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Prediction of electroconvulsive therapy response and remission in late-life depression: a review

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Summary

Electroconvulsive therapy is an effective and well-tolerated antidepressant treatment for the elderly population. The place of electroconvulsive therapy in the treatment sequence for depression in the elderly is currently not well established. This review aims to identify the factors that contribute to a positive response and remission in elderly patients with depression undergoing electroconvulsive therapy treatment.

We searched five bibliographic databases (Medline ALL Ovid, Embase.com, APA PsycInfo Ovid, Cochrane Library Wiley and Web of Science Core Collection) for articles published between 1995 and June 2023. Of the 2149 articles screened, 19 were included in the review.

No significant associations were found between remission and/or response and salivary cortisol, baseline hippocampal and white matter hyperintensities, total amyloid load or global cortical atrophy. The reviewed articles did not show a significant difference in remission between unilateral and bilateral electroconvulsive therapy treatment. Other interesting findings are that moderately elevated levels of CRP and S100B levels, lower retardation scores, poorer performance on the word reading task at baseline and longer post-ictal reorientation time may be associated with higher remission and/or response rates. Medial temporal atrophy can be associated with lower Montgomery-Åsberg Depression Rating Scale (MADRS) decrease after electroconvulsive therapy. Finally, elderly patients had higher rates of electroconvulsive therapy response; retardation and psychotic features may mediate this association.

Incorporation of this data into clinical practice may facilitate a personalised approach to electroconvulsive therapy. However, research on this topic is scarce and there are few studies that focus specifically on older people.

Introduction

Depression in the elderly is a complex mood disorder with high comorbidity with both psychiatric and physical diseases [1]. Rates of major depressive disorder in older people range from 5% to 10% in primary care and 37% after intensive care hospitalisation [1, 2]. Older adults with depression are at increased risk for suicide and for impairment in daily functioning [1].

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Electroconvulsive therapy (ECT) is a crucial treatment in psychiatric medicine for severe mood and psychotic disorders [3]. In most guidelines for the treatment of depressive disorder, electroconvulsive therapy is considered a first-line treatment for life-threatening severe depressive episodes and when a rapid response is required [4, 5]. In addition, for psychiatric inpatients with severe mood disorders, electroconvulsive therapy may reduce readmissions [6]. The presence of psychotic features, catatonia, high suicide risk and/or food or fluid refusal are indications for the use of electroconvulsive therapy [4, 7, 8]. Indications for first-line use of electroconvulsive therapy include a previous positive response to electroconvulsive therapy and patient preference [4, 7]. With a remission rate of 60–80%, electroconvulsive therapy is the most efficacious treatment for late-life major depression [3, 9]. In fact, electroconvulsive monotherapy has demonstrated superior efficacy compared with pharmacotherapy in the treatment of late-life depression [9, 10]. In addition, the combination of electroconvulsive therapy with medication exceeds the effectiveness of medication alone [10].

When comparing the efficacy of electroconvulsive therapy, ketamine and transcranial magnetic stimulation (TMS), one systematic review and meta-analysis suggests an efficacy advantage of electroconvulsive therapy over ketamine in adults with a major depressive episode [11]. To our knowledge, there are no trials comparing the effectiveness of electroconvulsive therapy and ketamine in late-life depression. Concerning other neuromodulation techniques, electroconvulsive therapy for late-life depression is usually considered the “gold-standard” therapy. Transcranial magnetic stimulation has few cognitive or somatic side effects, but it has not been shown to be as effective as electroconvulsive therapy in the treatment of psychotic depression or treatment-resistant depression in older people [12].

On the other hand, electroconvulsive therapy is a safe and well-tolerated antidepressant treatment for the elderly population [5, 13, 14]. However, some patients and clinicians may be reluctant to use this treatment because of the risks associated with general anaesthesia and cognitive side effects [15, 16].

Previous meta-analyses have identified predictors of good response to electroconvulsive therapy for treating depression, such as the presence of psychotic features, psychomotor retardation, female sex and older age [17, 18].

However, these factors are often interrelated and have been mostly studied in the general population.

Although electroconvulsive therapy is the most effective treatment for severe depression, there is not enough research evidence to make precise recommendations about the place of electroconvulsive therapy in the treatment sequence for depression, particularly in the older population. Therefore, a review of factors predictive of response to electroconvulsive therapy in late-life depression is needed. To our knowledge, no review has focused on the specific factors associated with response to and/or remission following electroconvulsive therapy in the elderly population.

Materials and methods

Eligibility criteria

In order to obtain details of original studies on the different factors predictive of the effectiveness of electroconvulsive therapy (as it is currently practised) in elderly patients with depression, we applied the following eligibility criteria:

- Studies assessing the effect of electroconvulsive therapy on depression in older participants (>50 years of age). To prioritise the older population, we initially established an age limit of 65 years. However, due to the limited availability of relevant articles meeting our inclusion criteria within this age range, we adjusted our approach and reduced the minimum age to 50 years.
- Selected studies included patients with uni- or bipolar depression as confirmed by Research Diagnostic Criteria, DSM-III-R, DSM-IV, DSM-IV-TR, DSM-5, ICD-10 or ICD-11 criteria.
- Classification of patients as "responder/non-responder" or "remitter/non-remitter" based on scores on valid clinician-rated depression scales (Hamilton Rating Scale for Depression [HRSD] or Montgomery-Åsberg Depression Rating Scale [MADRS]) that were administered before and after the end of the electroconvulsive therapy course.
- Prospective or retrospective studies.
- Observational or interventional studies.
- Articles written in English or French.
- Articles from January 1995 to June 2023.

Data sources and study selection

We conducted a literature search with the collaboration of a medical librarian (J. R. A.) in five bibliographic databases in June 2023: Medline ALL Ovid, Embase.com, APA PsycInfo Ovid, Cochrane Library Wiley and Web of Science Core Collection. All searches were done without language or date restrictions. The detailed search strategies, keywords and index terms are presented in the appendix, supplementary data.

Additional searches were conducted (B. P. M.) to identify possible additional papers by backward citation search, Google Scholar and Google.

In order to acquire an overview of predictors of the effectiveness of electroconvulsive therapy as it is currently applied, we decided to limit our search to papers published between 1995 and June 2023.

The titles and abstracts were first screened for relevance by the first author (B. P. M.). The inclusion of papers, after the first screening, in the review was evaluated separately by two independent researchers (B. P. M. and JP. S.). Disagreements were resolved via consensus (B. P. M., JP. S. and K. L. S.). If no agreement was reached, there was further discussion with a senior researcher (A. v. G.).

Data extraction

We used a data extraction sheet with the following data: (a) study characteristics: year, country and design of the study, diagnostic classification and depression severity scale used; (b) characteristics of the study sample: number of participants, percentage of female participants, mean age of the participants; (c) predictive factor investigated; (d) electroconvulsive therapy related: psychotropic drug modification, position of electrodes, pulse width, duration of seizures, electroconvulsive therapy sessions, number of treatments per week, anaesthetic drugs; (e) main results.

Outcome measures

The primary outcome was remission, the secondary outcome was response to electroconvulsive therapy in the elderly population with depression. In the selected studies, remission was defined as a depression scale score equal to or below 7 (for HRSD-17) or 10 (for HRSD-21, HRSD-24 and MADRS). Response was defined as a reduction of at least 50% from the baseline Hamilton Rating Scale for Depression (HRSD) or Montgomery and Åsberg Depression Rating Scale (MADRS) score.

Results

Selection of studies

After removal of duplicates and studies published before 1995 (figure 1), the literature search yielded 1779 potentially relevant articles. We excluded 1676 articles after review of titles and/or abstracts. We analysed the full text of the 103 remaining studies; 87 of them did not meet eligibility criteria and were excluded. Furthermore, we found 9 further articles via other methods that could potentially be included in the review. After reading these articles, only 3 of them met the criteria for inclusion. In total, we selected 19 articles (figure 1).

Studies had between 8 and 268 participants. Seventeen studies were age-restricted to the elderly (including only patients older than 50 years old) [19–35] and two other articles included all age populations [36, 37]. Although the latter two trials did not meet the age criterion, they were included because they have the rare advantage of age stratification, permitting comparison of the older population with the younger population.

There was one retrospective study [35] and all the others were prospective. Tables S1–S6 (in the appendix) show the mean age and percentage of women and men in each study. 73.7% of the studies were carried out in Europe. Three studies analysed biological markers, two had data on morphological markers, four on associated symptoms, five on electroconvulsive therapy parameters, two on treatment for the maintenance of remission and three on age.

Biological markers (table S1)

We found three articles [19–21] that focused on the impact of biomarkers in depression remission and/or response after treatment with electroconvulsive therapy.

No significant relation was found between pre-ECT salivary cortisol values and response or remission [19]. We found one study concluding that moderately elevated levels of CRP at baseline (3 to 10 mg/l), but no other inflammatory markers, were associated with higher remission rates [20].

Carlier et al. aimed to investigate whether higher S100B was associated with favourable treatment outcomes following electroconvulsive therapy and to further explore whether S100B reflects a state marker of depression activity. Patients with S100B levels in the intermediate tertile, that is, between 33 ng/l and 53 ng/l, had higher odds of remission, and were more likely to remit from depression over time, compared with patients in the lowest tertile. However, there was no significant decrease in levels of S100B after electroconvulsive therapy in both remitters and non-remitters [21].

Morphological markers (table S2)

We found no evidence that baseline hippocampal volume, white matter hyperintensity volume or total amyloid burden were predictive of response or remission at 1 and 4 weeks post-ECT, nor of relapse at 4 weeks post-ECT [22].

However, Oudega et al. showed that patients without medial temporal lobe atrophy were three times more likely to remit their depression than patients with moderate or severe medial temporal lobe atrophy [23]. This study found no differences in changes in MADRS scores and white matter hyperintensities or global cortical atrophy [23].

Associated symptoms (table S3)

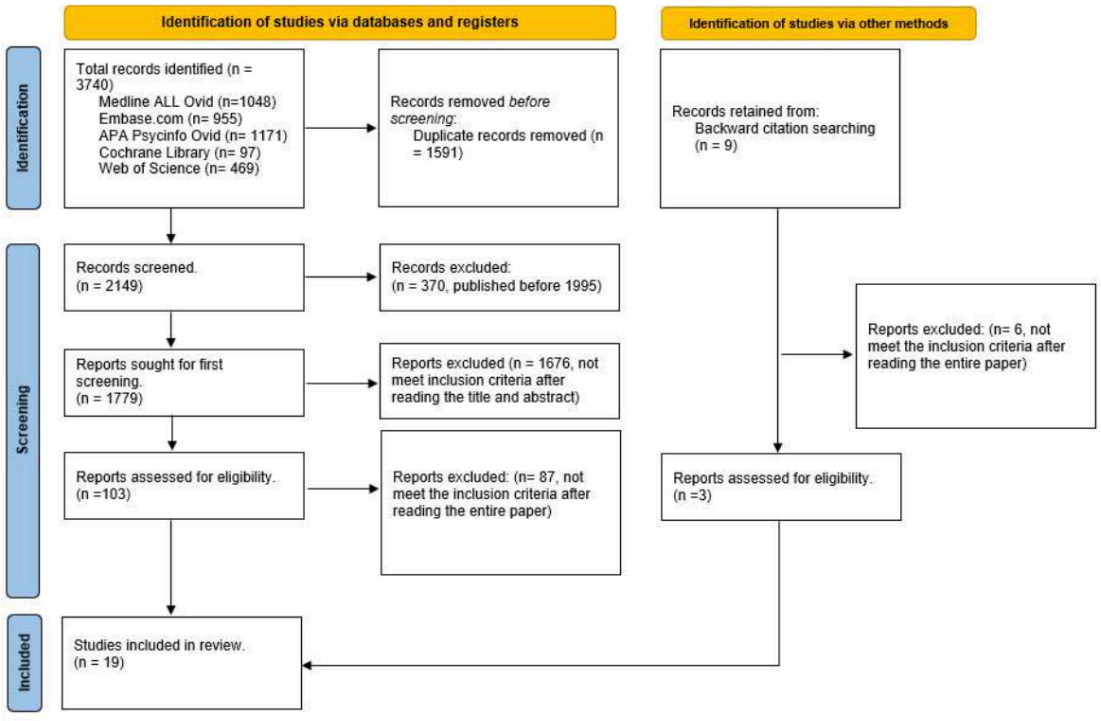
We found one study [24] that analysed the effects of differential response to electroconvulsive therapy in older people with depression using the 3-factor MADRS structure proposed by Suzuki et al. [38], in which factors 1, 2 and 3 represent dysphoria (three items), retardation (four items) and vegetative symptoms (three items), respectively. They concluded that the mean pretreatment score for retardation (factor 2) was significantly lower in responders than in non-responders.

On the other hand, in patients with melancholic depression, the total CORE score (an observational instrument for identifying melancholic depression by assessing psychomotor disturbance [39]) did not predict electroconvulsive therapy outcome [25]. However, another study concluded that the association between age and electroconvulsive therapy efficacy was mediated by psychomotor retardation and, to a lesser extent, by psychotic features [36].

Regarding cognitive functions, poorer performance on the word reading task of the Colour Word Interference Test was associated with a higher likelihood of achieving remission during electroconvulsive therapy in non-demented patients [26]. However, we found no other evidence of significant associations between the outcome of electroconvulsive therapy and cognitive performance parameters at baseline.

Regarding the speed of recovery from disorientation, Magne Bjølseth et al. concluded that a longer post-ictal reorientation time at the first and third treatment sessions predicted a more rapid decline and a lower endpoint on the HRSD17 continuous scores [27].

Figure 1: PRISMA 2020 Flow diagram. www.prisma-statement.org.



Electroconvulsive therapy parameters (table S4)

Several researchers have compared the efficacy of electroconvulsive therapy by right unilateral (RUL ECT) vs bilateral (BL ECT) stimulation. Evidence shows similar results for RUL ECT and BL ECT with more adverse effects in the BL ECT group, such as short-term cognitive impairment [28, 29], whereas improvements in neuropsychological scores were seen in both groups [28].

In another study, elderly patients with major depression were treated with a course of formula-based bifrontal (BF) electroconvulsive therapy or RUL ECT. At the end of the electroconvulsive therapy course, response rates for the BF and RUL groups were 63.9% and 67.6%, respectively. Short-term remission was achieved in 38.9% patients in the BF group and 51.4% patients in the RUL group; however there were no significant differences between the groups [30].

Phase 1 of the large PRIDE study [31] evaluated the efficacy of RUL ultrabrief pulse electroconvulsive therapy combined with venlafaxine for the treatment of geriatric depression. 61.7% of the participants met remission criteria. Among them, the mean decrease in the HAM-D score was 24.7 points. The authors concluded that RUL ultrabrief pulse electroconvulsive therapy, combined with venlafaxine, is a rapidly acting and highly effective treatment option for depressed geriatric patients, with excellent safety and tolerability [31].

From an electrophysiological point of view, a study involving 8 patients with late-life treatment-resistant depression tested whether the mean and regional frontal cortex theta cordance (TC) were able to differentiate early responders from non-responders [32]. TC is a well-documented quantitative electroencephalography measure of cerebral energy consumption [40]. Prefrontal cortex TC has been associated with antidepressant response [41]. The study found that, compared with non-responders, early responders exhibited a greater change in TC specifically within the right prefrontal cortex [32].

Treatment for the maintenance of remission (table S5)

A Finnish study observed the acute response and outcome in a 1-year follow-up of elderly depressive inpatients with major depressive disorder treated with electroconvulsive therapy and/or antidepressant therapy. The acute response was good in both groups. In this study, electroconvulsive therapy was continued until patients were asymptomatic or had received at least 8 treatments without improvement during the last 2 treatments. However, there was no significant difference in the 1-year rehospitalisation rate with 43% in the electroconvulsive therapy and 38% in the antidepressant group [33].

Phase 2 of the PRIDE study [34] evaluated the efficacy and tolerability of continuation electroconvulsive therapy plus medication compared with medication alone in depressed geriatric patients after a successful course of electroconvulsive therapy (phase 1) [31]. They found that additional electroconvulsive therapy after remission (operationalised as four continuation electroconvulsive treatments followed by further electroconvulsive therapy only as needed) was beneficial in sustaining mood improvement for most patients.

Age (table S6)

In terms of age, one study compared characteristics and treatment outcomes of adult (up to 59 years), young-old (60 to 74 years) and old-old (75 years or older) patients treated with electroconvulsive therapy for major depression. The authors found that both older groups had shorter index depressive episodes and were less likely to have had inadequate responses to adequate medication trials before electroconvulsive therapy. Despite a higher level of physical illness and cognitive impairment, even the oldest patients with severe major depression tolerate electroconvulsive therapy in a manner similar to younger patients and demonstrate similar or better acute response [37]. This article does not meet the formal inclusion criteria, but it has the rare advantage of age stratification, particularly at older ages.

A team from the Netherlands wondered whether the greater efficacy of electroconvulsive therapy in older depressed people was related to psychomotor disturbance and/or psychotic features. They compared three age groups (under 50, 50–69 and ≥70) and found no significant differences in HAM-D reduction between the three age groups. However, they did examine the mediating effects of symptomatology and found that the association between age and electroconvulsive therapy efficacy was mediated by psychomotor retardation and, to a lesser extent, by psychotic features [36].

Finally, the BrainAge gap (the difference between predicted biological and chronological age) [42] was not a predictor of response to electroconvulsive therapy in late-life depression patients [35].

Discussion

In this review, we screened 2149 journal articles and selected 19 articles that contained information about the factors predictive of response and/or remission following electroconvulsive therapy in an elderly population with depression. Two meta-analyses had already reviewed the predictors of response to electroconvulsive therapy (ECT) in depression, focusing on the general population [17, 18]. To our knowledge this is the first published attempt to comprehensively describe the different factors predictive of response and/or remission following electroconvulsive therapy in late-life depression. Very few of the screened articles explicitly examined the response to electroconvulsive therapy in depression after the age of 65. Therefore, we had to include studies that investigated the response to electroconvulsive therapy in patients aged 50 and over.

We stratified the predictive factors according to biological [19–21] and morphological markers [22, 23], associated symptoms [24–27], treatment for the maintenance of remission [33, 34] and age [35–37].

The debate about biological markers is wide-ranging. Even if severe subtypes of major depressive disorder are associated with elevated baseline cortisol levels [43], Suijk et al. did not find a significant relationship between pre-electroconvulsive therapy salivary cortisol levels and response or remission [19]. Further studies should focus on the relationship between response and remission following electroconvulsive therapy and variations in cortisol levels following electroconvulsive therapy in the older population.

Moderately elevated levels of CRP and S100B were associated with greater efficacy of electroconvulsive therapy in the treatment of depression [20, 21]. One meta-analysis reported that the increase in S100B correlates with the severity of major depressive disorder [44]. However, another study showed that mildly elevated plasma levels of CRP (above 3.2 mg/l) in later life are associated with higher scores for clinically relevant symptoms of depression [45]. Further research should assess whether the positive relationship between depression severity and electroconvulsive therapy response, but not remission as described by van Diermen et al. [18], can also be mediated by these two biomarkers in late life.

In the elderly, some studies show an association between depression and a decrease in right hippocampal volume [46], and a smaller hippocampal volume predicts poorer outcome with pharmacotherapy treatment [47]. However, Bouckaert et al. [22] did not find an association between hippocampal volume and response or remission following electroconvulsive therapy in late-life depression. One reason for this discrepancy may be the "gold-standard" used as manual segmentation to measure hippocampal volume was used in the former study unlike Oudega et al. [23] who used visual rating of medial temporal atrophy as an approximate stand-in for hippocampal volume.

Bouckaert et al. did not find any relationship between global brain amyloid load and electroconvulsive therapy response in patients with late-life depression [22]. However, one study found an increase in Aβ1-42 in the cerebrospinal fluid after electroconvulsive therapy in patients who responded to treatment, and this increase correlated with the number of electroconvulsive therapy sessions [48]. Consequently, one hypothesis that could be tested in further research is that electroconvulsive therapy has an impact on the risk of developing Alzheimer's disease in later life in major depressive disorder patients. More generally, treatment resistance in late-life depression has been associated with prodromal dementia, mainly Alzheimer's disease and vascular dementia [49]. This differential diagnosis should always be considered in cases of non-response to electroconvulsive treatment.

In adults with depression, RUL ECT did not differ from BL electroconvulsive therapy in efficacy and is advantageous in terms of safety and tolerability [50]. It is important to highlight that across the three studies assessing varying efficacy based on electrode position, the average number of electroconvulsive therapy sessions in both the RUL groups and the BL/BF groups was similar (see table S4 in the appendix). These results could be optimised with adjunctive treatment with venlafaxine [31]. This also applies to adults, with several studies agreeing on the similar efficacy of unilateral and bilateral treatment, with the advantage of fewer cognitive side effects with unilateral treatment [28–30].

The post-ictal time to reorientation was a predictor of greater retrograde amnesia effects following electroconvulsive therapy [51, 52]. However, a longer post-ictal reorientation period was associated with a more rapid reduction in the severity of depressive symptoms throughout the course of electroconvulsive therapy [27]. In light of these two findings, cognitive side effects may not necessarily be considered detrimental when seeking an optimal response to electroconvulsive therapy for depressive symptoms.

Studies focusing on adult populations associated psychomotor retardation with a favourable response to electroconvulsive therapy [53, 54]. The results regarding retardation in the elderly were ambiguous. Tominaga et al. concluded that the retardation score of elderly patients with depression was significantly lower in responders to electroconvulsive therapy than in non-responders [24]. Veltman et al. [25] concluded that the psychomotor symptoms were not related to remission or response. However, Heijnen et al. [36] maintained that retardation may be one of the mediators by which elderly people respond better to electroconvulsive therapy compared to younger patients. The results of this study are particularly reliable, since, unlike the others, the researchers systematically stopped benzodiazepines before starting electroconvulsive therapy.

We have taken into account two meta-analyses [17, 18] that analysed articles involving patients aged 18 years or older. These reviews complement the systematic review by van Shaik et al. about the continuation and maintenance of electroconvulsive therapy in elderly patients with depression [14].

Taken together, our results, along with those of van Dierman et al. [18], indicate that age was positively associated with a better response to electroconvulsive therapy. In our review, we found no clear difference in predictive factors between the younger adults and the elderly. This may be because most studies focused on the response to electroconvulsive therapy in the elderly included patients aged from 50 or 55 years. Consequently, the possible differences may be minimised. Further research is needed in the elderly population to identify possible specific factors predictive of response and remission in people aged over 65 years.

The principal study limitation is the age of inclusion. Although the population of geriatric psychiatry is usually defined as being at least 65 years old, we have included articles on subjects aged 50 years or older making sure, however, that the mean age of study participants in the articles was always over 65 years. There is only one article including exclusively patients over 65 years [29]. However, the average age of most of the studies is above 70 years old (table S1 in the appendix). Another limitation of the present review was that participants experiencing various types of depression and undergoing diverse pharmacological treatments were merged together into one analysis. Despite these limitations, we felt compelled to adopt this approach due to the scarcity of existing research and the restricted number of participants across various studies.

Ultimately, even with efforts to separate the factors predictive of response and remission into distinct subgroups (biological markers, radiological markers, correlated symptoms), the groups remained quite heterogeneous, which makes generalisation very challenging. In addition, the small number of studies focusing on this topic makes it particularly difficult to draw valid conclusions.

The thoroughness with which this review was conducted constitutes one of its strengths. Furthermore, this article focuses on a population group in which predictors of good

response to electroconvulsive treatment in depression have not yet been studied as a whole.

In conclusion, electroconvulsive therapy is an effective and safe technique for the elderly population. There are already some markers that may help predict response or remission following electroconvulsive therapy in the elderly depressed population; however clinical trials involving larger population samples are needed to draw more reliable conclusions.

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Potential competing interests
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Appendix

Appendix I : Bibliographic database search strategies

Embase.com

955 results, 27 June 2023

('aged'/exp OR 'late life depression'/exp OR 'geriatric patient'/exp OR 'geriatrics'/de OR 'gerontopsychiatry'/exp OR 'aging'/exp OR (elder* OR eldest OR geriatr* OR "old age*" OR (older NEXT/1 (patient* OR people OR subject* OR age* OR adult* OR men OR women OR population* OR person*)) OR "oldest old*" OR "very old*" OR geronto* OR psychoger* OR geriatr*):ab,ti,kw) AND ('electroconvulsive therapy'/exp/mj OR (electroconvulsive OR electroconvulsant OR "electric convulsive therapy" OR electroshock* OR ECT):ab,ti,kw) AND ('depression'/exp/mj OR (depression OR depressive OR bipolar OR unipolar OR melancholia):ti,kw) AND ('comparative effectiveness'/exp OR 'therapy effect'/exp OR 'treatment outcome'/exp OR 'treatment response'/exp OR 'relapse'/exp OR 'hospital readmission'/exp OR 'remission'/exp OR (effectiveness OR efficacy OR ((clinical OR treatment OR therap* OR ECT) NEXT/1 outcome*) OR "outcome assessment" OR "clinical improvement" OR relapse* OR Recurrence* OR readmission* OR rehospitali* OR remission OR (ECT NEAR/2 response) OR ((therap* OR treatment*) NEXT/3 (response* OR effect*))):ab,ti,kw) NOT ([conference abstract]/lim OR [conference paper]/lim) NOT ([animals]/lim NOT [humans]/lim)

1.1 Medline ALL Ovid

Ovid MEDLINE(R) ALL 1946 to June 26, 2023
1048 results, 27 June 2023

(exp "Aged"/ OR Geriatrics/ OR Geriatric Psychiatry/ OR exp Aging/ OR (elder* OR eldest OR geriatr* OR "old age*" OR (older ADJ1 (patient* OR people OR subject* OR age* OR adult* OR men OR women OR population* OR person*)) OR "oldest old*" OR "very old*" OR geronto* OR psychoger* OR geriatr*).ab,ti,kf,jw.) AND (*Electroconvulsive Therapy/ OR (electroconvulsive OR electroconvulsant OR "electric convulsive therapy" OR electroshock* OR ECT).ab,ti,kf.) AND (exp *depressive disorder/ OR (depression OR depressive OR bipolar OR unipolar OR melancholia).ti,kf.) AND (Comparative Effectiveness Research/ OR exp treatment outcome/ OR Recurrence/ OR Patient Readmission/ OR Remission Induction/ OR (effectiveness OR efficacy OR ((clinical OR treatment OR therap* OR ECT) ADJ1 outcome*) OR "outcome assessment" OR "clinical improvement" OR relapse* OR Recurrence* OR readmission* OR rehospitali* OR remission OR (ECT ADJ2 response) OR ((therap* OR treatment*) ADJ3 (response* OR effect*))).ab,ti,kf.) NOT (exp Animals/ NOT Humans/)

1.2 **APA PsycInfo Ovid**

APA PsycInfo 1806 to June Week 3 2023

1171 results, 27 June 2023

(geriatric patients/ OR exp geriatrics/ OR exp aging/ OR late life depression/ OR (380 OR 390).ag. OR (elder* OR eldest OR geriatr* OR "old age*" OR (older ADJ1 (patient* OR people OR subject* OR age* OR adult* OR men OR women OR population* OR person*)) OR "oldest old*" OR "very old*" OR geronto* OR psychoger* OR geriatr*).mp.) AND (*electroconvulsive shock therapy/ OR (electroconvulsive OR electroconvulsant OR "electric convulsive therapy" OR electroshock* OR ECT).mp.) AND (exp *major depression/ OR late life depression/ OR (depression OR depressive OR bipolar OR unipolar OR melancholia).mp.) AND (exp treatment effectiveness evaluation/ OR treatment outcomes/ OR "relapse (disorders)"/ OR "recovery (disorders)"/ OR psychiatric hospital readmission/ OR exp "remission (disorders)"/ OR (effectiveness OR efficacy OR ((clinical OR treatment OR therap* OR ECT) ADJ1 outcome*) OR "outcome assessment" OR "clinical improvement" OR relapse* OR Recurrence* OR readmission* OR rehospitali* OR remission OR (ECT ADJ2 response) OR ((therap* OR treatment*) ADJ3 (response* OR effect*))).mp.)

1.3 **Web of Science Core Collection**

Search option : Advanced search, Exact search

469 results, 27 June 2023

TS=((elder* OR eldest OR geriatr* OR "old age*" OR (older NEAR/1 (patient* OR people OR subject* OR age* OR adult* OR men OR women OR population* OR person*)) OR "oldest old*" OR "very old*" OR geronto* OR psychoger* OR geriatr*) AND (electroconvulsive OR electroconvulsant OR "electric convulsive therapy" OR electroshock* OR ECT) AND (depression OR depressive OR bipolar OR unipolar OR melancholia) AND (effectiveness OR efficacy OR ((clinical OR treatment OR therap* OR ECT) NEAR/1 outcome*) OR "outcome assessment" OR "clinical improvement" OR relapse* OR Recurrence* OR readmission* OR rehospitali* OR remission OR (ECT NEAR/1 response) OR ((therap* OR treatment*) NEAR/2 (response* OR effect*))) NOT (animal* NOT human*))

1.4 **Cochrane Library**

Cochrane Database of Systematic Reviews, Issue 6 of 12, June 2023

0 results, 27 June 2023

Cochrane Central Register of Controlled Trials, Issue 6 of 12, June 2023

97 results, 27 June 2023

((elder* OR eldest OR geriatr* OR (old NEXT age*) OR (older NEXT/1 (patient* OR people OR subject* OR age* OR adult* OR men OR women OR population* OR person*)) OR (oldest NEXT old*) OR (very NEXT old*) OR geronto* OR psychoger* OR geriatr*):ab,ti,kw AND (electroconvulsive OR electroconvulsant OR "electric convulsive therapy" OR electroshock* OR ECT):ab,ti,kw AND (depression OR depressive OR bipolar OR unipolar OR melancholia):ti,kw AND (((clinical OR treatment OR therap* OR ECT) NEXT/1 outcome*) OR "outcome assessment" OR "clinical improvement" OR relapse* OR Recurrence* OR readmission* OR rehospitali* OR remission OR (ECT NEAR/2 response) OR ((therap* OR treatment*) NEXT/3 (response* OR effect*))):ab,ti,kw**)**

Appendix II Supplementary tables

Reference	Year and country	Study design	Population clinical assessment	Female participants (%)	Minimum age; mean age and range	Diagnostic classification and depression severity scale	Biological marker	ECT parameters (psychotropic drug (PD)/ position of electrodes (PE)/pulse(P)/duration of seizures (DS)/ECT sessions, median (ES)/ week frequency (WF)/ anesthetic drugs (AD))
(1)	2019, The Netherlands	Prospective study	102	64.7	≥ 50 years old (y.o.); 72.8 (SD ± 8.6)	DSM-IV/ MADRS	Salivary cortisol	PD: patients withdrawn from any psychotropic drug at least 2 weeks before ECT treatment if clinical condition allowed. PE: bilateral (BL) ECT was administered when clinical condition worsened, or no clinical improvement occurred after 6 unilateral sessions. P: no data. DS: a seizure of 20 seconds (s) or more was considered adequate. ES: no data. WF: twice weekly. AD: etomidate and succinylcholine.
(2)	2019, The Netherlands	Prospective study	110	68.4	≥ 55 y.o.; 73.1 (SD ± 8.2)	DSM-IV/ MADRS	CRP, interleukin-6, interleukin-10, and tumor necrosis factor–α	PD: discontinued at least one week before ECT or kept stable before ECT and during the ECT course if necessary. PE: preferably started with right unilateral (RUL) ECT, when the clinical condition worsened treatment was switched to BL. P: brief-pulse ECT (1.0 ms). DS: no data. ES: 11. WF: twice weekly. AD: no data.
(3)	2019, The Netherlands	Prospective study	91	69.2	> 55 y.o.; 73.0 (SD ± 8.0)	DSM-IV/ MADRS	S100 calcium-binding protein B	PD: no data. PE: RUL, stimulation was changed to BL when clinical conditioned worsened or after six UL ECT sessions without improvement. P: brief-pulse ECT (1.0 ms). DS: A seizure of less than 20 s motor activity or less than 25 s EEG activity, was considered inadequate. ES: 11.6. WF: treated twice weekly. AD: no data.

Table 1: Characteristics of the studies focusing on biological markers.

Reference	Year and country	Study design	Population clinical assessment	Female participants (%)	Minimum age; mean age and range	Diagnostic classification and depression severity scale used	Radiological marker	ECT parameters (psychotropic drug (PD)/ position of electrodes (PE)/pulse(P)/duration of seizures (DS)/ECT sessions, median (ES)/ week frequency (WF)/ anesthetic drugs (AD))
(4)	2019, Belgium	Prospective study	34	67.6	≥ 55 y.o.; 73 (SD ± 7.8)	DSM-IV/ MADRS	Hippocampal volume, white matter hyperintensity volume and total amyloid load	PD: psychotropic medication was discontinued at least 1 week prior to ECT. PE: subjects were all treated with RUL, switching to bitemporal was applied when the clinical condition worsened. P: brief pulse (0.5–1.0 ms). DS: no data. ES: 11.2. WK: twice a week. AD: etomidate and succinylcholine.
(5)	2009, The Netherlands	Prospective study	81	61.7	≥ 55 y.o.; 74.0 (SD ± 7.8)	DSM-IV/ MADRS	White matter hyperintensities, medial temporal lobe atrophy, global cortical atrophy	PD: psychotropic medications were tapered off within 2 weeks before starting ECT. PE: started preferably with RUL. P: no data. DS: A motor seizure of less than 20 s was considered inadequate. ES: 12.8. WF: twice weekly. AD: no data.

Table 2: Characteristics of studies focusing mainly on morphological markers.

Reference	Year and country	Study design	Population clinical assessment	Female participants (%)	Minimum age; mean age and range	Diagnostic classification and depression severity scale used	Associated symptoms	ECT parameters (psychotropic drug (PD)/ position of electrodes (PE)/pulse(P)/duration of seizures (DS)/ECT sessions, median (ES)/ week frequency (WF)/ anesthetic drugs (AD))
(6)	2011, Japan	Prospective study	18	77.7	≥ 60 y.o.; 70.9 (SD ± 6.91)	DSM-IV/ MADRS	Dysphoria, retardation, vegetative symptoms	PD: patients maintained on the same drug treatment for at least one week before ECT and during the entire study period. PE: bifrontotemporal scalp. P: brief bipolar pulse. DS: no data. ES: 6. WF: twice a week. AD: propofol and suxamethonium.
(7)	2019, Belgium	Prospective study	110	66.7	≥ 55 y.o.; 73.0 (SD ± 8.4)	DSM-IV/ MADRS	Melancholic symptoms	PD: patients were withdrawn from psychotropic medication 1 week before starting ECT if clinical condition allowed, or pharmacotherapy was kept stable 6 weeks before and during ECT. PE: Switching to BL ECT occurred in case of clinical worsening or no improvement after 6 UL sessions. P: brief-pulse ECT (0.5–1.0 milliseconds). DS: motor seizure of 20 s or more was considered adequate. ES: 11. WF: twice weekly. AD: no data.
(8)	2015, Norway	Prospective study	65	55.4	≥ 60 y.o.;74.9 (SD ± 6.5)	DSM-IV-TR/ HRSD-17	Cognitive function	PD: 86.2% patients had not responded to at least one adequate trial of an antidepressant (AD) prior to admission. For those individuals, AD were reduced or withdrawn 3–10 days before starting ECT. 61.5% patients continued receiving AD. 60.0% were in need of benzodiazepines (BZD) for anxiety. In 7.7% patients, anti-epileptic drugs or mood stabilizers were discontinued one week prior to ECT. Olanzapine or quetiapine were prescribed to 41.5% patients with psychotic symptoms or agitation. PE: bifrontal (BF) or RUL. P: brief-pulse (0.5–1.0 ms pulse width). DS: no data. ES: 9.3. WF: twice a week. AD: atropine, thiopental and succinylcholine.
(9)	2015, Norway	Prospective study	57	52.6	≥ 60 y.o.; 75.5 (SD ± 6.3)	DSM-IV-TR/ HRSD-17	Post-ictal reorientation time	PD: 84.2% patients had not responded to at least one adequate trial of an AD prior to admission. For those individuals, AD were reduced or withdrawn 3–10 days before starting ECT. 59.6% patients received AD in sub-therapeutic doses during the ECT course, whereas AD were withdrawn in 24.6%. 77.2% patients were in need of oxazepam for anxiety. Zopiclon was accepted in case of insomnia. In 17.5% patients, anti-epileptic drugs or mood stabilizers were discontinued one week prior to ECT. Olanzapine or quetiapine were prescribed to 27 47.4% patients with psychotic symptoms or agitation. PE: BF or RUL. P: brief-pulse (0.5–1.0 ms pulse width). DS: seizure was missed or aborted if clonic movements in the cuffed arm and EEG manifestations of less than 15 s duration. ES: 9.55. WF: twice a week. AD: atropine, thiopental and succinylcholine.

Table 3: Characteristics of the studies focusing mainly on associated symptoms.

Reference	Year and country	Study design	Population clinical assessment	Female participants (%)	Minimum age; mean age and range	Diagnostic classification and depression severity scale used	ECT parameters	ECT parameters (psychotropic drug (PD)/ position of electrodes (PE)/pulse(P)/duration of seizures (DS)/ECT sessions, median (ES)/ week frequency (WF)/ anesthetic drugs (AD))
(10)	Brasil, 2006	Prospective study	39	RUL: 35.3%; BL: 72.7%	> 60 y.o.;RUL: 75.58 (SD ± 9.57); BL: 74.82 (SD ± 6.78)	DSM-IV/ MADRS	Right unilateral (RUL) vs bilateral (BL)	PD: PD were discontinued at least 1 week before ECT treatment. PE: randomly assigned to receive either BL ECT (n = 22) or RUL ECT (n = 17). P: 1 ms. DS: > 25 seconds per electroencephalogram monitoring. ES: 10.0 for RUL ECT and 10. For BL ECT (sessions to achieve remission) WF: 3 sessions per week. AD: atropine, etomidate, and succinilcoline chlorhydrate.
(11)	Poland, 2020	Prospective study	29	48.27	> 65 y.o.; 70.9 (SD ± 5.1)	ICD-10/ HDRS-21	RUL vs frontotemporal BL	PD: Before the first ECT treatment, all antidepressants, lithium, antipsychotics, benzodiazepines or anticonvulsant medications were discontinued. The mean duration of the discontinuation of medications before the first ECT was 7.3 days. PE: either in right frontotemporal and parietal for RUL or bilateral fronto-temporal for bilateral method. P: 0.5 ms. DS: duration of seizure of at least 20 s (EEG). ES: 10.5 for BT and 11 for RUL. WF: twice a week. AD: no data.
(12)	Norway, 2015	Prospective study	73	RUL: 56.8%; BF: 50%	≥ 60 y.o.; RUL: 75.5 (SD ± 6); BF: 74.1 (SD ± 6.6)	DSM-IV-TR/ HRSD-17	RUL vs BL	PD: antidepressants were reduced or withdrawn 3–10 days before starting ECT. Patients were allowed to use oxazepam if needed for anxiety. Zopiclon was accepted in case of insomnia. In 15.1% patients, anti-epileptic drugs or mood stabilizers were discontinued 1 week prior to ECT. Olanzapin or quetiapin were prescribed to 42.5% patients with psychotic symptoms or agitation. PE: BF or RUL. P: square-wave brief pulse (0.5–1.0 ms pulse width). DS: seizure missed if clonic movements in the cuffed arm and EEG manifestations of less than 15 s duration. ES: among remitters: 14 (BF) and 19 (RUL)/ among non-remitters: 22 (BF) and 18 (RUL) WF: twice a week. AD: atropine, thiopental and succinylcholine.
(13)	2016, USA	Prospective study, PRIDE phase 1	172	57.5	≥ 60 y.o.; 69.9 (SD ± 7.6)	DSM-IV-R/ 24-item HAM-D	RUL ultra brief pulse ECT, combined with venlafaxine	PD: discontinued within 1 week of starting phase 1. PE: RUL. P: 0.25 ms. DS: the seizure adequacy criterion was a motor seizure ≥15 seconds. ES: 7.3 (to achieve remission) WF: three times per week. AD: glycopyrrolate, methohexital, succinylcholine.
(14)	USA, 2020	Prospective study	8	75	≥ 50 y.o; responders: 66 (SD ± 5); non-responders: 61 (SD ± 7)	DSM-IV/ HDRS-17	Baseline theta cordance differences	PD: no data. PE: RUL. P: no data. DS: no data. ES: 7. WF: two to three times per week. AD: no data.

Table 4: Characteristics of the studies focusing mainly on ECT parameters.

Reference	Year and country	Study design	Population clinical assessment	Female participants (%)	Minimum age□mean age and range	Diagnostic classification and depression severity scale used	Drug added to the ECT treatment	ECT parameters (psychotropic drug (PD)/ position of electrodes (PE)/pulse(P)/duration of seizures (DS)/ECT sessions, median (ES)/ week frequency (WF)/ anesthetic drugs (AD))
(15)	Finland, 2004	Prospective study	51	73.3% (ECT group), 95.2% (ADT group)	≥ 60 y.o.; ECT group: 69.6 (SD ± 6.2); ADT group: 73.1 (SD ± 7.5)	DSM-IV/ MADRS	ECT versus conventional antidepressant drug treatment	PD: medication was kept constant during the follow-up. PE: standard bilateral (bifrontotemporal). P: brief-pulse. DS: at least of 20 seconds motor response and 25 seconds of EEG seizure activity. ES: 8. WF: 3 times a week. AD: methohexital and muscle relaxation with succinylcholine.
(16)	2016, USA	Prospective study (PRIDE, phase 2)	120 remitters (from PRIDE phase 1)	61.7	≥ 60 y.o.;70.5 (SD ± 7.2)	DSM-IV/ 24-item HAM-D	Medication only arm (venlafaxine plus lithium, over 24 weeks) versus ECT plus medication arm (four continuation ECT treatments over 1 month, while continuing venlafaxine plus lithium)	PD: venlafaxine and lithium in addition to ECT. PE: RUL. P: ultrabrief. DS: seizure adequacy criterion was a motor seizure ≥15 s. WF: 4 ECT treatments in the 1st month. In weeks 5-24 treatment frequency was 0-2 ECT based on the patient HAM-D scores. AD: glycopyrrolate, methohexital, succinylcholine.

Table 5: Characteristics of the studies focusing on associated treatment for the maintenance of remission.

Reference	Year and country	Study design	Population clinical assessment	Female participants (%)	Minimum age; mean age and range	Diagnostic classification and depression severity scale used	Age compared	ECT parameters (psychotropic drug (PD)/ position of electrodes (PE)/pulse(P)/duration of seizures (DS)/ECT sessions, median (ES)/ week frequency (WF)/ anesthetic drugs (AD))
(17)	The Netherlands, 2023	Retrospective	42	66.7	≥ 55 y.o.; 72.7 (SD ± 9.4)	DSM-IV-TR/ MADRS	Difference between predicted and observed BrainAge	No data
(18)	The Netherlands, 2019	Prospective study	96	67	Range 33-96 y.o.; 63.9 (SD ± 12.3),	MADRS/ HAM-D/ DSM-IV	Young age group (<50 y.o.), middle age group (50-59 y.o.) and old age group (≥ 70 y.o.)	PD: patients were withdrawn from all psychotropic medication at least 5 days prior to the first ECT treatment and the majority of patients were maintained medication-free during the course of ECT. 16 patients were treated with nortriptyline during the course of ECT. In case of severe agitation, incidental use of haloperidol was allowed, the use of BZD was not allowed. PE: bilateral. P: brief-pulse. DS: seizure of at least 25s. ES: 15. WF: twice weekly. AD: glycopyrrolate and etomidate, alfentanil and succinylcholine.
(19)	USA, 1999	Prospective study	268	Adult group: 66.2%; young-old group: 65.1%; old-old: 65.3%	Adult group: 41.9 (SD ± 10.3); young-old group: 68.9 (SD ± 4.1); old-old: 80.4 (SD ± 3.9)	DSM-III-R/ 24-item HAM-D	Adult (59 and younger), young-old (60 to 74 years), and old-old (75 and older)	PD: All psychotropic medications (with the exception of lorazepam) were tapered before ECT was started. PE: either RUL or BL with the bifrontotemporal placement. P: brief-pulse. DS: no data. ES: adult group: 13.8, young-old group: 13.1, old-old group: 12.1. WF: 3 per week. AD: Atropine, methohexital and succinylcholine.

Table 6: Characteristics of the studies focusing on age.

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