TECHNICAL COMMENTARY

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Electroconvulsive therapy

Introduction

Electroconvulsive therapy (ECT) involves the delivery of an electrical stimulus to the brain via electrodes placed either bilaterally or unilaterally to elicit a generalised seizure. Seizure thresholds vary between people and are affected by factors such as medication, age and sex. Thresholds may be estimated by applying a patient profile average or they may be empirically determined, e.g., in an initial titration session, the dose is increased gradually until a seizure eventuates. ECT's efficacy and safety are affected by several factors such as where electrodes are placed, the frequency of treatment, the degree to which the stimulus dose exceeds the seizure threshold and the dose and duration of concurrent medication.

Over the past 30 to 40 years, many studies have established the efficacy of ECT in the treatment of depression, however there has been little investigation, by comparison, for its efficacy for the treatment of schizophrenia. Most commonly, ECT has been tested as a short-term treatment schedule, usually between 12 and 20 treatments given two to three days per week to people who are not adequately responding to antipsychotic medication. It has also been tested as continuation treatment lasting for 6 months or as maintenance treatment lasting longer than 6 months. In continuation and maintenance ECT, treatments are spaced more widely (e.g., up to every 4 weeks) to prevent relapse and maintain wellness.

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2000 that report results separately for people with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder or first-episode schizophrenia. Reviews were identified by searching the databases MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO and the Cochrane library. Hand searching reference lists of identified reviews was also conducted. When multiple copies of reviews were found, only the most recent version was included. Reviews with pooled data are prioritised for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews rated as having less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large, there is a dose dependent response or if results are reasonably consistent, precise and direct with low

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associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found six systematic reviews that met our inclusion criteria[3-8].

- Moderate to high quality evidence suggests a small, short-term benefit of ECT compared to sham ECT (placebo) for symptom improvement in people with schizophrenia who are or who are not being treated with antipsychotics. However, there was more memory impairment, headache, and EEG abnormalities with ECT.
- Antipsychotics have been found to be more effective than ECT for global improvement, but not mental state, in people who are not necessarily resistant to antipsychotics.
- In people who are antipsychotic-resistant, moderate to high quality evidence finds a small effect of better mental state with ECT compared to standard care. Lower quality evidence also finds better functioning with ECT.
- Moderate to low quality evidence suggests small to medium-sized benefits of ECT alone over psychoanalytic psychotherapy alone for mental state, behaviour, and social functioning 6 months after treatment, and for global improvement for 2 years after treatment.

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Painuly N, Chakrabarti S

Combined Use of Electroconvulsive Therapy and Antipsychotics in Schizophrenia: the Indian Evidence. A Review and a Meta-analysis

Journal of ECT 2006; 22(1): 59-66

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Comparison	**8 to 18 unilateral or bilateral ECT sessions over 3 to 6 weeks + antipsychotics vs. sham ECT + antipsychotics.**
Summary of evidence	**Moderate quality evidence (small sample, consistent, imprecise, direct) indicates a short-term benefit of ECT + antipsychotics over sham ECT + antipsychotics for improving mental state.**
Mental state Measured by BPRS	
At the end of treatment *Small effect favouring ECT + antipsychotics over sham ECT + antipsychotics;* 4 RCTs, N = 113, *d* = -0.36, 95%CI -1.08 to 0.36, *p* = 0.33, I^2 = 31%, *p* = 0.10	
Risks	"Few" side effects were reported.
Consistency in results	Consistent
Precision in results	Imprecise
Directness of results	Direct

Pompili M, Lester D, Dominici G, Longo L, Marconi G, Forte A, Serafini G, Amore M, Girardi P

Indications for electroconvulsive treatment in schizophrenia: A systematic review

Schizophrenia Research 2013; 146(1-3): 1-9

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Comparison	**ECT vs. sham ECT.**
Summary of evidence	**Moderate to low quality evidence (small to medium-sized samples, unable to assess consistency or precision, direct) suggests a benefit of ECT over sham ECT for non-medicated or medication-resistant patients. Low quality evidence (small samples or appears inconsistent) is unclear of the benefit for medicated patients or patients with catatonia.**
Global improvement	
In non-medicated patients, 3 RCT (N = 419) reported greater efficacy of real ECT over sham ECT. *In medication-resistant patients*, 5 studies (N = 163) reported greater efficacy of real ECT when combined with medication. *In medicated patients*, 1 RCT (N = 22) reported greater efficacy of real ECT over sham ECT, but only in the short-term, and 1 study (N = 112) reported greater efficacy of adjunctive ECT over medication alone in adolescents with first-episode psychosis. However, 5 RCT (N = 196) reported no differences. *In patients with catatonia*, 1 study (N = 50) reported greater efficacy of ECT over medication. 1 study (N = 202) reported the most frequent reason for ECT use was to augment pharmacotherapy while the most common symptoms necessitating the use of ECT use were catatonia, aggression and suicide attempts. Another study (N = 19) reported that patients with catatonia responded faster to ECT than patients without catatonia.	
Risks	1 study (N = 18) reported no long-term harmful effects on cognitive ability.
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Sinclair DJ, Zhao S, Qi F, Nyakyoma K, Kwong JS, Adams CE

Electroconvulsive therapy for treatment-resistant schizophrenia

Cochrane Database of Systematic Reviews 2019; 3: CD011847

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Comparison 1	**ECT plus standard care vs. sham-ECT plus standard care.**

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Summary of evidence	**Low quality evidence (very small sample, imprecise, direct) is unclear of the effects of ECT vs. sham.**
Mental state	
No difference between groups; 1 study, N = 25, MD = 3.60, 95%CI -3.69 to 10.89, $p > 0.05$	
Hospitalisation	
Fewer readmissions in the ECT group; 1 study, N = 25, RR = 0.29, 95%CI 0.10 to 0.85, $p < 0.05$	
Risks	Not reported
Consistency in results	Not applicable – 1 study
Precision in results	Imprecise
Directness of results	Direct
Comparison 2	**ECT plus standard care vs. clozapine plus standard care.**
Summary of evidence	**Moderate to low quality evidence (medium-sized sample, imprecise, direct) finds a small effect of better mental state in people receiving ECT vs. clozapine.**
Response to treatment	
No difference between groups; 1 study, N = 162, RR = 1.23, 95%CI 0.95 to 1.58, $p > 0.05$	
Mental state	
Better mental state with ECT; 1 study, N = 162, MD = -5.20, 95%CI -7.93 to -2.47, $p < 0.05$	
Risks	Not reported
Consistency in results	Not applicable – 1 study
Precision in results	Imprecise
Directness of results	Direct

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Comparison 3	**ECT plus standard care vs. standard care.**
Summary of evidence	**Moderate to high quality evidence (large samples, imprecise, consistent, direct) finds a small effect of better mental state in people receiving ECT vs. standard care. Lower quality evidence (inconsistent) finds better functioning after ECT.**
Mental state	
There was better mental state in the ECT group; 6 studies, N = 432, MD = -7.62, 95%CI -9.49 to -5.74, $p < 0.05$, $I^2 = 32\%$ *There was more clinically important response in the ECT group;* 9 studies, N = 819, RR = 2.06, 95%CI 1.75 to 2.42, $p < 0.05$, $I^2 = 21\%$	
Functioning	
There was better general functioning in the ECT group; 2 studies, N = 97, MD = 10.66, 95%CI 6.98 to 14.34, $p < 0.05$, $I^2 = 81\%$	
Leaving the study early	
No difference between groups; 3 studies, N = 354, RR = 1.18, 95%CI 0.38 to 3.63, $p > 0.05$, $I^2 = 0\%$	
Risks	Memory deterioration was reported.
Consistency in results	Consistent, apart from functioning.
Precision in results	Imprecise
Directness of results	Direct
Comparison 4	**ECT alone vs. flupenthixol alone.**
Summary of evidence	**Low quality evidence (very small sample, imprecise, direct) is unclear of the effects of ECT alone vs. flupenthixol alone.**
Mental state	
No difference between groups; 1 study, N = 30, MD = -0.93, 95%CI -6.95 to 5.09, $p > 0.05$	
Functioning	

No difference between groups; 1 study, N = 30, MD = -0.66, 95%CI -3.60 to 2.28, *p* > 0.05	
Risks	Not reported
Consistency in results	Not applicable – 1 study
Precision in results	Imprecise
Directness of results	Direct

Tharyan P, Adams CE

Electroconvulsive therapy for schizophrenia

Cochrane Database of Systematic Reviews 2005; 2: CD000076

View review abstract online

Comparison 1	**9 to 45 treatments of bilateral or unilateral ECT vs. 9 to 45 treatments of sham ECT. Most studies included antipsychotics in both groups.**
Summary of evidence	**Moderate to high quality evidence (mixed samples, consistent, precise, direct) shows a small benefit for global improvement at the end of treatment with ECT over sham ECT, however this benefit was not maintained by 6 weeks after treatment. Moderate to low quality evidence (small sample, imprecise) suggests a small to medium-sized benefit for increased hospital discharge at the end of treatment with ECT and improved mental state for up to 6 weeks after treatment.** **Moderate quality evidence (imprecise) indicates no differences between ECT and sham ECT for study retention. Moderate to low quality evidence (small samples) also suggests no differences in mental state or relapse prevention for up to 6 months after treatment. There were also no differences between ECT and psychotherapy for global symptoms.**
Global improvement	

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Small effect favouring ECT over sham ECT, with or without antipsychotics in both groups; 10 RCTs, N = 392, RR = 0.72, 95%CI 0.59 to 0.86, *p* = 0.05, NNT = 6, I^2 = 48%, *p* = 0.05 Results were similar after deleting one small trial with the largest effect *Small effect favouring ECT over sham ECT, without antipsychotics in both groups;* 3 RCTs, N = 189, RR = 0.70, 95%CI 0.49 to 0.98, *p* value not stated, NNT = 7, I^2 = 0% *Small effect favouring ECT over sham ECT, with antipsychotics in both groups;* 6 RCTs, N = 183, RR = 0.81, 95%CI 0.66 to 1.00, *p* = 0.05, I^2 = 45%
At 6 weeks after treatment *No differences between ECT and sham ECT, with antipsychotics in both groups;* 1 RCT, N = 30, RR = 0.71, 95%CI 0.29 to 1.75, *p* = 0.46
At 6 months after treatment *No differences between ECT and sham ECT, with antipsychotics in both groups;* 1 RCT, N = 30, RR = 0.43, 95%CI 0.14 to 1.35, *p* = 0.15
Likelihood of hospital discharge
At the end of treatment *Small to medium-sized effect favouring ECT over sham ECT, without antipsychotics in both groups;* 1 RCT, N = 98, RR = 0.59, 95%CI 0.34 to 1.01, *p* = 0.053
Relapse
At 6 weeks after treatment *No differences between ECT and sham ECT, with antipsychotics in both groups;* 2 RCTs, N = 47, RR = 0.26, 95%CI 0.03 to 2.20, *p* = 0.22, I^2 = 0%, *p* = 0.85
At 6 months after treatment *No differences between ECT and sham ECT, with antipsychotics in both groups;* 1 RCT, N = 20, RR = 7.00, 95%CI 0.41 to 120.16, *p* = 0.18
After 6 months

No differences between ECT and sham ECT, without antipsychotics in both groups; 1 RCT, N = 98, RR = 0.69, 95%CI 0.26 to 1.84, *p* = 0.46
Global improvement **Measured by MHS scale**
At 6 weeks after treatment *No differences between ECT and psychotherapy, without antipsychotics in both groups;* 1 RCT, N = 90, WMD = -1.80, 95%CI -6.57 to 2.97, *p* = 0.46 *d* = -0.16, 95%CI -0.57 to 0.26, *p* = 0.46
At 2 years after treatment; *No differences between ECT and psychotherapy, without antipsychotics in both groups;* 1 RCT, N = 93, WMD = 1.30, 95%CI -3.31 to 5.91, *p* = 0.58 *d* = 0.12, 95%CI -0.30 to 0.54, *p* = 0.58
Mental state **Measured by BPRS**
At the end of treatment *Medium-sized effect favouring ECT over sham ECT, with antipsychotics in both groups;* 2 RCTs, N = 52, WMD = - 6.14, 95%CI -10.01 to -2.27, *p* = 0.0019, I^2 = 0%, *p* = 0.84 *d* = -0.81 95%CI -1.38 to -0.24, *p* = 0.005 There were no differences between groups at the end of treatment in one study that included only people who were not responding to antipsychotic treatment.
At 6 weeks after treatment *Medium-sized effect favouring ECT over sham ECT, with antipsychotics in both groups;* 2 RCTs, N = 52, WMD = -6.38, 95%CI -10.74 to -2.02, *p* = 0.0042, I^2 = 0%, *p* = 0.88 *d* = -0.75, 95%CI -1.32 to -0.19, *p* = 0.009 No differences were reported after 6 weeks in 1 small RCT.
Mental state **Measured by Jenkin scale**
At 6 months after treatment *No differences between ECT and sham ECT, without antipsychotics in both groups;* 1 RCT, N = 90, WMD = -2.10, CI -5.19 to 0.99, *p* = 0.18 *d* = -0.28, 95%CI -0.70 to 0.13, *p* = 0.18

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Behaviour and social functioning Measured by MACC	
At the end of treatment *No differences between ECT and sham ECT, without antipsychotics in both groups;* 1 RCT, N = 90, WMD = 4.10, 95%CI -0.40 to 8.60, *p* = 0.074 *d* = 0.38, 95%CI -0.04 to 0.80, *p* = 0.08	
Leaving the study early	
At the end of treatment *No differences between ECT and sham ECT, with or without antipsychotics in both groups;* 12 RCTs, N = 405, RR = 0.85, 95%CI 0.58 to 1.25, *p* = 0.41, I^2 = 0%, *p* = 0.73	
Risks	*One small trial reported reduced visual memory capacity immediately after ECT treatment;* WMD = -14.00, 95%CI -23.11 to -4.89, *p* = 0.0026 No differences between groups were found on verbal memory or headache.
Consistency in results	Consistent where applicable (> 1 RCT)
Precision in results	Precise for global clinical improvement at treatment end, global improvement – MHS, mental state – Jenkins, and social functioning – MACC. Imprecise for global clinical improvement at 6 weeks and 6 months post treatment, likelihood of hospital discharge, relapse, mental state – BPRS, and leaving the study early.
Directness of results	Direct
Comparison 2	**20 to 45 treatments of bilateral or unilateral ECT vs. antipsychotics.**
Summary of evidence	**Moderate quality evidence (mixed samples, consistent, imprecise, direct) suggests small to medium-sized benefits of antipsychotics over ECT for global improvement (but not mental state), hospital discharge, and improved behaviour and social functioning for 6 months after treatment.** **Low quality evidence (1 small RCT, imprecise) is uncertain of the differences between groups for prevention of relapse.**

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Global clinical impression **Measured by CGI scale**
At the end of treatment *Medium-sized effect favouring antipsychotics over ECT;* 3 RCTs, N = 175, RR = 2.18, 95%CI 1.31 to 3.63, *p* = 0.0026, I^2 = 4%, *p* = 0.35
Likelihood of hospital discharge
At the end of treatment *Medium-sized effect favouring antipsychotics over ECT;* 2 RCTs, N = 135, RR = 1.98, 95%CI 0.97 to 4.03, *p* = 0.059, I^2 = 44%, *p* = 0.18
Relapse
At 6 weeks after treatment *Medium-sized effect favouring ECT over antipsychotics;* 1 RCT, N = 33, RR = 0.33, 95%CI 0.13 to 0.85, *p* = 0.021
Global improvement **Measured by MHS scale**
At 6 weeks after treatment *Medium-sized effect favouring antipsychotics over ECT;* 1 RCT, N = 95, WMD = -5.30, 95%CI -9.31 to -1.29, *p* = 0.0095 *d* = -0.53, 95%CI -0.94 to -0.12, *p* = 0.01
At 2 years after treatment *No differences between ECT and antipsychotics;* 1 RCT, N = 90, WMD = -1.20, 95%CI -5.60 to 3.20, *p* = 0.59 *d* = -0.11, 95%CI -0.53 to 0.30, *p* = 0.60
Mental state **Measured by Jenkin scale**
At 6 months after treatment *No differences between ECT and antipsychotics;* 1 RCT, N = 94, WMD = 2.20, 95%CI -0.35 to 4.75, *p* = 0.091 *d* = 0.35, 95%CI -0.06 to 0.75, *p* = 0.10

Behaviour and social functioning Measured by MACC	
At 6 months after treatment *Medium-sized effect favouring antipsychotics over ECT;* 1 RCT, N = 95, WMD = -6.00, 95%CI -9.18 to -2.82, *p* = 0.00022 *d* = -0.75, 95%CI -1.17 to -0.34, *p* = 0.0004	
Leaving the study early	
At the end of treatment *No differences between ECT and antipsychotics;* 9 RCTs, N = 529, RR = 0.99, CI 0.78 to 1.27, *p* = 0.95, I^2 = 0%, *p* = 0.95	
At 5 years post treatment *No differences between ECT and antipsychotics;* 1 RCT, N = 102, RR = 0.97, CI 0.77 to 1.23, *p* = 0.82	
Risks	No effects on extra pyramidal symptoms or memory.
Consistency in results	Consistent where applicable (> 1 RCT).
Precision in results	Precise, apart from global clinical improvement, likelihood of hospital discharge, relapse, and leaving the study early.
Directness of results	Direct
Comparison 3	**6 to 13 treatments of bilateral ECT + placebo antipsychotic vs. antipsychotics + sham ECT.**
Summary of evidence	**Moderate to low quality evidence (very small sample, consistent, imprecise, direct) suggests no differences between ECT and antipsychotics for global improvement or study retention.**
Global clinical impression Measured by CGI scale	
At the end of treatment *No differences between ECT and antipsychotics;* 2 RCTs, N = 52, RR = 1.10, 95%CI 0.74 to 1.63, *p* = 0.64, I^2 =0%, *p* = 0.84	
Leaving the study early	

At the end of treatment No early departures reported in either group	
Risks	*A large effect of fewer extra pyramidal side effects in those receiving ECT + placebo antipsychotics;* 2 RCTs, N = 52, RR = 0.09, CI 0.01 to 0.69, p = 0.020, I^2 = 0% No differences between groups on memory, drowsiness, pain, weakness, dizziness or allergic reaction.
Consistency in results	Consistent
Precision in results	Imprecise
Directness of results	Direct
Comparison 4	**8 to 18 treatments of bilateral or unilateral ECT + antipsychotics vs. antipsychotics.**
Summary of evidence	**Moderate quality evidence (small to medium-sized samples, consistent, imprecise, direct) suggests no difference between ECT + antipsychotics and antipsychotics for global improvement or study retention. Low quality evidence (1 RCT, small samples, imprecise) is uncertain as to the benefit of ECT + antipsychotics for mental state.**
Global clinical impression Measured by CGI scale	
At the end of treatment *No differences between ECT and antipsychotics;* 3 RCTs, N = 151, RR = 1.15, 95%CI 0.73 to 1.82, p = 0.54, I^2 = 43%, p = 0.17	
Mental state Measured by BPRS	
At the end of treatment *Medium-sized effect favouring ECT + antipsychotics over antipsychotics;* 1 RCT, N = 40, WMD = - 3.90 95%CI -5.52 to -2.28, p = 0.00001 d = -1.46, 95%CI -2.17 to -0.76, p < 0.0001	
At 6 weeks after treatment *No differences between ECT and antipsychotics;* 1 RCT, N = 40, WMD = -2.00, 95%CI -9.57 to 5.57, p = 0.60	

d = -0.16, 95%CI -0.78 to 0.46, *p* = 0.61	
At 6 months after treatment *Small effect favouring ECT + antipsychotics over antipsychotics;* 1 RCT, N = 40, WMD = -7.2, 95%CI -14.08 to -0.32, *p* = 0.040 *d* = -0.64, 95%CI -1.27 to 0.00, *p* = 0.05	
Leaving the study early	
At the end of treatment *No differences between ECT and antipsychotics;* 9 RCTs, N = 529, RR = 0.99, 95%CI 0.78 to 1.27, *p* = 0.95, I^2 = 0%, *p* = 0.95	
Risks	*Reduced visual memory capacity immediately after ECT treatment;* 1 RCT, N = 40, WMD -4.90, CI -9.02 to 0.78, *p* = 0.020 No differences in memory 9 weeks after treatment or for extra pyramidal side effects or hypertension.
Consistency in results	Consistent where applicable (> 1 RCT).
Precision in results	Imprecise
Directness of results	Direct
Comparison 5	**Bilateral or unilateral ECT alone vs. psychoanalytic psychotherapy alone.**
Summary of evidence	**Moderate to low quality evidence (1 small RCT some imprecision) suggests small to medium-sized benefits of ECT over psychoanalytic psychotherapy for mental state, behaviour and social functioning 6 months after treatment, and for global improvement for 2 years after treatment. No differences were found for global improvement or study retention.**
Global clinical impression Measured by CGI scale	
At the end of treatment *No differences between ECT and psychoanalytic psychotherapy;* 1 RCT, N = 102, RR = 0.74, 95%CI 0.42 to 1.30, *p* = 0.29	
Global improvement Measured by MHS scale	

At 6 weeks after treatment *No differences between ECT and psychoanalytic psychotherapy;* 1 RCT, N = 93, *d* = 0.31, 95%CI -0.10 to 0.72, *p* = 0.14	
At 2 years after treatment *Medium-sized effect favouring ECT over psychoanalytic psychotherapy;* 1 RCT, N = 90, *d* = 0.43, 95%CI 0.01 to 0.85, *p* = 0.04	
Mental state **Measured by Jenkin scale**	
At 6 months after treatment *Medium-sized effect favouring ECT over psychoanalytic psychotherapy;* 1 RCT, N = 93, *d* = -0.51, 95%CI -0.92 to -0.09, *p* = 0.02	
Behaviour and social functioning **Measured by MACC**	
At 6 months after treatment *Small effect favouring ECT over psychoanalytic psychotherapy;* 1 RCT, N = 93, WMD = 4.40, 95%CI 0.14 to 8.66, *p* = 0.043 *d* = 0.42, 95%CI 0.01 to 0.83, *p* = 0.05	
Leaving the study early	
At the end of treatment *No differences between ECT and psychoanalytic psychotherapy;* 1 RCT, N = 100, RR = 1.28, 95%CI 0.30 to 5.43, *p* = 0.74	
At 5 year follow up *No differences between ECT and psychoanalytic psychotherapy;* 1 RCT, N = 100, RR = 0.96, 95%CI 0.76 to 1.21, *p* = 0.74	
Risks	Not reported
Consistency in results	Not applicable
Precision in results	Precise apart from global clinical improvement and leaving the study early (by end of treatment)
Directness of results	Direct

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Comparison 6	**Bilateral or unilateral ECT alone vs. psychoanalytic psychotherapy + antipsychotics.**
Summary of evidence	**Moderate quality evidence (1 small RCT, precise) suggests a small to medium-sized benefit of psychoanalytic psychotherapy + antipsychotics over ECT for global improvement 6 weeks after treatment, and mental state, and behaviour and social functioning 6 months after treatment. Moderate to low quality evidence (imprecise) suggests no differences between ECT and psychotherapy + antipsychotics for global improvement or study retention.**
Global clinical impression Measured by CGI scale	
At the end of treatment *No differences between ECT and psychoanalytic psychotherapy + antipsychotics;* 1 RCT, N = 100, RR = 1.92, 95%CI 0.85 to 4.36, *p* = 0.12	
Global improvement Measured by MHS scale	
At 6 weeks after treatment *Medium-sized effect favouring psychotherapy + antipsychotic treatment over ECT;* 1 RCT, N = 90, WMD = -5.00, 95%CI -9.46 to -0.54, *p* = 0.028 *d* = -0.46, 95%CI -0.88 to -0.04, *p* = 0.03	
At 2 years after treatment *No differences between ECT and psychoanalytic psychotherapy + antipsychotics;* 1 RCT, N = 91, WMD = -.50, 95%CI -5.04 to 4.04, *p* = 0.83 *d* = -0.04, 95%CI -0.46 to 0.37, *p* = 0.83	
Mental state Measured by Jenkin scale	
At 6 months after treatment *Small effect favouring psychotherapy + antipsychotic treatment over ECT;* 1 RCT, N = 91, WMD = 2.60, 95%CI 0.27 to 4.93, *p* = 0.029 *d* = 0.45, 95%CI 0.03 to 0.87, *p* = 0.03	
Behaviour and social functioning Measured by MACC	

At 6 months after treatment *Small effect favouring psychotherapy + antipsychotic treatment over ECT;* 1 RCT, N = 91, WMD = -6.10, 95%CI -9.23 to -2.97, *p* = 0.00013 *d* = -0.79, 95%CI -1.21 to -0.36, *p* = 0.0003	
Leaving the study early	
At the end of treatment *No differences between ECT and psychoanalytic psychotherapy + antipsychotics;* 1 RCT, N = 100, RR = 0.77, 95%CI 0.22 to 2.70, *p* = 0.68	
At 5 year follow up *No differences between ECT and psychoanalytic psychotherapy + antipsychotics;* 1 RCT, N = 100, RR = 0.91, 95%CI 0.73 to 1.14, *p* = 0.41	
Risks	Not reported
Consistency in results	Not applicable
Precision in results	Precise apart from global clinical improvement and leaving the study early (by end of treatment).
Directness of results	Direct
Comparison 7	**Bilateral or unilateral ECT alone vs. insulin coma therapy.**
Summary of evidence	**Low quality evidence (1 very small RCT, imprecise) is uncertain as to the benefits of ECT over insulin coma therapy for global improvement, preventing relapse, or retention in treatment.**
Global clinical impression Measured by CGI scale, not improved	
At the end of treatment *No differences between ECT and insulin coma therapy;* 1 RCT, N = 33, RR = 0.69, 95%CI 0.26 to 1.83, *p* = 0.46	
Relapse	
At the end of treatment *No differences between ECT and insulin coma therapy;*	

1 RCT, N = 33, RR = 0.67, 95%CI 0.22 to 2.05, *p* = 0.48	
Leaving the study early	
At the end of treatment *No differences between ECT and insulin coma therapy;* 1 RCT, N = 33, RR = 0.28, 95%CI 0.03 to 2.40, *p* = 0.24	
Risks	Not reported
Consistency in results	Not applicable
Precision in results	Imprecise
Directness of results	Direct
Comparison 8	**6 months of continuation bilateral ECT (weekly for 1 month, bimonthly for 5 months) without antipsychotics vs. flupenthixol.**
Summary of evidence	**Low quality evidence (1 very small RCT, small sample, some imprecision) is uncertain as to the benefits of ECT over flupenthixol for preventing relapse, global improvement, mental state or study retention.**
Global clinical improvement Measured by GAF scale	
At the end of treatment *No differences between ECT and flupenthixol;* 1 RCT, N = 30, WMD = -1.24, 95%CI -6.36 to 3.88, *p* = 0.64 *d* = -0.17, 95%CI -0.89 to 0.55, *p* = 0.64	
Relapse	
After treatment *No differences between ECT and flupenthixol;* 1 RCT, N = 30, RR = 1.00, 95%CI 0.83 to 1.21, *p* = 1.00	
Mental state Measured by BPRS	

At the end of treatment *No differences between ECT and flupenthixol;* 1 RCT, N = 30, WMD = -1.63 95%CI -9.07 to 5.81, *p* = 0.67 *d* = -0.15, 95%CI -0.87 to 0.56, *p* = 0.68	
Leaving the study early	
At the end of treatment *No differences between ECT and flupenthixol;* 1 RCT, N = 30, RR = 0.33, 95%CI 0.04 to 2.85, *p* = 0.32	
Risks	No significant differences reported on cognitive measures.
Consistency in results	Not applicable.
Precision in results	Imprecise for all outcomes apart from relapse after treatment.
Directness of results	Direct
Comparison 9	**6 months of continuation bilateral ECT (weekly for 1 month, bimonthly for 5 months) alone vs. 6 months of continuation bilateral ECT (weekly for 1 month, bimonthly for 5 months) + flupenthixol.**
Summary of evidence	**Low quality evidence (1 very small RCT, small sample, imprecise) is uncertain as to the benefit of continuation ECT over continuation ECT + flupenthixol for improving mental state, retention in treatment, preventing relapse, and for global improvement.**
Global clinical improvement Measured by GAF scale	
At the end of treatment *Large effect favouring continuation ECT + flupenthixol over ECT alone;* 1 RCT, N = 30, *d* = 1.41, 95%CI 0.60 to 2.22, *p* = 0.0007	
Relapse	
At the end of treatment *Large effect favouring continuation ECT + flupenthixol over ECT alone;* 1 RCT, N = 30, RR = 0.43, 95%CI 0.23 to 0.81, *p* = 0.00089	

Mental state Measured by BPRS	
At the end of treatment *Large effect size favouring continuation ECT + flupenthixol over ECT alone;* 1 RCT, N = 30, *d* = -1.45, 95%CI -2.27 to -0.63, *p* = 0.0005	
Leaving the study early	
At the end of treatment *No differences between continuation ECT + flupenthixol over ECT alone;* 1 RCT, N = 30, RR = 0.67, 95%CI 0.13 to 3.44, *p* = 0.63	
Risks	No significant differences reported on cognitive measures.
Consistency in results	Not applicable
Precision in results	Imprecise
Directness of results	Direct
Comparison 10	**Unilateral vs. bilateral ECT with or without antipsychotics in both groups.**
Summary of evidence	**Moderate to low quality evidence (small samples, consistent, imprecise, direct) suggests no benefit for unilateral over bilateral ECT for global improvement. Low quality evidence (1 very small RCT) is uncertain as to the effects for mental state.**
Global clinical impression Measured by CGI scale	
At the end of treatment *No differences between unilateral or bilateral ECT;* 2 RCTs, N = 78, RR = 0.79, 95%CI 0.45 to 1.39, *p* = 0.42, I^2 = 0%, *p* = 0.76	
At 3 months after treatment *No differences between unilateral or bilateral ECT;* 1 RCT, N = 54, RR = 0.69, 95%CI 0.40 to 1.21, *p* = 0.19	
Mental state Measured by BPRS	

At the end of treatment *No differences between unilateral or bilateral ECT;* 1 RCT, N = 36, *d* = -0.05, 95%CI -0.71 to 0.60, *p* = 0.87	
Risks	No differences between groups for memory.
Consistency in results	Consistent where applicable (> 1 RCT).
Precision in results	Imprecise
Directness of results	Direct
Comparison 11	**10 + bilateral ECT sessions - stimulus intensity just above titrated seizure threshold vs. 2 times seizure threshold with flupentixol in both groups.**
Summary of evidence	**Low quality evidence (1 very small RCT, imprecise) is uncertain as to the differences between 2 times seizure threshold and seizure threshold for global improvement, study retention and fewer sessions required.**
Global clinical impression Measured by CGI scale	
At the end of treatment *No differences between titrated seizure threshold and 2 times seizure threshold;* 1 RCT, N = 46, RR = 1.00, 95%CI 0.58 to 1.74, *p* = 1.00	
Leaving the study early	
At the end of treatment *No differences between titrated seizure threshold and 2 times seizure threshold;* 1 RCT, N = 46, RR = 1.00, 95%CI 0.15 to 6.51, *p* = 1.00	
Fewer ECT sessions to first reporting global improvement	
At the end of treatment *Large effect size favouring 2 times seizure threshold over titrated seizure threshold;* 1 RCT, N = 22, *d* = 1.32, 95%CI 0.38 to 2.26, *p* = 0.006	
Risks	Not reported
Consistency in results	Not applicable

Precision in results	Imprecise
Directness of results	Direct
Comparison 12	**10 + bilateral ECT sessions; stimulus intensity just above titrated seizure threshold vs. 4 times seizure threshold with flupentixol in both groups.**
Summary of evidence	**Low quality evidence (1 very small RCT, imprecise) is uncertain as to the differences between titrated seizure threshold and 4 times seizure threshold for global improvement, study retention and fewer sessions required.**
Global clinical impression Measured by CGI scale	
No differences between titrated seizure threshold and 4 times seizure threshold; 1 RCT, N = 44, RR = 1.00, 95%CI 0.57 to 1.75, *p* = 0.99	
Leaving the study early	
At the end of treatment *No differences between titrated seizure threshold and 4 times seizure threshold;* 1 RCT, N = 44, RR = 1.83, 95%CI 0.18 to 18.70, *p* = 0.61	
Number of ECT sessions for global improvement	
At the end of treatment *Large effect size favouring 4 times seizure threshold over titrated seizure threshold;* 1 RCT, N = 22, *d* = 2.45, 95%CI 1.29 to 3.61, *p* = 0.0001	
Risks	Not reported
Consistency in results	Not applicable
Precision in results	Imprecise
Directness of results	Direct
Comparison 13	**10 + bilateral ECT sessions - stimulus intensity 2 times titrated seizure threshold vs. 4 times seizure threshold, with flupentixol in both groups.**
Summary of evidence	**Low quality evidence (1 very small RCT, imprecise) is uncertain as**

	to the differences between 2 and 4 times seizure threshold.
Global clinical impression Measured by CGI scale	
At the end of treatment *No differences between 2 and 4 times seizure threshold;* 1 RCT, N = 44, RR = 1.00, 95%CI 0.57 to 1.75, *p* = 0.99	
Leaving the study early	
At the end of treatment *No differences between 2 and 4 times seizure threshold;* 1 RCT, N = 44, RR = 1.83, 95%CI 0.18 to 18.70, *p* = 0.61	
Number of ECT sessions to first reporting of global improvement	
At the end of treatment *Large effect favouring 4 times seizure threshold over 2 times seizure threshold;* 1 RCT, N = 22, *d* = 1.10, 95%CI 0.19 to 2.01, *p* = 0.02	
Risks	Not reported
Consistency in results	Not applicable
Precision in results	Imprecise
Directness of results	Direct
Comparison 14	**12 vs. 20 unilateral treatments with no antipsychotics in either group.** **Half of each group received 5 per week for 1 week, 3 per week for 2 weeks, and 1 per week for 1 week; the other half received 3 per week for 3 weeks, and 1 per week for 1 week.**
Summary of evidence	**Low quality evidence (1 very small RCT, imprecise) is uncertain as to the differences between 12 and 20 ECT treatments.**
Global clinical impression Measured by CGI scale	
At the end of treatment *Medium-sized effect favouring 20 over 12 treatments;* 1 RCT, N = 43, RR = 2.53, 95%CI 1.13 to 5.66, *p* = 0.023	

Risks	No differences on cognitive and memory measures between 3 days and 5 days per week of unilateral ECT.
Consistency in results	Not applicable
Precision in results	Imprecise
Directness of results	Direct

Wang G, Zheng W, Li XB, Wang SB, Cai DB, Yang XH, Ungvari GS, Xiang YT, Correll CU

ECT augmentation of clozapine for clozapine-resistant schizophrenia: A meta-analysis of randomized controlled trials

Journal of Psychiatric Research 2018; 2006; 105: 23-32

View review abstract online

Comparison	**6 to 24 unilateral or bilateral ECT sessions over 4 to 12 weeks + clozapine vs. clozapine in Chinese people with treatment-resistant schizophrenia.**
Summary of evidence	**Moderate quality evidence (large samples, inconsistent, mostly imprecise, direct) finds medium to large effects of greater improvement in symptom severity with adjunctive ECT in people with treatment-resistant schizophrenia. This effect lasted for around 5.3 weeks post-treatment.**

Mental state
Measured by BPRS or PANSS

Early assessment (1-2 weeks of treatment)

A medium-sized effect of more improved symptoms with adjunctive ECT;

8 RCTs, N = 739, SMD = -0.54, 95%CI -0.88 to -0.20, $p = 0.002$, $I^2 = 77\%$, $p < 0.0001$

At the end of treatment (mean 5.8 weeks of treatment)

A large effect of more improved symptoms with adjunctive ECT;

10 RCTs, N = 703, SMD = -0.88, 95%CI -1.33 to -0.44, $p = 0.0001$, $I^2 = 86\%$, $p < 0.00001$

At endpoint assessment (mean 5.3 weeks post treatment)

A large effect of more improved symptoms with adjunctive ECT;

13 RCTs, N = 1,235, SMD -1.44, 95%CI -2.05 to -0.84, $p < 0.00001$, $I^2 = 95\%$, $p < 0.00001$ Subgroup analysis found these effects were significant for positive but not negative or general symptoms. Meta-regression analyses found smaller effect sizes in larger studies, studies with longer trial/ECT duration, and longer illness duration. Higher clozapine dose in the ECT-clozapine combination group was significantly associated with greater symptomatic improvement. There were no effects of patient age, gender, study quality, and baseline symptom severity.	
Risks	There was more memory impairment (RR = 16.10) and headache (RR = 4.03) with adjunctive ECT.
Consistency in results	Inconsistent
Precision in results	Precise for early assessment only.
Directness of results	Direct

Zheng W, Tong G, Ungvari GS, Ng CH, Chiu HFK, Xiang YQ, Cao XL, Liu ZR, Meng LR, Gazdag G, Xiang YT

Memory Impairment Following Electroconvulsive Therapy in Chinese Patients with Schizophrenia: Meta-Analysis of Randomized Controlled Trials

Perspectives in Psychiatric Care 2018; 54: 107-14

View review abstract online

Comparison	**6 to 18 unilateral or bilateral ECT sessions over 2 to 12 weeks + antipsychotics vs. antipsychotics in Chinese people with schizophrenia.**
Summary of evidence	**Moderate quality evidence (medium-sized samples, inconsistent, some imprecision, direct) finds a large effect of more memory impairment with adjunctive ECT. There was also more headache and EEG abnormalities.**
Memory **Assessed by the Wechsler Memory Scale-Revised, Chinese version**	

Electroconvulsive therapy

At the end of treatment *A significant, large effect of more memory impairment with adjunctive ECT;* 4 RCTs, N = 220, SMD = -1.43, 95%CI -2.80 to -0.05, p = 0.04, I^2 = 95%, p < 0.00001 Subgroup analysis of specific tasks found this effect was evident for picture recall, counting, recognition and associative learning. Performance on the Wisconsin Card Sorting Task showed better performance in the ECT group on response administered and response errors, but not response corrects, perseverative errors, non-perseverative errors, and categories complete. At follow-up (2 weeks) *This effect was not maintained at follow up;* 4 RCTs, N = 426, SMD = -0.21, 95%CI -0.66 to 0.39, p = 0.37, I^2 = 77%, p = 0.005	
Risks	There was more headache (RR = 17.27) and EEG abnormalities (RR = 4.45) with ECT. There were no differences in all-cause discontinuation, akathisia, blurred vision, dry mouth, drowsiness, dizziness, weight gain, ECG readings, rigidity, tremor, insomnia, tachycardia, constipation, elevated liver enzymes, and nausea/vomiting.
Consistency in results	Inconsistent
Precision in results	Precise for follow-up only.
Directness of results	Direct

Explanation of acronyms

BPRS = Brief Psychiatric Rating Scale, CGI = Clinical Global Impression scale, CI = Confidence Interval, d = Cohen's standardised mean difference, EEG = electroencephalogram, g = Hedges' standardised mean difference, GAF = Global Assessment of Functioning scale, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - see ‡ below for interpretation, MACC = Motility Affect Co-operation Communication Scale, MD = mean difference, MHS = Meninger Health Sickness scale, N = number of participants, NNT = the number of people needing to receive treatment for one to show an effect, p = statistical probability of obtaining that result (p < 0.05 generally regarded as significant), PANSS = positive and negative syndrome scale, Q = Q statistic (chi-square) for the test of heterogeneity, RCT = randomised controlled trial, RR = relative risk, vs. = versus, WMD = weighted mean difference

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Electroconvulsive therapy

Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results, publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[9].

† Different effect measures are reported by different reviews.

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, an RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. An RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[10]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. 0.2 represents a small effect, 0.5 a medium effect, and 0.8 and over represents a large treatment effect[9].

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They are an indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the dependent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the

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number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

‡ Inconsistency refers to differing estimates of treatment effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent substantial heterogeneity and 75% to 100%: considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, this criteria should be relaxed[11].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available so is inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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