Cognitive Effects of Electroconvulsive Therapy in Schizophrenia:

A Systematic Review

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Abstract

Objective: To determine the objective cognitive effects of electroconvulsive therapy (ECT) in treatment-resistant schizophrenia (TRS).

Data Sources: A database search of MEDLINE, PsycINFO, and Embase was conducted on September 22, 2022, using the search terms "schizophrenia" and "electroconvulsive therapy." The search was limited to the articles published from 1985 to present, in English, and human studies.

Study Selection: A total of 4293 articles were identified. After screening by title and full text, 17 articles met eligibility criteria. Controlled, open-label, and retrospective studies of acute, maintenance, or continuation ECT were included. An objective cognitive measure(s) had to be the primary or secondary outcome of the study, with no other interventions administered, besides standard-of-care treatment (ie, antipsychotics).

Data Extraction: Data regarding the study design, type of ECT provided, cognitive outcome measures, and change in cognitive performance pre- to post-ECT were extracted. Results are presented as a narrative review.

Results: Overall, ECT was not associated with any significant cognitive deficits in participants with TRS across the domains of global cognition, attention, language, visuospatial function, and executive function. Findings for immediate effects on memory were equivocal, but the majority of studies found no change or an improvement in memory after treatment.

Conclusions: The current evidence supports the conclusion that ECT does not have negative long-term effects on cognition among patients with TRS. Larger, sham-controlled trials are needed to support these conclusions. All studies in this review assessed ECT adjunct to antipsychotics; therefore, the cognitive effects of ECT independent of antipsychotics remain unclear.

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Schizophrenia is a debilitating psychotic disorder characterized by positive and negative symptoms, as well as cognitive impairment. It has been suggested that schizophrenia is associated with generalized dysfunction in higher-order cognitive functions, as opposed to deficits in specific cognitive domains.[1] However, some studies have found specific impairments in attention, working memory, executive functioning, and verbal learning and memory.[2] Interestingly, neurocognitive impairment appears to be independent of positive symptom severity in schizophrenia.[3] While most patients with schizophrenia experience some form of cognitive impairment, there is variability in the severity and specific cognitive domains affected.[2] Cognitive deficits are strong predictors of functional outcomes in schizophrenia,[4] including poor performance on activities of daily living and social functioning, and decreased quality of life.[5] These associations have been found at all stages of schizophrenia, including adolescent and late life, and in both chronic and first-episode schizophrenia.[5]

Antipsychotic medications (APs) are the recommended first-line treatment for schizophrenia.[6,7] First- and second-generation APs are associated with small, but significant, improvements in neurocognitive functioning.[8,9] However, approximately 25% of individuals with schizophrenia do not respond to first-line APs.[10] In these patients, clozapine is typically prescribed. While clozapine is the most effective treatment for schizophrenia and the only medication indicated for treatment-resistant schizophrenia (TRS),[7,11] 60% of individuals continue to be unresponsive to clozapine[12]; consequently, nearly 20% of patients diagnosed with schizophrenia do not respond to any

Clinical Points

- Evidence shows that electroconvulsive therapy (ECT) is an effective treatment for treatment-resistant schizophrenia, yet it is underutilized in practice—likely (at least in part) because of many misconceptions surrounding ECT and its effect on cognition.
- In patients with treatment-resistant schizophrenia, there is no evidence demonstrating long-term cognitive impairments after a course of ECT.

pharmacologic intervention.[12,13] In most texts, "TRS" is defined as failure to respond to 2 or more antipsychotics at adequate dosage and duration.[14]

To address this issue of nonresponse, several nonpharmacologic treatment options have been developed. Electroconvulsive therapy (ECT) has shown efficacy for improving symptoms in TRS, specifically when given as augmentation therapy to clozapine or other antipsychotics.[15–17] During ECT, electric stimulation is applied to the brain to induce a brief tonic-clonic seizure. The exact mechanism of action of ECT is unknown, but it is hypothesized that the induction of seizures causes changes in neurotransmitters, neuroplasticity, and functional connectivity in the brain[18–20]; several studies have found structural and functional neuroimaging changes in distinct brain regions, such as the hippocampus and insula, after ECT for schizophrenia.[21,22]

While ECT was originally developed for the treatment of psychotic disorders,[23] the use of ECT for schizophrenia has greatly decreased in Western countries over the past several decades.[24] However, in Asian and African countries, the use of ECT for psychotic disorders remains prevalent.[24] Further, several Western treatment guidelines, including the American Psychiatric Association, National Institute for Health and Care Excellence, and Royal College of Psychiatrists guidelines, recommend the use of ECT in catatonic schizophrenia, in those who respond poorly to neuroleptic medications, and in clozapine nonresponders.[25–27] ECT shows impressive efficacy in TRS populations: 1 review found a response rate (defined as ≥20% improvement in schizophrenia symptoms) of 70–85% when ECT was added to AP.[16]

Despite the efficacy of ECT, the risk of cognitive impairment, specifically memory impairment, is a major concern.[28] Between 29% and 55% of patients receiving ECT report persistent memory loss.[29] However, the cognitive effects of ECT have been studied extensively in major depressive disorder (MDD), and the evidence supports that ECT is not associated with objective, long-term cognitive deficits in this population.[30] ECT may even be associated with improvements in cognitive performance, with previous studies showing an improvement in many cognitive domains—including processing speed, working memory, anterograde memory, and some aspects of executive function—approximately 2 weeks posttreatment.[30] However, certain ECT parameters may increase the risk of cognitive impairment in MDD populations: specifically, bitemporal electrode placement (versus unilateral) and more frequent administrations.[30,31]

Cognitive effects of ECT have been less studied in schizophrenia. Several review papers have explored this topic as a secondary outcome, finding acute cognitive disturbances, but no long-term cognitive impairments.[16,32,33] One meta-analysis focused on memory impairment following ECT in schizophrenia and found that ECT + AP was associated with greater transient memory impairment compared to AP alone.[34] However, this study only looked at Chinese patients and did not consider other cognitive domains.[34] Therefore, there is no definitive conclusion on whether or not ECT causes objective cognitive impairment in people with schizophrenia. Considering the enormous prevalence of cognitive impairment in schizophrenia, the persistent fear of memory loss associated with ECT, and the high proportion of schizophrenia patients who are treatment-resistant and may be referred to ECT, it is crucial that clinicians and researchers, as well as patients and their families, gain a clearer understanding of how ECT affects memory and overall cognitive function in schizophrenia populations.

The aim of the present systematic review is to assess and synthesize research addressing the objective cognitive effects of ECT in schizophrenia using a comprehensive and systematic approach.

METHODS

Search Methods

A comprehensive database search of MEDLINE, PsycINFO, and Embase was conducted through Ovid using the search terms *schizophrenia, schizophrenic disorder, electroconvulsive therapy, electroconvulsive, electric convulsive, electric shock, electroshock,* and *ECT*. Clinical trial registries were also searched using the terms schizophrenia and electroconvulsive therapy: specifically, ClinicalTrials.gov, the European Union Clinical Trials Register, and the World Health Organization International Standard Randomised Controlled Trial Number registry. The search was completed on September 22, 2022 (databases), and September 25, 2022 (clinical trial registries). The full search strategy is presented in Supplementary Appendix 1. The authors screened all results independently to assess for eligibility. Irrelevant articles were excluded based on title and abstract. The remaining articles were assessed for eligibility criteria using the full text; reasons for exclusion were recorded. The reference sections of included articles were searched

Table 1.
GRADE Criteria Checklist

GRADE Item[a]	Results
Selection bias: Was random sequence generation used?	All controlled trials met criterion NA: open-label, retrospective, and naturalistic studies
Performance bias: Was there blinding of participants?	Met criterion: Jiang et al[38]; Stryjer et al[39]
Detection bias: Was there blinding of outcome assessments?	Met criterion: Jiang et al[38]; Petrides et al[40]; Stryjer et al[39]; Yang et al[41]
Reporting bias: Were more than 80% of participants enrolled included in the analysis?	Met criterion: Bansod et al[42]; Chan et al[43]; Chanpattana[44]; Chanpattana and Kramer[45]; Davarinejad et al[46]; Jiang et al[38]; Liu et al[47]; Mishra et al[48]; Petrides et al[40]; Simsek et al[49]; Tan et al[50]; Vuksan Ćusa et al[51]; Wysokinski et al[52]; Yang et al[41]
Selective reporting: Were data reported consistently for the outcome of interest?	All studies met this criterion
Did the trials end as scheduled?	All studies met this criterion

[a]GRADE criteria checklist derived from Guyatt et al[36] and Meader et al.[37]
Abbreviations: GRADE = Grading of Recommendations, Assessment, Development, and Evaluation, NA = not applicable.

for any additional sources. Discrepancies between authors were discussed to reach consensus.

Eligibility Criteria

Controlled trials, open-label trials, and retrospective studies were included in this systematic review. Case studies or studies where statistical analysis could not be completed due to small sample size were excluded. Study participants must have received ECT in the year 1985 or later. Prior to 1985, strict guidelines for ethical and scientifically validated ECT administration were not applied internationally.[35] Therefore, before 1985, cognitive deficits linked to ECT may have been the result of the conditions under which ECT was administered, not ECT itself.

In addition to the criteria above, the following inclusion criteria were applied:

1. Written in English.
2. Study population between the ages of 18 and 65 years.
3. Study participants must be diagnosed with schizophrenia or schizophrenic psychosis according to the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*)-*III*, -*IV*, or -*5* or the WHO *International Classification of Diseases* 9th, 10th, or 11th Revision.
4. Primary or secondary outcomes include an objective and validated measure(s) of cognition.
5. No other investigational drug may be given with ECT; only standard-of-care treatment is permitted, such as antipsychotics.
6. Acute, maintenance, or continuation ECT trials were included.

Data Extraction and Synthesis

For all studies, the following data were extracted: background information (authors and year of publication), study sample demographics (number of participants enrolled, mean age of study population, and percent of study population that is female), number of ECT sessions, type of ECT provided (ie, bilateral versus unilateral, and if it was a maintenance/continuation ECT trial), study design, cognitive outcome measures used, cognitive outcome results, discontinuation/dropout rates, and study limitations.

A meta-analysis was not completed as part of this review because of the heterogeneity among the cognitive measures used and time points at which cognition was measured, thus significantly limiting the feasibility and value of quantitative synthesis.

Quality of Assessment

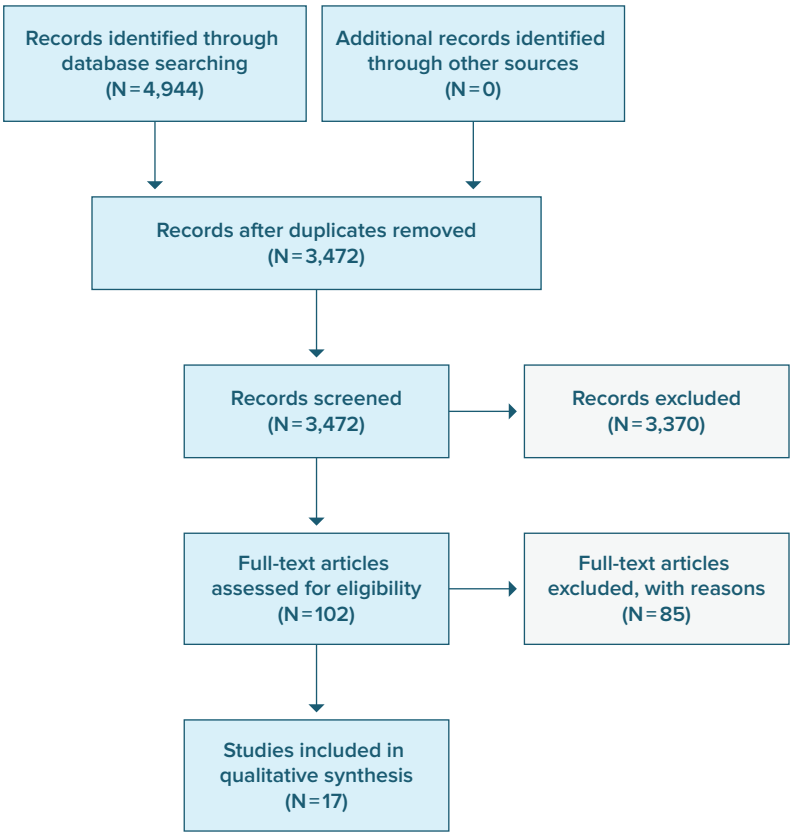
Quality of assessment of included articles was conducted using the Grading of Recommendations, Assessment, Development, and Evaluation criteria checklist.[36,37] The results of this review are presented in Table 1. Only Jiang et al[38] blinded patients to treatment, as they compared magnetic seizure therapy to ECT; no other studies were free of performance bias, as participants were not blinded to treatment. This was not unexpected, as it is impossible to blind participants in ECT versus medication studies without using sham ECT, which is often deemed unethical in severely ill populations.[53] A majority of studies (13 of 17) did not blind outcome assessments, which may have led to expectancy effects. Three studies included less than 80% of enrolled and/or eligible participants in their final analysis[47,54,55]; another did not include data to calculate this value.[56] However, this was deemed acceptable for the clinical population being investigated and the retrospective nature of many of these studies. Finally, there was no evidence of selective reporting, and no studies were terminated prematurely.

Additionally, clinical trial registries were searched to reduce the likelihood of publication bias.

RESULTS

Of 4293 articles identified through the database search, 102 full-text articles were screened for eligibility,

Figure 1.
PRISMA Flow Diagram of Studies Identified, Screened, and Assessed for Inclusion



Abbreviation: PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

and 17 studies were included in this review (Figure 1). The main reasons articles were excluded were because they did not measure cognition, they used subjective measures of cognition only, or the study sample included other psychiatric disorders in the analysis. No additional articles were identified from clinical trial registries or the reference section of included articles.

Description of Studies

Seventeen studies published between 2000 and 2022 were identified. The majority of studies were completed in Asian countries (N = 12). Participants were allowed to take APs during their course of ECT. All studies followed patients during an acute course of ECT for schizophrenia; 4 of these studies continued to follow patients during maintenance ECT (MECT) for 6–12 months.[41,44,45,48] MECT involves administering ECT less frequently over an extended period of time to individuals who previously responded well to acute ECT, with the goal of maintaining response and preventing relapse. These MECT studies reported long-term cognitive data during the treatment course. In addition, one study completed a follow-up assessment 4 weeks after completing a course of ECT.[39] All remaining studies only completed cognitive assessments immediately after the final ECT session, within a week of last treatment.

The majority of studies (N = 14) used bilateral electrode placement (including bitemporal and/or bifrontal) for ECT. Two studies used either bilateral or right unilateral placements.[50] Only one study used unilateral placement exclusively.[46] Most studies (N = 12) used propofol as the anesthetic during ECT; other anesthetic agents included thiopental (N = 4), methohexital (N = 2), etomidate (N = 1), and dexmedetomidine (N = 1), with some studies using more than 1 agent. All studies used succinylcholine as a paralytic agent. Several studies also gave adjunct anticholinergics, such as atropine, clemastine, and glycopyrrolate, with anesthesia.

Description and results of all studies are presented in Tables 2 and 3. Further details on the specific cognitive assessment tools and corresponding cognitive domains measured for each study are included as Supplementary Table 1.

Table 2.

Summary of Included Studies

First author, year	Location	N	Study design	Antipsychotics	Mean (SD) age	% Female	No. of ECT sessions (SD)	Type of ECT	Outcome measures	Outcome time points (after last ECT session)	Main cognitive findings[a]
Tan et al, 2022[50]	Singapore	132	Retrospective database analysis	Any	38.9 (13.8)	44%	6.0 (0.0)	BT, BF, or RUL	MoCA	Not specified	No change in MoCA score (mean baseline score: 18.1 ± 0.7, end of study: 19.6 ± 0.7)
Bansod et al, 2018[42]	India	82	Controlled trial	Any	29.5 (6.1)	40%	8.0 (0.0)	BT, BF, or RUL	WMS, AMI	Days 1–2	Decreased performance WMS and AMI Impairment was worst with BL electrode placement
Simsek et al, 2015[49]	Turkey	61	Naturalistic	Any	33.3 (10.9)	26%	6.8 (1.2)	BT	FAB	Days 2–7	Improvement in FAB score
Chan et al, 2019[43]	Singapore	50	Retrospective database analysis	Any	39.2 (15.3)	52%	9.8 (2.9)	BT, BF	MoCA	Not specified	Improvement in MoCA score (mean baseline score: 18.5 ± 8.0, end of study: 22.5 ± 6.9)
Chanpattana and Kramer 2003[45]	Thailand	46	Open label	Flupenthixol	32.0 (6.4)	UNK	12.3 (4.5)	BL; MECT	MMSE	After last treatment (not specified), 1 y	Improvement in MMSE score (mean baseline score: 26.8 ± 3.2, end of study: 29.0 ± 1.7) Maintained after 1 y MECT
Li et al, 2022[47]	China	37	Open label	Any	31.5 (8.0)	32%	8.0 (0.0)	BF	MCCB	Days 1–2	Improvement in visual learning Decreased performance in verbal learning after 4 sessions, but returned to baseline by end of treatment course No change in processing speed, attention, working memory, verbal learning, or problem-solving
Jiang et al, 2021[38]	China	37	Controlled trial	Any	33.8 (10.8)	61%	10.0 (0.0)	BT	RBANS	Not specified	Decreased performance in immediate and delayed memory, and total RBANS score No change in visuospatial function, language, or attention
Vuksan Ćusa et al, 2018[51]	Croatia	31	Open label	Any	34.1 (11.2)	48%	10.2 (UNK)	BT	CVLT, BVRT, digit span, verbal fluency, Stroop test	Day 1	Improvement in immediate and delayed verbal memory (CVLT), and executive function/ cognitive flexibility (Stroop interference) No change in visual memory, working memory, attention, verbal fluency, or psychomotor speed
Mishra et al, 2022[48]	India	30	Open label	Any excl. clozapine	34.5 (10.3)	40%	UNK	BL; MECT	MoCA	6 wk, 3 mo, 6 mo	No change from baseline MoCA (19.1 ± 0.4) score after 6 wk (20.3 ± 0.4), 3 mo (20.4 ± 0.4), and 6 mo (20.5 ± 0.4) of MECT

(continued)

Table 2 (continued).

First author, year	Location	N	Study design	Antipsychotics	Mean (SD) age	% Female	No. of ECT sessions (SD)	Type of ECT	Outcome measures	Outcome time points (after last ECT session)	Main cognitive findings[a]
Pawelczyk et al, 2015[55]	Poland	27	Open label	Any	32.8 (UNK)	48%	13.1 (UNK)	BT	TMT, WCST	Days 1–3	No change in attention (TMT-A), executive function (TMT-B, WCST)
Yang et al, 2016[41]	China	27	Controlled trial	Risperidone	33.6 (6.9)	45%	10.8 (1.9)	BT; MECT	MCCB	After last acute treatment (not specified), 2 wk, 4 wk, then monthly until 1 y	Improvement in verbal and visual memory after acute and MECT No change in processing speed, attention, working memory, or problem-solving after acute and MECT
Chanpattana 2000[44]	Thailand	21	Open label	Flupenthixol	32.3 (7.2)	76%	11.4 (5.0)	BL; MECT	MMSE	1 wk, 1 y	Improvement in MMSE score (mean baseline score: 26.9 ± 3.2, end of study: 29.2 ± 1.6) Maintained after 1 y MECT
Petrides et al, 2015[40]	USA	17	Controlled trial	Clozapine	35.7 (2.3)	25%	15.8 (4.2)	BL	MMSE, RAVLT, RMB paired-word and story-recall subsets, letter-number span, TMT, COWAT, CPT, set-shifting	1 wk	Decreased scores on measures of processing speed No change in MMSE, visual or verbal memory, or executive function
Davarinejad et al, 2019[46]	Iran	14	Open label	Any	31.1 (8.1)	50%	8.0 (0.0)	UL	MMSE	1 wk, 4 wk, 12 wk	Decreased MMSE score after completion of ECT (mean baseline score: 25.1 ± 2.2, end of study: 23.1 ± 2.7), but performance returned to baseline levels at 4 and 12 wk follow-up (24.6 ± 2.3 and 25.2 ± 2.0, respectively)
Li et al, 2017[56]	China	13	Open-label	Any	29.4 (8.5)	UNK	9.1 (1.1)	BL	Digit span (forward, backward), digit symbol coding, verbal fluency	Not specified	No change in working memory (digit span) or verbal fluency performance
Stryjer et al, 2012[39]	Israel	12	Controlled trial	Any	30.7 (11.7)	58%	7.8 (2.3)	BL	MMSE, ADAS-cog	After last treatment (not specified), 4 wk	No change in ADAS-cog from baseline to end of treatment, improved at week 4 follow-up No change in MMSE from baseline to end of treatment (mean baseline score: 26.3 ± 2.9, end of study: 24.8 ± 4.0), improved at 4-week follow-up
Kim et al, 2018[54]	Korea	7	Naturalistic	Clozapine	36.6 (12.5)	50%	14.9 (4.6)	BL	MMSE	Not specified	No change in MMSE score (mean baseline score: 24.9 ± 3.4, end of study: 27.4 ± 1.8)

[a]All significant results with $P < .05$, measures from baseline to after completion of ECT course, unless otherwise specified.

Abbreviations: ADAS-cog = Alzheimer Disease Assessment Scale—Cognitive Subscale, AMI = autobiographical memory interview, BF = bifrontal, BL = bilateral (unspecified temporal vs frontal), BT = bitemporal, BVRT = Benton Visual Retention Test, COWAT = Controlled Oral Word Association Test, CPT = Continuous Performance Task, CVLT = California Verbal Learning Test, ECT = electroconvulsive therapy, FAB = Frontal Assessment Battery, MCCB = MATRICS Consensus Cognitive Battery, MECT = maintenance electroconvulsive therapy, MMSE = Mini-Mental State Examination, MoCA = Montreal Cognitive Assessment, RAVLT = Rey Auditory Verbal Learning Test, RBANS = Repeatable Battery for the Assessment of Neuropsychological Status, RMB = Randt Memory Battery, RUL = right unilateral, TMT = Trail Making Test, UL = unilateral, UNK = unknown, WCST = Wisconsin Card Sorting Test, WMS = Wechsler Memory Scale.

Table 3.

Change in Cognitive Domain Scores at Different Follow-Up Points Across Studies[a]

	Post-ECT[b]	1–7 d	4 wk	6 wk	12 wk	6 mo	1 y
Global cognition	151[c]	52[d]	14	30	44	30	67
Global memory		82					
Working memory	40	82[e]	27				27
Verbal memory	27	167[f]					27
Visual memory	27	167[g]	27				27
Autobiographical memory		82					
Immediate recall	37						
Delayed recall	37						
Attention	64	95	27				27
Processing speed	27	68[h]	27				27
Language	37						
Verbal fluency	13	31					
Visuospatial function	37						
Reasoning/problem-solving	27	37	27				27
Executive function		92[e]					

LEGEND: No change from baseline; Improved from baseline; Worsened from baseline; Equivocal results

[a]Total numbers of participants assessed at each time point across studies are listed in the table.
[b]Measured after completion of ECT, but exact time point not specified.
[c]Improvement was observed in other studies with smaller sample sizes.
[d]n = 21 improved, n = 17 no change, and n = 14 worsened from baseline.
[e]No change observed in other studies with smaller sample sizes.
[f]n = 31 improved, n = 54 no change, and n = 82 worsened from baseline.
[g]n = 37 improved, n = 48 no change, and n = 82 worsened from baseline.
[h]Worsened performance observed in other studies with smaller sample sizes.
Abbreviation: ECT = electroconvulsive therapy.

Measures of Cognitive Impairment (MMSE and MoCA)

Nine studies assessed cognition using formal scales that assess severity of cognitive impairment, namely, the Mini-Mental State Examination (MMSE)[57] and Montreal Cognitive Assessment (MoCA).[58] In 5 of the studies, the average MMSE/MoCA score at baseline qualified as clinically significant cognitive impairment (MMSE score <25 or MoCA score <26; details in Table 1).

Across all studies, regardless of baseline cognitive function, global cognition either remained stable or improved after completing ECT. In Tan et al,[50] the largest study identified (n = 132) that there was no significant difference in MoCA score before and after 6 ECT sessions. Five additional studies assessed the immediate effects on cognition after an acute course of ECT. Chan and colleagues[43] found a clinically significant improvement in MoCA score from baseline to end of treatment. Stryjer et al,[39] Petrides et al,[40] and Kim et al[54] found no change in MMSE from baseline to end of treatment; in fact, in the study by Stryjer et al,[39] an improvement in MMSE was actually identified at 4-week follow-up. In the study by Darivenjad et al,[46] there was a significant decrease in MMSE score within the first week after treatment, but at 4- and 12-week follow-up, scores were no longer significantly different from baseline, demonstrating no long-term adverse cognitive effects.

Three studies examined the cognitive effects of MECT. Both studies by Chanpattana[44] and Chanpattana and Kramer[45] found an improvement in MMSE score after the initial acute course of ECT; this improvement was maintained after 1 year of MECT. Mishra et al[48] found no change from baseline MoCA at week 6, month 3, and month 6 of MECT.

Memory

Across studies, 7 domains of memory were assessed: verbal memory, visual memory, working memory, recognition memory, autobiographical memory, immediate recall, and delayed recall. In the 2018 study by Bansod and colleagues,[42] which was the largest study assessing memory (n= 82), memory significantly worsened after 8 ECT sessions across the domains of verbal, visual, working, recognition, and autobiographical memory. No other studies assessed recognition or autobiographical memory. The remainder of studies assessing memory subdomains found no change, or an improvement, from baseline to end of treatment. Liu et al[47] demonstrated no change in verbal or working memory and improvement in visual memory, after 8 ECT sessions. Vuksan Ćusa and colleagues[51] demonstrated no change in visual or working memory after an average of 10 ECT sessions. Petrides et al[40] found no change in verbal or visual memory performance after an average of 16 sessions, while Li et al[56] demonstrated no change in working memory before vs after average 9 sessions. Finally, Yang and colleagues[41] demonstrated an improvement in verbal and visual memory and no change in working memory, after average 11 ECT sessions, and these findings were maintained at 1-year follow-up.

Two studies assessed immediate and delayed recall performance before vs after a course of ECT: Liu et al[47] found performance on both measures worsened after ECT, while Yang et al[41] found performance improved. Improvement was maintained at 1-year follow-up by Yang and colleagues.

Speed of Processing

Speed of processing was measured in 4 studies. There was no change in speed of processing after a standard course of ECT in studies by Liu et al, Vuksan Ćusa et al, and Yang et al.[41,47,51] In long-term follow-up by Yang and colleagues,[41] this finding was persistent after 1 year. However, Petrides and colleagues[40] demonstrated worsened speed of processing in the study population after ECT.

Attention

There was no change in performance on measures after an acute course of ECT across 5 studies.[38,41,47,51,55] In long-term follow-up by Yang and colleagues,[41] this finding persisted after 1 year.

Language

In the study by Jiang et al,[38] there was no change in overall language performance, as measured on the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) after 10 ECT sessions.[59] Vuksan Ćusa et al[51] and Li et al[56] both demonstrated no change in verbal fluency after an acute ECT course.

Problem-Solving

There was no difference from baseline to end of treatment on measures of problem-solving in studies by Liu et al and Yang et al.[41,47] This finding was maintained at 1-year follow-up in Yang et al.[41]

Visuospatial Function

The 2021 study by Jiang et al[38] was the only study to compare visuospatial function before and after 10 ECT treatments: they found no difference in average performance at baseline vs end of treatment.

Executive Function

The largest study to assess executive function, Simsek et al[49] (n = 61), found an improvement in performance after ECT course. This was also found by Vuksan Ćusa and colleagues.[51] No change from baseline to end of treatment was found in the studies by Pawelczyk et al or Petrides et al.[40,55]

DISCUSSION

The current systematic review demonstrates that, based on the synthesis of available studies, ECT is not associated with significant cognitive deficits in participants with schizophrenia, specifically in the domains of global cognition, attention, language, visuospatial function, problem-solving, and executive function. Findings for the immediate effects of ECT on memory are equivocal, as the study with the largest sample size found a negative effect within 1–2 days after completing an ECT course.[42] Only 1 study with a smaller sample size (n = 27) assessed longer-term memory changes after 4 weeks and 1 year post-ECT, finding no change or improvement across several memory subdomains.[41]

Approximately a quarter of people with schizophrenia are classified as "treatment-resistant."[10] TRS remains a major social and economic burden, as it is associated with higher rates of substance abuse, physical comorbidities, unemployment, and social and functional impairment.[60,61] Moderate-to-severe cognitive dysfunction is a core feature of schizophrenia, with deficits consistently demonstrated in the domains of attention, memory, and executive function.[2] Cognitive deficits are more severe in TRS than in treatment-responsive patients, particularly in the domains of verbal memory and language.[62] Therefore, it is important that treatments for TRS do not cause further cognitive impairments in this already vulnerable population.

Previous systematic reviews have explored the cognitive effects of ECT in MDD and have found no long-term negative cognitive effects of ECT in this population.[30,63,64] One possible exception to this is autobiographical memory, for which the data are equivocal.[65] The cognitive effects of ECT have been less studied in schizophrenia, perhaps because of the underutilization of ECT for TRS in clinical practice.[66] Despite its underutilization, ECT is consistently shown to be an effective treatment for TRS, and treatment with ECT plus antipsychotics is associated with higher rates of

clinical improvement compared to antipsychotics alone.[67,68] Regardless of the compelling evidence for the clinical effectiveness of ECT, many are still resistant to its use, most likely because of the long history of misconceptions surrounding ECT—with one of the commonest misconceptions being that it will cause brain damage and memory loss.[69] However, as presented in this review, evidence fails to demonstrate the negative long-term effects of ECT on cognitive function. In fact, many studies demonstrate a cognitive benefit of ECT in patients with TRS.[41,43–45,47,49,51] One potential exception is memory performance, with 1 larger-scale study (n = 82) showing worsening memory performance immediately after ECT[42]; while the remainder of the studies do not support this conclusion, particularly in the long-term, these studies had a smaller sample size.

By synthesizing the current evidence regarding the cognitive effects of ECT in schizophrenia, this article aims to address the question of whether ECT causes long-lasting and severe cognitive impairments. Across the 17 identified studies that objectively measured cognitive function before and after an ECT course, the majority demonstrate that ECT is not associated with impaired cognitive functioning, with the exception of memory within a few days after completing ECT. All studies assessing long-term changes in cognitive function, including memory, found no change, or an improvement, in cognitive performance at 1-month to 1-year follow-up. Of note, cognitive improvement in these study populations may be, at least in part, due to improvements in organization of thought, a key symptom of schizophrenia that is known to improve with treatment.[70] There is an established association between neurocognitive performance and disorganized thinking in schizophrenia.[71]

Limitations

There are several limitations that must be considered when interpreting the results of this systematic review. First, most studies had a relatively small sample size, affecting the power of their results. Second, no sham treatment and/or double-blind conditions were used; this is a common limitation in ECT research, as it is often unethical and technically difficult to blind patients to ECT. Third, the vast majority of participants were prescribed antipsychotics. It has been previously found that antipsychotics may exert small but beneficial effects on cognition[8,9]; therefore, the lack of cognitive changes seen after ECT may have been related to neuroprotective effects of antipsychotics. Furthermore, only patients who were well enough to complete cognitive testing could be included in the studies. Therefore, these findings cannot be extended to individuals with poorer functional capacity, such as patients with severe catatonia or who are uncooperative due to their condition. The decision to exclude patients over 65 was made in order to reduce the confound of the neurocognitive impairments associated with aging; however, this may limit the generalizability of results. Additionally, many studies assessed cognitive function with the MMSE or MoCA, which are brief screening tools developed for mild cognitive impairment and dementia.[57,58] Therefore, they may not be sensitive enough to detect cognitive changes in populations with less severely impaired cognition. Further, while the MMSE has been validated for serial testing of cognitive changes over a period of 10–20 days, similar research on serial MoCA administrations to quantify cognitive changes over a short period of time has been limited. We did not assess for the role of electrode placement on cognitive performance; however, this was explored in a previous review, which found right unilateral and bifrontal electrode placement more cognitively favorable than bitemporal.[72] Finally, the majority of studies included in this review were conducted in Asian and Middle Eastern countries, which may limit the generalizability of the findings.

CONCLUSION

In conclusion, based on the current literature, there is no compelling evidence suggesting cognitive impairment following a standard course of ECT in populations with schizophrenia. The majority of studies found a neutral or beneficial effect of ECT on global cognition, attention, language, visuospatial function, and executive function. There were equivocal results for performance on various memory domains shortly after finishing an ECT course, but no evidence of long-term impairment. There were several limitations to the current review, most importantly that the included studies were limited by small sample size and did not have a control group, and all studies allowed concomitant antipsychotic use during ECT. Larger, sham-controlled trials are therefore needed to further support the conclusions of this review.

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Supplementary Material

Article Title: Cognitive Effects of Electroconvulsive Therapy in Schizophrenia: A Systematic Review

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

DISCLAIMER

Version Date: February 19, 2024

Cognitive Effects of Electroconvulsive Therapy in Schizophrenia: A Systematic Review

SUPPLEMENTARY MATERIAL

Supplementary Appendix 1: Database Search Strategies

I. MEDLINE Database (via Ovid)

#	Searches	Results
1	exp Schizophrenia/	112994
2	Schizophrenia*.tw,kf.	126079
3	schizophrenic disorder*.tw,kf.	1110
4	exp Electroconvulsive Therapy/	13999
5	electroconvulsive.tw,kf.	10541
6	electric convulsive.tw,kf.	103
7	electric shock.tw,kf.	3055
8	electroshock.tw,kf.	4355
9	ECT.tw,kf.	10122
10	1 or 2 or 3	155811
11	4 or 5 or 6 or 7 or 8 or 9	26998
12	10 and 11	2052
13	limit 12 to (english language and humans)	1435
14	limit 13 to yr="1985 -Current"	983

Date of search: September 22, 2022

II. PsycInfo Database (via Ovid)

#	Searches	Results
1	exp Schizophrenia/	96559
2	Schizophrenia*.tw.	116979
3	schizophrenic disorder*.tw.	1413
4	exp Electroconvulsive Shock Therapy/	7116
5	electroconvulsive.tw.	8594
6	electric convulsive.tw.	81
7	electric shock.tw.	3238
8	electroshock.tw.	1381
9	ECT.tw.	8182
10	1 or 2 or 3	129291
11	4 or 5 or 6 or 7 or 8 or 9	15090
12	10 and 11	1559
13	limit 12 to (human and english language)	1219
14	limit 13 to yr="1985 -Current"	1055

Date of search: September 22, 2022

III. Embase Database (via Ovid)

#	Searches	Results
1	exp schizophrenia/	194797
2	schizophrenia.tw,kw.	168388
3	schizophrenic disorder.tw,kw.	559
4	exp electroconvulsive therapy/	20246
5	electroconvulsive.tw,kw.	12479
6	electric convulsive.tw,kw.	42
7	electric shock.tw,kw.	3081
8	electroshock.tw,kw.	3850
9	ECT.tw,kw.	14296
10	1 or 2 or 3	222859
11	4 or 5 or 6 or 7 or 8 or 9	33177
12	10 and 11	3571
13	limit 12 to (human and english language)	2977
14	limit 13 to yr="1985 -Current"	2906

Date of search: September 22, 2022

IV. ClinicalTrials.gov

"schizophrenia" AND "electroconvulsive therapy"

Date of search: September 25, 2022

V. World Health ISRCTN registry

"schizophrenia" AND "electroconvulsive therapy"

Date of search: September 25, 2022

VI. European Union Clinical Trials Register

"schizophrenia" AND "electroconvulsive therapy"

Date of search: September 25, 2022

Supplementary Table 1: Cognitive Assessment Tools and Corresponding Domains

First Author, Year	Measure	Domain(s)
Bansod 2018 [1]	Wechsler Memory Scale	General memory, attention/ concentration, verbal memory, visual memory, delayed recall
	Autobiographical Memory Interview	Autobiographical memory
Chan 2019 [2]	Montreal Cognitive Assessment	Global cognition
Chanpattana 2000 [3]	Mini Mental State Exam	Global cognition
Chanpattana 2003 [4]	Mini Mental State Exam	Global cognition
Davarinejad 2018 [5]	Mini Mental State Exam	Global cognition
Jiang 2021 [6]	Repeatable Battery for the Assessment of Neuropsychological Status	Immediate recall, visuospatial function, language, attention, delayed recall
Kim 2018 [7]	Mini Mental State Exam	Global cognition
Li 2017 [8]	Digit span - forward & backward Digit Symbol Coding Verbal fluency test	Working memory, attention Processing speed Verbal fluency
Liu 2022 [9]	MATRICS Consensus Cognitive Battery	Processing speed, attention, working memory, verbal learning, visual learning, reasoning/problem solving, social cognition
Mishra 2022 [10]	Montreal Cognitive Assessment	Global cognition
Pawelczyk 2015 [11]	Trail Making Test A Trail Making Test B Wisconsin Card Sorting Test	Attention, processing speed Executive function Executive function
Petrides 2015 [12]	Mini Mental State Exam Rey Auditory Verbal Learning Test Randt Memory Battery paired-word subset Randt Memory Battery story-recall subset Letter-number span Trail Making Test A Trail Making Test B Controlled Oral Word Association Test Continuous Performance Task Set-shifting	Global cognition Verbal memory Visual memory Verbal memory Executive function Attention, processing speed Executive function Verbal fluency Attention Executive function
Simsek 2015 [13]	Frontal Assessment Battery	Executive function
Stryjer 2012 [14]	Mini Mental State Exam Alzheimer's Disease Assessment Scale – Cognitive Subscale	Global cognition Global cognition
Tan 2022 [15]	Montreal Cognitive Assessment	Global cognition
Vukan-Cusa 2017 [16]	California Verbal Learning Test Benton Visual Retention Test Digit span Verbal fluency test Stroop test	Verbal memory Visual memory Working memory, attention Verbal fluency Executive function, cognitive flexibility
Yang 2016 [17]	MATRICS Consensus Cognitive Battery	Processing speed, attention, working memory, verbal memory, visual memory, reasoning/problem solving, social cognition

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