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Evaluating the effect of electroconvulsive therapy (ECT) on post-traumatic stress disorder (PTSD): A systematic review and meta-analysis of five studies

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ABSTRACT

ECT has been proposed as a potential treatment for PTSD. There is a small number of clinical studies to date, but no quantitative review of the efficacy has been conducted. We performed a systematic review and meta-analysis to evaluate the effect of ECT in reducing PTSD symptoms. We followed the PICO and the PRISMA guidelines and searched PubMed, MEDLINE (Ovid), EMBASE (Ovid), Web of Science, and the Cochrane Central Register of Controlled Trials (PROSPERO No: CRD42022356780). A random effects model meta-analysis was conducted with the pooled standard mean difference, applying Hedge's adjustment for small sample sizes. Five within-subject studies met the inclusion criteria, containing 110 patients with PTSD symptoms receiving ECT (mean age 44.13 ± 15.35; 43.4% female). ECT had a small but significant pooled effect on reducing PTSD symptoms (Hedges' g = −0.374), reducing intrusion (Hedges' g = −0.330), avoidance (Hedges' g = −0.215) and hyperarousal (Hedges' g = −0.171) symptoms. Limitations include the small number of studies and subjects and the heterogeneity of study designs. These results provide preliminary quantitative support for the use of ECT in the treatment of PTSD.

1. Introduction

Post-traumatic stress disorder (PTSD) is a debilitating psychiatric condition that affects some victims of severe psychological trauma. Symptoms include intrusive re-experiencing of the trauma, avoidance, and persistent hyperarousal (Brewin et al., 2017; Oakley et al., 2021). PTSD has an annual incidence between 0.2% and 3.8% and a prevalence of 1.3%–12.2% (Benjet et al., 2016; Karam et al., 2014), with approximately half of PTSD patients also diagnosed with co-morbid major depressive disorder (MDD) (Flory and Yehuda, 2022).

Current treatment consists mainly of cognitive-behavioural and other psychotherapies and pharmacological treatment with selective serotonin reuptake inhibitor antidepressants. However, existing treatments have limited efficacy, and exploring additional PTSD treatments is warranted (Akiki and Abdallah, 2019; Ho et al., 2016; Hoogsteder et al., 2022; Kowalik et al., 2011; Lee et al., 2016). Brain stimulation treatments, including repetitive transcranial magnetic stimulation (rTMS) and electroconvulsive therapy (ECT), have been proposed for PTSD (Rosson et al., 2022). A recent review paper identified two meta-analyses of rTMS in PTSD but none for ECT. Some have proposed using ECT to disrupt traumatic memory reconsolidation (Andrade et al., 2016), and others have summarised the existing evidence for treating PTSD with ECT (Youssef et al., 2017).

National Institute for Health and Care Excellence (NICE) guidelines list ECT as an option for treating depression, schizophrenia, catatonia and mania but have not for PTSD (NICE, 2003; Rami-Gonzalez et al., 2001). ECT is not recommended as a first-line treatment because of significant adverse effects, including autobiographical memory

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impairment (Donahue, 2000). Empirical evidence for the efficacy of ECT in reducing PTSD symptoms has been reported in case studies (Nielsen et al., 2014; Pacilio et al., 2019) and in a study of ECT for treating depression with comorbid borderline personality disorders or PTSD (Kaster et al., 2018). Isolated observational studies also support this (Ahmadi et al., 2016, 2018). Overall, the evidence for ECT in PTSD is limited and of variable quality, and there are no meta-analyses or quantitative evaluations of existing data. Consequently, the current study consists of a systematic review and meta-analysis of the effects of ECT on PTSD symptoms.

2. Materials and methods

2.1. Study registration

This study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). A protocol for this quantitative review was registered with and reviewed by the PROSPERO International prospective register of systematic reviews (Reference No: CRD42022356780). The protocol is available at: https://www.crd.york.ac.uk/PROSPEROFILES/356780_PROTOCOL_20220830.pdf.

2.2. Search strategy

The literature search was conducted on September 5, 2022 on the PubMed, MEDLINE (Ovid), EMBASE (Ovid), Web of Science, and Cochrane Central Register of Controlled Trials databases. The search was based on the PICO format (population, intervention, comparison, outcome) and adapted according to each database thesaurus and Medical Subject Headings (MeSH) terms (Bramer et al., 2018). The Supplementary material (p2-13) provides further details, including the search terms used. The search was repeated before the final data analysis.

2.3. Eligibility criteria

Inclusion criteria were 1) population: participants who had PTSD symptoms measured with quantitative scales or who were diagnosed with PTSD using standardised measures and had an odds ratio reported (counts), where participants could have a comorbid diagnosis in addition to PTSD (e.g., depression); 2) Intervention: studies that applied any type of ECT to treat PTSD symptoms.; 3) Comparators: studies with a between-subjects design included a control group that did not receive ECT. Patients in either group could receive other treatments, such as antidepressant medications or psychotherapy. Studies using a within-subject design could measure PTSD symptoms before and after ECT; 4) Outcomes: studies measured PTSD symptoms with quantitative scales.

The exclusion criteria were studies: 1) not in English; 2) with insufficient information to estimate effect sizes or missing other essential information; 3) that were case reports.

2.4. Study screening and data extraction

Papers were retrieved in RIS format and managed using Endnote software (Bld13966, EndNote X9.3.3, 2022). PRISMA 2020 guidelines were applied for reporting the screening process (Page et al., 2021). Authors MZ and QL undertook the removal process through independent screens. First, all duplicate articles were removed, followed by those not meeting the inclusion criteria. The full text of the papers meeting the inclusion was downloaded. Discussions between the reviewers resolved discrepancies.

Authors MZ and QL extracted the study characteristics (e.g., author, public year, country, population, age, sex), intervention characteristics (e.g., ECT delivery settings), research methodology (e.g., between-subject & within-subject design), and raw data (mean; standard deviation; sample size).

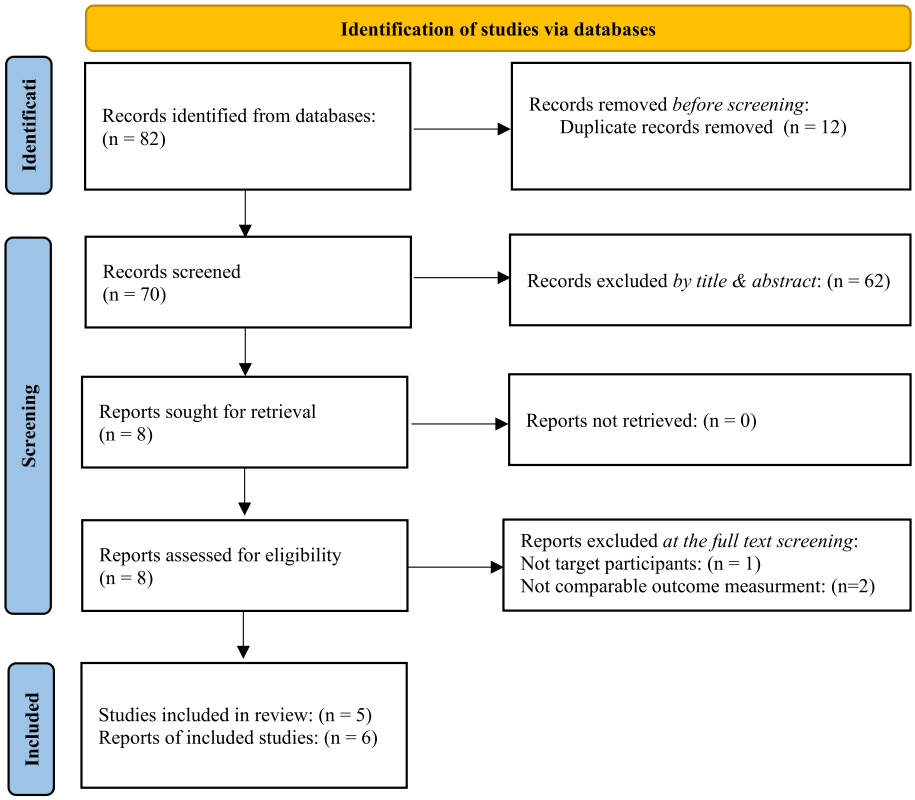

Fig. 1. The PRISMA flow.

Table 1
Study characteristic information.

Study	Study country	Study Design	PTSD criteria	PTSD measurement	PTSD score baseline (SD)	PTSD score post (SD)	Baseline N (dropped out from ECT)	Post-intervention available N	Baseline depression score (scale)	Effect Size g	Mean age (SD)	Sex (female ratio)	ECT device	ECT method	Subsidy ECT method	Comparator design	Valid control group	Main ECT ST (subsidy ST)	average ECT sessions (extra sessions)	Summary
Tang et al., 2021a	Canada	mixed design	DSM-IV diagnosis	CAPS-5	15.6 (2.7)	11.9 (6.6)	14 (3)	11	23.2 (QIDS)	−0.223	37.1 (12.3)	100%	MECTA spECTrum 5000Q	RUL ECT	BL ECT	Traumatic Memory Vs Neutral Memory	NA	600% (150%)	10.8 (2.5)	Tang et al. (2021) compared reactivation of traumatic versus non-traumatic memory in patients receiving ECT. There was no control condition for ECT, so the results reflected within patient changes with open-label ECT treatment. This data set was the neutral memory group
Tang et al., 2021b	Canada	mixed design	DSM-IV diagnosis	CAPS-5	15.4 (2.6)	8.4 (4.9)	14 (3)	14	23.2 (QIDS)	−0.527	37.1 (12.3)	100%	MECTA spECTrum 5000Q	RUL ECT	BL ECT	Traumatic Memory Vs Neutral Memory	NA	600% (150%)	14.3 (NA)	Tang et al. (2021) compared reactivation of traumatic versus non-traumatic memory in patients receiving ECT. There was no control condition for ECT, so the results reflected within patient changes with open-label ECT treatment. This data set was the traumatic memory group
Youssef et al. (2020)	USA	mixed design	DSM-IV diagnosis	PCL	64.7 (1.15)	41 (15.62)	4 (0)	3	NR	−0.659	NR (NR)	NR	MECTA spECTrum 5000Q	RUL ECT	NA	Low amplitude seizure therapy VS RUL ECT treatment	NA	500% (NA)	6 (NA)	Youssef et al. (2020) compared RUL ECT with a low amplitude seizure therapy and found no difference between the groups. However, the low amplitude seizure therapy is a reasonable but not a favourable control condition.

(*continued on next page*)

Table 1 (*continued*)

Study	Study country	Study Design	PTSD criteria	PTSD measurement	PTSD score baseline (SD)	PTSD score post (SD)	Baseline N (dropped out from ECT)	Post-intervention available N	Baseline depression score (scale)	Effect Size g	Mean age (SD)	Sex (female ratio)	ECT device	ECT method	Subsidy ECT method	Comparator design	Valid control group	Main ECT ST (subsidy ST)	average ECT sessions (extra sessions)	Summary
Margoob et al. (2010)	India & USA	within-subject design	DSM-IV diagnosis	CAPS	90.5 (17.3)	59.4 (25.2)	20 (3)	20	22.3 (MADRS)	−0.420	38 (12.1)	50%	MECTA-SR1	BL ECT	NA	baseline vs after 6 sessions ECT	NA	100% (NA)	6 (NA)	Margoob et al. (2010) was an open-label trial with no comparator for ECT, reflecting within patient changes with open-label ECT treatment
Watts and Groft (2010)	USA	mixed design	DSM-IV diagnosis	PCL	54.7 (8.3)	44.9 (8.5)	32 (0)	32	40.2 (MADRS)	−0.339	54.1 (14.39)	12.50%	MECTA spECTrum 5000Q	RUL ECT	BL ECT	dexamethasone enhance vs dexamethasone vs no dexamethasone	NA	250% (NR)	9.5 (4.8)	Watts and Groft (2010) was a retrospective chart review study (1998–2002) of patients with comorbid MDD and PTSD.
Watts (2007)	USA	within-subject design	DSM-IV diagnosis	PCL	71.08 (4.72)	55.62 (9.04)	26 (0)	26	40.5 (MADRS)	−0.645	55 (NR)	15%	MECTA spECTrum 5000Q	RUL ECT	BT ECT	baseline vs after 8 sessions ECT	NA	250% (NR)	9.65 (4.6)	Watts (2007) was a retrospective chart review study (2002–2008) of patients with comorbid MDD and PTSD.
Summary							110 (9)	106			44.13 (15.35)	43.40%								

Note. Baseline N was the number of initially included participants who reported baseline ratings. The numbers in the bracket (dropped out from ECT) refer to those who did not complete the full ECT courses but may still have been assessed after receiving ECT. The post-intervention available N refers to those who were rated after receiving ECT treatment, including those who dropped out. NR refers to not reported; NA refers to not applicable. CAPS refers to the Clinician-Administered PTSD Scale, and CAPS-5 refers to the Clinician-Administered PTSD Scale for DSM-5; PCL refers to PTSD Checklist; QIDS refers to the Quick Inventory of Depressive Symptomatology; MADRS refers to the Montgomery Asberg Depression Rating Scale; RUL ECT refers to the Right Unilateral ECT; BL ECT refers to the Bilateral ECT; BT ECT refers to the Bitemporal ECT. ST refers to the seizure threshold.

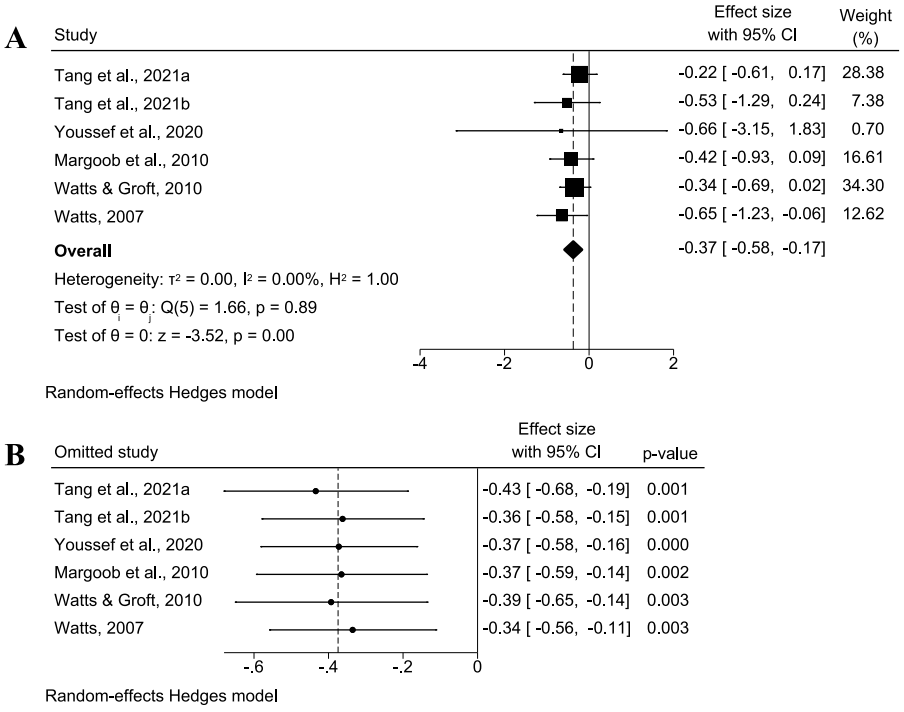

Fig. 2. Forestplot of the pooled effect size and leave-one-out sensitivity analysis.

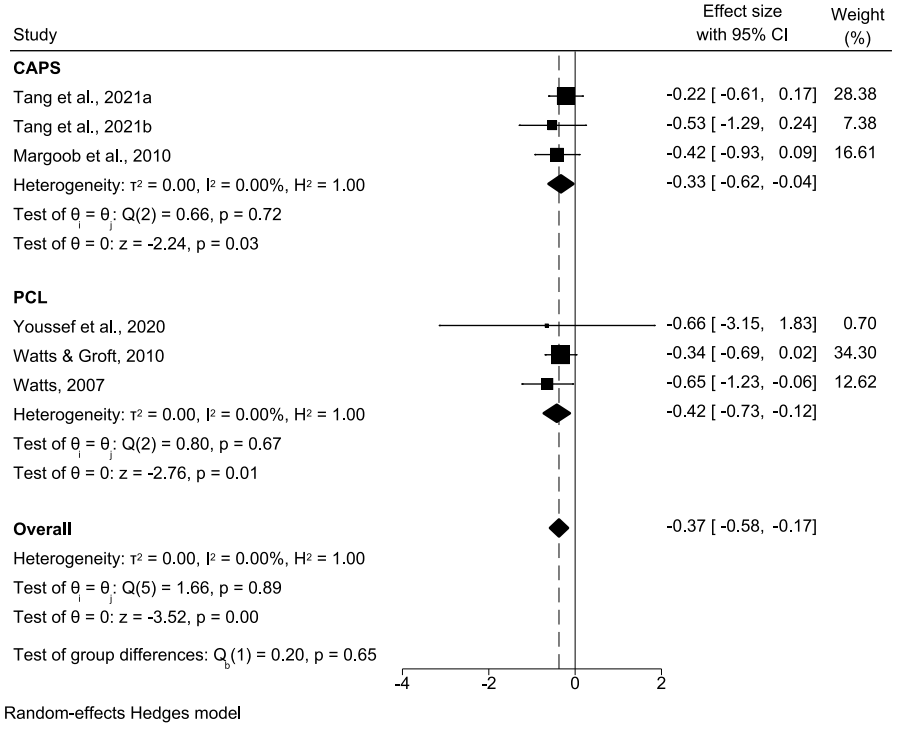

Fig. 3. Forestplot of subgroup analysis between CAPS & PCL measurements.

2.5. Risk of bias (data quality) assessment

Two authors (MZ and QL) independently scored the studies according to the guidelines of the National Heart, Lung, and Blood Institute of the National Institutes of Health quality assessment scales (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). The quality assessment focused on the specification of eligibility criteria, generalisability, intervention description, outcome assessment and incomplete data (Hale et al., 2021). There were 14 items assessed in each quality assessment, as shown in the Supplementary material (p15-16). The tool grades the studies as good, fair, or poor. Good quality studies have less bias risk and are more valid. A fair study is prone to some bias that is insufficient to invalidate its findings, and a poor study has a high risk of bias and is considered invalid (Mogre et al., 2017).

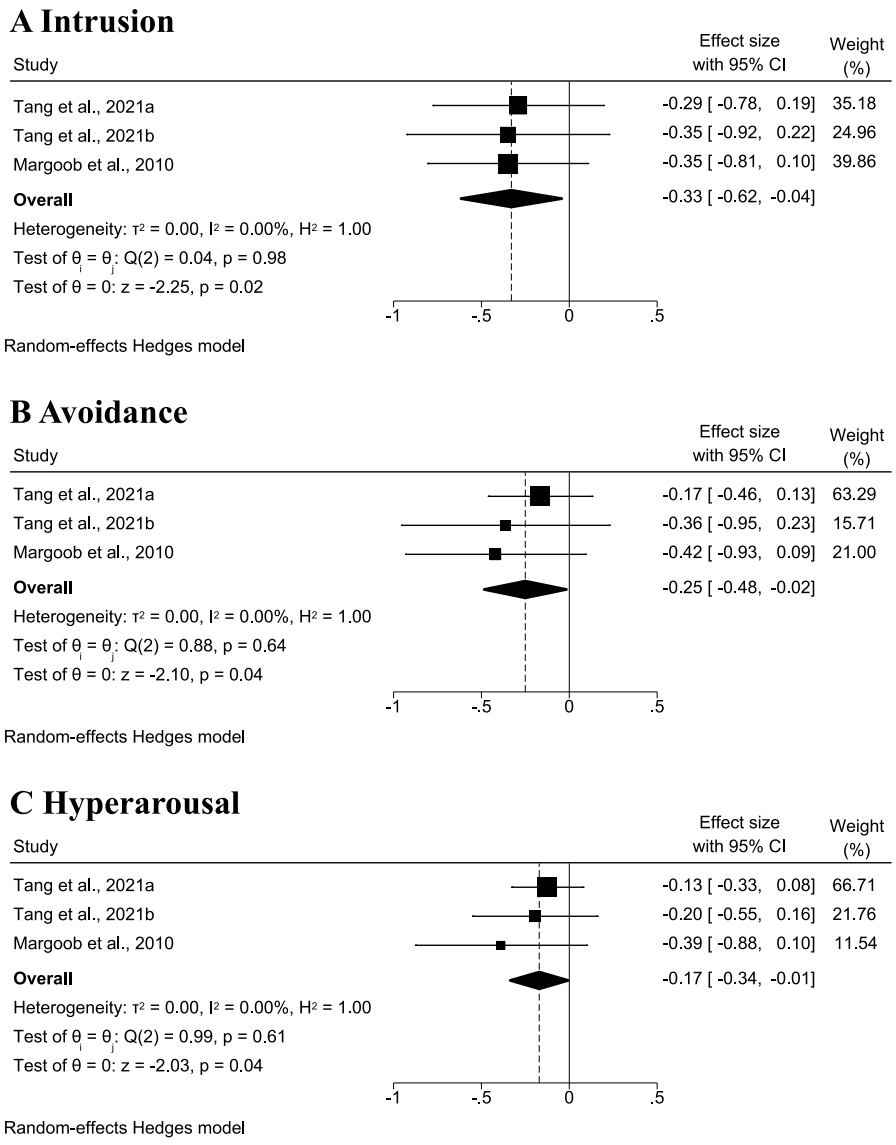

Fig. 4. Forestplots of PTSD subscale measurements.

2.6. Effect size estimation

The current quantitative review aimed to include studies that applied between-subject, within-subject and mixed designs. Consequently, the pooled effect size of the standard mean difference (SMD) was calculated for each study design and adjusted with Hedge's g to account for small sample sizes. The formula for effect size estimation is shown in the Supplementary material (p17-18).

2.7. Statistical analysis

The effect size for ECT on reducing PTSD symptoms was calculated using STATA v17. A random effects model meta-analysis was carried out to generate pooled effect sizes. Data heterogeneity was assessed with the random effects model. The heterogeneity I^2 is considered moderate when $I^2 > 50\%$ and high when $I^2 > 75\%$ (Higgins et al., 2003). Leave-one-out analysis was used to test the sensitivity of the random effects model. Studies without sufficient data to calculate SMD were excluded from pooling. The effect size was considered small when SMD is between 0.2 and 0.5, medium when it is between 0.5 and 0.8, and large when it is above 0.8. Outcomes were reported with 95% confidence intervals (CI). Egger's test was used to assess potential publication bias.

The same meta-analysis was performed on PTSD measurement tool subscales to assess the effect of ECT on subsets of PTSD symptoms. The pooled effect size, baseline depression ratings, treatment seizure threshold, treatment session number, treatment intensity, sample age and sex were included in the meta-regression analysis to explore whether these variables predicted the effect of ECT on PTSD symptoms.

Funding

There was no funding source for this study.

3. Results

As shown in Fig. 1, searching keywords in PubMed, Medline (Ovid), Embase (Ovid), Web of Science and the Cochrane Central Register of Controlled Trials produced 82 articles. Seven studies meeting PRIMA guidelines were initially identified, but two were excluded because they used only the CGI scale as the outcome measurement, which could not be combined with the other studies (Ahmadi et al., 2016, 2018). This left five studies with six datasets for the subsequent analysis. The study screening process is described in more detail in the Supplementary material (p14) .

Among the five studies, two had a mixed design (Tang et al., 2021; Youssef et al., 2020), one was an open-label trial, and two were retrospective chart review within-subject studies (Margoob et al., 2010; Watts, 2007; Watts and Groft, 2010). However, as shown in Table 1, none of the studies had control groups without ECT treatment. Therefore, all five studies were within-subject designs comparing change from the baseline. One study contained two intervention groups (Tang et al., 2021), in which PTSD patients were randomised to reactivate either the traumatic memory related to their PTSD or a neutral memory before each ECT session. Each patient group was therefore treated as a separate dataset for this meta-analysis.

There were 110 participants included who had PTSD symptoms measured at baseline and who received ECT; 101 completed the course of ECT, and 106 completed post-intervention measurements of PTSD symptoms. The pooled mean age of the sample was 44.13 ± 15.35 years old. Among the five studies, four studies delivered right unilateral ECT (RUL ECT) (Tang et al., 2021; Watts, 2007; Watts and Groft, 2010; Youssef et al., 2020), and one applied bilateral ECT (BL ECT) (Margoob et al., 2010). Among the four studies that administered primarily RUL ECT, three also treated patients with BL or bitemporal ECT (BT ECT) (Tang et al., 2021; Watts, 2007; Watts and Groft, 2010), in patients who did not respond sufficiently to the initial RUL ECT treatment. ECT was delivered with seizure thresholds from 100% to 600% in 6–14 sessions (Table 1).

The results of the risk-of-bias assessment are shown in Supplementary Tables 1 and 2 (p15-16). Among the five studies, three were gauged as being of good quality (Margoob et al., 2010; Tang et al., 2021; Youssef et al., 2020), and the remaining two were considered fair (Watts, 2007; Watts and Groft, 2010). Most reports did not control for covariates. Overall, the included studies were limited due to the lack of control groups without ECT but were of acceptable quality to estimate effect sizes.

The pooled effect size revealed a significant overall effect of ECT on PTSD symptoms from five studies and six datasets (Random effects; Hedges' $g = -0.374$, $SE = 0.11$, $z = -3.52$, $p < .001$; Fig. 2A). Estimation of heterogeneity suggested that the chance of inconsistent distribution of the pooled effect sizes was not significant, $Q_{(5)} = 1.66$, $p = .893$, with a low heterogeneity across the effect sizes of the studies, $I^2 = 0\%$. As shown in Fig. 2B on p19 of the Supplementary material, leave-one-out sensitivity analysis on the six datasets suggests that the overall effect remains significant after each study was removed (Hedges' $g = -0.374$, $p < .001$). When each study was omitted, the overall effect size estimate ranged from −0.335 to −0.434, suggesting that the results of the meta-analysis are relatively robust. Egger's regression-based tests did not suggest publication bias, $\beta = -0.74$, $SE = 1.00$, $z = -0.74$, $p = .457$. These results suggest a small but significant effect of ECT in reducing PTSD symptoms.

The PTSD symptom scale (CAPS vs PCL) was entered into the subgroup analysis to determine whether the main effect changed between PTSD measurements. No group difference between the subgroups (CAPS vs PCL) was found, $Q_{b(1)} = 0.2$, $p = .652$ (shown in Fig. 3 at Supplementary material p20). The chance of inconsistent distribution of the pooled effect sizes was not significant in both the CAPS measurements, $Q_{(3)} = 0.66$, $p = .72$, or the PCL measurements, $Q_{(3)} = 0.80$, $p = .67$. This suggests that the measurement of PTSD symptoms with either the CAPS or PCL did not affect the overall results.

The CAPS PTSD subscale ratings were entered into the same random Hedges' g model to determine the effect of ECT on specific PTSD symptoms. The pooled effect size revealed a significant effect of ECT on intrusion symptom ratings from three datasets drawn from two studies (Random effects; Hedges' $g = -0.330$, $SE = 0.15$, $z = -2.25$, $p = .024$), with nonsignificant heterogeneity ($Q_{b(2)} = 0.04$, $p = .982$) (Fig. 4A, Supplementary material p21). The pooled effect size revealed a significant effect of ECT on avoidance symptom ratings from the same two studies and three datasets (Random effects; Hedges' $g = -0.215$, $SE = 0.12$, $z = -2.1$, $p = .036$), with nonsignificant heterogeneity ($Q_{b(2)} = 0.88$, $p = .643$) (Fig. 4B). As shown in Fig. 4C, the pooled effect size revealed a significant effect of ECT on hyperarousal symptom ratings in three datasets from two studies (Random effects; Hedges' $g = -0.171$, $SE = 0.08$, $z = -2.03$, $p = .042$), with nonsignificant heterogeneity ($Q_{b(2)} = 0.99$, $p = .610$).

Finally, the seizure threshold, number of sessions, participant sex and age were not entered into the meta-regression analysis because of insufficient power. Baseline depression ratings were not entered into the meta-regression model because only two baseline QIDS scores and three baseline MADRS scores were available, below the usual threshold of four datasets for this type of analysis (Higgins et al., 2019).

4. Discussion

We conducted a meta-analysis of five studies, including 110 patients receiving ECT to treat PTSD symptoms. To our knowledge, this is the first such quantitative review. We found a small but significant beneficial effect of ECT in reducing overall PTSD symptoms. Our analysis found a low degree of heterogeneity among the studies and a low probability of publication bias. In addition to a general reduction in PTSD symptoms, ECT had a specific effect on reducing intrusion, avoidance, and hyperarousal symptoms. Overall, our analysis suggests that ECT could benefit patients with PTSD symptoms that have not responded to conventional treatments. The high prevalence of comorbid depression could be an independent indication for a trial of ECT in such patients, with existing evidence supporting that clinical option.

There are three important limitations of this meta-analysis: a small sample size, the lack of control groups with patients who did not receive ECT, and the presence of comorbid depression that could confound our analysis. We were able to analyse only five studies with 110 participants, among which two used the CAPS, and three used the PCL symptom rating scales. Only the two CAPS studies provided PTSD symptom subscale data. The non-ECT control subjects meant that none of the studies was blinded. This is a common limitation in ECT research because of the ethical and technical challenges in delivering sham ECT and general anaesthesia. Consequently, we had to rely only on within-subject designs, which are less rigorous. The third limitation is the presence of comorbid depression, which itself is an indication of ECT. One way of addressing this would be to investigate the relationship between depressive symptoms and the effect of ECT on PTSD, but there was insufficient data for this analysis. Therefore, the current results are preliminary and must be treated with caution.

We did not examine the neurobiological mechanisms by which ECT might have therapeutic effects on PTSD. Some studies have suggested that ECT may induce the arborisation of dendrites in the basolateral amygdala, altering structural plasticity and thereby influencing negative emotional memories (Andrade et al., 2016; Khaleel et al., 2013). It is also possible that the beneficial effects of ECT in PTSD are simply due to improvement in comorbid depressive symptoms, even if those symptoms are below the threshold for a formal MDD diagnosis (NICE, 2003; Rami-Gonzalez et al., 2001). On the other hand, our analysis suggests

that ECT has effects on symptoms specific to PTSD and not depression, as captured by the intrusion, avoidance and hyperarousal subscales of the CAPS. As well, changes in depression and PTSD symptoms were not always correlated (Tang et al., 2021) or only weakly correlated (Margoob et al., 2010). Lastly, there are likely shared neurobiological mechanisms for MDD and PTSD, such as a dysfunctional stress response system (Schulze et al., 2019). There are existing treatments, such as SSRIs, used for both MDD and PTSD, so it is not implausible that ECT could also be effective for both disorders.

Despite the uncertainty about the role of antidepressant effects of ECT in PTSD patients, this current study still provides useful clinical findings. PTSD is frequently comorbid with depression, with estimates of 50% having a diagnosis of MDD (Flory and Yehuda, 2022). ECT is typically reserved for severe, treatment-resistant depression, where rates of comorbidity and a history of trauma are common (Rybak et al., 2021). Finally, given the invasiveness of the procedure, ECT will be reserved for treatment-resistant cases of PTSD in which co-morbid depression is more common (Dewar et al., 2020). Further research into the efficacy of ECT for PTSD symptoms is needed to replicate the preliminary findings reported here, but ECT may be a useful treatment in PTSD patients with refractory symptoms and co-morbid depression.

5. Contributors

YL originated the study and drafted the protocol documents for registration. MZ and QL were the independent investigators to conduct the study's review, quality assessment, and data extraction. YL, MZ and LL completed the data analysis and drafted the manuscript. VT, AW, LL and QL revised the draft.

Declaration of competing interest

"none."

Abbreviations

ECT	Electroconvulsive therapy
PTSD	Post-traumatic stress disorder
MDD	Major depression disorder
CBT	Cognitive behavioural therapy
PE	Prolonged exposure therapy
EMDR	Eye movement desensitisation and reprocessing
SSRIs	Selective serotonin reuptake inhibitors
SMD	Standard mean difference
CGI	Clinical Global Impressions Scale
CAPS	Clinician-Administered PTSD Scale
CAPS-5	Clinician-Administered PTSD Scale for DSM-5
PCL	PTSD Checklist
QIDS	Quick Inventory of Depressive Symptomatology
MADRS	Montgomery Asberg Depression Rating Scale
RUL ECT	Right Unilateral ECT
BL ECT	Bilateral ECT
BT ECT	Bitemporal ECT
ST	Seizure threshold
NA	Not applicable
NR	Not reported

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychires.2023.05.080.

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