ความสัมพันธ์ระหว่างประสบการณ์อันไม่พึงประสงค์ในวัยเด็กกับประสิทธิภาพของการรักษาทางจิตเวชด้วยไฟฟ้าในผู้ป่วยภาวะซึมเศร้าในโรคซึมเศร้าและโรคไบโพลาร์วัยผู้ใหญ่

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**ภาควิชาจิตเวชศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล*

บทคัดย่อ

วัตถุประสงค์ เพื่อศึกษาความสัมพันธ์ระหว่างประสบการณ์อันไม่พึงประสงค์ในวัยเด็กกับการตอบสนองการรักษาทางจิตเวชด้วยไฟฟ้าในผู้ป่วยโรคซึมเศร้าวัยผู้ใหญ่ของโรงพยาบาลรามาธิบดี

วิธีการศึกษา การศึกษาเชิงพรรณนาและวิเคราะห์แบบย้อนหลังในกลุ่มผู้ป่วยที่มีภาวะซึมเศร้า อายุตั้งแต่ 18 ปีขึ้นไป ที่ได้รับการรักษาทางจิตเวชด้วยไฟฟ้าที่โรงพยาบาลรามาธิบดี ระหว่างเดือนมกราคม พ.ศ. 2558 ถึงเดือนมิถุนายน พ.ศ. 2566 เก็บรวบรวมข้อมูลโดยใช้แบบสอบถาม Adverse Childhood Experiences (ACE) Questionnaire ฉบับภาษาไทย วิเคราะห์ข้อมูลทางสถิติโดยใช้ Chi-square test, Fisher's Exact test, independent t-test และ binary logistic regression

ผลการศึกษา ผู้ป่วยเข้าร่วมวิจัย 38 คน ได้รับการวินิจฉัย major depressive disorder, persistent depressive disorder และ bipolar depression อายุเฉลี่ย 45.0 ± 17.4 ปี ส่วนใหญ่ (ร้อยละ 71.1) เป็นเพศหญิง โดยพบว่าประสบการณ์อันไม่พึงประสงค์ในวัยเด็กที่พบมากที่สุดสามอันดับแรก คือ การละเลยทอดทิ้งทางใจ (ร้อยละ 31.6) การเจ็บป่วยทางจิตเวชในครอบครัว (ร้อยละ 31.6) และการละเลยทอดทิ้งทางกาย (ร้อยละ 26.3) พบว่าผู้ป่วย 20 คน (ร้อยละ 52.6) ตอบสนองต่อการรักษาทางจิตเวชด้วยไฟฟ้าหลังทำการรักษาไปได้ 6 ครั้ง จากการวิเคราะห์ด้วย binary logistic regression ไม่พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติระหว่างประสบการณ์อันไม่พึงประสงค์ในวัยเด็ก กับการตอบสนองต่อการรักษาทางจิตเวชด้วยไฟฟ้า (OR = 0.42, 95% CI = 0.05-3.21, p = 0.40) นอกจากนี้พบว่าปัจจัยที่สัมพันธ์กับการตอบสนอง คือ ผู้ป่วยอายุน้อย (OR = 0.91, B = -0.09, 95% CI = 0.84-0.96, p = 0.02) และความแรงของการกระตุ้นไฟฟ้า (Odds ratio = 1.01, B = 0.01, 95%CI = 1.00-1.03, p = 0.05)

สรุป การศึกษานี้ไม่พบความสัมพันธ์ระหว่างประสบการณ์อันไม่พึงประสงค์ในวัยเด็กกับการตอบสนองต่อการรักษาทางจิตเวชด้วยไฟฟ้าในผู้ป่วยโรคซึมเศร้า ดังนั้นการรักษาทางจิตเวชด้วยไฟฟ้ายังคงเป็นการรักษาที่มีประสิทธิภาพ ไม่ว่าผู้ป่วยจะมีประสบการณ์อันไม่พึงประสงค์ในวัยเด็กหรือไม่ก็ตาม อย่างไรก็ตามยังมีความจำเป็นในการศึกษาเพิ่มเติมเกี่ยวกับประสบการณ์อันไม่พึงประสงค์ในวัยเด็ก เพื่อพิจารณาเลือกการรักษาที่เหมาะสม

คำสำคัญ ประสบการณ์อันไม่พึงประสงค์ในวัยเด็ก โรคซึมเศร้า การรักษาทางจิตเวชด้วยไฟฟ้า

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Association Between Adverse Childhood Experiences and Efficacy of ECT in Adults with Unipolar and Bipolar Depression

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ABSTRACT

Objective: This study aimed to examine the association between adverse childhood experiences (ACEs) and response to electroconvulsive therapy (ECT) in adult patients with unipolar and bipolar depression at Ramathibodi Hospital.

Methods: A retrospective-observational study was conducted on patients with unipolar and bipolar depression (≥18 years) who received inpatient ECT at Ramathibodi Hospital, Thailand, from January 2015 to June 2023. ACEs were assessed using the Adverse Childhood Experiences (ACE) Questionnaire - Thai version. The data were analyzed using Chi-square test, Fisher's Exact test, independent t-test, and binary logistic regression.

Results: The study involved 38 patients diagnosed with major depressive disorder, persistent depressive disorder, or bipolar depression, with a mean age of 45.0 ± 17.4 years. Most of the patients were female (71.1%). This study found that the most prevalent ACE categories were emotional neglect (31.6 %), household mental illness (31.6 %), and physical neglect (26.3 %). After 6 sessions of ECT, 20 patients (52.6%) achieved response. Binary logistic regression showed that no significant association was found between ACE and ECT response (OR = 0.42, 95% CI = 0.05 - 3.21, p = 0.40). However, younger age (Odds ratio = 0.91, B = -0.09, 95%CI = 0.84 - 0.96, p = 0.02). and higher stimulus intensity (Odds ratio = 1.01, B = 0.01, 95%CI = 1.00 - 1.03, p = 0.05) were significant predictors of ECT response.

Conclusion: This study did not find a correlation between ACE and the response to ECT in patients with major depressive disorder. Therefore, ECT may be an effective treatment option for patients with depression, regardless of their history of childhood trauma. However, further research is necessary to understand how adverse childhood experiences affect treatment decisions.

Keywords: adverse childhood experiences, depressive disorder, electroconvulsive therapy

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INTRODUCTION

Mental disorders are the leading cause of disability globally, with depression being the largest contributor to the global burden of these disorders.[1] Its debilitating effects can significantly impair an individual's quality of life.[2] Despite the availability of various treatments, such as antidepressant medications and psychotherapy, many patients do not achieve adequate response or remission.[3] Electroconvulsive therapy (ECT) is an effective acute treatment for patients with severe and treatment-resistant depression.[4] It involves delivering brief electrical pulses to the brain under general anesthesia, which induces seizures. However, the mechanisms of ECT are not fully understood. According to some previous imaging studies, treatment response is linked to sequential changes in functional connectivity within the intralimbic and limbic–prefrontal networks, and ECT induces volume increases in fronto-limbic areas.[5,6] A recent survey has indicated that ECT is frequently employed in Thailand.[7]

However, not all patients respond equally to ECT, and some may experience adverse effects such as memory loss or confusion.[8,9] Therefore, it is important to identify the factors that influence the response to ECT and optimize its effectiveness and safety. Predictors that could affect the outcome of ECT for people living with depression remain a subject of ongoing research. These predictors include age, sex, psychotic depression, duration of episode, polarity of mood disorder, and melancholic features.[10-15] Treatment- resistant depression (TRD) is also a factor that lower the response to ECT.[16-18]

Childhood trauma is one of the most influential factors leading to the subsequent development of Major Depressive Disorder (MDD).[19,20] Moreover, childhood trauma may also influence the course, severity, and treatment outcomes of depression.[21,22] The International Study to Predict Optimized Treatment for Depression (iSPOT-D) examined how childhood trauma affects depression treatment with three different antidepressants.[23] 1,008 patients were randomly assigned to take escitalopram, sertraline, or venlafaxine for 8 weeks, with doses adjusted by their doctors. The iSPOT-D trial reported that, although the overall trauma was not a significant predictor of response or remission, abuse occurring at ≤7 years of age predicted poorer outcomes after 8 weeks of antidepressant treatment in adults. Moreover, meta-analysis of studies conducted before 2010 showed a generally poorer effect of monotherapy, combination therapy, and psychotherapy in adults with MDD and a history of childhood maltreatment.[24]

One study by Finnegan et al examined the effect of childhood trauma and personality disorder on the response to brief-pulse electroconvulsive therapy in patients with depression. The study found that patients with a history of childhood trauma had a lower response rate to ECT (38.5%) than those who did not report any childhood trauma (83.3%). However, there is limited research in Thailand that examined how exposure to childhood trauma would influence the benefit of ECT treatment. The aim of this study was to investigate the potential association between adverse childhood experiences (ACEs), as measured by the ACE-Thai questionnaire, and efficacy of ECT in patients with depressive disorders. We hypothesize that patients with a history of ACEs will exhibit lower response and remission rates compared to those without ACEs. Understanding the relationship between ACEs and ECT response holds significant clinical implications. If ACEs are found to negatively impact ECT efficacy, clinicians can consider this information when making treatment decisions for patients with depression. Additionally, identifying the specific ACEs that are most strongly associated with poorer ECT response could inform the development of targeted interventions to improve ECT outcomes in patients with a history of trauma.

METHODS

Study design and participants

The study protocol was approved by the Ethics Committee on Human Experimentation of the Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand (COA. No.: MURA2022/384). Participants provided written informed consent if they were

physically present at the outpatient department or verbal consent if they were enrolled via telephone.

The study was a retrospective, observational study of adult patients (≥18 years old) who received inpatient ECT at Ramathibodi Hospital from January 2015 to June 2023. Participants were diagnosed with major depressive disorder, persistent depressive disorder, or bipolar depression, with or without psychotic features. Psychiatric diagnoses were performed by psychiatrists based on the DSM-IV-TR criteria.[26] Exclusion criteria included a history of seizure disorder, epilepsy, organic mood disorder, schizophrenia, schizoaffective disorder, or any other psychotic disorder; individuals who did not complete the recommended six sessions of ECT; and known medical conditions or sensory impairments that could interfere with assessments.

The sample size was calculated by n4StudieS applications, using this formula.:

$$n_1 = \left[\frac{z_{1-\frac{\alpha}{2}} \sqrt{\bar{p}\bar{q}\left(1+\frac{1}{r}\right)} + z_{1-\beta} \sqrt{p_1 q_1 + \frac{p_2 q_2}{r}}}{\Delta} \right]^2$$

Response rates to ECT for patients with and without childhood traumas from the previous study were used for sample size calculation.[27] The estimated sample size for each group is 18.

Procedure

Data Collection

Chart reviews were conducted for all participants to collect demographic data, clinical characteristics, physical and mental illness, and ECT data (e.g., indications, stimulus dose, and electrode placement method). The Adverse Childhood Experiences (ACE) questionnaire-Thai version was administered to assess exposure to childhood trauma and adversity.[28] For participants who presented at the clinic in person, the questionnaire was provided in paper format. Participants who were enrolled via telephone provided their responses to the same questionnaire verbally during the telephone interview by a psychiatric resident. Montgomery Asberg Depression Rating Scale (MADRS) for depression was used to assess the severity of symptoms at baseline (24 hours before ECT), after every 3 sessions of ECT treatment, and after the last ECT session. The MADRS is a 10-item rating scale used to assess the severity of depressive symptoms.[29] Each item is scored from 0 to 6, with higher scores indicating worse symptoms. Assessments were performed by staffs and psychiatric residents who had received appropriate training. Assessments of inter-rater reliability were performed using the intraclass correlation coefficient (ICC). The ICC was 0.9.

Questionnaire: Adverse childhood experiences questionnaire-Thai version

The ACE-Thai questionnaire is a 28-item, self-reported measure that assesses exposure to specific traumatic events that occurred before the age of 18. The questionnaire covers 10 domains of adversities, including physical abuse, emotional abuse, sexual abuse, physical neglect, emotional neglect, domestic violence, household substance abuse, household mental illness, parental separation or divorce, and incarcerated household member.[28] Each item is endorsed on a dichotomous (present or absent) scale and summed to compute a total ACE score. The total ACE score 0 means no exposure to childhood trauma, and total ACE ≥ 1 means patient exposed to at least one type of ACEs.

ECT treatment

Before commencing ECT treatment, a thorough assessment of all patients was conducted by psychiatrists and anesthesiologists. The administration of benzodiazepines was typically ceased at least 15 hours prior to the scheduled treatment sessions. The ECT procedures took place in the post-anesthetic care unit (PACU) and involved a collaborative effort from a team comprising psychiatric staff, psychiatric residents, anesthesia staff, psychiatric nurses, and anesthesia nurses. Anesthesia was induced using either thiopental (2-5 mg/kg IV) or propofol (1-2 mg/kg IV), along with the muscle relaxant succinylcholine (0.5-1 mg/kg IV). ECT was then performed using a modified technique involving

a brief pulse wave generated by a Mecta Spectrum 5000Q (Mecta Corp, USA) or Thymatron® System IV. ECT was performed three times per week. The placement of the electrodes was determined by the psychiatrists who prescribed ECT. At the first ECT session, the initial seizure threshold (IST) is the lowest dose of electrical stimulation that causes a generalized motor seizure and at least 25 seconds of EEG seizure, which is considered adequate seizure. If the EEG seizure following ECT stimulation lasts less than 25 seconds, restimulation at a higher dose may be attempted after 45 seconds. The titration schedules were shown in Table 1 and Table 2 of supplementary file. Stimulus intensity was then adjusted according to the selected electrode placement. For right unilateral (RUL) electrode placement, the stimulus was increased to 500% above the ST, whereas for bilateral (BL) electrode placement, the stimulus was set at 50% above the ST.[30] Treatment usually ended when patients achieved clinical remission or there was no further improvement in symptoms, as measured by MADRS scale, after 2 consecutive ECT sessions. Treatment is also discontinued if patients experience severe adverse effects such as postictal delirium, aspiration pneumonia, life-threatening arrhythmias, or myocardial infarction. In case of milder adverse effects, such as ECT-related cognitive deficit, nausea, vomiting, or headache, supportive treatment is considered.

Outcomes

The primary outcome was the rate of response (≥50% decrease in MADRS scores from baseline) after the 6 sessions of ECT, which was used as an indicator of ECT efficacy.[31]

Statistical analysis

SPSS version 21.0 for Windows was used to conduct all statistical analyses (IBM Corp., Armonk, NY, USA). Prior to each analysis, relevant statistical assumptions were verified, and a two-sided P-value ≤0.05 was considered significant. Categorical parameters were compared using Chi-squared and Fisher's Exact tests, as indicated. Continuous variables were compared using independent t-tests. Descriptive statistics were used to summarize the characteristics of the participants and the treatment outcomes. Continuous variables were presented as means and standard deviations (SD), while categorical variables were presented as percentages. The total ACEs scores and the specific domains of ACEs were also analyzed as continuous and categorical variables, respectively. Binary logistic regression analysis was conducted to evaluate the relative importance of various factors in predicting the ECT outcomes.

RESULTS

Demographic Characteristics

The study included a total of 38 adult depressed patients who underwent inpatient ECT. For exposure to ACE, 11 (28.9%) had no exposure, and 27 (71.1%) had exposure to at least one type of ACE. The demographic characteristics of all participants and comparison between responder group and non-responder group were shown in Table 1. The MADRS score of the patients was 30.4 (SD = 8.8), indicating severe depression. There were no statistical differences between responder and non-responder group, regarding baseline characteristics, clinical variables, and treatment variables. However, age, average electrical charge, electrode placement, and antipsychotic use had a tendency towards statistical significance. We then used these variables in a binary logistic regression analysis.

Adverse childhood experiences exposure versus response rate

The most commonly reported ACE categories were emotional neglect (N = 12, 31.6%), household mental illness (N = 12, 31.6%), and physical neglect (N = 10, 26.3%) (Table 2). When comparing responders and non-responders to ECT, there were no significant differences in overall ACE exposure (Table 1) or specific ACE categories. Binary logistic regression analysis also showed no significant difference in ACE exposure between responder and non-responder groups (Table 3).

TABLE 1 demographics and baseline clinical characteristics

Characteristic	N (%) or Mean ± SD	N (%) or Mean ± SD	N (%) or Mean ± SD	Group difference		
	All patient (N=38)	Responders (N=20)	Non-responders (N=18)	Chi-square	T	p-value
Mean age	45.0 ± 17.4	40.35 ± 14.3	50.06 ± 19.5		-1.764	0.086
Sex						
Male	11 (28.9)			0.752		0.485
Female	27 (71.1)	13 (65.0)	14 (77.8)			
Education						
Bachelor's degree or higher	29 (76.3)	15 (75.0)	14 (77.8)	0.40		1.000
Marital status						
Single	24 (63.2)	12 (60.0)	12 (66.7)	3.237		0.338
Married & live together	12 (31.6)	8 (40.0)	4 (22.2)			
Married & live separately	1 (2.6)	0 (0.0)	1 (5.6)			
Divorced or widow	1 (2.6)	0 (0.0)	1 (5.6)			
Chronic medical diseases (diabetes mellitus, Hypertension, Dyslipidemia)	22 (57.9)	11 (55.0)	11 (61.1)	0.145		0.752
Diagnosis						
Unipolar depression	35 (92.1)	17 (85.0)	18 (100.0)	2.931		0.232
Bipolar depression	3 (7.9)	3 (15.0)	0 (0.0)			
Psychotic symptoms	13 (34.2)	6 (30.0)	7 (38.9)	0.333		0.734
History of previous ECT	10 (26.3)	4 (20.0)	6 (33.3)	0.869		0.468
Electrode placement						
Right unilateral	35 (92.1)	20 (100.0)	15 (83.3)	3.619		0.097
Bilateral	3 (7.9)	0 (0.0)	3 (16.7)			
Average charge (mC)	219.6 ± 102.1	248.7 ± 123.0	187.2 ± 60.5		1.984	0.057
Concurrent medications						
Antidepressants	6 (15.8)	3 (15.0)	3 (16.7)	0.020		1.000
Antipsychotics	27 (71.1)	17 (85.0)	10 (55.6)	3.993		0.074
Lamotrigine	1 (2.6)	1 (5.0)	0 (0.0)	0.924		1.000
Benzodiazepines	3 (7.9)	1 (5.0)	2 (11.1)	0.487		0.595
Baseline MADRS score	30.4 ± 8.8	29.70 ± 7.1	31.11 ± 10.6		-0.487	0.629
Total ACEs score	1.74 ± 1.7	1.65 ± 1.8	1.83 ± 1.7		-0.324	0.784

Abbreviations: N, number, SD, standard deviation; ECT, electroconvulsive therapy; mC, millicoulombs, MADRS, Montgomery-Åsberg Depression Rating Scale; ACE, Adverse childhood experiences

Factors associated with response to ECT.

Out of 38 patients, 20 (52.6%) responded after 6 sessions of ECT while 18 (47.4%) had no response to 6 sessions of ECT (Table 1). 4 patients discontinued ECT before 6 sessions, so they were excluded from this study.

Among the variables examined, binary logistic regression analysis revealed that the average charge used during ECT sessions showed a significant association with ECT response (Odds ratio = 1.01, B = 0.01, 95%CI [1.00, 1.03], p = 0.05). In other words, for every 1 milliCoulomb

(mC) increase in the electrical charge delivered during ECT, the odds of a response increase by 1%. This suggests that the stimulus intensity, represented by the average charge, influences the likelihood of a positive response to ECT. Furthermore, younger age at the time of ECT was associated with a higher likelihood of a positive response (Odds ratio = 0.91, B = -0.09, 95%CI [0.84, 0.96], p = 0.020). Specifically, for each one-year increase in age, the likelihood of a response to ECT decreases by 9%. However, there is no association between response rate and ACE exposure (Table 3).

DISCUSSION

Our study examined an association between adverse childhood experiences and response to ECT. This study included 38 participants who were diagnosed

TABLE 2 Prevalence of adverse childhood experience in patients with depressive disorders

Adverse childhood experiences	N (%); Total (N=38)	N (%) Responders (N=20)	N (%) Non-responders (N=18)	X^2	P-value
Exposure to at least 1 type of ACE	27 (71.1)	13 (65.0)	14 (77.8)	0.752	0.485
Patients without exposure to ACE	11 (28.9)	7 (35.0)	4 (22.2)		
ACE exposure by category					
Physical abuse	3 (7.9)	1 (5.0)	2 (11.1)	0.487	0.595
Emotional abuse	6 (15.8)	4 (20.0)	2 (11.1)	0.563	0.663
Sexual abuse	3 (7.9)	2 (10.0)	1 (5.6)	0.257	1.000
Emotional neglect	12 (31.6)	6 (35.0)	5 (27.8)	0.229	0.734
Physical neglect	10 (26.3)	4 (20.0)	6 (33.3)	0.869	0.468
domestic violence	5 (13.2)	2 (10.0)	3 (16.7)	0.368	0.653
household substance abuse	6 (15.8)	2 (10.0)	4 (22.2)	1.064	0.395
household mental illness	12 (31.6)	5 (25.0)	7 (38.9)	0.846	0.489
parental separation or divorce	5 (13.2)	3 (15.0)	2 (11.1)	0.125	1.000
incarcerated household member	4 (10.5)	3 (15.0)	1 (5.6)	0.897	0.606

Abbreviations: N, number; ACE, Adverse childhood experiences

TABLE 3 Logistic regression analysis for response to ECT

Variables	Comparison between responder and non-responder	
	Adjusted odds ratio (95% CI)	P-value
Age on ECT (year)	0.91 (0.84 - 0.96)	0.02*
Average charge (mC)	1.01 (1.00 - 1.03)	0.05*
Antipsychotics use	5.18 (0.72 - 37.14)	0.10
Bilateral electrode placement	0.00 (-)	1.00
Exposure to ACE	0.42 (0.05 - 3.21)	0.40

Abbreviations: CI, confidence interval; ECT, electroconvulsive therapy; mC, millicoulombs, *p < .05; ACE, Adverse childhood experiences

with either major depressive disorder, persistent depressive disorder, or bipolar depression. This study found no significant association between the ACE score or the specific types of ACEs and the response outcome after ECT, which is contrary to the previous study by Finnegan et al. which reported that patients who were exposed to childhood trauma were associated with poorer response to ECT than those who had no exposure to childhood trauma.[25] This may be explained by, in our study, we measured outcome after 6 sessions of ECT treatment, whereas some patients may require more sessions to respond. The optimal timing of outcome measurement is unclear. A study by Nygren et al. reported that most patients with TRD or non-TRD received six to ten sessions of ECT to achieve response.[16] Therefore, the timing of outcome measurement in our study may not have been enough for some patients to achieve the benefit of ECT.

This study also examined other factors associated with ECT response. Contrary to previous literature suggesting that older age is associated with better ECT response, our study identified younger age as a predictor for a positive response to ECT. This study supported a study by Liang et al. that reported that older age groups responded less to ECT treatment.[32] However, existing studies examining the association between age and response to ECT yielded mixed results. Some studies suggested that older age might hold an advantage in response to ECT,[10,16] while others have found no association.[33] One possible explanation for this discrepancy is that there are methodological differences in outcome assessment and definitions of response across various studies. For example, O' Connor et al. used bitemporal electrode placement in all patients and measured the outcome as the change from baseline in total Hamilton Depression Rating Scale (HAMD) score at the end of treatment. They found that older age was associated with better response to ECT.[10] A randomized trial by Loo et al. used MADRS scale to evaluate response, defined by a ≥50% reduction from baseline MADRS scores or if criterion for remission was met, after the first week of ECT. They found no association between age and response to one week of ECT treatment in patients with major depressive disorder.[33] However, one-week period of outcome measurement may not be long enough to conclude the association between age and ECT treatment. Another possible explanation for the inconsistent findings is that the age-response relationship may be confounded by other factors, such as duration of depressive episode.[18]

Regarding stimulus intensity, measured in terms of mean charge delivered, we found that higher stimulus intensity was associated with better ECT response. However, this finding should be interpreted cautiously, as the analysis used mean charge per treatment, and the dose-response relationship in ECT is complex. A previous study demonstrated that high electrical dosage is associated with a more rapid response.[34] Anyway, in the same study, the author also mentioned that the efficacy of ECT is more influenced by exceeding the patient's seizure threshold than by the absolute electrical dose administered.

This study has some limitations to consider when interpreting the findings. First, the sample size of this study was relatively small, which may have reduced the statistical power to detect any meaningful differences between groups. However, we tried to calculate the sample size needed in this study and obtained the minimum number of participants required for each group. Second, the study was a retrospective, observational study that relied on chart reviews and self-reported measures, which may introduce recall biases and errors in the data collection and analysis. Bias may also have occurred in patients' reports of childhood adversity, where they may have underreported certain ACEs for fear of negative consequences, weakening the observed associations. Third, regarding the assessment of ACE, the measure of ACE exposure that we used, the Adverse Childhood Experiences Questionnaire Thai version, may not have captured the full range and severity of ACEs that the participants experienced. Moreover, although this questionnaire assesses the frequency of ACEs, it does not assess the duration, intensity, or timing of the ACEs, which may affect the impact of the ACEs on the brain and

the development of depression. It is important to acknowledge that the questionnaire's validity for telephone administration has not been established. This raises concerns about potential biases or inaccuracies in the collected data. Fourth, for patients who had been treated at psychiatric departments at Ramathibodi Hospital before 2015, some of the data may not have been available in the electronic medical records, which may limit the accuracy and completeness of the information. Additionally, some of the factors that may influence treatment response to ECT were not recorded, such as the duration of depressive episodes, the presence of melancholic features, psychiatric comorbidities, number of failed medications, and the duration of pharmacologic treatment. Therefore, we could not control these factors in the analysis. The presence of psychiatric comorbidities and the degree of treatment resistance can confound the effectiveness of ECT. This is because these factors may independently reduce a patient's response to the treatment. This study did not gather information on anesthetic agents that could impact the seizure threshold during ECT treatment. Consequently, this data was not adjusted in the analysis. Fifth, during titration of dosage of ECT, we adjusted ECT parameter according to dose titration schedule. This study did not determine a new seizure threshold for each patient after adjusting pulse width during dose titration. Since changes in pulse width can influence seizure threshold, this may have confounded the observed association between higher stimulus dose and response to ECT.[35] Lastly, this study only examined the immediate outcomes of ECT and did not assess the long-term prognosis or remission rates of the patients. Many patients still had some depressive symptoms after meeting the response criteria. These limitations require careful interpretation and suggest future research directions to overcome these challenges and improve knowledge in this complex area.

CONCLUSION

Our findings suggest that ACEs may not have a significant impact on the response to ECT in patients with depressive disorders. This implies that ECT may be an effective treatment option for patients with depression, regardless of their history of childhood trauma. However, further research with larger, diverse samples, comprehensive ACE assessment, and long-term outcome evaluation is necessary to definitively confirm these results and optimize ECT usage for patients with various childhood trauma histories.

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Conflict of interest

The authors report no conflicts of interest.

Authors' contributions

Nontapat Pitukkitronnagorn: conceptualization, methodology, data collection, data analysis, writing - original draft, writing - review & editing; Pichai Ittasakul: conceptualization, methodology, data analysis, writing - review & editing, supervision, approval of final version; Umporn Pitidhammabhorn: conceptualization, methodology, data analysis, writing - review & editing; Thidarat Yamnim: conceptualization, methodology, data collection, writing - review & editing; Nujaree Sombatcharoennon: conceptualization, methodology, data collection, writing - review & editing.

REFERENCES

1. Collaborators GBDMD. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry 2022; 9(2): 137-50.
2. Demyttenaere K. Quality of life in depression and anxiety: does it matter? Int J Psychiatry Clin Pract 2006; 10 Suppl 1(sup1): 27-30.
3. Sinyor M, Schaffer A, Levitt A. The sequenced treatment alternatives to relieve depression (STAR*D) trial: a review. Can J Psychiatry 2010; 55(3): 126-35.
4. Kellner CH, Greenberg RM, Murrough JW, Bryson EO, Briggs MC, Pasculli RM. ECT in treatment-resistant depression. Am J Psychiatry 2012; 169(12): 1238-44.

5. Cano M, Cardoner N, Urretavizcaya M, Martinez-Zalacain I, Goldberg X, Via E, et al. Modulation of limbic and prefrontal connectivity by electroconvulsive therapy in treatment-resistant depression: A preliminary study. Brain Stimul 2016; 9(1): 65-71.
6. Gbyl K, Videbech P. Electroconvulsive therapy increases brain volume in major depression: a systematic review and meta-analysis. Acta Psychiatr Scand 2018; 138(3): 180-95.
7. Kittayarak K, Ittasakul P. Electroconvulsive Therapy Practice in Thailand: A nationwide survey. Neuropsychiatr Dis Treat 2022; 18: 2477-84.
8. Semkovska M, McLoughlin DM. Objective cognitive performance associated with electroconvulsive therapy for depression: a systematic review and meta-analysis. Biol Psychiatry 2010; 68(6): 568-77.
9. Li X, Cheng N, Deng Y, Du J, Zhang M, Guo Y, Hei Z. Incidence and risk factors for postictal delirium in patients after electroconvulsive therapy in China. Asian J Psychiatr 2020; 53: 102361.
10. O'Connor MK, Knapp R, Husain M, Rummans TA, Petrides G, Smith G, et al. The influence of age on the response of major depression to electroconvulsive therapy: a C.O.R.E. report. Am J Geriatr Psychiatry 2001; 9(4): 382-90.
11. Petrides G, Fink M, Husain MM, Knapp RG, Rush AJ, Mueller M, et al. ECT remission rates in psychotic versus nonpsychotic depressed patients: a report from CORE. J ECT 2001; 17(4): 244-53.
12. Bloch Y, Ratzoni G, Sobol D, Mendlovic S, Gal G, Levkovitz Y. Gender differences in electroconvulsive therapy: a retrospective chart review. J Affect Disord 2005; 84(1): 99-102.
13. Agarkar S, Hurt S, Lisanby S, Young RC. ECT use in unipolar and bipolar depression. J ECT 2012; 28(3): e39-40.
14. Chen CC, Lin CH, Yang WC, Chen MC. Clinical factors related to acute electroconvulsive therapy outcome for patients with major depressive disorder. Int Clin Psychopharmacol 2017; 32(3): 127-34.
15. Pinna M, Manchia M, Oppo R, Scano F, Pillai G, Loche AP, et al. Clinical and biological predictors of response to electroconvulsive therapy (ECT): a review. Neurosci Lett 2018; 669: 32-42.
16. Nygren A, Reutfors J, Brandt L, Boden R, Nordenskjold A, Tiger M. Response to electroconvulsive therapy in treatment-resistant depression: nationwide observational follow-up study. BJPsych Open 2023; 9(2): e35.
17. Heijnen WT, Birkenhager TK, Wierdsma AI, van den Broek WW. Antidepressant pharmacotherapy failure and response to subsequent electroconvulsive therapy: a meta-analysis. J Clin Psychopharmacol 2010; 30(5): 616-9.
18. Dombrovski AY, Mulsant BH, Haskett RF, Prudic J, Begley AE, Sackeim HA. Predictors of remission after electroconvulsive therapy in unipolar major depression. J Clin Psychiatry 2005; 66(8):1043-9.
19. Chapman DP, Whitfield CL, Felitti VJ, Dube SR, Edwards VJ, Anda RF. Adverse childhood experiences and the risk of depressive disorders in adulthood. J Affect Disord. 2004; 82(2): 217-25.
20. Mandelli L, Petrelli C, Serretti A. The role of specific early trauma in adult depression: A meta-analysis of published literature. Childhood trauma and adult depression. Eur Psychiatry 2015; 30(6): 665-80.
21. Negele A, Kaufhold J, Kallenbach L, Leuzinger-Bohleber M. Childhood trauma and its relation to chronic depression in ddulthood. Depress Res Treat 2015; 2015: 650804.
22. Fuller-Thomson E, Baird SL, Dhrodia R, Brennenstuhl S. The association between adverse childhood experiences (ACEs) and suicide attempts in a population-based study. Child Care Health Dev 2016; 42(5): 725-34.
23. Williams LM, Debattista C, Duchemin AM, Schatzberg AF, Nemeroff CB. Childhood trauma predicts antidepressant response in adults with major depression: data from the randomized international study to predict optimized treatment for depression. Transl Psychiatry 2016; 6(5): e799.
24. Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. Am J Psychiatry 2012; 169(2): 141-51.
25. Finnegan M, Galligan T, McLoughlin DM. Response to electroconvulsive therapy for depression: investigating the effects of childhood trauma and personality disorder. Brain Stimulation 2019; 12(2): 557.
26. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (4th ed., text rev.). Washington, DC; 2000.
27. Bernard R. Fundamentals of biostatistics. 5 ed. Duxbury: Thomson learning; 2000.
28. Lertsak R, Napakkawat B, Parichawan C, Wantipa W. Development of the adverse childhood experiences (ACE) questionnaire Thai version. Chulalongkorn Med Bull 2019; 1: 251-60.
29. Kongsakon R, Zartrungpak S, Rotjananirunkit A, Buranapichet U. The reliability and validity of montgomery asberg depression rating scale (MADRS) Thai version. J Psychiatr Assoc Thai 2003; 48: 211-9.
30. Ittasakul P, Likitnukul A, Pitidhrammabhorn U, Waleeprakhon P, Goldman MB. Stimulus intensity determined by dose-titration versus age-based methods in electroconvulsive therapy in Thai patients. Neuropsychiatr Dis Treat 2019; 15: 429-34.
31. Leucht S, Fennema H, Engel RR, Kaspers-Janssen M, Lepping P, Szegedi A. What does the MADRS mean? Equipercentile linking with the CGI using a company database of mirtazapine studies. J Affect Disord 2017; 210: 287-93.
32. Su L, Zhang Y, Jia Y, Sun J, Mellor D, Yuan TF, Xu Y. Predictors of electroconvulsive therapy outcome in major depressive disorder. Int J Neuropsychopharmacol 2023; 26(1): 53-60.
33. Loo CK, Mahon M, Katalinic N, Lyndon B, Hadzi-Pavlovic D. Predictors of response to ultrabrief right unilateral electroconvulsive therapy. J Affect Disord 2011; 130(1-2): 192-7.
34. Sackeim HA, Prudic J, Devanand DP, Kiersky JE, Fitzsimons L, Moody BJ, et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. N Engl J Med 1993; 328(12): 839-46.
35. Girish K, Gangadhar BN, Janakiramaiah N, Lalla RK. Seizure threshold in ECT: effect of stimulus pulse frequency. J ECT 2003; 19(3): 133-5.

Supplementary Data

TABLE 1 Dose Titration Schedule and Parameter Settings for Mecta Spectrum 5000Q

Step	Right Unilateral Electrode Placement					Bilateral Electrode Placement				
	Pulse-Width (ms)	Frequency (Hz)	Duration (Sec)	Current (mA)	Charge (mC)	Pulse width(ms)	Frequency (Hz)	Duration (Sec)	Current (mA)	Charge (mC)
1	0.5	50	0.5	800	20	1	40	0.75	800	48
2	0.5	40	1	800	32	1	40	1.25	800	80
3	0.5	40	1.5	800	48	1	40	2	800	128
4	0.5	40	1.5	800	77	1	60	2	800	192
5	1	40	2	800	128	1	60	3	800	288
6	1	60	2	800	192	1	60	4.5	800	432
7	1	60	3	800	288	1	60	6	800	576
8	1	60	4.5	800	432					
9	1	60	6	800	576					

TABLE 2 Dose Titration Schedule and Parameter Settings for Thymatron System IV

Step	Right Unilateral Electrode Placement				Bilateral Electrode Placement			
	Pulse-Width (ms)	Frequency (Hz)	Energy Level (%)	Charge (mC)	Pulse Width (ms)	Frequency (Hz)	Energy Level (%)	Charge (mC)
1	0.5	40	5	25	0.5	40	10	50
2	0.5	40	10	50	0.5	40	15	76
3	0.5	40	15	76	0.5	40	25	126
4	0.5	40	25	126	0.5	40	35	176
5	0.5	40	35	176	0.5	40	50	252
6	0.5	40	50	252	0.5	60	70	353
7	0.5	60	70	353	1	40	100	504
8	1	40	100	504				