.45; 50% males); 40 healthy controls (mean age 48.31; 55% female, and education matched	Cross-sectional case–control study	MECT, 12 sessions, 3/week; initiated with stable-dose antidepressants	NLRP3 inflammasome, IL-18, NF-κB	Baseline: NLRP3 ↑, IL-18 ↑, NF-κB ↑ in patients vs. controls; Post-MECT: further ↑ in all markers in MDD group only.	70% showed cognitive impairment (WMS-R score < 50) after MECT; this group showed significantly higher post-ECT levels of NLRP3, IL-18, and NF-κB compared to cognitively preserved participants ($p < 0.05$).	Inflammatory cytokines, such as NLRP3, IL-18, and NF-κB, may predict cognitive impairment risk after MECT. Elevated levels were significantly correlated with worse cognitive performance.
Ryan et al., 2022b (24)	62 patients with depression (mean age: 56.8; 66.1% female)	Prospective observational study	Bilateral ECT (frequency not specified); mean 7.6 sessions.	NLR, PLR, MLR, SII (pre-ECT)	Baseline: PLR and SII inversely correlated with depression severity; higher NLR, PLR, and SII predicted longer time to reorientation post-ECT.	Patients experienced variable disorientation post-ECT, with longer time to reorientation associated with higher baseline NLR, PLR, and SII; Depression outcome not reported.	Greater peripheral inflammatory burden may predict longer disorientation time post-ECT; suggests link between systemic inflammation and acute cognitive adverse events.
Belge et al, 2021 (25)	62 patients with major depressive episodes (mean age = 58.2; 77.4% female)	Prospective longitudinal study	Right unilateral brief-pulse ECT, 2 sessions/week; switched to bilateral if no response or faster effect needed; mean 11 sessions (range 2–27).	Serum IL-6	Post-ECT: IL-6; ↓ correlated with psychomotor improvement.	HDRS-17 decreased (24.6 → 8.7, $p < 0.0001$) post-treatment; psychomotor symptoms improved; IL-6 decrease correlated with psychomotor retardation improvement.	ECT-related improvement in psychomotor retardation may be associated with IL-6 decrease, supporting the role of inflammation in motor symptom improvement.
Carlier et al., 2021b (26)	97 older adults with unipolar depression (mean age: 73.1; 67% female)	Prospective cohort study	Right unilateral ECT with dose titration; bilateral after 6 sessions if non-response; median 11 sessions	CRP, IL-6, IL-10, TNF-α (baseline only)	Higher baseline TNF-α and IL-10 were associated with lower MMSE scores during treatment. Elevated baseline CRP predicted poorer post-ECT MMSE performance.	Cognitive performance affected during the ECT course, particularly among those with higher baseline levels of TNF-α and IL-10. Elevated baseline CRP was associated with lower MMSE scores post-ECT. IL-6 showed no significant associations.	Baseline inflammation markers may predict cognitive vulnerability to ECT in older adults.

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TABLE 1 Continued

Study, year	Sample	Study Design	ECT Protocol	Biomarkers Assessed	Key Findings	Clinical Outcomes	Conclusions & Implications
Kirlioglu Balcioglu et al., 2025 (27)	156 patients with psychotic and mood disorders (mean age 36.09; 58.3% male)	Retrospective cohort study	Bilateral ECT, Thymatron System IV, 2–3 sessions/ week, avg. 8.53 ± 2.05 sessions	CRP, CRP-albumin ratio, NLR, MLR, PLR, CAR	Post-ECT: CRP ↓, NLR ↓, MLR ↓, PLR ↓, CAR ↓	Significant reductions in BPRS and CGI-S.	ECT reduces systemic inflammation but improvements do not directly correlate with symptom reduction; suggests multiple independent therapeutic mechanisms.
Ali et al., 2024 (28)	72 BD patients (median age 30; 55.6% male)	Prospective cohort study	Bitemporal brief-pulse ECT, 3 sessions/week; total of 4 sessions over 10 days	RDW, PDW (hematological inflammatory markers)	Post-ECT: PDW ↑ (platelet activation), RDW ↓ (reduced systemic inflammation)	Clinical improvement observed; No significant differences in platelet count, mean platelet volume, or plateletcrit.	ECT appears to modulate systemic inflammation via hematological pathways, particularly platelet-related immune activity; findings suggest potential for immune-targeted adjunctive therapies in BD.
Hough et al., 2024 (29)	40 TRD patients (mean age 41.78; 55% female); 26 healthy controls (mean age 40.50; 65% female)	Longitudinal observational study	Predominantly right unilateral ultrabrief pulse ECT (5x seizure threshold), switched to bilateral if needed; mean 11.5 sessions (range 6–22)	CRP, IL-6, TNF-α	Biphasic inflammatory trajectory post-ECT: IL-6 and CRP ↑ (T1→T2); IL-6 ↓ to baseline levels at T3, CRP remained ↑ at T3.	IL-6 early elevations (T2) were linked to greater affective/cognitive improvement if IL-6 remained high at T3; the opposite was observed in those with lower IL-6 at T3. Similar trend seen with CRP and neurovegetative symptoms.	ECT induces an early immune activation phase followed by partial resolution. Persistently elevated CRP post-treatment suggests that long-term immune modulation remains incomplete, highlighting the need for adjunctive anti-inflammatory approaches.
Gaarden et al., 2025 (30)	64 elderly TR-MDD patients (mean age 75.2; 54.7% female); 18 non-depressed controls (mean age 78.1; 66.7% female)	Longitudinal exploratory study	Bilateral/unilateral ECT, avg. 9 sessions, 2 per week	27 immune markers (TNF, IFN-γ, PDGF-BB, IL-6, etc.)	Post-ECT: 19 immune markers ↓; 23 markers remained ↑ in patients vs. controls at follow-up.	47% remission rate (HDRS-17 <8); no significant difference in inflammation between responders and non-responders.	Persistent pro-inflammatory trait in elderly post-ECT suggests chronic low-grade inflammation in TR-MDD patients.

ECT, Electroconvulsive Therapy; MDD, Major Depressive Disorder; TRD, Treatment-Resistant Depression; TR-MDD, Treatment-Resistant Major Depressive Disorder; LLD, Late-Life Depression; BD, Bipolar Disorder; HDRS, Hamilton Depression Rating Scale; MADRS, Montgomery-Åsberg Depression Rating Scale; BPRS, Brief Psychiatric Rating Scale; CGI-S, Clinical Global Impression, Severity Scale; IL-1β, Interleukin-1 Beta; IL-2R, Interleukin-2 Receptor; IL-4, Interleukin-4; IL-5, Interleukin-5; IL-6, Interleukin-6; IL-8, Interleukin-8; IL-10, Interleukin-10; IL-17, Interleukin-17; IL-18, Interleukin-18; TNF-α, Tumor Necrosis Factor Alpha; CRP, C-Reactive Protein; CRP-albumin ratio, C-Reactive Protein to Albumin Ratio; CAR, Cortisol-to-Albumin Ratio; NLR, Neutrophil-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; RDW, Red Cell Distribution Width; PDW, Platelet Distribution Width; SII, Systemic Immune-Inflammation Index; NF-κB, Nuclear Factor Kappa B; NLRP3, NLR Family Pyrin Domain Containing 3 Inflammasome; RANTES, Regulated on Activation, Normal T Cell Expressed and Secreted; IP-10, Interferon Gamma-Induced Protein 10; MIP-1α, Macrophage Inflammatory Protein 1-alpha; IFN-γ, Interferon Gamma; PDGF-BB, Platelet-Derived Growth Factor Subunit B; HMGB1, High Mobility Group Box-1 Protein; sRAGE, Soluble Receptor for Advanced Glycation End Products; BDNF, Brain-Derived Neurotrophic Factor; CSF, Cerebrospinal Fluid; CNS, Central Nervous System; WMS-R, Wechsler Memory Scale–Revised; MMSE, Mini-Mental State Examination.
↑ = increased levels or expression; ↓ = decreased levels or expression.

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improved more significantly in the ECT group. The findings of this study suggested that ECT led to significant symptomatic improvement and may influence neuroplasticity and inflammation in severe MDD (31).

Several studies explored neuroimmune interactions and cellular changes associated with ECT. Xu et al. (2023) investigated astrocytic markers and inflammatory cytokines in 40 TRD patients (mean ± SD age: 22.2 ± 4.5; 60% female) undergoing ECT and 35 healthy controls (mean ± SD age: 23.1 ± 3.9; 65.7% female). Pre-ECT, levels of glial fibrillary acidic protein (GFAP), S100 calcium-binding protein B (S100β), CD81, IL-1β, IL-4, IL-6, IL-10, IL-17, tumor necrosis factor-alpha (TNF-α), and inflammatory markers interferon γ (IFN-γ) were significantly higher in TRD patients than in controls. These elevations were positively correlated with cognitive dysfunction ($r = 0.62$, $p < 0.001$). Following ECT, there were significant decreases of GFAP, S100β, CD81, as well as IL-4 and IFN-γ in the TRD group compared to controls. Alongside these changes, patients showed significant improvement in all subscales of the Montgomery-Åsberg Depression Rating Scale (MADRS). Furthermore, the IL-4 decrease correlated with reductions in the MADRS vegetative subscale scores. This study added that ECT may also exert anti-inflammatory effects through astrocytic activity modulation in depressed individuals (32).

Abe et al. (2023) investigated the role of high mobility group box-1 protein (HMGB1) and soluble receptor for advanced glycation end-products (sRAGE) in the context of ECT, analyzing 25 MDD patients (median age [range]: 54.2 [48–63]; 56% female) and 25 healthy controls (median age [range]: 53.2 [47–61]; 56% female). HMGB1 is a damage-associated molecular pattern protein involved in neuroinflammation, blood-brain barrier dysfunction, and immune activation, while sRAGE functions as a decoy receptor that neutralizes pro-inflammatory HMGB1 signaling. Given prior evidence linking elevated HMGB1 to depression and stress-related neuroimmune dysregulation, it was hypothesized that ECT might exert therapeutic effects by downregulating HMGB1-mediated inflammatory pathways or modulating sRAGE expression. Surprisingly, however, no significant differences in HMGB1 or sRAGE levels at baseline were found between MDD patients and healthy controls. While ECT led to symptoms improvement (as assessed by the 21-item HDRS), it did not induce any significant post-treatment changes (HMGB1: $p = 0.677$; sRAGE: $p = 0.922$) (33).

A study by Brooks et al. (2024) assessed inflammation patterns, neuroimaging data, and its correlations with depressive symptoms in 20 TRD patients (mean ± SD age: 42.5 ± 13.7; 50% female) undergoing ECT. Magnetic resonance imaging (MRI) and inflammation markers (e.g., IL-6, IL-8, and TNF- α) from blood samples were obtained after an index ECT and six months after. MRI was evaluated with voxel-based morphometry. The results showed a correlation between IL-8 decrease and depression symptoms improvement, as evaluated by the 17-item HDRS ($r = 0.65$; $p = 0.01$). However, despite this correlation, inflammatory changes did not directly mediate neuroimaging structural changes and depressive symptoms. Four clusters of gray matter volume significant reductions were found; one cluster, including Brodmann's area 22 and right insula, correlated with higher severity of symptoms in HAM-D over six months. The author discussed that such structural changes may not necessarily be a sign of neurotoxicity but part of a dynamic neuroadaptive process (34).

In another study exploring possible correlations between neuroinflammation and structural brain changes following neuromodulation, Andreou et al. (2022) investigated 42 TRD patients (mean age ± SD: 43.15 ± 13.82; 54.8% female) undergoing ECT (right unilateral ultra-brief pulse stimulus; 3 sessions/week; ~30% transitioned to bilateral). Pre- and post-treatment serum levels of IL-6, IL-8, TNF-α, and CRP were measured alongside diffusion-weighted MRI to assess free-water corrected fractional anisotropy (FAt) in 17 white matter tracts. Among responders (≥50% MADRS reduction), changes in IL-8 significantly correlated with FAt alterations in the right cingulum and superior longitudinal fasciculus ($r = 0.65–0.70$), suggesting a role for IL-8 in glia-mediated white matter remodeling. These neuroimmune associations were absent in non-responders, reinforcing the hypothesis that inflammatory signaling may support therapeutic plasticity induced by ECT (35).

Furthermore, post-mortem histopathological analyses contributed to elucidating the neurobiological effects of ECT. In 2023, Loef et al. published a first explorative study assessing direct histopathological evidence of ECT-induced neuroplasticity in human post-mortem brain tissue, examining hippocampal samples from 12 patients with bipolar or unipolar depression (mean ± SD age: 54.25 ± 21.85; 58.3% male) who had received ECT within the five years preceding death, compared to 10 depressed donor patients who were not treated with ECT (mean ± SD age: 66.9 ± 13.47; 60% female), and 15 healthy control donors (mean ± SD age: 68.87 ± 16.02; 53.3% female). In subjects previously treated with ECT, the analyses showed a significantly higher proportion of cells positive for doublecortin (DCX) in the hippocampal CA4 area (compared to healthy control donors) and subgranular zone (compared to both non-ECT depressed patients and healthy controls donors). DCX is a marker for the presence of young neurons and cellular plasticity. In addition, a higher percentage of positive stathmin 1 cell (STMN1), another marker for neuroplasticity, was found in the hippocampal subgranular zone of ECT-treated subjects compared with non-ECT depressed patients and healthy control donors. Notably, there were no evident differences in inflammatory markers reflecting microglial or astrocytic activity, as well as in structural changes (e.g., major hippocampal cell loss, overt cytoarchitectural changes) among the three groups. Based on these results, the authors discussed that ECT may enhance hippocampal neurogenesis without promoting chronic inflammatory responses or gliosis (36).

The main characteristics of studies investigating neuroplastic and structural brain changes in relation to ECT in mood disorders are shown in Table 2.

TABLE 2 Main features of studies evaluating neuroplasticity, neuroimmune processes, and brain changes related to ECT in mood disorders.

Study, year	Sample	Study Design	ECT Protocol	Biomarkers Assessed	Key Findings	Clinical Outcomes	Conclusions & Implications
Han et al., 2023 (31)	204 severe MDD patients (102 ECT-treated: mean age 46.3; 56.86% male 102 non-ECT: mean age 45.8; 58.82% male)	Prospective cohort study	Bilateral ECT, 3 sessions/week, up to 12 sessions	IL-6, BDNF, Cortisol	In ECT patients post-treatment: IL-6 ↑ (less than in non-ECT group); BDNF ↓ in both groups but better preserved in ECT; Cortisol unchanged.	ECT group showed greater depression symptom relief, improved QoL and cognition, with 68% achieving remission vs. 42% in the non-ECT group.	ECT may attenuate excessive inflammatory responses in MDD but does not fully normalize IL-6 levels; findings support ECT's role in neuroplasticity; relative BDNF preservation post-ECT.
Xu et al., 2023 (32)	40 TRD patients (mean age 22.2; 60% female); 35 healthy controls (mean age 23.1; 65.7% female)	Prospective cohort study	Modified bifrontal ECT, Thymatron IV; 3 sessions/week until remission (HAMD ≤7); mean duration 14.6 ± 5.8 days	GFAP, S100β, CD81, IL-1β, IL-4, IL-6, IL-10, IL-17A, TNF-α, IFN-γ	Post-ECT: significant ↓ in GFAP, S100β, CD81, IFN-γ, and IL-4; suggesting astrocytic deactivation and immune modulation. IL-4 ↓ correlated with MADRS vegetative symptom improvement.	Significant reduction in MADRS total score, with improvement across all symptom subscales; higher baseline astrocyte/ inflammatory markers correlated with greater symptom severity and cognitive dysfunction.	ECT reduces astrocyte activation and neuroinflammation, potentially contributing to therapeutic efficacy in TRD; findings support targeting glial and immune mechanisms in future interventions.
Abe et al., 2023 (33)	25 MDD patients (median age 54.2; 56% female); 25 healthy controls (median age 53.2; 56% female)	Prospective cohort study	Bilateral ECT, Thymatron System IV, avg. 10.5 sessions	HMGB1, sRAGE	HMGB1 and sRAGE: no difference at baseline (MDD vs. controls); no post-ECT change in either marker.	Significant reduction in HDRS scores post-ECT; No correlation between inflammatory markers and symptom improvement.	Findings challenge the hypothesis that HMGB1 and sRAGE play a role in the inflammatory response to ECT. Suggests a more complex relationship between these markers and depression pathophysiology.
Brooks et al., 2024 (34)	20 TRD patients (mean age 42.5; 50% female)	Longitudinal observational study	Predominantly right unilateral ultra-brief pulse ECT (6x seizure threshold); switched to bilateral brief-pulse (2x ST) if no response after 10 sessions; mean 11.1 sessions (range 6–16), 3 sessions/week	L-6, IL-8, TNF-α, MRI (voxel-based morphometry)	Post-ECT IL-8 ↓ correlated with symptom improvement; GM volume ↓ in 4 clusters (incl. right insula & Brodmann's area 22), one associated with depression severity at 6 months.	No direct mediation between inflammatory changes and neuroimaging structural alterations.	Structural changes post-ECT may represent neuroadaptive processes rather than neurotoxicity; highlights the need for long-term studies on brain plasticity in ECT-treated TRD patients.
Andreou et al., 2022 (35)	42 patients with TRD (mean age: 43.15; 54.8% female)	Longitudinal cohort study	Right unilateral ultrabrief pulse ECT, 3 sessions/week; ~30% transitioned to bilateral; average 10.88 sessions	Serum IL-6, IL-8, TNF-α, CRP; diffusion-weighted DWI MRI assessing free-water corrected fractional anisotropy (FAt) in 17 white matter tracts	Baseline: IL-8 ↑ in patients vs. controls; Post-ECT: IL-8 change correlated with FAt changes in right cingulum and SLF (responders only).	Only responders showed neuroimmune coupling between IL-8 and FAt in the right cingulum and SLF; absent in non-responders.	ECT may promote glia-mediated white matter remodeling via IL-8 signaling in responders. Findings suggest neuroimmune modulation as a mechanistic component of ECT in TRD.
Loef et al., 2023 (36)	12 ECT-treated depressed patients (mean age 54.25); 10 non-ECT depressed patients (mean age 66.9); 15 healthy controls (mean age 68.87)	Post-mortem histopathological study	ECT-treated patients received right unilateral and/or bilateral ECT within 5 years prior to death. Detailed parameters (number of sessions, frequency, stimulus intensity) not reported.	DCX, STMN1 (neuroplasticity markers), GFAP, Iba1 (astrocytic/ microglial markers)	Post-ECT: ↑ DCX+ cells in CA4 (vs. controls) & SGZ (vs. non-ECT & controls); ↑ STMN1+ in SGZ (ECT group); no microglial/ astrocytic activation or cytoarchitectural damage.	Neuroplasticity markers suggest an ECT-induced increase in neuronal differentiation, which may contribute to long-term symptom improvement in mood disorders.	ECT enhances hippocampal neurogenesis without triggering chronic inflammation or gliosis, reinforcing its effect in neuroplasticity and potentially sustaining its antidepressant effects.

ECT – Electroconvulsive Therapy; MDD – Major Depressive Disorder; TRD – Treatment-Resistant Depression; QoL – Quality of Life; HDRS – Hamilton Depression Rating Scale; MADRS – Montgomery-Åsberg Depression Rating Scale; IL-1β – Interleukin-1 Beta; IL-4 – Interleukin-4; IL-6 – Interleukin-6; IL-8 – Interleukin-8; IL-10 – Interleukin-10; IL-17A – Interleukin-17A; TNF-α – Tumor Necrosis Factor Alpha; IFN-γ – Interferon Gamma; CRP – C-Reactive Protein; BDNF – Brain-Derived Neurotrophic Factor; GFAP – Glial Fibrillary Acidic Protein; S100β – S100 Calcium-Binding Protein B; CD81 – Cluster of Differentiation 81; STMN1 – Stathmin 1; DCX – Doublecortin; Iba1 – Ionized Calcium-Binding Adapter Molecule 1; MRI – Magnetic Resonance Imaging; DWI – Diffusion-Weighted Imaging; FAt – Free-Water Corrected Fractional Anisotropy; GM – Gray Matter; SLF – Superior Longitudinal Fasciculus; SGZ – Subgranular Zone; CA4 – Cornu Ammonis Area 4 (hippocampal subregion).
↑ = increased levels or expression; ↓ = decreased levels or expression.

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Molecular, epigenetic, and mitochondrial function modifications

Adding novelty to the field, molecular and epigenetic analyses investigated ECT-induced changes. In 2024, Carvalho Silva et al. published an epigenome-wide longitudinal study investigating DNA methylation in 32 TRD patients (mean ± SD age: 56.9 ± 14.3; 68.7% female) undergoing ECT. Clinical severity (evaluated with the MADRS) and ECT outcomes were assessed at baseline (T0) and 1 month after intervention (T1); genome-wide methylation was analyzed at T0 and T1. Analyses showed three differentially methylated probes (DMPs), with two annotated in genes CYB5B and PVRL4; nonetheless, these probes were not significant after false discovery rate (FDR) correction. In a covariate analysis including changes in clinical symptoms (as assessed by the MADRS), four DMPs were found annotated in the genes FAM20C, EPB41, OTUB1, and ADARBI1. Considering response status as a covariate to the model, three DMPs were detected, with two annotated in the genes IQCE and FAM20C. However, none of these probes remained significant after the FDR correction. Similarly, fifty-four differentially methylated regions (DMRs) were found, alongside the identification of 21 DMRs for symptoms variations and 26 DMRs for response status. Again, none of these regions remained significant after the FDR correction (37). In contrast to genome-wide approach, Moschny et al. (2020) analyzed DNA methylation patterns of tissue-type plasminogen activator (t-PA; gene: PLAT) and its inhibitor PAI-1 (SERPINE1) in sorted immune cells (B cells, T cells, monocytes, and NK cells), as well as in whole blood, from 87 TRD participants undergoing ECT (mean ± SD age: 51.9 ± 16.6; 51.7% female). Although significant variability in methylation across immune cell types was observed, no consistent differences in PLAT or SERPINE1 methylation were found between remitters and non-remitters. Clinical response (≥50% MADRS reduction) was achieved in 33 patients; however, methylation profiles were not associated with symptom improvement (38).

Maier et al. (2023) conducted a prospective observational study to examine the effects of ECT on DNA methylation in genes related to hypothalamic–pituitary–adrenal (HPA) axis regulation. The study included 31 patients with MDD (mean ± SD age: 55 ± 16; 64.5% female), alongside 19 unmedicated depressed controls and 20 healthy controls. All patients underwent right unilateral ECT (3 sessions/week; average of 10 ± 4 sessions) using the Thymatron IV system. Peripheral blood mononuclear cells (PBMCs) were collected to assess methylation patterns of NR3C1 (encoding the glucocorticoid receptor) and POMC. Results showed that NR3C1 methylation was significantly higher in ECT non-responders compared to responders at baseline; however, it decreased in both groups after treatment. In contrast, POMC methylation decreased in responders but increased in non-responders by the end of the ECT course. These findings suggest that ECT may induce short-term epigenetic modifications in stress-related genes and that NR3C1 methylation, in particular, could serve as a candidate biomarker for treatment response prediction (39).

Beyond methylation, new studies on small RNA sequencing have provided further insights into the molecular underpinnings of ECT response. In 2023, Kaurani et al. analyzed whole-blood miRNA profiles obtained from 64 patients with treatment-resistant MDD (mean ± SD age: 55.9 ± 16; 59.38% female) at three different times (e.g., before, after the first, and after the last ECT). Clinically, patients were assessed by the MADRS. The main outcome showed that miR-223-3p was down-regulated at baseline among responder subjects (e.g., 62.5% individuals with a reduction of ≥50% in MADRS total score) in comparison to non-responders. A ROC analysis showed that miR-223-3p distinguished these two groups with an area under curve of 0.76 (95% CI = 0.6–0.91; p = 0.0031), supporting its potential as a predictive biomarker. In addition, a negative correlation was observed between miR-223-3p expression and percentage changes in MADRS (r = -0.32; p = 0.04). This finding leads to an understanding that low miR-223-3p expression at baseline correlates with higher severity of depressive symptoms and that its higher post-treatment expression is associated with symptoms improvement. The results of this study also showed higher expressions of proinflammatory markers (NLRP3, IL-6, IL-1B, and TNF-α) at baseline in responders compared to non-responders, again underscoring the potential of ECT for inflammatory modulation (40). Similarly, Galbiati et al. (2025) performed miRNA analyses in 27 TRD individuals (mean ± SD age: 58.1 ± 11.2; 67% female) treated with ECT. Blood samples were obtained at baseline (T0) and 1 month after the last ECT session (T1); depression symptoms were assessed by the MADRS. Their outcomes showed that eight microRNAs were downregulated after ECT. Symptoms improvement among responders (18 out of 27 subjects) directly correlated with changes in miR-30c-5p (r = 0.616; p = 0.006) and miR-324-3p (r = 0.473; p = 0.048) levels between T0 and T1. In the whole sample (e.g., responders and non-responders), only miR-324-3p correlated with depressive symptoms relief (r = 0.460, p = 0.016) (41).

Moreover, mitochondrial function was investigated by Ryan et al. (2023) in a study including 100 individuals with depression (mean ± SD age: 56.36 ± 14.28; 62% female) treated with ECT and 89 healthy controls (mean age 53.42 ± 10.39; 66.29% female). Blood samples were obtained to measure mtDNAcn levels. Assessed outcomes were the depression severity, ECT response, telomere length, and inflammatory markers. The analyses showed significantly elevated mtDNAcn in depressed individuals compared to controls, even after adjustments for potential confounding factors. However, higher baseline mtDNAcn levels were insufficient as a biomarker for ECT outcome prediction, as no significant differences were observed between remitters and non-remitters or responders and non-responders. Alongside this finding, mtDNAcn was not associated with inflammatory markers levels, intensity of depression symptoms, or telomere length (42).

The main characteristics of studies investigating genetic, epigenetic, microRNA, and mitochondrial biomarkers in the context of ECT in mood disorders are shown in Table 3.

TABLE 3 Main features of studies on genetic, epigenetic, microRNA, and mitochondrial biomarkers after ECT in mood disorders.

Study, year	Sample	Study Design	ECT Protocol	Biomarkers Assessed	Key Findings	Clinical Outcomes	Conclusions & Implications
Carvalho Silva et al., 2024 (37)	32 TRD patients (mean age 56.9; 68.7% female)	Prospective longitudinal study	Bilateral brief-pulse ECT (Thymatron DG), 3 sessions/week; mean 7.4 ± 2.2 sessions; completed based on clinical judgment	DNA methylation changes, epigenetic markers	54 DMRs and 3 DMPs identified post-ECT; none remained significant after FDR correction.	No direct correlation between epigenetic changes and symptom severity.	ECT modulates epigenetic markers; however, findings did not reach statistical significance after correction; results highlight the need for further studies on epigenetic biomarkers predicting treatment response.
Moschny et al., 2020 (38)	87 patients with TRD (59 in cross-sectional, 28 in longitudinal cohort; mean age 51.9; 51.7% female)	Prospective observational study	Right unilateral ECT (3 sessions/week, up to 4 weeks); bilateral ECT considered after 2 weeks if non-response	DNA methylation of *PLAT* (t-PA) and *SERPINE1* (PAI-1) in B cells, T cells, monocytes, NK cells, and whole blood	No differences in t-PA or PAI-1 methylation between ECT remitters and non-remitters (baseline and post-ECT); significant variation in t-PA methylation across immune cell types, but stable across ECT course.	33 patients achieved remission; methylation profiles did not correlate with clinical improvement.	Epigenetic signatures of *t-PA* and *PAI-1* are not predictive of ECT response. Findings highlight the importance of analyzing DNA methylation in specific immune cell subtypes rather than whole blood samples.
Maier et al., 2023 (39)	31 patients with MDD (mean age: 55; 64.5% female); 19 unmedicated depressed controls; 20 healthy controls	Prospective observational study	Right unilateral ECT, 3 sessions/week, average of 10 ± 4 sessions; Thymatron IV system	DNA methylation of NR3C1 (glucocorticoid receptor) and POMC in PBMCs	Baseline: NR3C1 methylation ↑ in non-responders; Post-ECT: NR3C1 methylation ↓ in both responders and nonresponders; POMC methylation ↓ in responders but ↑ in nonresponders.	NR3C1 methylation was higher in non-responders at baseline but decreased in both groups post-ECT. POMC methylation decreased in responders and increased in non-responders, indicating an epigenetic signature associated with response.	ECT induces short-term epigenetic changes in HPA-axis-related genes. NR3C1 methylation may act as a baseline biomarker of treatment response; POMC methylation changes may reflect stress regulation dynamics associated with ECT outcome.
Kaurani et al., 2023 (40)	64 TRD patients (mean age 55.9; 59.38% female)	SmallRNA sequencing analysis	Bilateral ECT (placement adjusted as needed), avg. 12 sessions; titration based on seizure threshold or age	miR-223-3p, IL-6, IL-1β, TNF-α, NLRP3	Baseline: miR-223-3p ↓ and IL-6, TNF-α ↑ in responders; Post-ECT: miR-223-3p ↑, IL-6 and TNF-α ↓ in responders; miR-223-3p discriminated responders from non-responders.	Significant symptoms improvement (≥50% MADRS decrease) in 62.5% patients; miR-223-3p down-regulated at baseline among responders; higher post-ECT miR-223-3p expression associated with greater depressive symptom improvement.	miR-223-3p may serve as a biomarker for ECT response, linking immune-inflammatory pathways to antidepressant effects. Findings highlight the potential for miRNA-based diagnostics in TRD treatment and further research on inflammatory modulation.
Galbiati et al., 2025 (41)	27 TRD patients (mean age 58.1; 67% female	Prospective longitudinal study	Bilateral brief-pulse ECT (Thymatron DG); 3 sessions/week; mean 7.9 ± 2.7 sessions; dosing based on age or seizure threshold titration	miR-30c-5p, miR-324-3p, miR-95-3p, miR-194-5p, miR-195-5p, miR-19b-3p, let-7i-5p, miR-497-5p	Downregulation of 8 miRNAs post-ECT; symptom improvement correlated with changes in miR-30c-5p and miR-324-3p in responders; Only miR-324-3p correlated with symptom relief in the whole sample.	Significant symptoms improvement reduction in MADRS scores; 18 out of 27 classified as responders (≥50% symptom reduction).	Findings suggest that miR-30c-5p and miR-324-3p may be implicated in the antidepressant mechanism of ECT and could serve as potential biomarkers for treatment response.
Ryan et al., 2023 (42)	100 MDD patients (mean age 56.36; 62% female) treated with ECT; 89 healthy controls (mean age 53.42; 66.29% female)	Observational cohort study	Bilateral ECT (bitemporal at 1.5× ST or unilateral at 6× ST); mean 8.03 ± 2.51 sessions	mtDNAcn, telomere length, inflammatory markers (IL-6, IL-10, TNF-α, and CRP)	Baseline: mtDNAcn ↑ in MDD vs. controls; no correlation with inflammation, telomere length, or depression severity; mtDNAcn not predictive of ECT response/remission.	No association between mtDNAcn levels and ECT response or remission.	Findings suggest mitochondrial dysfunction in depression; however, mtDNAcn did not serve as a predictor for ECT treatment outcomes. Further research is warranted on mitochondrial pathways in depression.

ECT, Electroconvulsive Therapy; MDD, Major Depressive Disorder; TRD, Treatment-Resistant Depression; MADRS, Montgomery-Åsberg Depression Rating Scale; IL-1β, Interleukin-1 Beta; IL-6, Interleukin-6; IL-10, Interleukin-10; TNF-α, Tumor Necrosis Factor Alpha; CRP, C-Reactive Protein; NLRP3, NLR Family Pyrin Domain Containing 3 Inflammasome; miRNAs, microRNAs; miR-223-3p, microRNA 223-3p; miR-30c-5p, miR-324-3p, miR-95-3p, miR-194-5p, miR-195-5p, miR-19b-3p, let-7i-5p, miR-497-5p, Specific microRNAs studied; mtDNAcn, Mitochondrial DNA Copy Number; DMRs, Differentially Methylated Regions; DMPs, Differentially Methylated Positions; FDR, False Discovery Rate; NR3C1, Nuclear Receptor Subfamily 3 Group C Member 1 (Glucocorticoid Receptor Gene); POMC, Proopiomelanocortin; PLAT, Tissue-Type Plasminogen Activator Gene; SERPINE1, Plasminogen Activator Inhibitor-1 Gene; PBMCs, Peripheral Blood Mononuclear Cells; ST, Seizure Threshold.
↑ = increased levels or expression; ↓ = decreased levels or expression.

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Discussion

Our review assessed recent evidence on ECT and mood disorders. The analyzed studies highlight key pathways through which ECT exerts its effects, spanning systemic immune modulation, neuroplasticity, genetic regulation, and mitochondrial function. Despite heterogeneity in studies designs, the collective evidence suggests, in accordance with previous studies of the field, that ECT does not merely act at the neurotransmitter level but induces broader biological adaptations that may underpin its therapeutic efficacy (43). Importantly, these processes are not isolated, as neurotransmitter alterations may act as upstream modulators influencing these multimodal effects.

Regarding systemic inflammation following ECT, some studies reported marked reductions in pro-inflammatory markers such as CRP, IL-6, and TNF-α post-ECT (17, 27, 28), while others revealed a biphasic response, characterized by initial immune activation followed by partial resolution (29, 30). Whether these distinct patterns can reflect consequences of influence by other factors (such as sample profile and assessment methods) or epiphenomenon is still a knowledge gap. While most biomarker studies have emphasized peripheral inflammation, emerging evidence also points to ECT's capacity to modulate central immune activity. Findings from cerebrospinal fluid suggest that neuroimmune shifts may accompany clinical improvement, supporting a broader view of ECT as influencing both systemic and central pathways (18).

Interestingly, sex-specific immune responses to ECT—such as IL-8 increases associated with symptom improvement only in women—highlight the potential role of sex hormones and sex-linked immune regulation in treatment outcomes (19). Age-related differences have also been noted: adolescents with MDD exhibited a prolonged and sustained reduction in IL-1β and IL-6 post-ECT, alongside an increase in IL-10, an anti-inflammatory cytokine. These findings showed that younger individuals may exhibit a favorable profile in terms of ECT immune-inflammatory modulation, potentially due to greater immune plasticity or a lower baseline inflammatory burden (17). In contrast, among elderly TRD patients, inflammatory markers remained elevated in a subset of individuals, suggesting that, in this population, immune dysregulation may persist despite clinical symptom improvement; it raises concerns about whether residual inflammation contributes to long-term relapse risk (22). The differences between these age groups indicate the potential immune aging (inflammaging) on ECT response (22, 44). Future research should investigate whether baseline inflammatory profiles can predict differential responses to ECT across age groups and explore personalized approaches to optimize treatment efficacy.

Furthermore, specific symptom clusters may also be influenced by immune modulation. Psychomotor symptoms—often disabling and treatment-resistant—have been shown to associate with IL-6 shifts following ECT, suggesting that targeting immune pathways may have functional relevance beyond core mood symptoms (25). In parallel, cognitive vulnerability following ECT may be related to individual inflammatory profiles in patients with MDD. Inflammatory mediators such as NLRP3 inflammasome, IL-18, and NF-κB were significantly elevated after ECT in MDD patients and negatively correlated with memory scores. Similarly, higher pre-treatment TNF-α, IL-10, and CRP predicted poorer cognitive performance during or after ECT in depressed individuals. These findings suggest that pre-ECT immune phenotyping might aid in predicting short-term cognitive risk in this population (23).

Pharmacological strategies targeting neuroinflammation, such as the COX-2 inhibitor celecoxib, have been explored as potential adjuncts in mood disorders treatment (45–48). Indeed, Kargar et al. (2014) demonstrated that celecoxib, compared with placebo, effectively reduced TNF-α levels in patients with BD undergoing ECT. However, no reductions in other inflammatory markers (e.g., IL-6, IL-1, and high-sensitivity CRP) or direct link between TNF-α decrease and greater symptomatic improvement were observed. Specifically on age, a randomized controlled trial including a large sample of cognitively normal individuals with late-life depression showed that either celecoxib or naproxen was insufficient to improve depressive symptoms compared to placebo (47). Additionally, Kargar et al. (2015) explored the effects of celecoxib in manic patients receiving ECT, assessing its potential role in modulating BDNF levels, a critical mediator of neuroplasticity. While there was a trend toward increased BDNF in patients receiving celecoxib, it did not reach statistical significance, and no correlation was observed between BDNF changes and clinical response (48). These findings suggest that while anti-inflammatory strategies may modulate peripheral and central immune-inflammatory responses, their impact on neuroplasticity and symptomatic improvement remains uncertain (45–48).

The neuroplastic effects of ECT have been supported by studies demonstrating increased expression of hippocampal neurogenesis markers (36). These recent findings align with preclinical research showing that electroconvulsive seizures (ECS) in rodents stimulate neural progenitor cell proliferation and dendritic remodeling (49). The absence of significant microglial activation in post-mortem human hippocampal tissue from ECT-treated patients further suggests that ECT may promote structural brain recovery without triggering sustained neuroinflammation (36). However, contrasting results from animal models, such as ECS failing to prevent lipopolysaccharide-induced microglial activation and behavioral effects, reinforce that neuroimmune response to ECT may be context-dependent, varying with baseline inflammatory status and underlying pathology (50). Despite new data, it is still unclear whether neuroplastic changes correlate with long-term functional outcomes. Longitudinal studies assessing whether these biomarkers relate to relapse risk or cognitive effects could refine clinical decision-making; strategies for augmentation of ECT's neuroplastic effect may further enhance the precision of neuromodulatory interventions. Notably, emerging neuroimaging studies in humans suggest that glial activity may mediate ECT-induced white matter reorganization. Rather than reflecting nonspecific volumetric effects, structural adaptations appear selectively associated with inflammatory shifts in responders, reinforcing the view that glia-mediated immune signaling may support functional plasticity in TRD (35).

Identifying trends in DNA methylation following ECT in the study by Carvalho Silva et al., albeit lacking statistical significance after multiple corrections, suggests possible effects on cellular reprogramming, which may contribute to neuroplasticity and clinical outcomes in MDD (37). This new analysis contributed to pre-existing investigations; however, newer investigations with larger populations are necessary for robust conclusions (7). Beyond global methylation patterns, recent evidence suggests that ECT may epigenetically modulate components of the stress-response system. Changes in the methylation of NR3C1 and POMC—two key HPA-axis genes—were associated with treatment response, indicating that epigenetic regulation of stress-related pathways may represent a mechanistic link between biological vulnerability and ECT efficacy, particularly in stress-linked mood phenotypes (39).

Still within genetics, the valuable findings of two included studies in this review on microRNA among TRD patients treated with ECT (40, 41) fit within the general trajectory of omics research on treatment-resistant depression (51). The findings indicate that biomarker-driven stratification might enable precision-medicine techniques to select appropriate candidates for ECT. In this setting, translational studies showed that antidepressant treatments have been associated with changes in miRNA expression profiles (such as miR-1202) (52), and current research reinforces that interventions targeting miRNAs may regulate immune functions and improve mood disorders treatment outcomes (53–55). However, gaps within the field involving ECT still remain. The stability of DNA methylation and miRNA changes over time, their sensitivity to external factors such as medication use (53, 56), and their specificity to ECT rather than other antidepressant interventions require deep investigation. Longitudinal studies with repeated sampling, larger cohorts, and controlled confounders are essential to determine whether these molecular alterations can be effectively integrated into clinical decision-making.

Mitochondrial function has also emerged as a relevant domain, with one cited study showing elevated mtDNA copy number in MDD patients, though without clear differentiation between ECT responders and non-responders (42). A plausible explanation for the lack of association between mtDNAcn levels and ECT response is that mitochondrial adaptations may occur at a functional rather than a purely quantitative level. While mtDNAcn is an indirect measure of mitochondrial activity, it does not fully capture key parameters such as mitochondrial membrane potential, ATP production, or reactive oxygen species generation (57, 58). The observed variability in mitochondrial adaptations following ECT requires further studies on comprehensive metabolic profiling, particularly in the context of oxidative stress and neuroenergetics (58). Given that mitochondrial dysfunction is implicated in multiple psychiatric disorders, including MDD, BD, and schizophrenia, further exploration of ECT's role in mitochondrial resilience could refine understanding of its therapeutic potential (59–61). Additionally, interventions that enhance mitochondrial function, such as metabolic modulators or antioxidant therapies, may represent promising adjuncts to ECT, particularly for patients with high oxidative stress burden (58, 60, 61). Despite recent advances, interactions between mitochondrial function, inflammation, and neuroplasticity remain underexplored in mental disorders. Therefore, integrative research assessing these pathways could contribute to new mechanistic concepts.

Beyond ECT, other neuromodulation techniques have been investigated for their effects on immune, inflammatory, and cellular mechanisms in mood disorders. Repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), and vagus nerve stimulation (VNS) have all demonstrated varying degrees of immunomodulatory and neuroplastic effects. A systematic review encompassing both animal and human studies examined the impact of rTMS on inflammatory markers in psychiatric disorders. The review found that while animal models showed positive changes in microglial activity and anti-inflammatory effects associated with behavioral improvement, these findings were not consistently replicated in human studies focusing on TRD. Specifically, several human studies reported rTMS-induced alterations in peripheral inflammatory markers, but only a minority demonstrated an association with clinical treatment response. The review also noted that most studies exhibited poor or moderate quality in bias assessment, indicating a need for more rigorous research in this area (62). A pilot study published in 2024 by Lespérance et al. assessed the immunomodulatory effects of VNS in TRD patients over an extended period of up to four years. Plasma levels of 40 soluble inflammatory molecules, including cytokines, were measured before VNS implantation and throughout treatment. The results showed significant modifications in cytokine levels that were associated with clinical response in depressive symptoms, suggesting a potential relation between inflammatory modulation and response to treatment. Nonetheless, the small sample size and an extended follow-up of this study limits its generalizability (63). A study by Goerigk et al. (2020) examined the role of peripheral biomarkers associated with neuroplasticity and immune-inflammatory processes in patients with BD undergoing tDCS treatment. The findings suggested that tDCS modulates these biomarkers, particularly IL-8, which significantly reduced following active tDCS. Additionally, higher baseline IL-6 plasma levels were associated with symptomatic improvement post-tDCS (64), aligning with ECT and suggesting that pre-existing inflammatory states may influence treatment response (65, 66). Head-to-head comparisons between ECT and other modulatory interventions are needed to delineate their respective neurobiological mechanisms and optimize patient selection among different modalities.

The newer research in this review contributed to the field with noteworthy insights, yet numerous limitations still exist. First, different patients' profile across samples (e.g., age, sex, clinical history, body mass index, years of education, ethnicity), heterogeneous outcome variables, distinct ECT protocols, serum collections, and time of follow-up may halt the overall interpretation of the included studies. Secondly, the multimodal responses to ECT, even in studies with similar methods, demonstrate the difficulty in identifying standard modulatory mechanisms. Thirdly, while novel results (such as neuroplasticity and genetic/epigenetic findings) TRD mechanistic insights and phenomenological correlations, their clinical translation remains

preliminary, necessitating validation in larger cohorts/randomized controlled trials.

In summary, our review support the view that ECT may modulate immune-inflammatory, neuroplastic, and epigenetic mechanisms, reinforcing its function as a systemic neuromodulatory intervention rather than a purely neurotransmitter-based therapy. While these domains have often been studied in isolation, recent findings suggest a complex interplay between immune regulation, synaptic remodeling, and gene expression in underpinning ECT's therapeutic effects (65). Neuroinflammatory changes may facilitate neuroplasticity by mitigating cytokine-induced synaptic dysfunction and neurodegeneration. This aligns with post-mortem and imaging studies demonstrating hippocampal neurogenesis and structural remodeling in ECT-treated patients (36). Moreover, epigenetic modifications may be molecular switches linking inflammatory modulation to synaptic plasticity (40, 41). Mitochondrial function represents another critical intersection in this neuroimmune interface. Since mitochondria are key oxidative stress and ATP production regulators, their dysfunction could exacerbate neuroinflammation and impair synaptic remodeling. However, current studies suggest that ECT-induced mitochondrial adaptations may occur at a functional rather than a quantitative level, requiring advanced metabolic profiling to elucidate their clinical significance (42, 58).

Conclusion

Novel research has added important insights into immune-inflammatory, neuroplastic, and genetic mechanisms related to ECT in mood disorders. Despite remaining gaps, these findings pave the way for precision-based therapeutic strategies.

Author contributions

RJ: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing. JA: Conceptualization, Data curation, Investigation, Writing – original draft, Writing – review & editing. DP: Data curation, Investigation, Writing – original draft, Writing – review & editing. PR: Conceptualization, Data curation, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. PO: Conceptualization, Data curation, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing.

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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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Glossary

ADARB1	Adenosine Deaminase RNA Specific B1
BD	Bipolar Disorder
BDNF	Brain-Derived Neurotrophic Factor
BPRS	Brief Psychiatric Rating Scale
CAR	Cortisol-to-Albumin Ratio
CGI-S	Clinical Global Impression – Severity Scale
COX-2	Cyclooxygenase-2
CRP	C-Reactive Protein
CRP-albumin ratio	C-Reactive Protein to Albumin Ratio
CYB5B	Cytochrome B5 Type B
DBS	Deep Brain Stimulation
DCX	Doublecortin
DMP	Differentially Methylated Positions
DMR	Differentially Methylated Regions
DNA	Deoxyribonucleic Acid
ECT	Electroconvulsive Therapy
ECS	Electroconvulsive Seizures
EPB41	Erythrocyte Membrane Protein Band 4.1
FAM20C	Family with Sequence Similarity 20 Member C
FDR	False Discovery Rate
GABA	Gamma-Aminobutyric Acid
GFAP	Glial Fibrillary Acidic Protein
HAMD-24	Hamilton Depression Rating Scale 24-item version
HDRS	Hamilton Depression Rating Scale
HMGB1	High Mobility Group Box-1 Protein
Iba1	Ionized Calcium-Binding Adapter Molecule 1
IFN-γ	Interferon Gamma
IL-1β	Interleukin-1 Beta
IL-6	Interleukin-6
IL-8	Interleukin-8
IL-10	Interleukin-10
IL-18	Interleukin-18
IQCE	IQ Motif Containing E
MADRS	Montgomery-Åsberg Depression Rating Scale
MDD	Major Depressive Disorder
MEG	Magnetoencephalography
miRNA	MicroRNA
MLR	Monocyte-to-Lymphocyte Ratio
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
mtDNAcn	Mitochondrial DNA Copy Number
NF-κB	Nuclear Factor Kappa B
NLR	Neutrophil-to-Lymphocyte Ratio
NLRP3	NLR Family Pyrin Domain Containing 3 Inflammasome
NR3C1	Nuclear receptor subfamily 3 group C member 1 (glucocorticoid receptor)
OTUB1	OTU Deubiquitinase, Ubiquitin Aldehyde Binding 1
PDGF-BB	Platelet-Derived Growth Factor Subunit B
PDW	Platelet Distribution Width
PLR	Platelet-to-Lymphocyte Ratio
POMC	Proopiomelanocortin
PVRL4	Poliovirus Receptor-Related 4
QoL	Quality of Life
RDW	Red Cell Distribution Width
rTMS	Repetitive Transcranial Magnetic Stimulation
sRAGE	Soluble Receptor for Advanced Glycation End Products
SD	Standard Deviation
SII	Systemic Immune-Inflammation Index
STMN1	Stathmin 1
tDCS	Transcranial Direct Current Stimulation
TNF-α	Tumor Necrosis Factor Alpha
TRD	Treatment-Resistant Depression
TR-MDD	Treatment-Resistant Major Depressive Disorder
VNS	Vagus Nerve Stimulation
WMS-R	Wechsler Memory Scale–Revised
WHOQOL-BREF	World Health Organization Quality of Life – Brief Version

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Efficacy and influencing factors of modified electroconvulsive therapy for schizophrenia: a real-world retrospective observational study

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Background: Schizophrenia (SCZ) is a chronic and disabling psychiatric disorder. Modified Electroconvulsive Therapy (MECT), which involves electrical stimulation under general anaesthesia and muscle relaxation, is widely used to treat SCZ. Despite its rapid onset and robust therapeutic effect, the efficacy of MECT varies significantly between individuals. This study aimed to evaluate the clinical effectiveness of MECT in patients with SCZ and identify its influencing factors, with the goal of informing personalised treatment strategies.

Methods: This retrospective observational study included 237 inpatients with SCZ who received a full course of MECT at the Fourth People's Hospital of Nantong between January 2023 and December 2024. Treatment response was evaluated using the Positive and Negative Syndrome Scale (PANSS) reduction rate. Patients were classified into effective (≥50% reduction) and ineffective (<50% reduction) groups. Demographic, clinical, and treatment-related variables were compared between groups, and multivariate logistic regression was used to identify predictors of treatment response.

Results: The overall effectiveness rate of MECT was 70.46%. Multivariate analysis identified age ≥50 years (OR = 0.111–0.078, P = 0.010–0.002) and illness duration ≥10 years (OR = 0.028–0.003, P < 0.05) as negative predictors of response. In contrast, first-episode SCZ (OR=6.537, P = 0.003), higher baseline positive symptom scores (OR = 1.325, P<0.001), and longer EEG seizure duration (OR = 1.183, P<0.001) were positive predictors. No significant associations were found for sex, education level, or stimulus parameters such as current or frequency.

Conclusion: MECT remains a clinically valuable intervention for SCZ, particularly in younger, first-episode patients with prominent positive symptoms. Treatment efficacy is influenced by age, illness duration, baseline symptom severity, and seizure quality. These findings support the need for personalised MECT protocols guided by clinical and electrophysiological characteristics.

KEYWORDS

schizophrenia, SCZ, MECT, electroconvulsive therapy, EEG seizure duration, PANSS, treatment predictors, personalised psychiatry

1 Introduction

Schizophrenia (SCZ) is a chronic and disabling psychiatric disorder characterised by symptoms including positive symptoms (such as hallucinations, delusions, and disorganised thinking), negative symptoms (such as affective flattening and social withdrawal), and behavioural disturbances (1). Typically manifesting in adolescence or early adulthood, SCZ has become one of the global causes of disability (1, 2). Although antipsychotics have significantly improved clinical outcomes of patients (3), their adverse effects—particularly metabolic syndrome and extrapyramidal symptoms—remain a major clinical challenge (4). In this context, physical interventions have attention, and Modified Electroconvulsive Therapy (MECT) as a promising therapeutic approach owing to its unique mechanism of action (5, 6).

MECT involves the induction of brief, generalised cerebral seizures under anaesthesia, which may contribute to rebalancing neurotransmitter systems and modulating functional brain networks (7, 8). Existing evidence supports the efficacy of MECT in the treatment of SCZ episodes, agitation, and catatonia (8–11), and it is particularly beneficial for patients who are treatment-resistant or require urgent clinical intervention (12–15). Furthermore, several studies have demonstrated that MECT can significantly reduce the length of hospital stay in patients with schizophrenia, thereby alleviating the burden on families and healthcare systems (16–18).

Although previous studies have investigated individual predictors of MECT efficacy—for example patient demographics (age, illness duration), clinical measures (Positive and Negative Syndrome Scale scores) or single treatment parameters (stimulus intensity) (19, 20)—there is a clear lack of comprehensive, multivariable investigations that integrate these domains and examine their joint, potentially interacting effects. For instance, one influential study reported that bitemporal stimulus intensities above 1.5× the seizure threshold may accelerate improvement in positive symptoms, but it did not account for clinical or demographic covariates that could modify this relation (19).To address this evidence gap, the present retrospective study systematically evaluates how demographic characteristics, clinical phenotype and detailed MECT parameters jointly relate to symptomatic outcomes in patients with schizophrenia. Our objective is to generate robust, multivariable evidence to inform the optimisation and individualisation of MECT protocols in routine clinical practice.

Abbreviations: SCZ, Schizophrenia; MECT, Modified Electroconvulsive Therapy; PANSS, Positive and Negative Syndrome Scale; CGI, Clinical Global Impression; EEG, Electroencephalogram; BMI, Body Mass Index; VIF, Variance Inflation Factor; ASEI, Average Seizure Energy Index; PSI, Postictal Suppression Index.

2 Materials and methods

2.1 Participants

All consecutive adult in-patients diagnosed with schizophrenia at the Fourth People's Hospital of Nantong between January 2023 and December 2024 were screened for eligibility (n = 451). Of these, 205 patients were excluded because they met one or more exclusion criteria; note that category counts are not mutually exclusive and therefore do not sum to the overall exclusion total. 9 patients were not evaluable in the primary analysis owing to dropout. The remaining 237 patients comprised the analysed sample (see Figure 1 for full details).

1. Inclusion criteria: Patients who (a) were aged 18 - 65 years; (b) met the diagnostic criteria for SCZ according to either the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition or the International Classification of Diseases, Tenth Revision (21); (c) han no contraindications; (d) voluntarily accepted MECT and had not received MECT within the past six months; (e) completed ≥6 MECT sessions with complete pre- and post-treatment evaluation data; and (f) experienced no serious adverse events requiring treatment discontinuation occurred during the course.
2. Exclusion criteria: Patients with (a) other psychiatric disorders (e.g., bipolar disorder or major depressive episode) or neurological disorders (e.g. bipolar disorder, epilepsy); (b) substance use or drug dependence; (c) significant physical illnesses;(d) incomplete clinical data; or (e) serious adverse reactions to MECT.
3. Drop-out criteria: Patients who **(a)** voluntarily discontinued treatment; (b) lost to follow-up; or (c) who refused to complete post-treatment assessments.

2.2 Treatment procedure

All procedures were conducted in strict accordance with the Expert Consensus on Modified Electroconvulsive Therapy (2019 Edition) (7). Treatment was administered using a Thymatron IV device (Somatics, Lake Bluff, IL, USA). Pre-treatment protocols included fasting and water restriction, routine screening with Electrocardiograph, chest X-ray, and blood tests to exclude contraindications.

During treatment, vital signs were continuously monitored. Anaesthesia was induced using etomidate (0.16–0.2 mg/kg), muscle relaxation was achieved with succinylcholine (1.0 mg/kg), and atropine sulphate (0.01 mL/kg) was used to reduce airway secretions. Bilateral temporal electrodes were used to induce seizures (22). Initial stimulus dosing was calculated using an age-based formula, with subsequent adjustments based on seizure adequacy assessed by electroencephalographic (EEG) monitoring (18), as detailed in Supplementary 1 Seizure adequacy criteria and dose–titration algorithm.

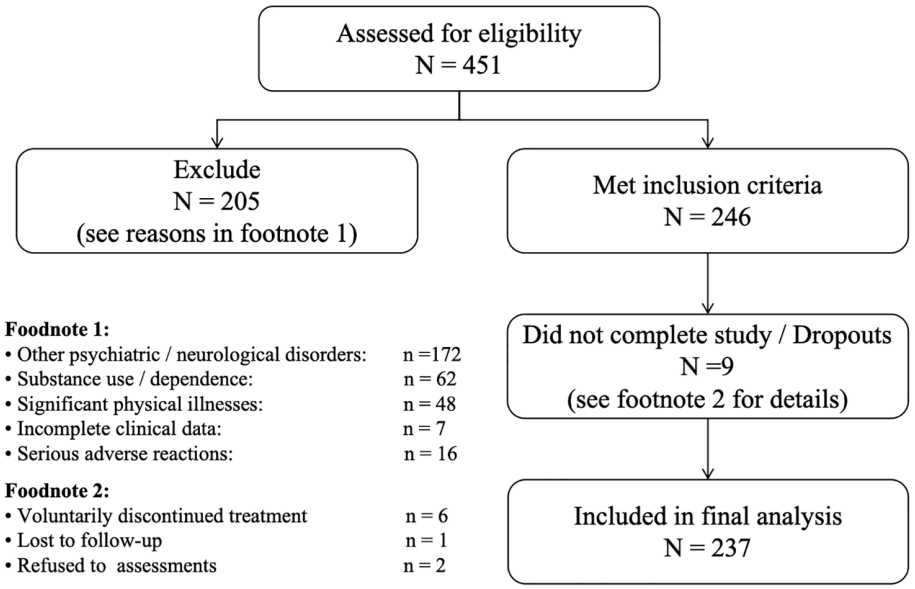

FIGURE 1
STROBE flow diagram of patient screening, exclusions, and inclusion in the final analysis.

MECT was administered three times during the first week (on alternate days) and twice weekly during the second week, resulting in a total of six sessions over two weeks. Each treatment was jointly supervised by an anaesthesiologist and a psychiatrist throughout the procedure (18).

2.3 Outcome assessment and grouping

The Positive and Negative Syndrome Scale (PANSS) was used to evaluate clinical efficacy. PANSS comprises three subscales: positive symptoms (7 items), negative symptoms (7 items), and general psychopathology (16 items), with total scores ranging from 30 to 210. Assessments were conducted at baseline (within 24 hours before the first MECT session) and post-treatment (within 24 hours after the final session).

Efficacy was determined based on the reduction rate of the PANSS total score, calculated as:

[(Baseline score − Post-treatment score)/Baseline score] × 100% (23).

We chose a ≥50% reduction in total PANSS score to define treatment response for three principal reasons. First, a 50% reduction is widely regarded in the MECT literature as representing a clinically meaningful improvement and is commonly used in studies that classify outcomes as "markedly effective" (≥75%), "effective" (50–74%), "improved" (25–49%) and "ineffective" (<25%) (24). This categorical scheme has precedent in prior MECT reports (11, 25, 26), facilitating direct comparability with the existing body of MECT evidence. Second, empirical work linking PANSS percentage change to the Clinical Global Impression (CGI) suggests that reductions in the order of ~40–50% correspond to CGI categories such as "much improved", whereas smaller reductions of 20–30% typically reflect only minimal-to-moderate clinical change (27). Thus, a 50% threshold better captures treatment effects that are likely to be meaningful to clinicians and patients. Third, selecting ≥50% strikes a pragmatic balance between sensitivity and specificity in a treatment context where rapid and substantial symptomatic relief (rather than marginal change) is the clinical aim.

2.4 Observational variables

Demographic characteristics included age, sex, and education. Health-related variables comprised smoking, alcohol consumption, family history of mental illness, and body mass index (BMI). Smoking status was dichotomised based on history (smoker vs non-smoker). Alcohol use was assessed in accordance with WHO guidelines (Global Status Report on Alcohol and Health), categorised as non-drinker, moderate drinker, or harmful drinker. Harmful drinking was defined as a daily average alcohol intake of ≥61g for men and ≥41g for women.

Clinical characteristics included illness duration, first-episode status, and antipsychotic medication dose converted to olanzapine equivalents (28, 29) (see Supplementary Table S1). Baseline scores for PANSS positive, negative, general psychopathology, and total score were also collected.

MECT treatment parameters included EEG seizure duration (30), Average Seizure Energy Index (ASEI), Postictal Suppression Index (PSI), static and dynamic impedance, energy percentage, stimulus dose, current, frequency, and duration. The ASEI represents the averaged ictal EEG power, reflecting the overall "potency" of the seizure, and is calculated over the entire seizure duration. The PSI quantifies the proportion of abrupt termination of ictal activity versus a gradual, undifferentiated decline. Dynamic impedance is measured

automatically by the Thymatron during stimulation, whereas static impedance whereas static impedance was measured after EEG electrode placement and prior to stimulation; both values are expressed in ohms (Ω).These definitions and calculations follow the Thymatron IV manual.

2.5 Assessment and quality control

All clinical evaluations were independently conducted by two psychiatrists with attending-level qualifications and formal training in PANSS assessment. Baseline assessments were conducted within 24 hours before MECT initiation, and post-treatment assessments were completed within 24 hours following the final session. Interviews using a standardised protocol.

Data were entered in real-time into an electronic database and double-checked by an independent data manager using a blinded approach. Ten percent of the sample was randomly selected for duplicate data entry verification before database locking.

2.6 Statistical analysis

Statistical analyses were performed STATA 16.0 (StataCorp LLC, USA). Continuous variables were inspected for normality using the Shapiro–Wilk test. Variables with approximately normal distributions are reported as mean ± standard deviation (SD) and compared using independent-samples t-tests. Variables with non-normal distributions are reported as median, interquartile range (IQR) and compared using the two-sided Mann–Whitney U test. Categorical variables are presented as counts (percentages) and compared by Pearson's χ^2 test.

A multivariable logistic regression model was used to explore predictors of MECT efficacy. To address potential multicollinearity among predictors, Variance inflation factor (VIF) analysis was performed; variables with VIF > 5 were considered to exhibit multicollinearity. A two-tailed p-value of <0.05 was considered statistically significant.

Sensitivity analyses (1) a worst-case (intention-to-treat) sensitivity analysis in which patients who dropout (discontinued treatment or lacked post-treatment PANSS) were assumed to be non-responders; and (2) Using alternative responder thresholds ≥30%, Results from these sensitivity analyses are reported in the Supplementary Material. Robustness Analyses (1) Ordinal logistic model using the four pre-specified categories (≥75%, 50–74%, 25–49%, <25%); (2) Using PANSS total in place of subscales to test robustness; (3) Using beta regression to test robustness. All primary conclusions were robust to these alternative specifications.

2.7 Ethical statement

This study adhered to the principles of informed consent, autonomy, confidentiality, and beneficence. Written informed consent was obtained from all participants or their legal guardians, after clear explanation of the study's objectives and procedures. Participation was voluntary and participants' data were anonymised. The study protocol was reviewed and approved by the Ethics Committee of the Fourth People's Hospital of Nantong City (Approval No. 2023-Ko37).

3 Results

Based on the percentage reduction in PANSS total scores, participants achieving a reduction rate of ≥50% (i.e. markedly effective or effective) were classified into the effective group (n = 167, 70.46%), while the remaining participants were assigned to the ineffective group (n = 70, 29.54%).

3.1 Comparison of baseline characteristics between groups

A comparison of demographic, health-related, and clinical characteristics between the effective and ineffective groups is presented in Table 1. The two groups were similar across most sociodemographic and clinical variables. The baseline differences of statistical significance were patient age distribution and first-episode status: a substantially greater proportion of non-responders were aged ≥50 years, whereas first-episode patients were more common among responders (both $p < 0.05$). All other baseline variables (sex, education, residence, BMI, family history, smoking and alcohol use, antipsychotic dose, and most illness-related categories) did not differ between groups (see Table 1).

3.2 Comparison of MECT treatment parameters between groups.

The principal electrophysiological difference between groups was EEG seizure duration: responders had significantly longer than non-responders ($p < 0.001$). No other procedural or device parameters showed differences in comparisons (Table 2).

3.3 Comparison of PANSS reduction rates between groups before and after treatment.

At baseline, the effective group had higher PANSS positive and total scores. After the MECT course, responders exhibited substantially greater reductions in positive symptoms, general psychopathology and total PANSS score (all $p < 0.001$). There was no significant between-group difference in negative-symptom reduction (Table 3).

3.4 Multivariate logistic regression analysis

We fitted a multivariable logistic regression to identify independent predictors of achieving ≥50% PANSS reduction. After addressing severe multicollinearity among candidate

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TABLE 1 Comparison of demographic and clinical characteristics between effective and ineffective groups.

Variable	Ineffective group (n=70)	Effective group (n=167)	$x^2/t/z$-value	p-value
Age group (years, %)				
<30	7(10.00)	35(20.96)	54.524	<0.001
30-40	10(14.29)	55(32.93)		
40-50	12(17.14)	56(33.53)		
50-60	20(28.57)	12(7.19)		
≥60	21(30.00)	9(5.39)		
Sex(%)				
Male	35(50.00)	77(46.11)	0.300	0.584
Female	35(50.00)	90(53.89)		
Education level(%)				
Less than lower secondary	53(75.71)	131(78.44)	1.643	0.440
upper secondary & vocational training	9(12.86)	25(14.97)		
tertiary	8(11.43)	11(6.59)		
Marital status(%)				
With partner	6(8.57)	24(14.37)	1.501	0.221
Single	64(91.43)	143(85.63)		
Residence(%)				
Urban	38(54.29)	106(63.47)	1.746	0.186
Rural	32(45.71)	61(36.53)		
BMI(kg/m², mean ± SD)	25.48 ± 6.76	26.53 ± 3.91	-1.490	0.138
Family history of SCZ(%)				
No	63(90.00)	139(83.23)	1.794	0.180
Yes	7(10.00)	28(16.77)		
Smoking(%)				
No	49(70.00)	111(66.47)	0.281	0.596
Yes	21(30.00)	56(33.53)		
Alcohol use(%)				
Non-drinker	50(71.43)	113(67.66)	1.786	0.409
Moderate drinking	9(12.86)	16(9.58)		
Harmful drinking	11(15.71)	38(22.75)		
Antipsychotic dose [mg/d, median (IQR)]	13.17 (10.06, 17.78)	13.15 (8.27, 18.36)	0.444	0.657
Illness duration(years, %)				
	6(8.57)	17(10.18)	0.898	0.826
5-10	6(8.57)	15(8.98)		
10-15	8(11.43)	13(7.78)		
≥15	50(71.43)	122(73.05)		

(Continued)

TABLE 1 Continued

Variable	Ineffective group (n=70)	Effective group (n=167)	$x^2/t/z$-value	p-value
First-episode status(%)				
No	54(77.14)	97(58.08)	7.750	0.005
Yes	16(22.86)	70(41.92)		

predictors (see Supplementary Materials S3 Methods for VIF-based variable selection), the model retained clinical and electrophysiological covariates. Key independent predictors were: older age (≥50 years) and longer illness duration (≥10 years) - both associated with a lower likelihood of being a responder - and first-episode status, higher baseline positive-symptom severity, and longer EEG seizure duration, which were associated with increased odds of response (all $P < 0.05$), as shown in Table 4.

3.5 Sensitivity and robustness analysis

To test the robustness of these conclusions we (a) inspected VIFs and removed variables with extreme collinearity prior to reporting the final model (Supplementary Table S2), and (b) report sensitivity analyses (alternative response thresholds, continuous outcome modelling and worst-case imputation for dropouts) in the Supplementary Material S4. These supplementary analyses are included to address information-loss concerns inherent to dichotomisation and to verify that the identified direction of associations is robust to reasonable variations in modelling choices.

3.6 Adverse events

Among 237 patients (1,422 MECT sessions), no serious adverse events (AE) occurred that required permanent discontinuation. Overall, 68 patients (28.7%) experienced at least one non-serious AE. The commonest events were headache (n = 40; 16.9%), transient confusion/delirium (n = 18; 7.6%), and transient memory complaints (n = 12; 5.1%). The majority (82%) of events were mild and resolved within 72 hours with symptomatic treatment; 12% were moderate and required brief pharmacological therapy or extended observation. There were no statistically significant differences in overall AE incidence between the effective and ineffective groups (29.3% vs 27.1%, p = 0.55). Full AE details are provided in Supplementary Materials S5.

TABLE 2 Comparison of MECT parameters between effective and ineffective groups.

Parameter	Ineffective group (n = 70)	Effective group (n = 167)	t/z-value	p-value
EEG seizure duration [s, median (IQR)]	39(29,51)	52(41,61)	-4.241	<0.001
ASEI [μV^2, median(IQR)]	41102.05 (35360.80,45555.00)	38844.20 (33714.90,45547.20)	1.314	0.189
PSI (%)	74.25 ± 9.00	74.10 ± 9.94	0.115	0.909
Static Impedance [Ω, median(IQR)]	1051.54 (849.28,1278.49)	1085.51 (879.73,1268.91)	-0.224	0.823
Dynamic Impedance [Ω, median (IQR)]	233.84 (199.51,268.47)	221.84 (191.78,251.18)	1.910	0.056
Energy Percentage [%, median(IQR)]	69.13 (58.88,76.26)	65.72 (56.45,73.79)	1.588	0.112
Stimulus Charge [mC, median(IQR)]	299.39 (254.60,349.91)	303.27 (258.24,344.92)	0.076	0.940
Stimulus Current (A)	0.81 ± 0.06	0.82 ± 0.07	–0.724	0.470
Stimulus Frequency [Hz, median (IQR)]	57.53 (50.57,64.22)	56.52 (49.71,62.47)	1.020	0.308
Stimulus Duration [s, median(IQR)]	3.11 (2.50,3.52)	2.91 (2.40,3.39)	1.111	0.267

TABLE 3 Comparison of PANSS scores and reduction rates between groups.

PANSS domain	Ineffective group (n = 70)	Effective group (n = 167)	t/z-value	p-value
Pre-treatment PANSS scores				
Negative symptoms [median(IQR)]	26(22,29)	27(24,30)	-1.601	0.110
Positive symptoms [median(IQR)]	28(25,31)	36(29,39)	-6.344	<0.001
General psychopathology	50.56 ± 8.81	52.77 ± 8.22	–1.853	0.065
Total PANSS score	105.73 ± 12.45	112.58 ± 15.58	–3.267	0.001
Post-treatment PANSS reduction rates				
Negative symptom reduction [%, median(IQR)]	33.06(14.44,48.02)	35.33(18.84,47.44)	0.144	0.885
Positive symptom reduction [%, median(IQR)]	26.61(15.52,42.07)	70.07(62.84,75.85)	-11.742	<0.001
General psychopathology reduction [%, median(IQR)]	30.22(7.05,56.42)	53.72(44.91,61.81)	-6.130	<0.001
Total PANSS reduction [%, median(IQR)]	31.17(19.25,43.85)	52.57(51.20,54.55)	-12.139	<0.001

4 Discussion

This study confirmed a response rate of 70.46% for MECT in the treatment of SCZ, which aligns with previously reported ranging from 55.5% to 76.7% in both domestic and international literature (15, 23, 31). These findings further support the clinical value of MECT as an effective intervention for SCZ. Multivariate logistic regression identified age, duration of illness, first-episode status, severity of positive symptoms, and EEG seizure duration as predictors of treatment outcome, offering an evidence-based foundation for individualised treatment optimisation.

4.1 Demographic predictors of treatment response

Age ≥50 years emerged as a negative predictor of MECT efficacy (OR = 0.111–0.078), with younger patients demonstrating significantly greater symptomatic improvement—consistent with existing findings (32–35). These findings support a model of age-related responsiveness, suggesting that stimulation dosage should be adjusted by age, with older patients potentially requiring higher stimulus intensities to induce adequate therapeutic seizures. There is a clear need for age-adjusted dose–response algorithms to be established in future protocols.

Additionally, illness duration ≥10 years significantly reduced treatment efficacy (OR = 0.028–0.003), a result in line with previous studies (36). Chronicity in SCZ may decrease neuronal responsiveness to MECT. Notably, first-episode patients showed superior outcomes (OR = 6.537), likely due to lower seizure thresholds and higher neuroplasticity observed in early-onset patients (32). This supports the concept of a "critical treatment window," highlighting the potential for early intervention to exert amplified effects and improve long-term outcomes (37).

Other demographic characteristics—including sex, education level, smoking and alcohol use, and family history of SCZ - were not independently associated with treatment efficacy (P > 0.05). While this finding is consistent with several prior reports (38–40), it is worth noting that one study found women to have lower seizure thresholds and more complete therapeutic seizures (41). These inconsistencies underscore the necessity of large-scale, multicentre randomised trials to determine sex-specific treatment responses and establish standardised evaluation frameworks.

4.2 Clinical characteristics and treatment response

MECT demonstrated substantial efficacy in reducing PANSS positive symptom scores, general psychopathology scores, and overall total scores. Although responders showed significantly greater post-treatment reductions in general psychopathology scores (Table 3), baseline general-psychopathology was not an independent predictor of achieving ≥50% PANSS reduction in our multivariable model. While higher baseline positive symptom scores were positively correlated with greater treatment response (OR = 1.325, p < 0.001), which was consistent with previous studies and may be involved in the recovery of cerebellar-cerebral connectivity following MECT (42).

4.3 Technical parameters and electrophysiological predictors

This study explored the association between MECT technical parameters and therapeutic efficacy in SCZ, identifying EEG seizure duration as a key electrophysiological predictor. The effective group exhibited a significantly longer EEG seizure duration compared to the ineffective group, with seizure duration strongly associated with treatment response (OR = 1.183, p < 0.001). These findings are consistent with prior research (43, 44) and suggest that monitoring EEG seizure duration provides useful information when titrating treatment.

No independent predictive value was found for the seizure index or suppression index, consistent with earlier studies (45, 46).

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TABLE 4 Multivariate logistic regression analysis of factors associated with MECT treatment response.

Variable	OR	SE	z	p-value	95% CI
Age group					
<30 (Ref.)	–	–	–	–	–
30–40	1.209	0.875	0.260	0.793	0.293 - 4.991
40–50	1.057	0.801	0.070	0.942	0.239 - 4.669
50–60	0.111	0.095	-2.560	0.010	0.021 - 0.597
≥60	0.078	0.065	-3.050	0.002	0.015 - 0.402
Sex					
Male (Ref.)	–	–	–	–	–
Female	2.763	1.824	1.540	0.124	0.757 - 10.078
Education level					
Less than lower secondary	–	–	–	–	–
upper secondary & vocational training	0.993	0.832	-0.010	0.993	0.192 - 5.129
tertiary	0.527	0.462	-0.730	0.465	0.095 - 2.937
Marital status					
With partner (Ref.)	–	–	–	–	–
Single	0.725	0.538	-0.430	0.665	0.169 - 3.109
Residence					
Urban (Ref.)	–	–	–	–	–
Rural	0.579	0.300	-1.050	0.292	0.209 - 1.599
BMI	1.059	0.056	1.090	0.274	0.955 - 1.175
Family history of SCZ					
No (Ref.)	–	–	–	–	–
Yes	3.113	2.556	1.380	0.166	0.623 - 15.557
Smoking					
No (Ref.)	–	–	–	–	–
Yes	1.793	1.221	0.860	0.391	0.472 - 6.814
Alcohol use					
Non-drinker (Ref.)	–	–	–	–	–
Moderate drinking	3.689	3.097	1.560	0.120	0.712 - 19.116
Harmful drinking	1.808	1.304	0.820	0.411	0.440 - 7.429
Antipsychotic Dose	0.983	0.035	-0.500	0.619	0.917 - 1.053
Illness duration					
<5 years (Ref.)	–	–	–	–	–
5–10 years	0.193	0.205	-1.550	0.122	0.024 - 1.550
10–15 years	0.028	0.036	-2.840	0.004	0.002 - 0.331
≥15 years	0.003	0.004	-4.120	<0.001	0.001 - 0.047

(Continued)

TABLE 4 Continued

Variable	OR	SE	z	p-value	95% CI
First-episode status					
No (Ref.)	–	–	–	–	–
Yes	6.537	4.060	3.020	0.003	1.935 - 22.083
MECT parameters					
EEG Seizure Duration	1.183	0.044	4.550	<0.001	1.100 - 1.272
ASEI*	0.202	0.226	-1.430	0.153	0.023 - 1.809
PSI	0.963	0.026	-1.400	0.162	0.914 - 1.015
Energy Percentage	1.005	0.020	0.270	0.787	0.966 - 1.046
Stimulus Current*	0.210	0.470	-0.700	0.486	0.003 - 17.005
Stimulus Duration	0.925	0.352	-0.210	0.837	0.439 - 1.949
Pre-treatment PANSS scores					
Negative symptoms	0.990	0.051	-0.190	0.848	0.896 - 1.094
Positive symptoms	1.325	0.071	5.240	<0.001	1.193 - 1.472
General psychopathology	0.960	0.027	-1.440	0.150	0.908 - 1.015

OR, Odds Ratio; SE, Standard Error; CI, Confidence Interval; BMI, Body Mass Index; EEG, Electroencephalogram; ASEI, Average Seizure Energy Index; PSI, Postictal Suppression Index.
*ASEI was log transformed and Stimulus Current was reciprocals transformed.

This study employed a personalised parameter adjustment strategy, modifying stimulus charge, current, frequency, and duration to balance efficacy with tolerability. These clinician-led adjustments, although beneficial for individual outcomes, may obscure population-level dose–response relationships due to variability and limited sample size. This could explain why no significant associations were observed between stimulation parameters and clinical outcomes in our analysis. Future studies with larger cohorts are needed to elucidate the complex interplay between electrical dosing and neural plasticity.

4.4 Strengths and limitations

This study presents a comprehensive multidimensional evaluation, encompassing demographic, clinical, and electrophysiological factors, thereby enhancing the representativeness and practical relevance of the findings. The integration of diverse predictors strengthens the external validity and clinical applicability of the results. However, several limitations must be acknowledged:

First, the retrospective, observational design limits causal inference. Treatment assignment and parameter adjustments were determined by clinical teams rather than by protocolised allocation, so unmeasured confounding and indication bias may have influenced both treatment choices and outcomes despite multivariable adjustment. Second, the study was conducted at a single tertiary psychiatric hospital; local clinical practice, patient demographics and device-setting routines may differ from other centres, which restricts the generalisability of our findings. Third, we included only patients who completed the six-session MECT course with complete pre- and post-treatment PANSS data. This inclusion criterion risks survivorship (selection) bias: patients who discontinued early because of adverse events, clinical deterioration, practical reasons or early non-response were not represented in the primary analysis and may differ systematically from completers. Although we performed sensitivity analyses treating early dropouts as non-responders (reported in the Supplementary Material), prospective intention-to-treat data would more robustly estimate real-world effectiveness.Fourth, the study did not include formal cognitive assessments or longer-term follow-up. As a result, we cannot comment on the cognitive safety profile of the six-session regimen, nor on durability of response or relapse rates beyond the immediate post-treatment window. These outcomes are clinically important when weighing short-term symptom improvement against potential cognitive adverse effects and relapse prevention strategies. Fifth, although PANSS ratings were performed by two trained psychiatrists under a standardised protocol, we did not compute inter-rater reliability (e.g., ICC or kappa) for this dataset; future prospective work should include formal rater-training and reliability testing. Finally, several electrophysiological and device parameters (for example, seizure index, suppression index and impedance measures) are susceptible to measurement variability (influenced by electrode placement, muscle relaxation, amplifier settings and artefact) and were adjusted in real-time by clinicians; this pragmatic approach improves individual care but reduces the internal control required to precisely estimate dose–response relationships. Taken together, these limitations motivate prospective, multicentre, randomised or adaptive-design studies with standardised titration algorithms, comprehensive cognitive testing and longer follow-up to confirm and extend the present findings.

Future research should aim to address these limitations through multicentre, prospective, randomised controlled trials to validate the present findings. Additionally, exploring the associations between stimulation modalities (e.g., unilateral vs bilateral electrode placement, stimulation frequency variations) and both therapeutic outcomes and adverse effects will be essential. The integration of neuroimaging, electrophysiological indices, and biological markers may also enable the development of more personalised and precise MECT protocols.

5 Conclusion

MECT is an effective therapeutic strategy for patients with schizophrenia, particularly during the acute phase. Treatment efficacy is influenced by several key factors, including age, illness duration, first-episode status, baseline severity of positive symptoms, and EEG seizure duration. These variables should be considered when formulating individualised MECT treatment plans, with the aim of maximising clinical efficacy and informing optimised decision-making in psychiatric practice.

Data availability statement

The datasets presented in this article are not readily available because access requires approval from the Fourth People's Hospital of Nantong City, Jiangsu Province, China. Requests to access the datasets should be directed to XW, xueting_wang2021@126.com.

Ethics statement

The studies involving humans were approved by the Ethics Committee of the Fourth People's Hospital of Nantong City (approval no.: 2023-Ko37). 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

WZ: Formal Analysis, Writing – original draft, Data curation, Conceptualization. QJ: Supervision, Project administration, Conceptualization, Writing – review & editing. PZ: Writing – original draft, Data curation, Investigation, Conceptualization. CM: Software, Project administration, Writing – review & editing, Methodology. WX: Methodology, Validation, Supervision, Writing – review & editing.

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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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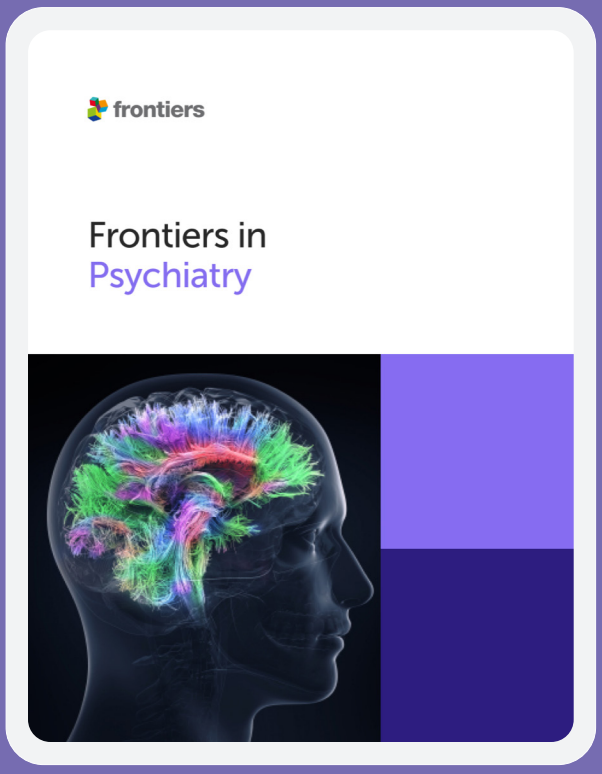

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