Effectiveness of electroconvulsive therapy in patients lacking decision making capacity: A systematic review and meta-analysis

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ABSTRACT
Background: Electroconvulsive therapy (ECT) is provided for patients with severe and often life-threatening illness, who lack decision making capacity to consent to treatment (DMC-T) in clinical settings.

Objective: The aim of this study is to summarize previous studies investigating clinical outcomes of ECT in patients lacking DMC-T.

Methods: A systematic review and meta-analysis of studies reporting clinical outcomes of ECT in patients lacking DMC-T with any psychiatric diagnoses was conducted. The primary outcome was clinical improvement. Secondary outcomes were cognitive outcomes and six month readmission rate. Hedges’ g and odds ratios were calculated using a random-effects model. The protocol was registered in Open Science Framework (https://osf.io/rxjkm).

Results: Of 3552 identified articles, 41 studies (n = 1299) were included. Approximately 80% of patients lacking DMC-T responded to ECT, and part of the patients regained capacity to consent and consented to further treatment with ECT. A total of seven studies (n = 1081) were included for meta-analysis. Patients without DMC-T showed superior clinical improvement and less cognitive side effects compared with those with DMC-T, whereas the groups did not show any difference in readmission rate. Several clinical characteristics at baseline and ECT techniques were significantly different between the groups.

Conclusion: ECT is equally, if not superiorly, effective in patients lacking DMC-T compared to patients with DMC-T. ECT can potentially enhance patients’ autonomy, without increasing the risk of cognitive side effects. These results support the clinical and ethical legitimacy of ECT provision for patients with the most severe illness who lack DMC-T at start of treatment.

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1. Introduction

Clinical studies have consistently provided evidence on the efficacy of electroconvulsive therapy (ECT) in pharmacotherapy-resistant severe major depressive disorder [1], bipolar disorder [2,3], and schizophrenia [4]. High-quality randomised controlled trials (RCTs) [5–8] are required as proof of the efficacy of a treatment, but clinical trials often exclude a subpopulation typically treated in real-world clinical practice, which may hamper the generalizability of the results. For instance, in real-world clinical settings ECT is often administered to patients with severe psychotic or catatonic symptoms, those who refuse to take food or drink and need rapid recovery from a life-threatening condition, and those exhibiting the most severe affective symptoms, including high suicide risk. The majority of these patients are likely to be excluded from clinical trials because they often lack decision making capacity to consent both to treatment and research (DMC-T and DMC-R). Indeed, the inability to obtain valid consent for study
participation has been identified as the only common exclusion criterion in ECT clinical trials [9]. However, ECT for patients lacking DMC-T is not an exception, as reported from several countries all over the world [10]. Nevertheless, the practice of obtaining informed consent varies from country to country and different countries have legislations or regulations [11], which can be obstacles to provide this effective and life-saving treatment for patients lacking DMC-T in a timely fashion [12]. Additionally, lack of evidence on the efficacy or effectiveness of ECT when administered in patients lacking DMC-T as well as possible ethical concerns may discourage clinicians to provide ECT for this subgroup of severely ill patients. As a general rule, it is not feasible to conduct RCTs for patients lacking DMC-T due to ethical, legal and practical reasons. Thus, reviewing observational studies may provide the best available evidence and useful information for clinicians, substitute decision makers (e.g., patients’ relatives and legal guardians), and also the courts.

The aim of our study is to systematically review and quantitatively summarize studies that investigated the effectiveness of ECT in patients lacking DMC-T. We hypothesize that ECT shows at least equal effectiveness in patients lacking DMC-T compared to patients who have DMC-T.

2. Methods

The literature search, decisions on inclusion, data extraction were performed independently by two of the authors (A.T. and D.Z.-W.). Disagreements were resolved by discussion with another author (P.S.). We followed the Meta-Analysis of Observational Studies in Epidemiology guidelines. The protocol was registered in Open Science Framework (https://osf.io/rxjkm/).

PubMed, PsycINFO, Web of Science, and Embase were searched to identify eligible studies meeting the inclusion criteria (last search: March 17, 2022). The following keywords were used: (Electroconvulsive OR ECT) AND (consent OR involuntary OR incapable OR capacity OR refusal OR autonomy OR coercion). A manual search of reference lists in relevant publications was conducted to supplement the electronic search. Using Covidence (https://www.covidence.org/), duplicates were removed, and titles and abstracts of studies were screened. Then, full-text articles were reviewed for eligibility according to the following inclusion criteria: a) original articles, b) peer-reviewed papers written in English, German, Dutch or Japanese, c) studies including adult patients with any diagnoses (e.g., major depressive disorder, bipolar disorder, or schizophrenia) who lack capacity to consent to receive ECT, and d) studies reporting clinical outcomes of ECT with/without any standardized clinical rating scales. We did not limit the diagnoses because patients lacking DMC-T may present with similar symptoms/conditions regardless of their primary diagnoses (e.g., catatonic stupor, severe psychotic symptoms, or a refusal of food or pharmacological treatment due to delusional thinking). Studies including only children or adolescents were excluded because their treatment always needs (additional) consent by their parents or relatives and legal guardians, and also the courts.

The clinical characteristics of the samples (e.g., age, sex, and baseline severity), ECT parameters (e.g., electrode placement, pulse width, number of ECT sessions), and clinical outcomes (e.g., clinical effectiveness and adverse effects) were extracted. When articles did not provide sufficient information, we contacted corresponding authors to request data.

All articles meeting the eligibility criteria were assessed for their quality by two authors (A.T. and D.Z.-W.). Risk of bias was assessed by using the Newcastle-Ottawa Scale [13], and scores were determined by consensus between the two authors.

We divided all relevant articles into two groups: a) studies including a control group to compare the clinical effectiveness of ECT between groups (i.e., patients with/without DMC-T), and b) studies including only patients lacking DMC-T without any comparison groups. We conducted a quantitative meta-analysis for the former studies, and we summarized the results from the latter studies qualitatively and/or quantitatively.

The primary outcome in our meta-analysis was clinical effectiveness of ECT defined by response rate or change in scores on a standardized clinical rating scale. When specific symptom rating scales, such as Hamilton Depression Rating Scale (HAM-D), Montgomery Asberg Depression Rating Scale (MADRS), the Positive and Negative Syndrome Scale (PANSS), Brief Psychiatric Rating Scale (BPRS), were not reported, assessments for global symptoms, namely Clinical Global Impression (CGI) were used. Secondary outcomes included tolerability (e.g., incidence of adverse effects, such as cognitive impairment), long-term clinical outcome (e.g., readmission rate), and patients’ perspective (e.g., satisfaction).

Meta-analyses were performed using Comprehensive Meta-Analysis version 3.0. The effect size (Hedges’ $g$ for continuous outcomes and odds ratio for dichotomous outcomes) was calculated with 95% confidence intervals, using random effect models. Heterogeneity was calculated using $I^2$, $Q$, and P values. To combine all extracted data as possible, odds ratio was converted into Hedges’ $g$. To investigate the effect of age, diagnosis, ECT parameters, types of clinical assessment (e.g., dichotomous or continuous rating scales), and quality of the studies on results, we conducted a subgroup/meta-regression analysis. Egger’s regression test, followed by Duval & Tweedie’s trim and fill method, were used to assess publication bias.

3. Results

The literature search yielded a total of 3552 articles. After duplicates were removed, 2144 studies were screened. At title and abstract level, 2044 articles were removed, and the remaining 100 full texts were screened. As a result, a total of 41 studies, including seven observational studies [14–20], seven case series [21–27], and 27 case reports [28–54], met the inclusion criteria for our systematic review. These studies include a total of 1299 patients (645 patients without DMC-T and 654 patients with DMC-T). The identified studies were reported from 14 different countries. Full details of the search results, including the reasons for exclusion, are presented in Supplementary Fig. 1.

3.1. Quantitative analysis: a meta-analysis

A total of 1081 participants from the seven independent observational studies, including 427 patients without DMC-T and 654 patients with DMC-T, were selected for the meta-analysis (Table 1). Participants in Tor et al. [16] were divided into two groups (i.e., psychosis and depression groups) and they were considered as two different study cohort because two different assessment scales (i.e., BPRS and MADRS) were used in the two different diagnostic groups (i.e., psychosis and depression). The results of quality assessments using a Newcastle-Ottawa Scale for the included studies are presented in Supplementary Table 1.
| Study Country | Study design | n | Group size (n), Diagnosis (Mean Age (SD)) %Female | ECT parameters | Baseline Severity | Clinical Results | Other Results |
|---------------|--------------|---|-------------------------------------------------|---------------|-----------------|-----------------|--------------|
| Takamiya et al., 2021 Japan | retrospective observational | 168 | DMC (±): n = 34 (27 MDD/7 BP) 69.1 (9.9) years old 64.7% Female DMC (±): n = 134 (115 MDD/19 BP) 59.6 (14.8) years old 54.5% Female | DMC (±): No. ECT = 9.1 (2.8) 3BL = 100% PW = 0.5 DMC (±): No. ECT = 9.2 (2.7) 3BL = 100% PW = 0.5 | DMC (±): CGI-S = 6.0 (QRI: 4–7) DMC (±): CGI-S = 4.0 (QRI: 4–6) | Remission/Response Rate | Postictal delirium (%) |
| Plahouras et al., 2021 Canada | retrospective observational | 238 | DMC (±): n = 159 (104 SZ/55 SA) 46 (15.6) years old 41.5% Female DMC (±): n = 79 (34 SZ/45 SA) 43 (11.2) years old 35.4% Female | DMC (±): No. ECT = 9.5 (5.1) 3BL = 85.5%, SRUL to BL = 9.4% PW = 1.0 (89.3%)/0.3to1 (3.8%)/0.3 to 1 (6.9%) DMC (±): No. ECT = 13.3 (6) 3BL = 69.6%, SRUL to BL = 22.8% PW = 1.0 (74.7%)/0.3 to 1 (20.3%) | DMC (±): CGI-S = 5.7 (0.64) DMC (±): CGI-S = 5.4 (0.74) DMC (±): CGI-S = 5.8 (0.74) | Response rate | Cognitive impairment (%) |
| Tor et al., 2020 Singapore | retrospective observational | 175 | DMC (±): n = 131 (74 SZ/31 Mania/26 D) 42.4 (15.3) years old 51.9% Female DMC (±): n = 44 (14 SZ/7 Mania/23 D) 42.3 (16.7) years old 56.8% Female | DMC (±): No. ECT = 9.6 (2.7) 3BL = 53.4% PW = 0.5 (bitemporal, bitemporal, bitemporal) DMC (±): No. ECT = 9.5 (3.0) 3BL = 27.3% PW = 0.5 (bitemporal, bitemporal, bitemporal) DMC (±): No. ECT = 7.8 (2.6) 3BL = 83% PW = 0.5 (bitemporal, bitemporal, bitemporal) | DMC (±): MADRS = 30.1 (11.6) DMC (±): MADRS = 30.1 (11.3) DMC (±): MADRS = 30.1 (10.5) | Post-treatment Scores | MoCA |
| Finnegan et al., 2018 Ireland | retrospective case-control (age-gender-matched) | 144 | DMC (±): n = 48 (31 MDD/5BP/3 Mania/2Catatonia/7SA) 69.3 (12.8) years old 77.6% Female DMC (±): n = 96 (71 MDD/17 BP/3 Mania/7SA) 64.9 (14.8) years old 74.6% Female | DMC (±): No. ECT = 8.1 (2.9) 3BL = 96% PW–NR (brief pulse) DMC (±): No. ECT = 7.8 (2.6) 3BL = 83% PW–NR (brief pulse) | DMC (±): CGI-S = 6.1 (0.79) DMC (±): CGI-S = 5.3 (0.94) | Response Rate (CGI–I = 1 or 2) | Readmission within 6 months |
| Enriquez et al., 2010 Ireland | retrospective observational | 153 | DMC (±): n = 21 DMC (±): n = 132 NR in each group, but only for total n: 146 depression/1 mania/5 psychosis 50.6 (16.7) years old 66% Female | DMC (±): No. ECT = NR 3BL = 100% PW = 0.5 | DMC (±): MADRS = 40.8 (9.0) DMC (±): MADRS = 34.4 (8.9) | MADRS reduction | Cognitive impairment (%) |
| Wheeldon et al., 1999 the UK | retrospective observational | 150 | DMC (±): n = 11 (11 MDD) 47.8 (22.7) years old 72.7% Female DMC (±): n = 139 (139 MDD) 54.8 (16.5) years old 65.4% Female | NR | DMC (±): HAM-D = 24.4 (6.5) DMC (±): HAM-D = 21.9 (5.6) | Response rate | Cognitive impairment (%)|

Abbreviation: DMC, decision making capacity; SZ, schizophrenia; SA, schizoaffective disorder; MDD, major depressive disorder; BP, bipolar disorder; BL, bilateral; RUL, right unilateral; PW, pulse width; NR, not reported.

*“Cognitive impairment” in these studies was not based on formal psychological assessments, but it was defined by an assessment of treating clinicians.”
3.2. Primary outcomes

Compared to patients with DMC-T, those without DMC-T showed a significant superior clinical improvement (i.e., higher response rate or larger reduction in symptom severity) (8 studies, n = 1081, Hedges’ g = 0.19, 95% CI 0.03 to 0.36, p = 0.02; heterogeneity: $\tau^2 = 0.01, I^2 = 0, Q = 6.8, p = 0.45$), regardless of diagnosis (Fig. 1). After imputing a ‘missing study’ to account for potential publication bias, the point estimate of the effect size increased (Hedges’ g = 0.21, 95% CI 0.05 to 0.37, p = 0.02) (Supplementary Fig. 2).

In the subgroup analysis, patients with depressive disorders who lack DMC-T showed a significant superior clinical improvement compared to patients who have DMC-T (6 studies, n = 697, Hedges’ g = 0.24, 95% CI 0.01 to 0.48, p = 0.04; heterogeneity: $\tau^2 = 0.1, I^2 = 10.5, Q = 5.6, p = 0.35$) (Fig. 2a). For the subgroup of patients with schizophrenia, there was no significant difference in clinical improvement between both groups (3 studies, n = 386, Hedges’ g = 0.08, 95% CI –0.18 to 0.34, p = 0.54; heterogeneity: $\tau^2 = 0, I^2 = 0, Q = 0.8, p = 0.68$) (Fig. 2b).

In another subgroup analysis, studies using continuous rating scales showed a significantly larger reduction in symptom severity in patients without DMC-T as compared to patients with DMC-T (4 studies, n = 381, Hedges’ g = 0.32, 95% CI 0.01 to 0.63, p = 0.04; heterogeneity: $\tau^2 = 0.18, I^2 = 32, Q = 4.4, p = 0.22$) (Supplementary Fig. 3a), whereas studies using a dichotomous outcome did not (4 studies, n = 700, OR = 1.20, 95% CI 1.08 to 1.81, p = 0.37; heterogeneity: $\tau^2 = 0, I^2 = 0, Q = 0.96, p = 0.81$) (Supplementary Fig. 3b).

In the meta-regression analyses, mean age (p = 0.22), age difference between groups (p = 0.63), proportion of participants receiving bilateral ECT between groups (p = 0.15), or total scores of the quality rating scale (p = 0.46) did not show significant correlations with the estimated effect sizes of clinical effect in each study.

When comparing reported clinical characteristics and ECT parameters between the groups, patients without DMC-T had higher baseline severity (7 studies, n = 928, Hedges’ g = 0.58, 95% CI 0.33 to 0.84, p < 0.001; heterogeneity: $\tau^2 = 0.07, I^2 = 61.3, Q = 15.5, p = 0.02$), and they were more likely to receive bilateral ECT (6 studies, n = 778, OR = 2.95, 95% CI 1.82 to 4.79, p < 0.001; heterogeneity: $\tau^2 = 0.1, I^2 = 0, Q = 3.8, p = 0.58$), whereas the number of ECT sessions did not differ between the groups (5 studies, n = 725, Hedges’ g = 0.21, 95% CI -0.11 to 0.52, p = 0.20; heterogeneity: $\tau^2 = 0.09, I^2 = 70.1, Q = 13.4, p = 0.01$). In addition, patients without DMC-T were older than those with DMC-T (7 studies, n = 928, Difference in means = 4.5, 95% CI 2.3 to 6.7, p < 0.001; heterogeneity: $\tau^2 = 0, I^2 = 0, Q = 5.6, p = 0.46$), whereas female proportion did not differ between the groups (7 studies, n = 928, OR = 1.2, 95% CI 0.8 to 1.8, p = 0.29; heterogeneity: $\tau^2 = 0.07, I^2 = 26.1, Q = 8.1, p = 0.23$) (Supplementary Figs. 4–8).

3.3. Secondary outcomes

Regarding adverse effects, only cognitive outcomes were meta-analyzed using data from three studies. As a result, compared to patients with DMC-T, those without DMC-T showed better cognitive outcomes following ECT (4 studies, n = 566, Hedges’ g = 0.52, 95% CI 0.11 to 0.93, p = 0.01; heterogeneity: $\tau^2 = 0.10, I^2 = 59.8, Q = 7.5, p = 0.06$) (Fig. 3). There was no significant difference in a readmission rate within 6 months after the last ECT (3 studies, n = 474, OR = 0.86, 95% CI 0.56 to 1.3, p = 0.49) (Supplementary Fig. 9).

Because patient satisfaction was assessed in one study [17], a meta-analysis for this outcome measure was not possible. The study reported no significant differences in treatment satisfaction between patients with/without DMC-T.

3.4. Qualitative analysis: a systematic review for case series/reports

Characteristics of published case reports, including 218 patients without DMC-T, are presented in Supplementary Tables 2 and 3 of 198 patients without DMC-T for whom response data were reported, 79.8% (158/198) showed response. In addition, 11/15 (73.3%) [21]; 7/8 (87.5%) [22], 4/7 (57.1%) [26], 1/1 (100%) [29], and 1/1 (100%) [33] regained capacity to consent and agreed to further treatment with ECT. Twenty-nine patients showed catatonic symptoms including cases with severe medical comorbidities, including a patient with subdural hematoma, seizure, neuroleptic malignant syndrome, and sepsis [30], a patient with aspiration pneumonia and deep vein thrombosis [32], and a patient with respiratory failure as well as increased intracranial pressure [50]. All 29 cases responded to ECT. One catatonic patient with aortic stenosis, labile hypertension, systemic lupus, and end-stage renal failure which required hemodialysis showed “a dramatic mood improvement” as early as after the second ECT, but ultimately died four days after the fourth treatment, most likely unrelated to ECT [47].

4. Discussion

This is the first systematic review and meta-analysis to thoroughly investigate the effectiveness of ECT in patients lacking DMC-T. Our results show that ECT is equally, if not superiorly, effective in patients without DMC-T when compared to patients with DMC-T,

![Fig. 1. Effectiveness of ECT. Squares are effect sized of single studies, diamonds are pooled results.](1249)
without increased risk of cognitive adverse effects or readmission rate within six months. In the absence of evidence from RCTs, our results represent the best available evidence on the effectiveness of ECT in this important and severely ill patient population.

4.1. Clinical effectiveness of ECT in patients without DMC-T

Our meta-analysis found that ECT was more effective in patients lacking DMC-T, especially in the subgroup of patients with depressive disorders (Fig. 2a). One possible explanation for this finding is that patients lacking DMC-T were older and showed higher baseline severity, both of which were associated with superior ECT outcomes [55]. Since all studies included in our meta-analysis were observational studies, these clinical variables were not adjusted between groups. Other explanations may include differences in indication for ECT and selection of ECT techniques. Many patients lacking DMC-T receive ECT for rapid symptom reduction [14–16,18], e.g., due to an inadequate fluid and food intake, suicidality, or physical deterioration, all of which might lead to shorter duration between onset of depressive symptom and introduction of ECT, which is associated with higher ECT response [56]. In addition, patients without DMC-T were more likely to receive bilateral ECT compared with those with DMC-T. Our results thus clearly support the effectiveness of ECT in patients lacking DMC-T who, by the very nature of their disorders, may show an accumulation of positive predictors of ECT response.

Although we found a statistically significant difference in the clinical effectiveness between the groups, the effect sizes were small. Therefore, the group differences may not be clinically relevant. However, it is important to note that both groups showed particularly high response rates (i.e., approximately 80%), which may have caused ceiling effects in the group comparisons limiting the detection of even more pronounced advantages of ECT in the group without DMC-T. From a clinical point of view, even a non-inferiority of ECT in patients lacking DMC-T would be sufficient to draw the main conclusion from our study, i.e., that lack of DMC-T should definitely be no reason to refrain from ECT.

4.2. Cognitive effects of ECT in patients without DMC-T

Previous studies have revealed that cognitive effects of ECT are mild and transient regardless of consent status [57]. Even in older

[Fig. 2. Results from subgroups of (a) patients with depressive disorders, and (b) patients with schizophrenia. Squares are effect sized of single studies, diamonds are pooled results.]

[Fig. 3. Cognitive outcomes of ECT. Squares are effect sized of single studies, diamonds are pooled results.]
patients, long-term follow-up does not reveal significant cognitive decline [58,59]. Additionally, ECT was well tolerated even in older patients with pre-existing cognitive impairment [60].

Although our study found less cognitive side-effects in patients without DMC-T compared to patients with DMC-T, this result is limited by missing thorough neuropsychological assessments. For instance, the included studies did not assess long-term autobiographical memory [61,62], which is associated with ECT technique, such as electrode placement [63] and pulse width [64]. However, it may be difficult to differentiate residual cognitive impairment from depression itself from the effects of ECT [65–67]. According to our clinical experience, many patients, especially those without DMC-T, are not able to perform formal cognitive testing prior to ECT. Thus, previous studies mostly used surrogate data like global cognitive measures or global ratings by treating physicians. Against the background of these limitations, no firm conclusions can be drawn from our meta-analysis regarding possibly differential cognitive side effects between the groups. However, the available data suggest an at least equal cognitive tolerability in patients without DMC-T. An assessment of patients’ perspectives post ECT [17], subjective measures of cognition [68], or level of functioning as a surrogate marker for cognitive function in daily life may yield additional evidence on the effect of ECT on cognition in patients lacking DMC-T.

4.3. Safety of ECT in patients without DMC-T

To weigh up the benefits and risks of a treatment, safety issues have to be considered. The mortality rate associated with ECT is 2.1 per 100,000 treatments [69], and all-cause mortality is approximately three per 10,000 ECT [70,71]. Additionally, ECT is associated with a lower one-year all-cause mortality compared with matched control subjects [72].

Our literature search revealed only one study that reported a sudden death four days after the fourth ECT in an patient who lacked DMC-T [47], most likely unrelated to ECT. It is important to note that patients without DMC-T who need ECT constitute a high-risk population, which is reflected by a three times higher mortality rate in comparison to age-and sex-matched patients with DMC-T [73]. For instance, mortality rate from acute malignant catatonia as an example of patients without DMC-T is reported up to 20% if an adequate treatment were not provided [74,75]. ECT can be a lifesaving treatment for certain populations, and in such cases it is essential to provide ECT without any delay.

4.4. Ethical considerations for ECT in patients lacking DMC-T

Our results may reassure clinicians, substitute decision makers and courts that the established clinical efficacy/effectiveness of ECT in general psychiatric populations are generalizable to patients who lack capacity to consent and are often among the most severely ill. This is an important and ethically relevant empirical finding for all those involved in decision-making processes about ECT in patients lacking DMC-T. Although the legal regulations of who the surrogate decision-maker is (e.g., a patient’s relative, a legal guardian), according to which normative standard he or she decides (e.g., the substituted judgment standard or the best interests standard), and which procedural safeguards are followed in this process (e.g., involvement of an external reviewer or a court), may vary greatly between different jurisdictions, decisions about ECT for patients lacking DMC-T should consider the broadly shared ethical principles of respect for patients’ autonomy, beneficence (doing good), nonmaleficence (inflicting not harm), and justice [11,12,14,76].

Regarding the principle of autonomy, clinicians should first check whether an advance directive exists. In clinical practice, patients already use psychiatric advance directives to specify their preferences - be it consent or refusal - regarding future ECT [77]. If a patient has not made an advance directive, clinicians should ask substitute decision-makers, i.e. the patient’s legal representative, about the patient’s presumed will. In such cases, nonvoluntary treatment implies treating a person who temporarily lacks DMC-T in the way how he or she would have most likely decided if he or she were currently capable of giving consent. ECT treats the illness which has compromised DMC-T, and can, therefore, be seen as an intervention that can promote the patient’s autonomy. In fact, as documented in several case reports, patients can regain their DMC-T, as their condition improves, and can decide whether or not to continue treatment [21,22,26,29,33,78].

Regarding the principle of beneficence, our meta-analysis indicates that ECT in patients lacking DMC-T has positive effects on their severe mental illness and successfully avert life-threatening conditions with at least equal effectiveness compared to patients with preserved DMC-T. Additionally, most involuntary patients retrospectively assess the treatment as helpful [17]. All these aspects support the view of ECT as a beneficial and potentially autonomy-enhancing treatment in patients lacking DMC-T.

Regarding nonmaleficence, our study revealed no increased risk of adverse cognitive effects in patients lacking DMC-T compared to patients with DMC-T. However, like any other medical treatments, ECT also has side effects. Additionally, no studies included in our meta-analysis investigated long-term autobiographical memory, which should be assessed in future studies.

Finally, patients lacking DMC-T have the right to receive the most effective and a lifesaving treatment in accordance with the principle of justice, just like patients with preserved DMC-T. In the name of ethical concerns, some countries or states have regulations which make ECT inaccessible for patients lacking DMC-T or which result in delayed administration of ECT to patients with life-threatening conditions [12]. However, denying or hampering patients who lack DMC-T access to a safe and effective treatment can be unethical [12,76].

4.5. Limitations and future perspectives

Some limitations should be acknowledged. First, this meta-analysis included only observational studies, and therefore, several confounding factors (e.g., baseline symptom and cognitive scores) were not adjusted between the groups as mentioned in the discussion. Additionally, information on how exactly DMC-T was assessed is widely missing in the original studies. Thus, the distinction between groups in this meta-analysis is subject to good clinical practice in real world settings and may not be perfectly accurate.

Nevertheless, our findings distinctly corroborate the clinical effectiveness of ECT in patients lacking DMC-T in real-world clinical settings. Second, systematic data regarding cognitive effects are very scarce in the included studies, most likely because formal neuropsychological testing before ECT was not feasible in the study populations. Furthermore, we found only one study reporting patients’ perspectives [17]. From both a medical and ethical viewpoint, future studies should include the first person’s perspective in terms of patient reported outcome measures as well as objective assessment scales. There is an urgent need to gain insight into this perspective as it may be particularly helpful when discussing the practice of ECT in patients lacking DMC-T with patients’ relatives and courts, and counter widespread skepticism against ECT in patients without DMC-T. Ultimately, many patients with severe psychiatric disorders may experience further episodes in the future in
which they lack DMC-T. At least for those patients who regain DMC-T after ECT, advance directives may be an instrument to determine their wishes and facilitate adequate treatment in the future. There is increasing evidence to show patient and broader support for such directives, including “self-binding directives” which allow patients to “bind” themselves to treatment during future episodes where they lack DMC-T and are unable or unwilling to give consent to treatment [79].

5. Conclusions
ECT is equally, if not superiorly, effective in patients lacking DMC-T compared to patients with DMC-T. Our results support the clinical and ethical legitimacy of ECT provision for patients with the most severe illness who lack DMC-T.

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Akihiro Takamiya: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Visualization. Pascal Sienaert: Writing – review & editing. Tania Gerigel: Writing – review & editing. Jakov Gather: Writing – review & editing. Taishiro Kishimoto: Writing – review & editing, Supervision. David Zilles-Wegner: Conceptualization, Methodology, Investigation, Supervision, Project administration.

Declaration of competing interest
None.

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Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.brain.2022.09.001.

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