Electroconvulsive Therapy for Young Minds: A Solution for Mental Dysfunction or a Problem for Cognition? A Systematic Review and Meta-Analysis

Nour Dabboussi

Abstract

Background

Decades of research have consistently demonstrated the efficacy of electroconvulsive therapy (ECT) for the treatment of major depressive disorders; however, there is a lack of studies regarding the efficacy of ECT in children and adolescents. The present study aims to address the question of whether ECT causes cognitive function deficits in the pediatric population.

Methods

A systematic review of the literature was conducted to investigate the effect of ECT on memory functions, and a meta-analysis addressed studies that used verbal learning test as an outcome in pediatric patients. MedLine, Embase, Google Scholar, Cochrane CENTRAL and Web of Science were searched. We examined the characteristics of each study and then compared them. The risk of bias of the studies was assessed using the Newcastle-Ottawa scale. A meta-analysis was performed for studies evaluating the effect of ECT on verbal learning specifically.

Results

Eleven studies met the inclusion criteria. Two studies were pooled together in one meta-analysis that yielded a pooled estimate with a positive value of 0.12 indicating that ECT can improve verbal learning. All studies showed that ECT does not induce cognitive impairment on the long term. Any short-term cognitive deterioration in specific fields was absent upon follow-up.

Conclusion

Our data analysis revealed that cognitive functions in children and adolescents were not significantly impacted by ECT. While this procedure could have adverse effects on children for the short-term, it is generally considered a safe procedure for pediatric cases, with no deleterious cognitive effects on the long-term.

Key words: electroconvulsive therapy, verbal learning, cognition, adolescents, children.

Introduction

The present-day use of electroconvulsive therapy (ECT) has been shown to be safe and efficacious. It is recommended for adolescents who fail to respond to multiple medications and psychotherapy or those with severe psychiatric symptoms (Puffer et al., 2016). Schizophrenia is one of the most common indications for ECT worldwide even though it is still not considered a standard treatment by US FDA (Kellner et al., 2020). As for depression, extensive studies have suggested that ECT is highly effective in improving depressive symptoms with few unwanted effects (Li et al., 2020). Similarly, catatonia typically responds very well to ECT where it may be used after benzodiazepines fail to be adequately helpful (Dhossche et al., 2019). Current professional guidelines support ECT use for pharmacotherapy-resistant mania, often as second- or third-line treatment (Elias et al., 2021). Several studies have been conducted to elucidate the mechanisms of ECT action in the brain (Li et al., 2020; Njau, et al., 2017; Merkl et al., 2011; Zhang et al., 2013; Landauet al., 2011; Wang et al., 2017; Wang al., 2019; Takamiya et al., 2019; Erchinger et al., 2021). Pre-clinical studies have shown that ECT induces neurogenesis to compensate for the loss of neurons and glial cells resulting from stress-induced damage and depression (Li et al., 2020). They also highlighted the modulatory effect of ECT on brain metabolism and related neural signaling (Landau et al., 2011; Erchinger et al., 2021). For example, a reduction in the levels of N-acetyl aspartate (Njau, et al., 2017; Merkl et al., 2011), an increase in choline, glutamate, and glutamine (Zhang et al., 2013) in addition to an increase in dopamine receptor binding and neurotransmission (Landau et al., 2011) were reported following ECT

treatment (Zhang et al., 2013; Erchinger et al., 2021) Clinical studies have shown that ECT enhances different aspects of brain plasticity (Wang et al., 2017, 2019; Takamiya et al., 2019).

Even though ECT is a fast, safe, and life-saving treatment modality, it is rarely recommended for children and adolescents potentially due to its long-term adverse effects (Bilginer & Karadeniz, 2019). These side effects include different kinds of seizures (Whittaker et al., 2007; Cristancho et al., 2008; Andrade et al., 2016), cardiovascular, and respiratory problems (Andrade et al., 2016; Rabheru, 2001). However, there is a lack of studies addressing the possible effect of ECT on cognitive function. This is important to consider especially when ECT is used as a last resort for specific pediatric cases. Most observed cognitive deficits are temporary, and cases of severe permanent memory loss are usually hard to confirm (Kellner et al., 2020). Accounts of retrograde and anterograde amnesia upon ECT exposure are usually resolved yet with lingering memory deficits for retrograde amnesia (Andrade et al., 2016). Acute cognitive adverse effects of ECT may include attention deficits, postictal confusion, and delirium (Andrade et al., 2016).

A systematic review by Lima and colleagues showed that ECT use in adolescents has high remission rates and presents few and relatively non-problematic adverse effects (Lima et al., 2013). Similarly, the most recent systematic review of the current literature and guidelines for ECT in children and adolescents stated that there are no absolute contraindications for ECT in children and adolescents (Dossing & Pagsberg, 2021). Also, fears regarding cognitive dysfunction have not been reproduced in studies (Dossing &

Pagsberg, 2021). Perhaps, the single-most important unaddressed concern is retrograde amnesia, which has been shown to persist for up to 2 months post ECT (Weiner & Reti, 2017). ECT is shown to provoke anterograde amnesia, a temporary functional memory deficit, which may become progressively more pronounced over a course of ECT (Porter et al., 2020). It resolves within one or two weeks following completion of the acute course of ECT and is the reason for restricting cognitively demanding work in patients (Zolezzi, 2016). It also causes retrograde amnesia manifested by mostly forgetting recent events, which occurred during the time of the ECT (Weiner & Reti, 2017). Until this day, there is no systematic study discussing the cognitive risks of the use of ECT in adolescents. Most of the publications in this field remain in the form of observational studies or case reports and case series. It is imperative that clinicians exercise special caution when prescribing therapies with potential cognitive side effects, particularly for children and adolescents, whose brain is still under development. A new and safer method is needed to alleviate the psychiatric symptoms exhibited in the pediatric population at this critical age period.

The first objective of this study is to systematically review the literature and provide evidence pertaining to the adverse effect of ECT on cognitive functions in the pediatric population compared to those not receiving the intervention or to the patients' baseline state. A second objective is to perform a meta-analysis of the effect of ECT on verbal learning in our population of interest. Verbal learning is defined, following the dictionary of the American Psychological Association (APA), as "The process of learning about verbal

stimuli and responses, such as letters, digits, nonsense syllables, or words" (American Psychiatric Association, 2013).

Methods

Data sources and search strategies

This systematic review was reported with more than 90% adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009). We prospectively submitted the systematic review protocol for registration on PROSPERO (International prospective register of systematic reviews (CRD42020218692)). The protocol can be accessed from https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020218692. MedLine (through Ovid), Embase (through Elsevier) and Google Scholar were searched on 9 February 2021 and Cochrane CENTRAL and Web of Science (through Clarivate) on 26 January 2021. These databases were searched again on the 31st of May 2022 (Medline, Embase, Cochrane, Web of Sciences) and on the 7th of July 2022 (for Google Scholar) with the application of the date filters (since 8 of February for Web of Science, Cochrane and since 2022 for Medline, Embase and Google scholar). A thorough search strategy was built for each of the mentioned databases with the supervision of a specialized librarian. Screening was performed over 2 phases: title and abstract screening as a preliminary screening and full text screening of the included studies. The search strategy is presented in the supplementary material part. For the title abstract screening, 2 reviewers participated in

the process in duplicates and independently. Disagreements were resolved by consensus or by referring to a third reviewer. No IRB oversight or informant consent are needed.

Study selection and data extraction

Our inclusion criteria were: (1) Population of pediatric patients aged below 19 years; (2) Patients being subjected to ECT; (3) Study comparator being either the patients themselves before and after ECT (self-control) or a second arm of patients not receiving ECT; (4) Any aspect of cognitive performance of patients being assessed objectively in response to ECT. Study designs eligible for inclusion were case reports, case series, retrospective or prospective cohort studies, case controls, single arm studies and RCTs. Studies that did not meet the aforementioned requirements were excluded, as well as those with no objective measurement for the outcome of interest or where the outcome was not measured at the adequate time points before or after ECT. We have also excluded reviews, editorials, study protocols, hypothesis abstracts. Any assessment of the cognitive functions at more than 5 months after the last session of ECT was considered a long-term follow-up point.

We have classified the studies in the narrative part of the results section according to the specific dimension of cognitive and intellectual ability they evoke. We recorded reasons for exclusion and reported the results of the selection process using a PRISMA flow diagram (Moher et al., 2009). Data were abstracted from the studies by 1 reviewer according to their designs and settings including country and year of the study. Data specific to patients like their number, gender, sociodemographic details, and diagnosis were

extracted as well as information about ECT settings, control groups, cognitive tests used, and the outcome they measure.

Quality assessment

The risk of bias was assessed using the Newcastle-Ottawa quality assessment scale of nonrandomized studies by 1 reviewer with consultation from another. We evaluated the quality of the studies by adding stars in each domain (Wells et al., 2000). We synthesized data in both narrative and tabular formats. Two reviewers rated the certainty of evidence in duplicate by following the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach for the studies included in our meta-analysis. Certainty was judged on the following factors: anticipated absolute effects (95% CI), relative effect (95% CI), number of participants (in the pooled studies) (Balshem et al., 2011).

Statistical analysis

We did a meta-analysis of association by pooling risk ratios (RRs) using Revman software version 5.4.1. (Review Manager, 2020). Depending on the availability of required numerical data, the presence of a second arm control group, and presence of a common measured aspect of cognitive functioning, we were able to pool only 2 studies, which studied the effect of ECT on verbal learning. There were missing data from one of the 2 studies (Cohen et al., 2000) concerning ECT parameters that possibly affected our outcome of interest (frequency, pulse duration, etc.). We have adopted a fixed-effects models and standardized mean difference as our outcome was measured by 2 different scales. We have calculated 95% confidence intervals and two-sided P values for each outcome. The

heterogeneity was assessed using the I^2 calculation (Higgins et al., 2022). Finally, the publication bias was planned to be visually assessed with a funnel plot, as asymmetry in a funnel plot may be indicative for publication bias or other reporting biases.

Results

General characteristics of the study

The result of the selection process is presented in the PRISMA flow diagram (Fig. 1). Our search of the electronic databases and additional searches yielded a total of 2621 unique citations. We removed 212 duplicate records and excluded 2376 studies at the title abstract stage. At the full text stage, 22 studies were excluded.

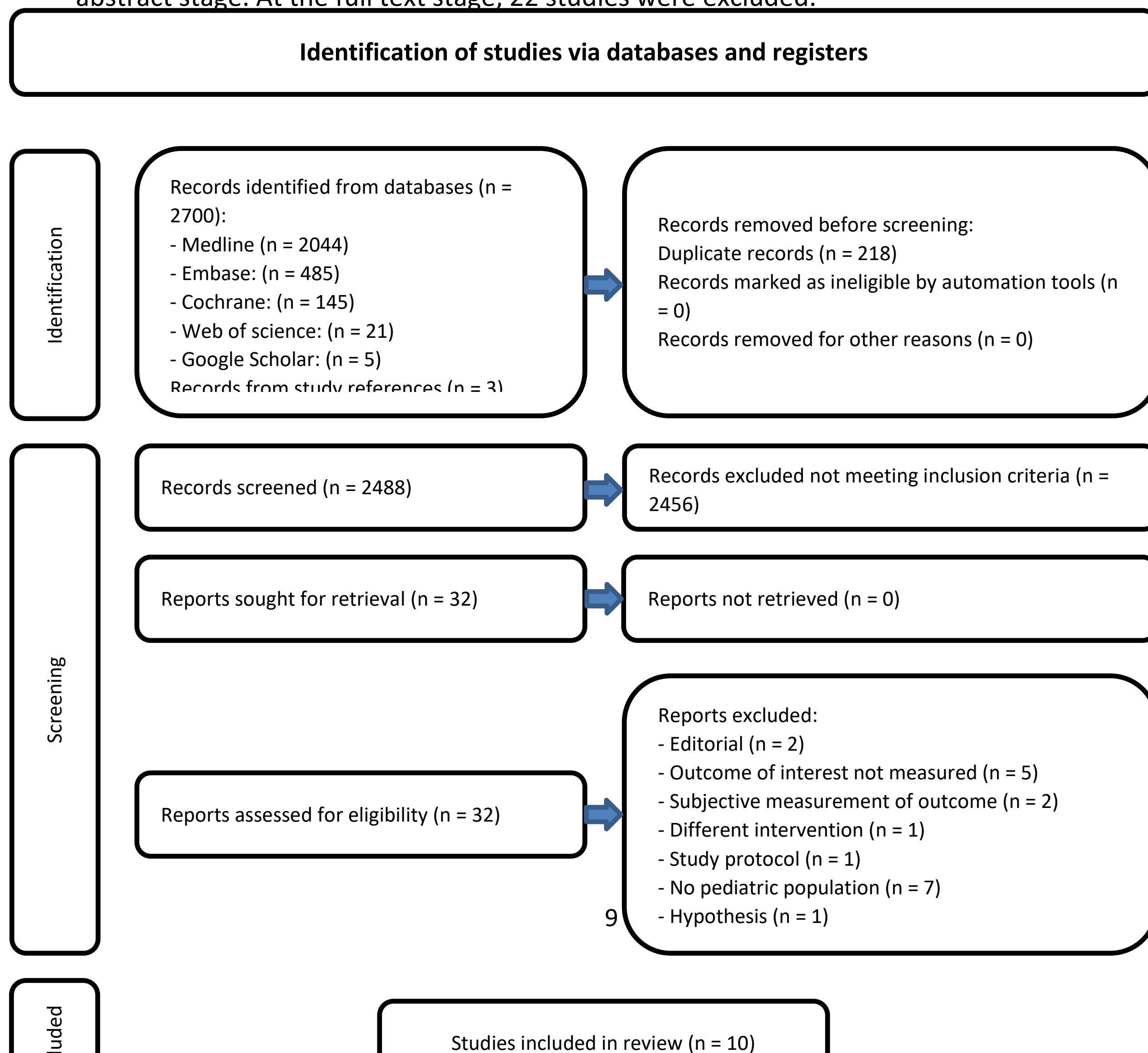


Fig. 1 PRISMA flow chart diagram

A total of 11 studies were included. Their designs were as follows: 2 cohorts, 2 single arm observational, 3 single arm experimental, 2 case reports and 2 case series. Studies varied in their short- or long-term follow-up timing of involved subjects. Out of these 11, only 2 had a control group of patients. Other studies compared the scores of the cognitive performance measuring tests for the patients before and after being subjected to bilateral ECT. The numbers and frequency of the ECT varied between the studies. Additionally, the number of participants in each ranged from 1 to 98, with a total of 183, including Asian, European, and American populations. All studies have been carried out in the pediatric population. Our search did not identify any eligible randomized trials. The specific reasons for exclusion for each of the initially retrieved articles are reported in supplementary materials (table S1).

In summary, the reasons for exclusion were the following: 2 studies were editorials, 3 studies were with different outcome measured, 2 studies were subjective (Surveys), 1 study had a different intervention, 1 study was a protocol, 7 studies did not include a pediatric population, 2 studies were without a measured outcome, 2 studies were with

inadequate time point collection of cognitive test results at baseline, 1 study did not specify time point of collection, and 1 study was an abstract. Tables 1 and 2 show a summary of the general characteristics of these studies. All of them have looked at the influence of ECT administered as a treatment for the disorder/disease of the involved subjects on their cognitive functioning measured with specialized mental tests. ECT settings in each study including electrode placement, pulse width, frequency, duration, current and number of sessions are listed in supplementary materials (table S2). The characteristics related to the study outcome including study results, cognitive outcome studied, used test, and time point of collection are listed in supplementary materials (table S3).

Table 1. Settings of the included studies including study method, year, number of participants and country.

Citation	Method	Number of participants	Country
Cohen et al., 2000	Cohort retrospective	10	France
De la Serna et al., 2011	Cohort retrospective	9	Spain
Etain et al., 2001	Case series	6 (2 had cognitive assessment in response to ECT)	France
Ghaziuddin et al., 1996	Single-arm observational	11	USA
Ghaziuddin et al., 1999	Case report	1	USA
Ghaziuddin et al., 2000	Single-arm experimental	16 (14 had cognitive assessment in response to ECT)	USA
Ghaziuddin et al., 2011	Case series	6	USA

Wachtel et al., 2012	Case report	1	USA
Bender et al., 1947	Single-arm observational	98	USA
Gurevitz et al., 1954	Single-arm observational	16	USA
Krislaty 2014	Single-arm observational	15	Not stated

NA, Not available.

Table 2. Characteristics of the patients included in each study including socio-demographic details, diagnosis, age, sex and their controls.

Citation	Socio-demographic characteristics	Diagnosis (number of patients)	Mean age	Sex	Control type
Cohen et al., 2000	11.1 years of education.	Bipolar disorder, manic, with psychotic features (3); Bipolar disorder, mixed, with psychotic features (2); Major depressive episode with psychotic features of melancholic type (5)	17.6 y	4 M, 6 F	10 psychiatric comparison subjects not receiving ECT matched for sex, age, and diagnosis
De la Serna et al., 2011	2.22 on the Hollingshead Redlich scale	Schizophrenia (7); Schizoaffective disorder (2)	15.78 ± 1.3 y	2 M, 6 F	9 adolescent subjects not receiving ECT matched by age, socioeconomi

					c status, and diagnostic
Etain et al., 2001	NA	Bipolar disorder, major depressive episode (6)	16 y	2 M	Comparison of pre-ECT and post-ECT
Ghaziuddin et al., 1996	NA	MDD (9); Organic mood disorder (1); Bipolar disorder (1)	16.3 ± 1.7 y	1 M, 10 F	NA
Ghaziuddin et al., 1999	Superior student with national percentile Rankings falling above the 90.	Bipolar mania (1)	16 y	1 F	NA
Ghaziuddin et al., 2000	Mean education in grades was 10.2 ± 1.8 y; mean IQ was 103.7 ± 13.5	Unipolar depression (14); Bipolar depression (2)	15.9 ± 1.6 y	3 M, 13 F	Comparison of pre-ECT and post-ECT
Ghaziuddin et al., 2011	NA	Severe treatment resistant major depression (6)	15.3 y	4 M, 2 F	Comparison of pre-ECT and post-ECT
Wachtel et al., 2012	NA	Malignant catatonia (1)	16 y	M	Comparison of pre-ECT and post-ECT

Bender et al., 1947	NA	Schizophrenia (98)	from 4.3 to 11.10 y	70 M, 28 F	Comparison of pre-ECT and post-ECT
Gurevitz et al., 1954	NA	Schizophrenia (16)	9.11 y	15 M, 1 F	Comparison of pre-ECT and post-ECT
Krislaty 2014	NA	MDD	15.9 y	7 M, 8 F	Comparison of pre-ECT and post-ECT

Forest plot and meta-analysis

We have constructed a forest plot and conducted a meta-analysis based on 2 studies only (Cohen et al., 2000; De la Serna et al., 2011). As for the remaining 8 studies, the absence of control group caused the risk of bias to be significantly high and their inclusion in the meta-analysis statistically inadequate. Cohen et al. (2000) and De la Serna et al. (2011) examined the effect of ECT on verbal learning by comparing the results obtained from ECT-exposed patients with those of normal subjects. Pooling the results of the 2 studies together in one meta-analysis has yielded a pooled estimate with a positive value of 0.12 and a forest plot both indicating that ECT can improve verbal learning compared to the controls. However, the value of the pooled estimate is considered small, and the confidence interval is large crossing 0 and ranging from negative to positive values (CI: -0.51; 0.74). The favourability for ECT over no ECT for the improvement of verbal learning test scores used

by the 2 studies implies that the use of ECT is considered a safe and effective intervention for patients suffering from severe psychiatric disorders (Fig. 2).

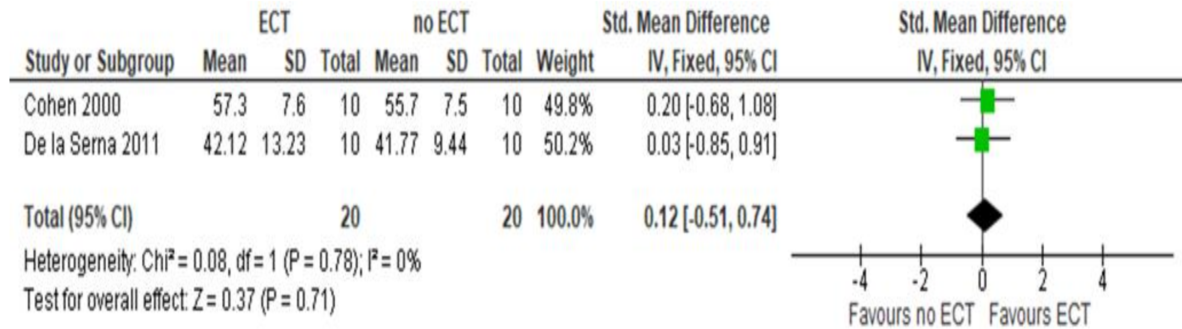


Fig. 2 Forest plots of verbal learning for ECT versus no ECT application

Risk of bias

For the 2 studies included in the meta-analysis, the risk of bias assessment demonstrated a good quality (low bias) after considering the observational designs. For the other 6 single arm studies, the quality showed to be poor (high bias). Table S4 shows the components of evaluation of the risk of bias of these studies (supplementary materials).

Publication bias

Given that only two studies were included in our meta-analysis, publication bias could not be assessed. As a rule of thumb, tests for funnel plot asymmetry should be used only when there are at least 10 studies included in the meta-analysis, because when there are fewer studies the power of the tests is too poor to distinguish chance from real asymmetry (Higgins et al., 2022).

Grading of the certainty of the evidence

The certainty of evidence of the effect of ECT on verbal learning, attention and/or concentration, IQ, general cognitive functioning, executive functions, academic achievement, visual memory, and verbal memory was measured using GRADEpro. A summary of our findings is presented in supplementary materials (table S5) and has shown that the certainty of evidence is very low.

Studies' details and findings

Not all the results of each included study were relevant to our research question. Some studies included assessment of additional outcomes such as depressive symptoms. In such cases, we solely abstracted data of cognitive tests of the included subjects.

Five studies investigated the effect of ECT on verbal tasks as a cognitive outcome. Cohen et al. (2000), De La Serna et al. (2011), Krislaty (2014), Ghaziuddin et al. (2000, 2011) reported the results of verbal learning tests in adolescents diagnosed with mood disorders or schizophrenia spectrum disorders. Cohen et al. (2000) and De La Serna et al. (2011) showed that the participating group of patients, constituting of 10 subjects for Cohen et al. (2000) and 9 for De La Serna et al. (2011), did not differ on any objective measure of verbal learning and attention. Similarly, Cohen et al. (2000) demonstrated no alterations in cognitive functions measured by the mini-mental status examination test, which included questions about orientation, attention, recall, and language (Galea & Woodward, 2005) or in the results of the attention section of the Wechsler Memory Scale-Revised. This is also the case for the results of De La Serna et al. (2011) concerning functions of working memory, executive functions, and IQ or their changes at the planned long-term follow-up periods. In

the studies of Ghaziuddin et al. (2000, 2011), the researchers examined the results of cognitive tests of adolescent patients diagnosed with various subtypes of depression and compared their scores before and after being subjected to ECT. By comparing pre-ECT and the first post-ECT testing administered less than 1 month after treatment, Ghaziuddin et al. (2000) showed that ECT resulted in significant impairments in verbal delayed recall, verbal fluency, attention, concentration, and visual- delayed recall yet with complete recovery at long-term treatment. They, however, found no change in the ability to problem solve during the initial or the subsequent testing. Ghaziuddin et al. (2011) even revealed a trend toward improved intellectual functioning [(which included IQ testing (Wechsler, 2011)], short-term memory, or verbal learning memory following ECT measured mostly at short-term intervals following treatment of 6 depressed adolescent patients. There was also significant improvement in long-term delayed memory recall (Ghaziuddin et al., 2011).

The study by Krislaty (2014) reported that verbal fluency and memory both showed improvement at the follow-up points ranging from 1 to 36 months after ECT in comparison to baseline in 15 subjects with major depressive disorder. The same trend of variation was observed for intellectual and executive functioning, academic achievement, story memory, and visual memory, although these results did not reach statistical significance. Like Cohen et al. (2000), other studies also focused on orientation, attention, memory, calculation, and language, which were evaluated by the Mini-mental state examination test. Of these studies, Ghaziuddin et al. (1996) reported that the Mini-mental State Examination showed no significant decline in cognitive functioning in 11 patients with pharmacotherapy

refractory depression at short-term follow-up. However, they also clarified that a significant decline in attention, concentration, and long-term memory occurred in 5 subjects as demonstrated by neuropsychological testing both before ECT and 1-5 days after the last treatment.

IQ was another aspect that was the focus of 4 studies as an indicator of cognitive functioning in response to ECT. Bender et al. (1947), prospectively evaluated the effect of ECT as a treatment for 98 schizophrenic children at Children's Ward of Psychiatric Bellevue Hospital. Children were followed before shock, immediately following shock, and at intervals thereafter whenever possible. There was no evidence of a lasting effect on the intellectual functioning and development of the child, although 5 children represented some alteration in function immediately after treatment. For this same outcome, Ghaziuddin et al. (1999) reported a case of a 13-year-old girl with bipolar mania subjected to 12 bilateral ECT sessions. Comparison of different cognitive test results pre-ECT at 2 weeks and 3 months post-ECT cognitive testing showed no change in IQ. The study reported other tests like the mini-mental state examination and academic achievement tests. These did not show any performance deterioration, although math ability improved between pre and post ECT time intervals. On verbal memory tasks, performance post-ECT suggested some decline in delayed memory tasks compared to 20 months pre ECT. The publication of Etain et al. (2001), reported a case series of 6 adolescents treated with ECT of which 2 had cognitive performance comparison of IQ levels before and after ECT. The study showed that ECT does not seem to cause alterations in short-term cognitive functions (based on our

definition of short- and long-term assessment periods) as compared to baseline for these 2 subjects. Another case report by Wachtel et al. (2012) of an adolescent with malignant catatonia who received 61 sessions of ECT confirmed no evidence of decline in intellectual functioning [including attention (Elsheikh et al., 2017) and IQ (Pearson, 2003)], acute memory, or delayed memory at the end of all the prescribed sessions that took place over 5 years. In the study by Gurevitz et al. (1954), 16 pediatric patients diagnosed with schizophrenia and subjected to series of 20 shocks had their IQ scores measured. Like previously reported studies, they compared the subjects' performance on IQ tests such as the Standford-Binet test and the Goodenough Draw-A-Man-test. They showed that intellectual efficiency and logical reasoning were significantly altered immediately after shock but recovered by the time of follow-up and even reported significant enhancement in non- verbal intelligence and IQ measurement.

Discussion

The aim of this meta-analysis was to investigate the effect of ECT on cognitive outcome in children and adolescents. We focused on the effects of ECT, which was once considered a controversial medical therapy, on verbal learning. Compiled studies included single arm and cohort studies in addition to case reports, which assessed cognitive performance on the short- and long-term following ECT. The findings of this meta-analysis indicate that ECT does not cause any significant long-term harmful effects on cognitive functions in the pediatric population. This result appears consistent with those of Gurevitz

et al. (1954) and Ghaziuddin et al. (2000). These studies reported significant impairment in intellectual efficiency, concentration, attention, verbal- and visual-delayed recall, and verbal fluency only at the short-term post treatment. In addition, Ghaziuddin et al. (2011) reported improvements in delayed story memory performance for most of the subjects including 3 subjects whose performance was collected at short- and long-term follow-up. This is also the case for the study of Krislaty (2014) that reported improvement in cognitive functions at post-ECT testing. This controversy in the literature could be attributed to differences between the studies such as their design, the specific cognitive outcome measured, and time point of the collection of test results.

The discrepancy between our findings and previous studies is likely due to the small sample size in each study, the non-randomly assigned experimental and control groups (when present), the variable testing time points in some observational single arm studies, and, lastly, the different types of selected studies. Moreover, the risk of bias assessment using the New Castle Ottawa scale signified a poor overall quality of many of our included studies, particularly due to the lack of a control group. In addition, the resulting values of the pooled estimate, the confidence interval, and the P value of the overall effect cannot, with certainty, confirm whether ECT has any short-term or long-term detrimental effects on cognitive functions in children and adolescents. It is also worth noting that one of the two studies included in this meta-analysis (Cohen et al., 2000) had no disclosure about the applied ECT settings on their subjects, which, if known, would possibly appear to be dissimilar to those applied by the other study (De la Serna et al., 2011). This fact would have

possibly rendered both studies impossible to be pooled together and the meta-analysis unfeasible. The certainty of evidence assessed in our study was also very low indicating low confidence in the estimated effect of the pooled outcome and/or of the unpooled outcome. This is possibly due to the inconsistency in the observational design of the 2 included studies, the high risk of bias, and the absence of control group in the other studies. Thus, ECT may have the ability to enhance verbal learning although the evidence is very uncertain. This uncertainty is likely attributable to the small number of participants in the studies included (n = 40). Also, it is supported by the confidence interval of the absolute effect that includes values reflecting both benefit and harm. As another limitation, we did not screen the reference lists of other systematic reviews published on or around the topic. However, despite our study's limitations, it is important to note that a rigorous search of the literature has been done regarding our question of interest. The results provided an access to the totality of studies addressing our research question and highlights the need to perform a controlled clinical trial or a randomized controlled clinical trial to elucidate the effect of ECT on cognitive functions.

Conclusion

Our findings indicate that it may be reasonable to recommend and prescribe ECT for a pediatric case resistant to other therapeutic strategies, with no serious concerns about lasting cognitive deterioration resulting from the procedure. Data also indicated that ECT has no deleterious effects on verbal learning in these patients. However, due to the

uncertainty of the findings of the meta-analysis and the primary limitations of the systematic review, the decision to recommend ECT should take into consideration the emergency of the case, the existence of an alternative therapeutic solution, and the potential side effects on cognition. Future controlled clinical trials or randomized controlled clinical trials should be performed to more accurately investigate the possible effect of ECT on cognitive function in the pediatric population.

References

American Psychiatric Association (APA) (2013): Diagnostic and statistical manual of mental disorders, 5th ed. Washington, DC.

Andrade, C., Arumugham, S. S., & Thirthalli, J. (2016). Adverse Effects of Electroconvulsive Therapy. *The Psychiatric clinics of North America*, *39*(3), 513–530. https://doi.org/10.1016/j.psc.2016.04.004

Balshem, H., Helfand, M., Schünemann, H. J., Oxman, A. D., Kunz, R., Brozek, J., Vist, G. E., Falck-Ytter, Y., Meerpohl, J., Norris, S., & Guyatt, G. H. (2011). GRADE guidelines: 3. Rating the quality of evidence. *Journal of clinical epidemiology*, *64*(4), 401–406. https://doi.org/10.1016/j.jclinepi.2010.07.015

Bender, L. (1947). Childhood schizophrenia; clinical study on one hundred schizophrenic children. *The American journal of orthopsychiatry*, *17*(1), 40–56. https://doi.org/10.1111/j.1939-0025.1947.tb04975.x

Bertagnoli, M. W., & Borchardt, C. M. (1990). A review of ECT for children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, *29*(2), 302–307. https://doi.org/10.1097/00004583-199003000-00022

Bilginer, Ç., & Karadeniz, S. (2019). Knowledge, attitudes, and experience of child and adolescent psychiatrists in Turkey concerning pediatric electroconvulsive therapy. *Asian journal of psychiatry*, *46*, 74–78. https://doi.org/10.1016/j.ajp.2019.09.035

Chess, S. (1968). An interactive concept of childhood schizophrenia. *International Journal* of *Psychiatry*, 5(3), 222-4

Cohen, D., Taieb, O., Flament, M., Benoit, N., Chevret, S., Corcos, M., Fossati, P., Jeammet, P., Allilaire, J. F., & Basquin, M. (2000). Absence of cognitive impairment at long-term follow-up in adolescents treated with ECT for severe mood disorder. *The American journal of psychiatry*, *157*(3), 460–462. https://doi.org/10.1176/appi.ajp.157.3.460

Cristancho, M. A., Alici, Y., Augoustides, J. G., & O'Reardon, J. P. (2008). Uncommon but serious complications associated with electroconvulsive therapy: recognition and management for the clinician. *Current psychiatry reports*, *10*(6), 474–480. https://doi.org/10.1007/s11920-008-0076-4

de la Serna, E., Flamarique, I., Castro-Fornieles, J., Pons, A., Puig, O., Andrés-Perpiña, S., Lázaro, L., Garrido, J. M., Bernardo, M., & Baeza, I. (2011). Two-year follow-up of cognitive functions in schizophrenia spectrum disorders of adolescent patients

treated with electroconvulsive therapy. *Journal of child and adolescent psychopharmacology*, *21*(6), 611–619. https://doi.org/10.1089/cap.2011.0012

Dhossche, D. M., & Withane, N. (2019). Electroconvulsive Therapy for Catatonia in Children and Adolescents. *Child and adolescent psychiatric clinics of North America*, *28*(1), 111–120. https://doi.org/10.1016/j.chc.2018.07.007

Døssing, E., & Pagsberg, A. K. (2021). Electroconvulsive Therapy in Children and Adolescents: A Systematic Review of Current Literature and Guidelines. *The journal of ECT*, *37*(3), 158–170. https://doi.org/10.1097/YCT.0000000000000761

Elias, A., Thomas, N., & Sackeim, H. A. (2021). Electroconvulsive Therapy in Mania: A Review of 80 Years of Clinical Experience. *The American journal of psychiatry*, *178*(3), 229–239. https://doi.org/10.1176/appi.ajp.2020.20030238

Elsheikh, S., Kuusikko-Gauffin, S., Loukusa, S., Omar, M., Riad, G., Ebeling, H. & Moilanen, I. (2017) Neuropsychological Performance of Egyptian Children with Autism Spectrum Disorder and Attention Deficit Hyperactivity Disorder. *Psychology*, *8*, 1280-1300. doi: 10.4236/psych.2017.89083

Erchinger, V. J., Ersland, L., Aukland, S. M., Abbott, C. C., & Oltedal, L. (2021). Magnetic Resonance Spectroscopy in Depressed Subjects Treated With Electroconvulsive Therapy-A Systematic Review of Literature. *Frontiers in psychiatry*, *12*, 608857. https://doi.org/10.3389/fpsyt.2021.608857

Etain, B., Le Heuzey, M. F., & Mouren-Simeoni, M. C. (2001). Electroconvulsive therapy in the adolescent: clinical considerations apropos of a series of cases. *Canadian journal of psychiatry*, *46*(10), 976–981. https://doi.org/10.1177/070674370104601012

Fink M. (1993). Electroconvulsive Therapy in Children and Adolescents. *Convulsive therapy*, *9*(3), 155–157

Galea, M., & Woodward, M. (2005). Mini-Mental State Examination (MMSE). *The Australian journal of physiotherapy*, *51*(3), 198. https://doi.org/10.1016/s0004-9514(05)70034-9

Ghaziuddin, N., DeQuardo, J. R., Ghaziuddin, M., & King, C. A. (1999). Electroconvulsive treatment of a bipolar adolescent postcraniotomy for brain stem astrocytoma. *Journal of child and adolescent psychopharmacology*, *9*(1), 63–69. https://doi.org/10.1089/cap.1999.9.63

Ghaziuddin, N., Dumas, S., & Hodges, E. (2011). Use of continuation or maintenance electroconvulsive therapy in adolescents with severe treatment-resistant depression. *The journal of ECT*, *27*(2), 168–174. https://doi.org/10.1097/YCT.0b013e3181f665e4

Ghaziuddin, N., King, C. A., Naylor, M. W., Ghaziuddin, M., Chaudhary, N., Giordani, B., Dequardo, J. R., Tandon, R., & Greden, J. (1996). Electroconvulsive treatment in adolescents with pharmacotherapy-refractory depression. *Journal of child and adolescent psychopharmacology*, *6*(4), 259–271. https://doi.org/10.1089/cap.1996.6.259

Ghaziuddin, N., Laughrin, D., & Giordani, B. (2000). Cognitive side effects of electroconvulsive therapy in adolescents. *Journal of child and adolescent psychopharmacology*, *10*(4), 269–276. https://doi.org/10.1089/cap.2000.10.269

Ghaziuddin, N., Shamseddeen, W., Gettys, G., & Ghaziuddin, M. (2020). Electroconvulsive Therapy for the Treatment of Severe Mood Disorders During Adolescence: A Retrospective Chart Review. *Journal of child and adolescent psychopharmacology*, *30*(4), 235–243. https://doi.org/10.1089/cap.2019.0054

Gurevitz, S., & Helme, W.H. (1954). Effects of electroconvulsive therapy on personality and intellectual functioning of the schizophrenic child. *The Journal of Nervous and Mental Disease, 120*, 213-26

Higgins, J. P. T., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M., & Welch, V. (Eds) (2022). *Cochrane Handbook for Systematic Reviews of Interventions version 6.3*. Cochrane.

Kaliora, S. C., Braga, R. J., Petrides, G., Chatzimanolis, J., Papadimitriou, G. N., & Zervas, I. M. (2013). The practice of electroconvulsive therapy in Greece. *The journal of ECT*, *29*(3), 219–224. https://doi.org/10.1097/YCT.0b013e31827e0d49

Kellner, C. H., Obbels, J., & Sienaert, P. (2020). When to consider electroconvulsive therapy (ECT). *Acta psychiatrica Scandinavica*, *141*(4), 304–315. https://doi.org/10.1111/acps.13134

Krislaty, V. (2014). The Effect of Electroconvulsive Therapy (ECT) on Neuropsychological Functioning in Adolescents who suffer from Major Depressive Disorder. Thesis (University of Michigan).

Landau, A. M., Chakravarty, M. M., Clark, C. M., Zis, A. P., & Doudet, D. J. (2011). Electroconvulsive therapy alters dopamine signaling in the striatum of non-human primates. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology*, *36*(2), 511–518. https://doi.org/10.1038/npp.2010.182

Li, M., Yao, X., Sun, L., Zhao, L., Xu, W., Zhao, H., Zhao, F., Zou, X., Cheng, Z., Li, B., Yang, W., & Cui, R. (2020). Effects of Electroconvulsive Therapy on Depression and Its Potential Mechanism. *Frontiers in psychology*, *11*, 80. https://doi.org/10.3389/fpsyg.2020.00080

Lima, N. N., Nascimento, V. B., Peixoto, J. A., Moreira, M. M., Neto, M. L., Almeida, J. C., Vasconcelos, C. A., Teixeira, S. A., Júnior, J. G., Junior, F. T., Guimarães, D. D., Brasil, A. Q., Cartaxo, J. S., Akerman, M., & Reis, A. O. (2013). Electroconvulsive therapy use in adolescents: a systematic review. *Annals of general psychiatry*, *12*(1), 17. https://doi.org/10.1186/1744-859X-12-17

Loiseau, A., Harrisson, M. C., Beaudry, V., & Patry, S. (2017). Electroconvulsive Therapy Use in Youth in the Province of Quebec. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, *26*(1), 4–11.

Meeter, M., Murre, J. M., Janssen, S. M., Birkenhager, T., & van den Broek, W. W. (2011). Retrograde amnesia after electroconvulsive therapy: a temporary effect?. *Journal of affective disorders*, *132*(1-2), 216–222. https://doi.org/10.1016/j.jad.2011.02.026

Merkl, A., Schubert, F., Quante, A., Luborzewski, A., Brakemeier, E. L., Grimm, S., Heuser, I., & Bajbouj, M. (2011). Abnormal cingulate and prefrontal cortical neurochemistry in major depression after electroconvulsive therapy. *Biological psychiatry*, *69*(8), 772–779. https://doi.org/10.1016/j.biopsych.2010.08.009

Mohapatra, S., & Rath, N. (2015). Electroconvulsive Therapy in a Child Suffering from Acute and Transient Psychotic Disorder with Catatonic Features. *Indian journal of psychological medicine*, *37*(4), 465–466. https://doi.org/10.4103/0253-7176.168603

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine*, *6*(7), e1000097. https://doi.org/10.1371/journal.pmed.1000097

Moise, F. N., & Petrides, G. (1996). Case study: electroconvulsive therapy in adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, *35*(3), 312–318. https://doi.org/10.1097/00004583-199603000-00012

Nelson, F. B., Reid, I. E., & Travers, R. M. (1965). Effect of electric shock as a reinforcer of the behavior of children. *Psychological reports*, *16*, 123–126. https://doi.org/10.2466/pr0.1965.16.1.123

Njau, S., Joshi, S. H., Espinoza, R., Leaver, A. M., Vasavada, M., Marquina, A., Woods, R. P., & Narr, K. L. (2017). Neurochemical correlates of rapid treatment response to

electroconvulsive therapy in patients with major depression. *Journal of psychiatry & neuroscience: JPN*, *42*(1), 6–16. https://doi.org/10.1503/jpn.150177

Oltedal, L., Kessler, U., Ersland, L., Grüner, R., Andreassen, O. A., Haavik, J., Hoff, P. I., Hammar, Å., Dale, A. M., Hugdahl, K., & Oedegaard, K. J. (2015). Effects of ECT in treatment of depression: study protocol for a prospective neuroradiological study of acute and longitudinal effects on brain structure and function. *BMC psychiatry*, *15*, 94. https://doi.org/10.1186/s12888-015-0477-y

Pearson, N. (2003). Comprehensive Test of Nonverbal Intelligence. In: McCallum, R.S. (eds) Handbook of Nonverbal Assessment. Springer, Boston, MA. https://doi.org/10.1007/978-1-4615-0153-4_7

Porter, R. J., Baune, B. T., Morris, G., Hamilton, A., Bassett, D., Boyce, P., Hopwood, M. J., Mulder, R., Parker, G., Singh, A. B., Outhred, T., Das, P., & Malhi, G. S. (2020). Cognitive side-effects of electroconvulsive therapy: what are they, how to monitor them and what to tell patients. *BJPsych open*, *6*(3), e40. https://doi.org/10.1192/bjo.2020.17

Puffer, C. C., Wall, C. A., Huxsahl, J. E., & Frye, M. A. (2016). A 20 Year Practice Review of Electroconvulsive Therapy for Adolescents. *Journal of child and adolescent psychopharmacology*, *26*(7), 632–636. https://doi.org/10.1089/cap.2015.0139

Rabheru K. (2001). The use of electroconvulsive therapy in special patient populations. *Canadian journal of psychiatry*, *46*(8), 710–719. https://doi.org/10.1177/070674370104600803

Rami-González, L., Boget-Llucià, T., Bernardo, M., Marcos, T., Cañizares-Alejos, S., Penadés, R., Portella, M. J., Castelví, M., Raspall, T., & Salamero, M. (2002). Selective alteration of the declarative memory systems in patients treated with a high number of electroconvulsive therapy sessions. *Revista de neurologia*, *35*(9), 805–808.

Review Manager (RevMan). (2020). Version 5.4. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration.

Rey, J. M., & Walter, G. (1997). Half a century of ECT use in young people. *The American journal of psychiatry*, *154*(5), 595–602. https://doi.org/10.1176/ajp.154.5.595

Schneekloth, T. D., Rummans, T. A., & Logan, K. M. (1993). Electroconvulsive Therapy in Adolescents. *Convulsive therapy*, *9*(3), 158–166.

Seow, L., Subramaniam, M., Chan, Y., Martin, D. M., Abdin, E., Chong, S. A., Liu, J., Peh, C. X., & Tor, P. C. (2019). A Retrospective Study of Cognitive Improvement Following Electroconvulsive Therapy in Schizophrenia Inpatients. *The journal of ECT*, *35*(3), 170–177. https://doi.org/10.1097/YCT.0000000000000569

Squire, L. R., Slater, P. C., & Chace, P. M. (1976). Anterograde amnesia following electroconvulsive therapy: No evidence for state-dependent learning. *Behavioral Biology, 17*(1), 31–41. https://doi.org/10.1016/S0091-6773(76)90227-3

Takamiya, A., Plitman, E., Chung, J. K., Chakravarty, M., Graff-Guerrero, A., Mimura, M., & Kishimoto, T. (2019). Acute and long-term effects of electroconvulsive therapy on human dentate gyrus. *Neuropsychopharmacology : official publication of the*

American College of Neuropsychopharmacology, *44*(10), 1805–1811. https://doi.org/10.1038/s41386-019-0312-0.

Tor, P. C., Ying, J., Ho, N. F., Wang, M., Martin, D., Ang, C. P., Tan, C., Yap, L. S., Lu, V., Simpson, B., Mok, Y. M., & Loo, C. (2017). Effectiveness of Electroconvulsive Therapy and Associated Cognitive Change in Schizophrenia: A Naturalistic, Comparative Study of Treating Schizophrenia With Electroconvulsive Therapy. *The journal of ECT*, *33*(4), 272–277. https://doi.org/10.1097/YCT.0000000000000422

Vila, F., Snyder, J., & Zhang, T. (2019). ECS-induced neurogenesis and cognitive side effects. *Brain stimul*,*12*, 585. https://doi.org/10.1016/j.brs.2018.12.942

Wachtel, L. E., Dhossche, D. M., Reti, I. M., & Hughes-Wheatland, R. (2012). Stability of intellectual functioning during maintenance electroconvulsive therapy. *Pediatric neurology*, *47*(3), 219–221. https://doi.org/10.1016/j.pediatrneurol.2012.05.012

Wang, J., Tang, Y., Curtin, A., Xia, M., Tang, X., Zhao, Y., Li, Y., Qian, Z., Sheng, J., Zhang, T., Jia, Y., Li, C., & Wang, J. (2019). ECT-induced brain plasticity correlates with positive symptom improvement in schizophrenia by voxel-based morphometry analysis of grey matter. *Brain stimulation*, *12*(2), 319–328. https://doi.org/10.1016/j.brs.2018.11.006

Wang, J., Wei, Q., Bai, T., Zhou, X., Sun, H., Becker, B., Tian, Y., Wang, K., & Kendrick, K. (2017). Electroconvulsive therapy selectively enhanced feedforward connectivity from fusiform face area to amygdala in major depressive disorder. *Social cognitive and affective neuroscience*, *12*(12), 1983–1992. https://doi.org/10.1093/scan/nsx100

Wechsler, D. (2011). Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II) [Database record]. *APA PsycTests*.

Weeks, H. R., 3rd, Tadler, S. C., Smith, K. W., Iacob, E., Saccoman, M., White, A. T., Landvatter, J. D., Chelune, G. J., Suchy, Y., Clark, E., Cahalan, M. K., Bushnell, L., Sakata, D., Light, A. R., & Light, K. C. (2013). Antidepressant and neurocognitive effects of isoflurane anesthesia versus electroconvulsive therapy in refractory depression. *PloS one*, *8*(7), e69809. https://doi.org/10.1371/journal.pone.0069809

Weiner, R. D., & Reti, I. M. (2017). Key updates in the clinical application of electroconvulsive therapy. *International review of psychiatry (Abingdon, England)*, *29*(2), 54–62. https://doi.org/10.1080/09540261.2017.1309362

Wells, G. A., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M., & Tugwell, P. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. Available from: URL: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm [cited 2016 Apr 25].

Whittaker, R., Scott, A., & Gardner, M. (2007). The prevalence of prolonged cerebral seizures at the first treatment in a course of electroconvulsive therapy. *The journal of ECT*, *23*(1), 11–13. https://doi.org/10.1097/01.yct.0000263253.14044.3a

Wong, V., Tor, P. C., Martin, D. M., Mok, Y. M., & Loo, C. (2019). Effectiveness and Cognitive Changes With Ultrabrief Right Unilateral and Other Forms of Electroconvulsive Therapy in the Treatment of Mania. *The journal of ECT*, *35*(1), 40–43. https://doi.org/10.1097/YCT.0000000000000519

Zhand, N., Courtney, D. B., & Flament, M. F. (2015). Use of Electroconvulsive Therapy in Adolescents With Treatment-Resistant Depressive Disorders: A Case Series. *The journal of ECT*, *31*(4), 238–245. https://doi.org/10.1097/YCT.0000000000000236

Zhang, J., Narr, K. L., Woods, R. P., Phillips, O. R., Alger, J. R., & Espinoza, R. T. (2013). Glutamate normalization with ECT treatment response in major depression. *Molecular psychiatry*, *18*(3), 268–270. https://doi.org/10.1038/mp.2012.46

Zolezzi M. (2016). Medication management during electroconvulsant therapy. *Neuropsychiatric disease and treatment*, *12*, 931–939. https://doi.org/10.2147/NDT.S100908

SUPPORTING INFORMATION

SUPPLEMENTARY MATERIALS

Appendix 1. Search Strategy

MedLine, Embase and Google Scholar were searched on 9 February 2020 and Cochrane CENTRAL and Web of Science on 26 January 2020. A thorough search strategy was built for each of the mentioned databases with the supervision of a specialized librarian. The strategy includes Mesh and keywords of concepts related to ECT, cognition and age groups of children and adolescents.

- **Medline search strategy was:**

1 psychiatric somatic therapies/ or convulsive therapy/ or electroconvulsive therapy/ or electric stimulation/ or electroshock/ or shock treatment/

2 (((Therap* or treatment) adj2 ((psychiatric adj2 somatic) or electroshock or (electr* adj2 shock) or (electr* adj2 convuls*) or electroconvuls* or shock? or convuls* or (convuls* adj2 shock?))) or elelctrotherapy or (electric* adj2 stimulation*) or electroplexy).ti,ab.

3 1 or 2

4 cognition/ or comprehension/ or executive function/ or learning/ or imprinting, psychological/ or memory/ or exp memory, long-term/ or mental recall/ or recognition, psychology/ or retention, psychology/ or spatial memory/ or overlearning/ or problem-based learning/ or problem solving/ or spatial learning/

5 ((cognitive adj2 (function? or task? or thinking)) or understand* or comprehen* or train* or (association * adj2 concept*) or (memor* adj2 (episodic or (long adj2 term) or spatial or anterograde or remote or event)) or (mental adj2 recall) or recogni* or (learning adj2 ((problem adj based) or spatial or verbal)) or (knowledge adj2 aquisition) or overlearn* or (over adj2 learn*) or (problem* adj1 solving)).ti,ab.

6 4 or 5

7 adolescent/ or exp child/ or infant/ or infant, newborn/

8 (child* or infan* or newborn? or adolescen* or toddler? or juvenil?e? or junior? or young? or youth? or teen* or bab* or youngster? or nenonate? or (little adj2 (m?n or wom?n or boy* or girl*))).ti,ab.

9 7 or 8

10 3 and 6 and 9

- **Embase search strategy was:**

1 'convulsive therapy'/de OR 'electroconvulsive therapy'/de OR 'electrotherapy'/de

2 electroplexy:ti,ab,kw OR ((treatment$ NEAR/2 convuls* NEAR/2 shock$):ti,ab,kw) OR ((therap* NEAR/2 convuls* NEAR/2 shock$):ti,ab,kw) OR ((treament$ NEAR/2 convul*):ti,ab,kw) OR ((therap* NEAR/2 convul*):ti,ab,kw) OR ((treament$ NEAR/2 shock$):ti,ab,kw) OR ((therap* NEAR/2 shock$):ti,ab,kw) OR ((treatment$ NEAR/2 electro NEAR/2 convuls*):ti,ab,kw) OR ((therap* NEAR/2 electro NEAR/2 convuls*):ti,ab,kw) OR ((treatment$ NEAR/2 electric NEAR/2 convuls*):ti,ab,kw) OR ((therap* NEAR/2 electric NEAR/2 convuls*):ti,ab,kw) OR ((treatment$ NEAR/2 electric NEAR/2 shock$):ti,ab,kw) OR ((therap* NEAR/2 electric NEAR/2 shock$):ti,ab,kw) OR ((treatment* NEAR/2 electroshock$):ti,ab,kw) OR ((therap* NEAR/2 electroshock$):ti,ab,kw) OR ((treatment* NEAR/2 psychiatric NEAR/2 somatic):ti,ab,kw) OR ((therap* NEAR/2 psychiatric NEAR/2 somatic):ti,ab,kw)

3 #1 OR #2

4 'cognition'/de OR 'comprehension'/de OR 'executive function'/de OR 'imprinting (psychology)'/de OR 'memory'/de OR 'long term memory'/exp OR 'learning'/de OR 'recognition'/de OR 'spatial memory'/de OR 'overlearning'/de OR 'problem based learning'/de OR 'problem solving'/de OR 'spatial learning'/de

5 (understading*:ti,ab,kw OR comprehen*or:ti,ab,kw) AND training*:ti,ab,kw OR recognit*:ti,ab,kw OR retention:ti,ab,kw OR ((problem NEAR/2 solving):ti,ab,kw) OR ((over NEAR/2 learning):ti,ab,kw) OR ((knowledge NEAR/2 acquisition):ti,ab,kw) OR ((learning NEAR/2

verbal):ti,ab,kw) OR ((learning NEAR/2 spatial):ti,ab,kw) OR ((recall NEAR/2 phenomenon):ti,ab,kw) OR ((mental NEAR/2 recall):ti,ab,kw) OR ((event NEAR/2 memory):ti,ab,kw) OR ((remote NEAR/2 memory):ti,ab,kw) OR ((anterograde NEAR/2 memory):ti,ab,kw) OR ((spatial NEAR/2 memory):ti,ab,kw) OR ((episodic NEAR/2 memory):ti,ab,kw) OR ((long NEAR/1 term NEAR/2 memory):ti,ab,kw) OR ((association$ NEAR/2 concept$):ti,ab,kw) OR ((cognitive NEAR/2 thinking):ti,ab,kw) OR ((cognitive NEAR/2 task$):ti,ab,kw) OR ((cognitive NEAR/2 function$):ti,ab,kw)

6 #4 OR #5

7 'adolescent'/de OR 'juvenile'/de OR 'child'/exp OR 'infant'/de

8 ((little NEAR/2 (m$n OR wom$n OR boy* OR girl*)):ti,ab,kw) OR child*:ti,ab,kw OR infan*:ti,ab,kw OR newborn$:ti,ab,kw OR adolescen*:ti,ab,kw OR toddler$:ti,ab,kw OR juvenil$e$:ti,ab,kw OR junior$:ti,ab,kw OR young$:ti,ab,kw OR youth$:ti,ab,kw OR teen*:ti,ab,kw OR bab*:ti,ab,kw OR youngster$:ti,ab,kw OR nenonate$:ti,ab,kw

9 #7 OR #8

10 #3 AND #6 AND #9

Some grey literature sources were searched electronically on 28 January.

Additional articles were included from references of previous systematic reviews on electroconvulsive therapy and cognition as well other relevant studies. We did not limit our search by language.

- **Cochrane Library search strategy was:**

#1 MeSH descriptor: [Convulsive Therapy] this term only

#2 MeSH descriptor: [Electroconvulsive Therapy] this term only

#3 MeSH descriptor: [Psychiatric Somatic Therapies] this term only

#4 MeSH descriptor: [Electric Stimulation] this term only

#5 MeSH descriptor: [Electroshock] this term only

#6 {OR #1-#5}

#7 (Electroplexy OR (treatment? NEAR/2 convul*) OR (therap* NEAR/2 convul*) OR (treatment? NEAR/2 shock?) OR (therap* NEAR/2 shock?) OR (treatment? NEAR/2 electric NEAR/2 convuls*) OR (therap* NEAR/2 electric NEAR/2 convuls*) OR (treatment? NEAR/2 electric NEAR/2 shock?) OR (therap* NEAR/2 electric NEAR/2 shock?) OR (treatment? NEAR/2 electroshock?) OR (therap* NEAR/2 electroshock?) OR (treatment? NEAR/2 psychiatric NEAR/2 somatic) OR (therap* NEAR/2 psychiatric NEAR/2 somatic)): ti,ab,kw

#8 {OR #6-#7}

#9 MeSH descriptor: [Comprehension] this term only

#10 MeSH descriptor: [Executive Function] this term only

#11 MeSH descriptor: [Learning] this term only

#12 MeSH descriptor: [Imprinting, Psychological] this term only

#13 MeSH descriptor: [Memory] this term only

#14 MeSH descriptor: [Memory, Long-Term] explode all trees

#15 MeSH descriptor: [Recognition, Psychology] this term only

#16 MeSH descriptor: [Retention, Psychology] this term only

#17 MeSH descriptor: [Spatial Memory] this term only

#18 MeSH descriptor: [Overlearning] this term only

#19 MeSH descriptor: [Problem-Based Learning] this term only

#20 MeSH descriptor: [Problem Solving] this term only

#21 MeSH descriptor: [Spatial Learning] explode all trees

#22 {OR #9-#21}

#23 (understading* OR comprehen* OR training* OR recognit* OR retention OR (problem NEAR/2 solving) OR (over NEAR/2 learning) OR (knowledge NEAR/2 acquisition) OR (learning

NEAR/2 verbal) OR (learning NEAR/2 spatial) OR (recall NEAR/2 phenomenon) OR (mental NEAR/2 recall) OR (event NEAR/2 memory) OR (remote NEAR/2 memory) OR (anterograde NEAR/2 memory) OR (spatial NEAR/2 memory) OR (episodic NEAR/2 memory) OR (long NEAR/1 term NEAR/2 memory) OR (association? NEAR/2 concept?) OR (cognitive NEAR/2 thinking) OR (cognitive NEAR/2 task?) OR (cognitive NEAR/2 function?)): ti,ab,kw

#24 {OR #22-#23}

#25 MeSH descriptor: [Adolescent] this term only

#26 MeSH descriptor: [Child] explode all trees

#27 MeSH descriptor: [Infant] this term only

#28 MeSH descriptor: [Infant, Newborn] this term only

#29 {OR #26-#29}

#30 (child* or infan* or newborn? or adolescen* or toddler? or juvenil?e? or junior? or young? or youth? or teen* or bab* or youngster? or nenonate? or (little NEAR/2 (m?n or wom?n or boy* or girl*))):ti,ab,kw

#31 {OR #30-#31}

#32 (#8 AND #25 AND #31)

- **Web of Science search strategy was:**

#1 TS= ((psychological NEAR/1 technique) OR electroplexy OR (treatment? NEAR/2 convuls* NEAR/2 shock?) OR (therap* NEAR/2 convuls* NEAR/2 shock?) OR (treatment? NEAR/2 convul*) OR (therap* NEAR/2 convul*) OR (treatment? NEAR/2 shock?) OR (therap* NEAR/2 shock?) OR (treatment? NEAR/2 electro NEAR/2 convuls*) OR (therap* NEAR/2 electro NEAR/2 convuls*) OR (treatment? NEAR/2 electric NEAR/2 convuls*) OR (therap* NEAR/2 electric NEAR/2 convuls*) OR (treatment? NEAR/2 electric NEAR/2 shock?) OR (therap* NEAR/2 electric NEAR/2 shock?) OR (treatment? NEAR/2 electroshock?) OR (therap* NEAR/2 electroshock?) OR (treatment? NEAR/2 psychiatric NEAR/2 somatic) OR (therap* NEAR/2 psychiatric NEAR/2 somatic))

#2 TS=(understading* OR comprehen* OR training* OR recognit* OR retention OR (problem NEAR/2 solving) OR (over NEAR/2 learning) OR (knowledge NEAR/2 acquisition) OR (learning NEAR/2 verbal) OR (learning NEAR/2 spatial) OR (recall NEAR/2 phenomenon) OR (mental NEAR/2 recall) OR (event NEAR/2 memory) OR (remote NEAR/2 memory) OR (anterograde NEAR/2 memory) OR (spatial NEAR/2 memory) OR (episodic NEAR/2 memory) OR (long NEAR/1 term NEAR/2 memory) OR (association? NEAR/2 concept?) OR (cognitive NEAR/2 thinking) OR (cognitive NEAR/2 task?) OR (cognitive NEAR/2 function?))

#3 TS= (child* or infan* or newborn? or adolescen* or toddler? or juvenil?e? or junior? or young? or youth? or teen* or bab* or youngster? or nenonate? or (little NEAR/2 (m?n or wom?n or boy* or girl*)))

#4 #3 AND #2 AND #1

- Google Scholar search strategy was:

Intitle:“psychiatric * therapy”|electroplexy|“convulsive * treatment”|“electroconvulsive therapy”|(cognition|learning|“anterograde memory”|“episodic memory”|“long-term memory”) (adolescent|child|youth|teen) (conference|presentation)

Appendix 2

Table S1. Exclusion reasons for the initially retrieved articles

Citation	**Title**	**Reason for exclusion**
Chess, 1968	An interactive concept of childhood schizophrenia	Editorial
Dhossche & Withane, 2019	Electroconvulsive therapy for catatonia in children and adolescents	Different outcome measured
Fink, 1993	Electroconvulsive therapy in children and adolescents	Editorial
Loiseau et al., 2017	Electroconvulsive therapy use in youth in the province of Quebec	Subjective (Survey)
Moise & Petrides, 1996	Case study: Electroconvulsive therapy in adolescents	Subjective (Survey)
Nelson et al., 1965	Effect of electric shock as a reinforce of the behavior of children	Different intervention
Oltedal et al., 2015	Effects of ECT in treatment of depression: study protocol for a prospective neuro-radiological study of acute and longitudinal effects on brain structure and function	Study protocol
Rey & Walter, 1997	Half a century of ECT use in young people	Outcome was not measured
Seow et al., 2019	A retrospective study of cognitive improvement following electroconvulsive therapy in schizophrenia inpatients	Not pediatric population
Schneekloth et al., 1993	Electroconvulsive therapy in adolescents	Different outcome measured
Squire et al., 1976	Anterograde amnesia following electroconvulsive therapy: No evidence for state-dependent learning	Not pediatric population
Tor et al., 2017	Effectiveness of electroconvulsive therapy and associated cognitive change in schizophrenia	Not pediatric population
Vila e al., 2019	ECS-induced neurogenesis and cognitive side effects	Abstract

Weeks et al., 2013	Antidepressant and neurocognitive effects of isoflurane anesthesia versus electroconvulsive therapy in refractory depression	Not pediatric population
Wong et al., 2019	Effectiveness and cognitive changes with ultra-brief right unilateral and other forms of electroconvulsive therapy in the treatment of mania	Not pediatric population
Zhand et al., 2015	Use of electroconvulsive therapy in adolescents with treatment-resistant depressive disorders, a case series	Different outcome measured
Rami-González et al., 2002	Selective alteration of the declarative memory systems in patients treated with a high number of electroconvulsive therapy sessions	Not pediatric population
Meeter et al., 2011	Retrograde amnesia after electroconvulsive therapy: A temporary effect?	Not pediatric population
Mohapatra & Rath, 2015	Electroconvulsive therapy in a child suffering from acute and transient psychotic disorder with catatonic features	Inadequate time point collection of cognitive test results at baseline
Bertagnoli & Borchardt, 1990	A review of ECT for children and adolescents	Outcome was not measured
Kaliora et al., 2013	The practice of electroconvulsive therapy in Greece	Time point of collection not specified
Ghaziuddin et al., 2020	Electroconvulsive therapy for the treatment of severe mood disorders during adolescence: A retrospective chart review	Inadequate time point collection of cognitive test results at baseline

T

able S2. ECT settings in each study including electrode placement, pulse width, frequency, duration, current and number of sessions.

Citation	Electrode placement	Pulse width	Frequency (hertz)	Duration (sec)	Current	Number of sessions
Cohen et al., 2000	Bilateral	NA	NA	NA	NA	9.8
De la Serna et al., 2011	Bifrontotemporal	1 ms	65	0.89	0.63 A	13
Etain et al., 2001	NA	NA	NA	NA	NA	9 for patient 1; NA for patient 2
Ghaziuddin et al., 1996	Bilateral for 7 patients; Non dominant right electrode for 2 patients	NA	NA	NA	NA	11.2 ± 2.0
Ghaziuddin et al., 1999	Bilateral	NA	NA	Clinical seizure 45.75 ; EEG seizure 71.1	NA	12
Ghaziuddin et al., 2000	Bilateral for 3 patients; unilateral for 3 patients;	NA	NA	NA	NA	10.8 ± 2.0

	combination of the two modes for 10 patients					
Ghaziuddin et al., 2011	NA	NA	NA	NA	NA	37 ± 4.7
Wachtel et al., 2012	Bilateral	1ms	90	4	0.8 A	61
Bender et al., 1947	NA	NA	NA	0.1 or 0.2	NA	6 children had fewer than 20; 9 children had 2 or more courses of treatment, up to 40 convulsive shocks.
Gurevitz et al., 1954	Bilateral	NA	NA	0.1-0.2	NA	Series of 20 shocks
Krislaty 2014	NA	NA	NA	NA	NA	NA

NA, not available

Table S3. Characteristics related to the study outcome including study results, cognitive outcome studied, used test, time point of collection.

Citation	Cognitive Outcome measured	Used test	Time point collected	Results about the effect of ECT on cognitive outcomes
Cohen et al., 2000	Attention; Verbal learning; Cognitive performance.	Attention section of the Wechsler Memory scale; California Verbal Learning Test; Mini-Mental State.	3.5 year follow- up.	All cognitive test scores of the patients treated with ECT were similar to those of the comparison subjects.
De la Serna et al., 2011	IQ; Working memory; Attention; Verbal memory; Executive functions	Wechsler Adult Intelligence Scale-III Revised (WAIS III); Wechsler Intelligence Scale for Children-Revised; Trail Making Test Parts A and B (TMT-A); Verbal Learning Test-Complutense (Spain); Wisconsin Card Sorting Test (WCST), the interference part of the Stroop test, Verbal Fluency Task (FAS), the TMT part B.	At baseline and 2 years after treatment.	At baseline, there was no statistically significant differences between the ECT group and the NECT group. Significant improvement was found in both groups in the semantic category of verbal fluency task and digits forward at follow-up. There was no significant differences between groups in any clinical or cognitive variable at follow-up.

Etain et al., 2001	QIP-QIV	Patient 1: NA Patient 2: Weschler III.	Patient 1: At baseline, at 15 days following ECT. Patient 2: At baseline, at 6 weeks following ECT.	ECT did not seem to cause cognitive impairment at long term.
Ghaziuddin et al., 1996	Cognitive functioning in the areas of memory, orientation, concentration, language, and calculation; General memory screening (Personal and current information, orientation, mental control, logical memory,	Mini-Mental State Examination; Wechsler Memory Scale-Russel Modification; Verbal fluency test.	For all patients, Mini-Mental State Examination before (1-5 days) and after (1-5 days) ECT. Neuropsychological testing for 5 patients before (1-5 days) and after (1-5 days) ECT.	The Mini-Mental State Examination showed no significant differences on memory quotient, orientation, passage learning, visual learning, associative learning, visual delayed recall, and IQ-related measures. Neuropsychological testing indicated a significant decline in attention, concentration, long-term memory search and verbal fluency.

	memory span, visual reproduction, associate learning); Fluency of speech			
Ghaziuddin et al., 1999	Verbal and performance IQ; Academic achievement; verbal memory.	WISCR, WISC III, WAIS-R; WRAT-R, WIAT; neuropsychological testing; Mini-Mental State Examination.	20 months prior ECT for WISC-R, WRAT R, neuropsychological testing; 2 weeks prior ECT for WISC-III; 3 months after ECT.	Comparison of 2-week pre-ECT and 3-month post-ECT cognitive testing revealed no change in IQ. No performance deterioration on the mini-mental state examination and academic achievement tests although her math ability, however, appeared to have improved between pre and post ECT time intervals. On verbal memory tasks, her performance post-ECT suggested some decline in delayed memory tasks compared to 20 months pre ECT.
Ghaziuddin et al., 2000	Attention and concentration; Immediate and delayed verbal	Digit span; For subjects ages 15 and younger, the Story Memory subtest of the Wide Range Assessment of Memory and Learning (WRAML) was	Cognitive tests administered prior to ECT were compared with results at 7.0 ± 10.3 days following the last treatment	Comparison of pre-ECT and the first post-ECT testing administered during the first 10 days of the treatment yielded significant impairments of concentration and attention, verbal- and visual-delayed recall, and verbal fluency. A complete recovery of these

	memory; Immediate and delayed visual memory; Verbal fluency (phonemics); Verbal fluency (semantics); Executive functions.	used. For subjects ages 16 and older, the Logical Memory subtest of the Wechsler Memory Scale; For subjects ages 15 and younger, the Design Memory subtest of the WRAML was used. For subjects ages 16 and older, the Visual Reproduction subtest of the WMS was used; Naming as many words as patient would think of in 1 min interval; Naming as many animals as patients would think of in 1 min interval; Halstead Category Test or the Boll Category Test	and with a second testing at 8.5 ± 4.9 months after the last treatment	functions was noted at the second post-ECT testing. There was no deficit in the ability to problem solve during the initial or the subsequent testing.
Ghaziuddin et al., 2011	Intellectual functioning; Academic achievement-reading; Verbal Memory; Visual	Wechsler Abbreviated Scale of Intelligence (WASI); Wide Range Achievement Test (WRAT-3); Wechsler Memory Scale (WMSIII); California Verbal Learning Test (CVLT-II); Trail making test.	Follow-up points ranged from 5 days to 5.5 month depending on each case.	Comparison of pre-ECT and post-ECT testing did not reveal decline in intellectual functioning, short-term memory or verbal learning; significant improvement was noted on long-term delayed memory recall.

	attention and working memory.			
Wachtel et al., 2012	Evaluation of intellectual functioning independent of spoken language	Comprehensive test of nonverbal Intelligence; Developmental Neuropsychological Assessment Test 2005 and the updated Neuropsychological Assessment Test, Second Edition, 2010 version.	Before treatment onset and after 61 ECT	No evidence of decline in intellectual functioning and acute or delayed memory.
Bender et al., 1947	IQ	IQ test	Before shock, immediately following shock, and at intervals thereafter whenever possible	Lack of any evidence for a lasting effect on the intellectual functioning and development of the child as a result of ECT, although 5 children showed some interference in function immediately after treatment.
Gurevitz et al., 1954	IQ	The revisited Standford-Binet; The Non Language Multi-Mental Test; The Goodenough Draw-A-Man test.	For the Standford-Binet, just before, 24-48 hours after ECT; For other 2 tests, just before, 24-48 hours and 5-27 months after ECT.	Intellectual efficiency was significantly reduced immediately after shock but recovered by the time of follow-up. Some evidence of the non-language test showed that logical reasoning processes where differently organized at time of follow-up than before shock. 5-27 months later there was significance enhancement in performance in tasks of non- verbal intelligence and IQ measurement.

Krislaty 2014	Intellectual functioning; Academic achievement; Verbal fluency; Story memory; Verbal memory, Visual memory; Executive functioning	WAIS-III, Wechsler Abbreviated Scale of Intelligence (WASI), the 2-subtest abbreviated Full Scale IQ, and for patients ranging in age from 6 to 16 years, the Wechsler Intelligence Scale for Children – Fourth Edition was used; Wide Range Achievement Test-Fourth Edition; COWA test; Logical memory subset from the Wechsler Memory Scale Third or Fourth Edition; California Verbal Learning Test-Second Edition; Rey-Osterrieth Complex Figure Test; The Wisconsin Card Sorting Test.	At baseline and at follow-up testing ranging between 1 and 36 months.	Patients' performance post-ECT improved across most domains, particularly memory, however these results did not reach statistical significance. Although memory complaints are typical in this group, the results show that patient's neuropsychological functioning appears to improve except for processing speed.

Table S4. The components of evaluation of the risk of bias.

Citation	Selection				Comparability	Outcome			Quality score
	Representative-ness of exposed cohort	Selection of the non-exposed cohort from same source as exposed cohort	Ascertainment of exposure	Outcome of interest was not present at start of study	Comparability of cohorts.	Assessment of outcome	Follow-up long enough for outcome to occur	Adequacy of follow- up	
Cohen et al., 2000	Truly representative of the population as patients were selected consecutively from chart review and all adolescents were treated with ECT for mood disorder before 19 years of age in five psychiatry departments in Paris. *	Yes *	Medical records *	* (inferred from the deterioration in cognitive test results (when present) after the treatment)	10 psychiatric comparison subjects were chosen who had never been given ECT but were individually matched with the ECT subjects for sex, age, date and place of hospitalization, and DSM-IIIR, except for 1 patient who couldn't be matched for the same subtype of mood disorder or clinical severity. In addition, global assessment of functioning score was not matched	Medical records *	Yes *	Yes, all subjects participated in the follow-up.	Good

					for both groups. For this reason, we will assign only 1 star for this section *			*	
De la Serna et al., 2011	Truly representative of the population as patients were selected consecutively and subjects admitted in the study were schizophrenic patients admitted to the inpatient ward of the Child and Adolescent Psychiatry and Psychology Department of Hospital Clinic of Barcelona. *	Yes *	Medical records *	* (inferred from the deterioration in cognitive test results (when present) after the treatment)	Subjects treated with ECT were compared with 9 subjects selected from the same schizophrenia or diagnosed patients treated during the same period. Schizophrenia (n = 7) or schizoaffective disorder (n = 2) was diagnosed in these controls, and they were treated with psychiatric drugs but without ECT. They were matched for age, socioeconomic status, and PANSS at baseline. Socioeconomic status of the sample was estimated with the Hollingshead Redlich scale. **	Medical records *	Yes *	Yes, all subjects participated in the follow-up. *	Good

Etain et al., 2001	Truly representative of the population as patients were selected consecutively and subjects admitted in the study were selected by a retrospective evaluation of records of adolescents treated by ECT and hospitalized during the last 20 years before the year of the study at the psychopathological service of the child and adolescent, Robert Debré hospital *	No control	Medical records *	* (inferred from the deterioration in cognitive test results (when present) after the treatment)	No control	Medical records *	Yes *	No, not all subjects ?	Poor
Ghaziuddin et al., 1996	Not sure	No control	Reported by the study *	* (inferred from the deterioration in cognitive test results (when present) after the treatment)	No control	Reported by the study *	Yes *	No, not all subjects participated in the follow-up.	Poor

								*	
Ghaziuddin et al., 1999	?	No control	Medical record *	* (inferred from the deterioration in cognitive test results (when present) after the treatment)	No control	Medical records *	Yes *	Yes *	Poor
Ghaziuddin et al., 2000	Not sure	No control	Medical records *	* (inferred from the deterioration in cognitive test results (when present)	No control	Medical records *	Yes *	No, not all subjects participated in	Poor

				after the treatment)				the follow-up.	
Ghaziuddin et al., 2011	Truly representative of the population as patients were selected consecutively and subjects admitted in the study were selected from documentation of adolescent subjects with major depression who were referred to a university-based Child and Adolescent program and were consecutively treated with M-ECT. *	No control	Medical records *	* (inferred from the deterioration in cognitive test results (when present) after the treatment)	No control	Medical records *	Yes *	Yes, all subjects participated in the follow-up. *	Poor
Wachtel et al., 2012		No control		* (inferred from the deterioration in cognitive test results (when	No control	Medical records *	Yes *		Poor

				present) after the treatment)					
Bender et al., 1947	Truly representative of the population as patients were selected consecutively from patients admitted to the Children Ward of the Psychiatric Division of Bellevue Hospital between the year 1942-1947. *	No control	Reported by the study *	* (inferred from the deterioration in cognitive test results (when present) after the treatment)	No control	Reported by the study *	Yes *	No, not all subjects participated in the follow-up.	Poor
Gurevitz et al., 1954	Not evident	No control	Reported by the study *	* (inferred from the deterioration in cognitive test results (when	No control	Reported by the study *	Yes *	No, few missed the Good enough or	Poor

				present) after the treatment)				the Bender-Gestalt test on 1 occasion. *	
Krislaty 2014	Truly representative of the population as patients were selected consecutively from a chart review of patients referred for pre- or post-treatment evaluation for the years spanning 1995 to 2014. *	No control	Reported by the study *	* (inferred from the deterioration in cognitive test results (when present) after the treatment)	No control	Reported by the study *	Yes *	Yes *	Poor

Table S5. Evidence table grading the certainty of evidence following the GRADEpro method.

Question: ECT compared to no ECT for Cognitive functioning deterioration

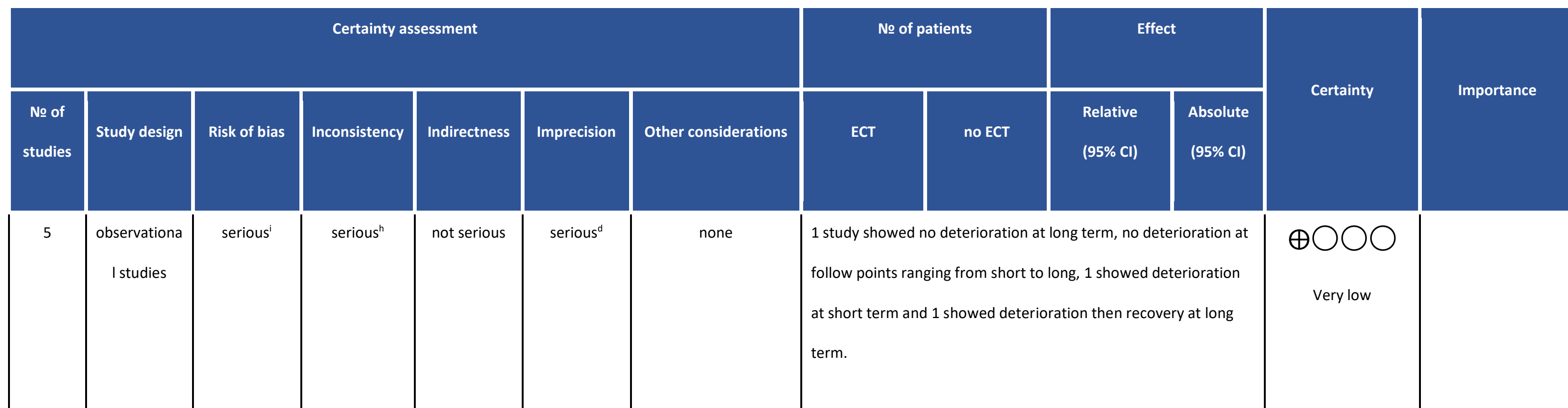
Setting: Children and adolescents

Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ECT	no ECT	Relative (95% CI)	Absolute (95% CI)		
Verbal Learning												
2	observational studies	not serious	not serious	not serious	very serious[a]	none	20	20	-	SMD **0.12 SD higher** (0.51 lower to 0.74 higher)	⨁◯◯◯ Very low	
Attention and/or concentration (follow-up: range 1-5 days to 3.5 years; assessed with: number of points of the test)												
5	observational studies	serious[b]	serious[c]	not serious	very serious[d]	none	2 studies found no deterioration at long term follow up, 2 showed no deterioration at follow up ranging from short to long term time points, and 1 found significant deterioration at short and recovery a follow up point of 8.5 ± 4.9 months.				⨁◯◯◯ Very low	

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ECT	no ECT	Relative (95% CI)	Absolute (95% CI)		
IQ (follow-up: range 1-2 days to 2 years; assessed with: test points)												
8	observational studies	serious[e]	not serious	not serious	very serious[d]	none	1 study found no deterioration at long term follow up, 1 showed no deterioration at follow up ranging from short term to long term time points, 3 studies showed no deterioration at short-term follow up, 1 showed deterioration at short term follow up, 2 studies showed deterioration at short term and recovery at long term.				⨁◯◯◯ Very low	
General cognitive functioning (memory, orientation, concentration, language, and calculation) (follow-up: range 1-5 days to 3.5 years; assessed with: number of points of the test)												
4	observational studies	serious[f]	not serious	not serious	very serious[d]	none	1 study found no deterioration at long term follow up and 2 studies showed no deterioration at short term follow up.				⨁◯◯◯ Very low	
Executive functions (including working memory) (follow-up: range 5-around 170 days to 2 years; assessed with: number of points of the test)												
5	observational studies	serious[g]	not serious	not serious	very serious[d]	none	1 study showed no deterioration at long term, 1 showed no deterioration at a follow up point of 8.5 ± 4.9 months, 1 showed no deterioration at short term and 2 showed no deterioration at follow up points ranging from long to short term.				⨁◯◯◯ Very low	

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ECT	no ECT	Relative (95% CI)	Absolute (95% CI)		
Academic achievement (follow-up: range 5-around 170 days to 3 months; assessed with: number of points of the test)												
3	observational studies	serious[g]	not serious	not serious	very serious[d]	none	2 studies showed no deterioration at short term and 1 showed no deterioration at follow up points ranging from short to long.				⨁◯◯◯ Very low	
Visual memory (follow-up: range 1-5 days to 36 months; assessed with: number of points of the test)												
3	observational studies	serious[f]	serious[h]	not serious	very serious[d]	none	1 study showed deterioration at short term then recovery at long term, 1 showed no deterioration at follow up points ranging from short to long term and 1 showed no deterioration at short term.				⨁◯◯◯ Very low	
Verbal fluency (assessed with: number of point of the tests)												
3	observational studies	serious[g]	serious[h]	not serious	serious[d]	none	1 study showed no deterioration at short term, 1 showed deterioration at short term and 1 showed deterioration then recovery at long term.				⨁◯◯◯ Very low	
Verbal memory (follow-up: range 7.0 ± 10.3 days to 2 years; assessed with: number of points of the test)												



Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ECT	no ECT	Relative (95% CI)	Absolute (95% CI)		
5	observational studies	serious[i]	serious[h]	not serious	serious[d]	none	1 study showed no deterioration at long term, no deterioration at follow points ranging from short to long, 1 showed deterioration at short term and 1 showed deterioration then recovery at long term.				⊕◯◯◯ Very low	

CI, confidence interval; **SMD,** standardised mean difference

Explanations

a, The total number of participants is small (n = 40). Also, the confidence interval of the absolute effect includes values reflecting both benefit and harm; b, Absence of control group (5 studies); c, There were reports of no effect and of deterioration in different studies even in those assessing the outcome at close follow-up points; d, No effect estimate measured; e, Absence of control group (6 studies); f, Absence of control groups; g, Absence of control group (3 studies); h, There were reports of no effect and of deterioration in different studies; i, Absence of control group (4 studies).