Current Behavioral Neuroscience Reports
https://doi.org/10.1007/s40473-024-00286-7

Predictors of Response to Electroconvulsive Therapy in Major Depressive Disorder: A Review of Recent Research Findings

Anuradha Baminiwatta[1] · **Vikas Menon**[2]

Accepted: 15 July 2024

Abstract

Purpose of Review In the context of the current global move towards precision medicine, considering the adverse effects, costs and efficacy limitations of electroconvulsive therapy (ECT) in major depression, this review aimed to identify predictors of ECT response based on recent research.

Recent Findings Established predictors such as older age, psychotic symptoms, melancholic features, shorter episode duration, higher baseline severity, medication failure, and comorbid personality disorder were replicated in recent studies. Genetic polymorphisms showed little utility, whereas potentially useful epigenetic predictors were identified. Neurotrophic factors offer some predictive value. Some evidence for inflammatory markers emerged. Structural neuroimaging mainly implicates the hippocampal structures, amygdala, cingulate cortex, and other frontal lobe regions. Functional neuroimaging suggests an important role of brain functional connectivity, especially involving the default mode network.

Summary Many previously recognized demographic and clinical predictors of ECT response were supported, but evidence for biological predictors remains largely inconclusive, and requires further exploration and replication in future research.

Keywords Electroconvulsive therapy · Precision medicine · Precision psychiatry · Prediction · Depression

Introduction

Electroconvulsive therapy (ECT) has been used in the treatment of major depressive disorder (MDD) for more than eight decades, and is considered one of the most effective treatments available for MDD [1, 2]. A meta-analysis of six randomized controlled trials (RCTs) showed a response rate of 70% for ECT and 40% for simulated treatment, with a number-needed-to-treat (NNT) of 3–4 [3]. Based on such evidence, most national and international professional bodies have approved ECT for a range of indications in MDD [4–6]. ECT is currently recommended for patients with MDD when there is high suicide risk, life-threatening illness due to refusal of foods and liquids, marked psychomotor retardation or stupor, psychotic depression, or treatment-refractory illness [7]. Since not all patients with MDD who undergo ECT for the above indications will respond well to ECT, and because of the potential adverse effects and costs associated with ECT, predicting which patients will respond to ECT is important in psychiatric practice.

Earlier narrative reviews have attempted to synthesize the evidence on predictors of response to ECT. Pinna et al. reviewed the literature on clinical and biological predictors of ECT response using studies published up to 2015 [8]. Yao et al. reviewed clinical, laboratory and physiological markers of ECT response or remission using studies published up to 2018 [9]. From the time these reviews were published, many more studies investigating various predictors of ECT response have been published. Considering the current global trend towards precision psychiatry, it is important to be updated with the recent findings on ECT response prediction [10]. The current review thus aims to synthesize the recent literature on pre-treatment and procedural factors predicting response or remission following ECT, including demographic, clinical, genetic, laboratory, neuroimaging, and neurophysiological predictors, based primarily on studies published between 2018 and 2024.

✉ Anuradha Baminiwatta
baminiwatta@kln.ac.lk

[1] Department of Psychiatry, Faculty of Medicine, University of Kelaniya, Kelaniya 11600, Sri Lanka

[2] Department of Psychiatry, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry 605006, India

Published online: 25 July 2024

Demographic Predictors

Age

Recent studies [11–14] confirmed the previous observation [15, 16] that older age predicts better response to ECT. A study that attempted to explain why older patients respond better to ECT by exploring the mediating effects of psychomotor retardation and psychotic features suggested that older patients respond better because they show a greater degree of psychomotor retardation and psychotic features, both of which, by themselves, are strong predictors of ECT response [11]. However, Su et al. reported that older patients with more severe depressive symptoms responded less well to ECT [17]. Real-world evidence of preserved efficacy of ECT across age groups in treating MDD has been demonstrated in a large cohort of adult patients, and among age subgroups within the 16–30-years range [18, 19].

Gender

Consistent with previous literature [15, 16], a study based on the Global ECT-MRI Research Collaboration (GEMRIC) showed that ECT was equally effective in males and females [20]. However, one recent study reported that females responded better [21].

Sexual Orientation

Oka et al. found that LGBTQ and non-LGBTQ patients with depression experienced similar clinical response to ECT [22].

Education

Su et al. identified three response trajectories following ECT (non-remit, rapid response and slow response) and found that the non-remit and rapid-response groups had fewer education years than the slow-response group [17]. However, the significance of this association was not retained on multivariate analysis. Previous literature on the effect of education on ECT response is scarce but suggests no significant effect [9].

Clinical Predictors

Psychotic Depression

In line with prior literature, recent studies showed that the presence of psychotic symptoms was a predictor of better response to ECT [13, 23–25]. A continuous severity measure known as the Psychotic Depression Assessment Scale did not confer any advantage over the dichotomous variable of absence/presence of psychotic symptoms in predicting ECT response [24].

Melancholic Features

A recent study confirmed the previous observation that melancholic features, specifically indicated by psychomotor disturbances, predicted better response to ECT [26]. They utilized objective measures such as accelerometry and a drawing task in addition to the observer-rated CORE measure to assess psychomotor disturbance, and showed that both higher CORE scores and longer cognitive and motor time on the drawing task predicted better ECT response. Patients with melancholic depression had about five times greater chance of response than those with non-melancholic depression. On the contrary, a study among depressed older inpatients treated with ECT did not reveal a significant association between CORE scores and response [27].

Duration of Episode

Recent evidence [12, 25, 28] confirms the earlier notion that shorter episodes of depression respond better to ECT.

Baseline Severity

Prior literature suggests that higher baseline severity predicts better response to ECT. However, both higher [12, 14, 29] and lower baseline severity [28] have been associated with ECT response in recent studies.

Medication Failure

Consistent with older studies, recent studies suggest that medication failure predicts lower response to ECT [13, 14, 25, 30], but in some studies, no such association was observed [29].

Comorbid Personality Disorder

Absence of personality disorder has been associated with better response to ECT [13, 31]. In a systematic review on borderline personality disorder (BPD) and outcome of ECT in patients with depression, five of the six included studies showed a less robust response to ECT in patients with BPD [32].

Family History

Family history of mood disorder has been shown to predict ECT response [23].

Body Mass Index (BMI)

Lower BMI has also been suggested as a predictor of ECT response in depression [28]. Opel et al. did not find a significant direct association between BMI and clinical response to ECT but found that higher BMI was associated with a lower increase in subcortical grey matter volume (GMV) following ECT, and that BMI moderated the association between subcortical GMV change and the clinical response to ECT [33]. In a separate analysis, where symptom dimensions were considered, higher BMI predicted better treatment response for the somatic disturbances and insomnia symptom dimensions and worse outcomes for the core mood and anhedonia symptom dimension [34].

Comorbid Alcohol Use Disorder

In a retrospective study in Germany, a history of alcohol use disorder (AUD) predicted a better response to ECT [35]. They hypothesized that excitatory/inhibitory neurotransmitter changes in AUD could possibly explain this phenomenon. Another study found that the ECT response rate among patients with comorbid AUD was not significantly different from those without the comorbidity [31].

Cognitive Impairment

Copersino et al. found that baseline cognitive impairment did not predict ECT response in depressed patients [36].

Individual MADRS Items

Carstens et al. showed that MADRS single items were good predictors of ECT response [21]. Specifically, baseline scores of items assessing affective symptoms (sadness and inability to feel) predicted ECT response.

Demographic and clinical predictors of response to ECT described above are summarized in Table 1.

Genetic and Epigenetic Predictors

Recent research on the genetic predictors of ECT response has delved mainly into the role of genes related to neurotrophins such as brain-derived growth factor (BDNF) and vascular endothelial growth factor (VEGF), telomere length, and the role of epigenetic processes such as DNA methylation and micro-RNAs.

Table 1 Demographic and clinical predictors of response to ECT

Predictor	Nature of association	Contrasting evidence
Age	Older age predicted a better response [11–14].	One study found that older patients with severe symptoms responded less well [17].
Gender	Gender was not associated with the response [20].	Females responded better in one study [21].
Education	No significant effect of education overall [17].	
Sexual orientation	No difference in response between LGBTQ and non-LGBTQ groups [22].	
Psychotic symptoms	Presence of psychotic symptoms predicted a better response [13, 23–25].	
Melancholic features	Presence of melancholic features (esp. psychomotor disturbance) predicted a better response [26].	No association with melancholic features found in one study [27].
Duration of episode	Shorter episodes responded better [25,28.29].	
Baseline severity of depressive symptoms	Higher baseline severity predicted a better response [12, 14, 29].	Lower baseline severity predicted a better response in one study [28].
Medication failure	Absence of medication failure predicted a better response [13, 14, 25, 30].	No association with medication failure found in one study [29].
Comorbid personality disorder	Absence of personality disorder predicted a better response [13, 31].	
Family history	Family history of mood disorder predicted better response [23].	
Body mass index (BMI)	Lower BMI predicted a better response [28].	Higher BMI predicted better response for biological symptoms but worse response for mood and anhedonia symptoms in one study [34].
Comorbid alcohol use disorder (AUD)	Patients with a history of AUD respond better [35] or equally well [31] compared to those without AUD.	
Baseline cognitive impairment	No significant association with response observed [36].	

Note LGBTQ = lesbian, gay, bisexual, transgender and queer

BDNF Gene

The Val66Met polymorphism in the BDNF gene (rs6265) has been investigated as a predictor of ECT response among patients with MDD but no significant effects were found [37, 38]. Maffioletti et al. studied the potential of the same polymorphism in predicting ECT outcome specifically in TRD patients, and again found no association [39]. These findings indicated that the BDNF genotype has poor predictive value for ECT response.

VEGF Gene

The role of genes regulating VEGF on predicting ECT response were explored by Maffioletti et al. using a genome-wide association study (GWAS) [40]. Alleles on a single nucleotide polymorphism (SNP) associated with lower VEGF levels in MDD patients (rs78355601) in the 6p21.1 locus predicted non-response to ECT.

Telomere Length

Telomere length has been studied as a potential predictor of ECT response in two recent studies. Neither of the studies found a significant predictive potential of telomere length for ECT responsiveness [41, 42].

Polygenic Risk Scores (PRS)

Several recent studies have explored the utility of PRS in predicting response to ECT. Based on the Swedish National Quality Register for ECT, which included 2320 participants who underwent ECT for MDD, Sigstrom et al. found that greater PRS for MDD was associated with less clinical improvement, and greater PRS for bipolar disorder was associated with greater improvement [43]. To explain this, they theorized that higher polygenic liability for bipolar disorder may reflect a propensity to develop more severe depression, thereby increasing ECT responsiveness. In this study, PRS for schizophrenia (PRS-SCZ) was not associated with improvement. Conversely, Luykx et al. studied 288 patients with depressive episodes from three countries and observed that PRS-SCZ was associated with ECT response and remission, whereas PRS for MDD was not [44]. Luykx et al. postulated that high PRS-SCZ in MDD patients may reflect a vulnerability for psychotic depression, which increases the likelihood of ECT-related response. However, this association between PRS-SCZ and ECT response was also observed in the subset of patients without psychotic features, suggesting that the psychosis trait severity may lie on a continuum in major depression [44].

DNA Methylation

Several studies have explored the predictive role of epigenetic factors in ECT response. Neyazi et al. have shown that higher promoter methylation of p11, a multifunctional protein involved in serotonin- and BDNF-mediated signaling, predicted response to ECT in patients with resistant MDD [45]. Another study investigated whether DNA methylation of genes encoding tissue-type plasminogen activator (t-PA) and plasminogen activator inhibitor-1 (PAI-1) could predict ECT response, considering the role of these genes in BDNF production [46]. Although no baseline blood DNA methylation differences were observed between ECT remitters and non-remitters, a significant difference in methylation of t-PA between the immune cell subtypes was found.

Epigenetics of the stress response system has also been implicated in predicting ECT response in a study by Maier et al., who analyzed the DNA methylation of genes encoding the glucocorticoid receptor (*NR3C1*) and proopiomelanocortin (*POMC*) among MDD patients undergoing ECT [47]. They found lower methylation rates in *NR3C1* among ECT responders.

A DNA methylome analysis in TRD patients undergoing ECT discovered five protein-coding candidate genes associated with ECT response (*RNF175*, *RNF213*, *TBC1D14*, *TMC5*, and *WSCD1*) [48]. Several gene regions encoding long non-coding RNA transcripts were also associated with ECT responder status (*AC018685.2* and *CLCN3P1*). The strongest association was observed for the *RNF213* gene, suggesting a potential role of angiogenesis and immune system functioning, and the *TBC1D14* gene suggested a possible role of autophagic mechanisms. On the contrary, another methylome-wide analysis found that baseline methylation was not associated with ECT response [49].

Micro-RNA

Micro-RNAs are short, non-coding RNA molecules regulating gene expression. In a study that compared the microRNAome between ECT responders and non-responders, miR-223-3p was down-regulated in responders at baseline, suggesting a role of inflammatory processes [50]. McGrory et al. analysed E2F1 micro-RNA (miR-126-3p and miR-106a-5p) levels from peripheral blood during a course of ECT [51] as a previous study by the same group identified E2F1 as a potential genetic target of micro-RNAs involved in ECT response [52]. However, no relationship was found between baseline E2F1 levels and treatment response.

Neurotrophic Factors

Lower serum BDNF levels have been shown to predict better response to ECT in MDD patients in some studies [37, 53] whereas no association has been observed in others [39, 54]. Conversely, Psomiades et al. distinguished between total BDNF and mature BDNF levels in serum in patients undergoing ECT and reported that higher baseline ature BDNF but not total BDNF levels significantly predicted remission [55]. Mindt et al. found that baseline levels of BDNF in cerebrospinal fluid (CSF) and serum were not associated response following ECT [56]. Lower baseline serum VEGF levels have also been shown to predict response [40].

Inflammatory and Immune Markers

With reference to the inflammatory hypothesis of depression and the effects of ECT on inflammatory and immune processes observed in previous literature [57], several studies have studied peripheral and central markers of inflammation as predictors of ECT response. Elevated baseline serum C-reactive protein (CRP) has been associated with better response to ECT in some studies [58–60] whereas no such association was found in others [61]. Kruse et al. found that CRP predicted response only among women [58]. In contrast, Yilmaz reported that higher CRP levels were associated with poor response to ECT [62]. Evidence for interleukin-6 (IL-6) was also conflicting, with elevated IL-6 levels being associated with better response to ECT in one study [58], and non-response in one study [62], with no association observed in others [60, 61]. Lower levels of IL-8 have been found to predict better response to ECT among women [61]. Lower TNFα levels have also been shown to predict ECT response [63]. These findings suggest that inflammatory processes in MDD play a complex role in determining ECT response.

CSF studies have explored possible inflammatory and immune markers in CSF that could predict ECT response. Mindt et al. studied 25 different cytokines in both CSF and blood as markers of ECT response, and found some evidence for CSF IP-10 levels in predicting remission, and serum levels of IP-10, MIP-1b, and IL-2R in predicting improvement in depressive symptoms [56]. Kranaster et al. studied CSF markers of neurodegeneration (e.g. tau proteins, β-amyloids and neurogranin), immune system (e.g. IL-6, neopterin, soluble CD14,), endocannabinoids, sphingolipids, and Klotho, and reported that higher baseline CSF levels of AEA, Aβ1–40, T-tau protein and P-tau, Ng, and sCD14 predicted the reduction of depressive symptoms during ECT [64].

Hypothalamo-Pituitary-Adrenal (HPA) axis Markers

Considering the involvement of the HPA axis in depression [65], a few studies have explored whether peripheral markers of the HPA axis can predict ECT response. Neither hair cortisol concentration nor salivary cortisol concentration has been shown to predict response to ECT in MDD patients [66, 67].

Structural Neuroimaging

Several recent studies have explored structural MRI (sMRI) findings of the brain which can predict response to ECT using both volumetric and morphometric approaches. Both whole brain and region of interest (ROI) analyses have been adopted. Machine learning models have been increasingly used for prediction.

Jiang et al. identified six gray matter regions as predictors of ECT response [68]. These included the right hippocampus/parahippocampus, right orbitofrontal gyrus, right inferior temporal gyrus, left postcentral gyrus/precuneus, left supplementary motor area, and left lingual gyrus. Their models achieved an accuracy of 86–90% for prediction of remission. Gartner et al. also identified gray matter volume (GMV) in the right anterior parahippocampal gyrus as predictive of ECT response, and reported an overall accuracy of 69% for the sMRI-based classification of ECT response [69]. Xu et al. studied the role of amygdala segments and hippocampal sub-regions in predicting ECT response and found that the hippocampus-amygdala transition area predicted ECT remission with the highest accuracy (83–87%) [70]. Cao et al. used volumetric information of hippocampal subfields in patients with severe MDD, and showed that hippocampal subfield volumes at baseline could predict response using machine learning algorithms [71]. Specifically, lower volumes of cornu ammonis subfields CA3 and CA4, granule cell layer, molecular layer, and subiculum were associated with better response. Accuracy for predicting remission reached 90%. The volume of the dentate gyrus has also been shown to predict ECT response [72].

A study that used surface-based morphometry from sMRI to identify cortical predictors of ECT response along with demographic and clinical predictors found that the rostral anterior cingulate thickness and depression score at baseline showed the greatest predictive power [73]. Redlich et al. had earlier found a positive association between pretreatment subgenual cingulate volume and ECT response, and reported an overall accuracy rate of 78.3% and sensitivity of 100% [74].

Various other brain regions have also been implicated in ECT response in recent studies. Takamiya et al. used both clinical and sMRI variables to predict ECT response, and

observed that volumes in the gyrus rectus, right anterior lateral temporal lobe, cuneus, and third ventricle were associated with response [23]. The prediction accuracy improved from 70 to 93% when sMRI data were added to clinical variables. Bruin et al. developed predictive models using multimodal data from both sMRI and fMRI from the GEMRIC study, and found that regions located in dorsomedial prefrontal cortex (DMPFC), precuneus and thalamus contributed the most to the predictive classification of remission [75]. Takamiya et al. also reported a potential predictive role of the thalamus, with pretreatment smaller GMV in the left thalamus predicting worse response to ECT [76].

A few studies have explored the role of structural connectivity of white matter tracts for ECT response prediction. A diffusion tensor imaging study reported that, among those who underwent ECT, baseline functional anisotropy was positively and mean diffusivity was negatively associated with depressive symptoms after ECT [77]. A study investigating whether baseline hippocampal structural connectivity relates to the clinical response to ECT found no association [78]. Tsolaki et al. reported that the structural connectivity between the subcallosal cingulate and medial prefrontal cortex was lower in ECT responders [79].

Functional Neuroimaging

Recent studies using functional MRI (fMRI) have explored the potential of various regional brain activity indicators and functional connectivity (FC) markers between different brain networks at baseline in predicting response to ECT. Most studies have used resting-state functional connectivity based on fMRI.

The role of global and regional cerebral blood flow (CBF) in predicting ECT response was studied by Leaver at al. using arterial spin-labelled fMRI in patients undergoing ECT for depression, who found that those who had lower baseline global CBF were more likely to respond to ECT [80]. They also observed that pre-treatment CBF in bilateral thalami was lower in ECT-responders.

Several recent studies suggested the significance of the pre-treatment default mode network (DMN) and its connectivity with other networks in predicting ECT response. Pang et al. used both whole-brain multi-voxel pattern analysis and ROI FC analysis among MDD patients undergoing ECT and showed that the baseline FC within the DMN and between the DMN and central executive network (CEN; also known as the frontoparietal network) predicted the improvement in depression scores [81]. Dini et al. observed that more negative connectivity between the cognitive control network (CCN) and DMN components before ECT could predict depression score reduction [82]. Li et al. demonstrated that static and dynamic FC features of the DMN before treatment could predict clinical improvement following ECT [83]. Moreover, Moreno-Ortega et al. have reported a potential role of the connectivity between the dorsolateral prefrontal cortex (DLPFC) and DMN in predicting ECT response [84].

An influence of connectivity involving the frontoparietal network (i.e. CEN), temporal networks, and subgenual ACC on ECT response was suggested by Leaver et al. [85]. A role of the connectivity between the CEN and the salience network in predicting ECT response has also been reported [86]. Moreover, important contributions from the fronto-limbic network connectivity in ECT response prediction have been demonstrated by two studies [84, 87]. One study reported a high baseline connectivity between the left amygdala and the right frontal pole among ECT responders, whereas the other reported a predictive role of reduced connectivity between the DLPFC and the subgenual ACC.

Sun et al. explored whether pre-ECT whole-brain FC predicted depressive score changes and remission after ECT among 122 patients, and showed that FC networks with the greatest predictive value were found in the prefrontal and temporal cortices and subcortical nuclei [88]. These included the inferior frontal, superior frontal, superior temporal, and inferior temporal gyri, as well as basal ganglia, and thalamus. Takamiya et al. investigated pre-treatment whole-brain fractional amplitude of low frequency fluctuations (fALFFs) to identify brain regions associated with post-ECT depression scores, and found that higher fALFFs in the right anterior insula, and lower fALFFs in the left thalamus and cerebellum predicted worse outcomes [76]. Li et al. reported that local brain activity in the insula, superior parietal gyrus, and angular gyrus as indicated by fALFFs, and FC in cortical-limbic circuits were predictive of ECT response in adolescents [89]. In a study of adolescents with MDD and suicidal ideation, amplitude of low frequency fluctuations in the right precentral gyrus and centrality of the left hippocampus were predictive of depressive score change after ECT [90].

A few studies have employed task-based fMRI to study the effects of ECT. Enneking et al. investigated the effects of ECT on the activity of the anterior cingulate cortex (ACC) and amygdala during a negative emotional stimuli processing paradigm, and showed that pre-treatment ACC activity was lower among ECT responders [91]. Another fMRI study that assessed neural activity in five key regions associated depression pathophysiology using an emotional working memory task did not identify any prognostic markers [92].

Magnetic resonance spectroscopy (MRS) is useful in identifying regional metabolism in the brain by measuring changes in tissue concentrations of various neurochemicals. A few recent studies have utilized 1 H-MRS to identify neurochemical predictors of ECT response, specifically based on metabolite levels in the ACC. Ermis et al., who

Table 2 Summary of biological predictors of response to ECT

Predictor	Nature of association	Contrasting evidence
Genetic polymorphisms		
rs6265 (Val66Met in BDNF gene)	No significant association observed [37–39].	
rs78355601 (SNP in VEGF gene)	Alleles associated with lower VEGF levels predicted non-response [40].	
Telomere length	No significant association observed [41, 42].	
Polygenic risk scores (PRS)		
PRS for MDD	Greater PRS for MDD predicts poor response [43].	No association with PRS for MDD found by Luykx et al. [44]
PRS for schizophrenia	Greater PRS for schizophrenia predicts better response [44].	No association with PRS for schizophrenia found by Sigström et al. [43]
PRS for bipolar disorder	Greater PRS for bipolar disorder predicts better response [43].	
Epigenetic factors		
DNA methylation of promoter region of p11	Higher methylation predicts better response [45].	
DNA methylation of *NR3C1* gene (glucocorticoid receptor gene)	Lower methylation predicts response [47].	
DNA methylation of proopiomelanocortin (*POMC*) gene	No significant association [47].	
DNA methylation of *RNF175*, *RNF213*, *TBC1D14*, *TMC5*, and *WSCD1*	Methylation of CpG sites in these regions predicted ECT response [48].	
miR-223-3p	miR-223-3p is down-regulated in ECT responders [50].	
miR-126-3p and miR-106a-5p	No significant association with response observed [51].	
Peripheral biomarkers		
Serum BDNF levels	Lower BDNF predicted a better response [37, 53].	No association with BDNF levels found in two studies [39, 54]. Higher mature BDNF predicted response [55].
Serum VEGF levels	Lower baseline VEGF predicted better response [40].	
Serum C-reactive protein (CRP)	Higher baseline CRP predicted a better response [58, 59].	No association found in one study [61]. Higher CRP predicted poor response in another [62].
Interleukin − 6	Higher IL-6 predicted a better response in one study [58].	No association observed in two studies [60, 61]. Lower IL-6 predicted response in one study [62].
Interleukin − 8	Lower IL-8 predicted response in women [61].	
TNFα	Lower TNFα predicted a better response [63].	
Salivary and hair cortisol concentrations	No significant association with salivary [66] or hair [67] cortisol levels.	
Structural MRI features	Right parahippocampal gyrus volume predicted response [68, 69].	
	Hippocampal subfield volumes predicted response [70, 71].	
	ACC volume predicted response [73, 74].	
	Precuneus volume predicted response [68, 75].	
	Thalamic volume predicted response [75, 76].	
	White matter connectivity markers predicted response [77, 79].	No association of hippocampal connectivity with response [78].
Functional MRI features	Lower global and thalamic cerebral blood flow predicted better response [80].	
	Default mode network connectivity predicted response [81, 83].	
	Frontolimbic network connectivity predicted response [84, 87].	
	Frontoparietal network [85, 86].	
Magnetic Resonance Spectroscopy (MRS) features	Higher baseline glutamate/glutamine and total creatine in ACC predicted response [93].	
	Lower baseline *N*-acetylaspartate levels in the dACC predicted response [94].	

Table 2 (continued)

Predictor	Nature of association	Contrasting evidence
Electroencephalographic features	Anterior delta coherence predicted improvement [96].	
	Higher beta-band power in right frontal and central regions predicted poor response [97].	
	Lower connectivity in cortical areas in the alpha 2 band (mainly frontal and left-hemispheric) predicted better response [98].	

Note ACC = anterior cingulate cortex, SNP = single nucleotide polymorphism

studied choline, glutamate/glutamine (Glx), myo-inositol, NAA, and total creatine in the ACC during ECT, found higher baseline levels of Glx and total creatine among ECT responders [93]. Njau et al. measured Glx, creatine, choline, and *N*-acetylaspartate (NAA) in the dorsal (dACC) and subgenual ACC, and bilateral hippocampi following ECT and showed that lower baseline NAA levels in the dACC predicted depressive symptom improvement [94]. In contrast, a MRS study on GABA levels in the ACC did not show significant differences at baseline between remitters and non-remitters [95].

Neurophysiological Predictors

Encephalography

Several recent studies have explored the utility of encephalographic markers in predicting ECT response. Scangos et al. examined the coherence and spectral amplitude in six EEG frequency bands and found that greater pre-ECT anterior delta coherence could predict improvement in MADRS scores [96]. The authors postulated that this could indicate an intact circuitry allowing for better seizure propagation. In a study of frontal theta coherence assessed using magnetoencephalography, there were no baseline differences between early responders and non-responders. In another study, higher beta-band power in right frontal and central regions has been associated with inadequate treatment response for ECT [97]. A study examining linear connectivity measures for the alpha 1 (8–10 Hz) and alpha 2 (10–12 Hz) frequency bands on EEG reported that ECT responders showed lower connectivity in cortical areas in the alpha 2 band mainly within frontal and left-hemispheric networks [98].

Ictal EEG features, which are influenced by ECT techniques, have also been found to predict response. In a systematic review on the relationship between ictal EEG features and clinical outcomes, authors noted modest effects of ictal EEG indices on response outcomes [99]. Similarly, postictal suppression on the EEG has also been associated with ECT response [100].

Findings on the biological predictors of ECT response are summarized in Table 2.

ECT Parameters as Predictors

ECT parameters including stimulus dose, electrode placement, pulse width and pulse amplitude have been implicated in the response to ECT. Recent studies indicate that right unilateral (RUL) ECT at high doses (about 6 times the seizure threshold) is as efficacious as moderate dose bitemporal [101, 102]and bifrontal ECT [103, 104]. It has been suggested that the stimulus dose relative to seizure threshold affect efficacy particularly for RUL ECT, where suprathreshold doses about 5–6 times the seizure threshold were more efficacious than doses closer to threshold; however, for bitemporal ECT, no remarkable increment in efficacy with higher doses has been observed [105]. With regard to the role of pulse width, Tor et al. conducted a systematic review of studies comparing brief pulse versus ultra-brief pulse RUL ECT, and found that the former was significantly more efficacious in depression than the latter, albeit with more cognitive adverse effects [106]. A study on the role of pulse amplitude on ECT efficacy showed that a higher amplitude (700 mA and 800 mA) was associated with better depressive outcomes than lower amplitude (600 mA) [107].

Conclusion

This narrative review explored the recent research findings on pre-treatment and procedural factors predicting response to ECT in MDD. Numerous demographic, clinical and biological predictors were identified. Many of the previously established predictors of ECT response appear to be supported in the recent literature, but some inconsistencies were also noted. In addition, new data on response predictors, particularly from neurobiological studies, have accrued over the last five years.

Older age has been shown to predict better response to ECT is most studies. Other demographic factors such as gender, education and sexual orientation do not seem to be important. In line with previous literature [8, 9, 15, 16], the presence of psychotic symptoms, melancholic features, shorter duration of episode, higher baseline severity, lack of medication failure, and absence of comorbid personality disorder predicted better response in recent studies. Some evidence linking a family history of mood disorder and

baseline BMI to ECT response has emerged. Neither comorbid alcohol use disorder nor baseline cognitive impairment seem to impede the efficacy of ECT.

Genetic and epigenetic studies on predicting ECT response have produced inconsistent results. In view of the role of neurogenesis in mediating therapeutic effects of ECT [108], recent studies have investigated genetic and epigenetic factors related to neurotrophins. Polymorphisms of the BDNF and VEGF genes do not seem to play an important role. DNA methylation studies have implicated epigenetic processes related to serotonin- and BDNF-mediated signalling, stress-response system, and immune/inflammatory processes. Findings regarding the utility of PRS in predicting ECT response were also contradictory, but PRS-SCZ and PRS-bipolar disorder may have some predictive value. Serum BDNF and VEGF may have some utility in predicting response. Attempts to identify other peripheral blood markers for successfully predicting response to ECT have not yielded consistent results.

Structural neuroimaging studies have identified baseline neuroanatomical features related to temporal lobe structures (e.g. hippocampus, amygdala) as important predictors of ECT response. This is in line with the evidence that ECT induces structural changes in these areas [109, 110]. Other regions such as the subgenual cingulate cortex, DMPFC, precuneus, and thalamus have also received support in more than one study. Several fMRI studies have identified connectivity features involving the DMN as predictors. This is consistent with the observation that DMN is altered in MDD and that ECT changes the connectivity of the DMN [111]. Baseline DMN connectivity has been shown to predict response with other treatment modalities for MDD as well [112]. Apart from the DMN, frontoparietal and frontolimbic connectivity have also revealed predictive markers. FC based on EEG has suggested connectivity within the alpha 2 band mainly in frontal and left-hemispheric networks as possible predictors.

A probable reason for the inconsistent results observed within most categories of predictors could be the heterogeneity of study methods including different study designs, ECT techniques, and patient characteristics. Large international studies such as GEMRIC and Gen-ECT-ic utilizing consistent methodologies are needed to better elucidate clinical and biological predictors to guide individualized treatment selection. However, despite these advances in neurobiological studies and identification of biomarkers for ECT response prediction, their clinical utility may be limited, particularly in low-resource settings.

Author Contributions A.B. performed the literature review and drafted the manuscript. V.M. reviewed and edited the manuscript. Both authors approved the final version.

Data Availability No datasets were generated or analysed during the current study.

Declarations

Human and Animal Rights This review is based solely on studies that have already been published. No new human or animal data are used.

Competing Interests The authors declare no competing interests.

References

1. Kirov G, Jauhar S, Sienaert P, Kellner CH, McLoughlin DM. Electroconvulsive therapy for depression: 80 years of progress. Br J Psychiatry. 2021;219(5):594–7.
2. Meechan CF, Laws KR, Young AH, McLoughlin DM, Jauhar S. A critique of narrative reviews of the evidence-base for ECT in depression. Epidemiol Psychiatr Sci. 2022;31:e10.
3. UK ECT Review Group. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. Lancet. 2003;361(9360):799–808.
4. Weiss A, Hussain S, Ng B, Sarma S, Tiller J, Waite S, et al. Royal Australian and New Zealand College of Psychiatrists professional practice guidelines for the administration of electroconvulsive therapy. Australian New Z J Psychiatry. 2019;53(7):609–23.
5. Milev RV, Giacobbe P, Kennedy SH, Blumberger DM, Daskalakis ZJ, Downar J, et al. Canadian Network for Mood and anxiety treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder. Can J Psychiatry. 2016;61(9):561–75.
6. National Institute for Clinical Excellence. Guidance on the use of electroconvulsive therapy. Guidance on the Use of Electroconvulsive Therapy; 2003.
7. Scott AIF. College guidelines on electroconvulsive therapy: an update for prescribers. Adv Psychiatr Treat. 2005;11(2):150–6.
8. Pinna M, Manchia M, Oppo R, Scano F, Pillai G, Loche AP, et al. Clinical and biological predictors of response to electroconvulsive therapy (ECT): a review. Neurosci Lett. 2018;669:32–42.
9. Yao Z, McCall WV, Essali N, Wohl E, Parker C, Rosenquist PB, et al. Precision ECT for major depressive disorder: a review of clinical factors, laboratory, and physiologic biomarkers as predictors of response and remission. Pers Med Psychiatry. 2019;17–18:23–31.
10. Manchia M, Pisanu C, Squassina A, Carpiniello B. Challenges and future prospects of Precision Medicine in Psychiatry. Pharmgenomics Pers Med. 2020;13:127–40.
11. Heijnen WTCJ, Kamperman AM, Tjokrodipo LD, Hoogendijk WJG, van den Broek WW, Birkenhager TK. Influence of age on ECT efficacy in depression and the mediating role of psychomotor retardation and psychotic features. J Psychiatr Res. 2019;109:41–7.
12. van Diermen L, Hebbrecht K, Schrijvers D, Sabbe BCG, Fransen E, Birkenhäger TK. The Maudsley Staging Method as predictor of electroconvulsive therapy effectiveness in depression. Acta Psychiatr Scand. 2018;138(6):605–14.
13. van der Does Y, Turner RJ, Bartels MJH, Hagoort K, Metselaar A, Scheepers F, et al. Outcome prediction of electroconvulsive therapy for depression. Psychiatry Res. 2023;326:115328.
14. Nygren A, Reutfors J, Brandt L, Bodén R, Nordenskjöld A, Tiger M. Response to electroconvulsive therapy in treatment-resistant depression: nationwide observational follow-up study. BJPsych Open. 2023;9(2):e35.

15. van Diermen L, van den Ameele S, Kamperman AM, Sabbe BCG, Vermeulen T, Schrijvers D, et al. Prediction of electroconvulsive therapy response and remission in major depression: meta-analysis. Br J Psychiatry. 2018;212(2):71–80.
16. Haq AU, Sitzmann AF, Goldman ML, Maixner DF, Mickey BJ. Response of Depression to Electroconvulsive Therapy. J Clin Psychiatry. 2015;76(10):1374–84.
17. Su L, Zhang Y, Jia Y, Sun J, Mellor D, Yuan TF, et al. Predictors of Electroconvulsive Therapy Outcome in Major Depressive Disorder. Int J Neuropsychopharmacol. 2023;26(1):53–60.
18. Luccarelli J, McCoy TH, Uchida M, Green A, Seiner SJ, Henry ME. The Efficacy and Cognitive effects of Acute Course Electroconvulsive Therapy are equal in adolescents, transitional Age Youth, and young adults. J Child Adolesc Psychopharmacol. 2021;31(8):538–44.
19. Luccarelli J, McCoy TH, Seiner SJ, Henry ME. Real-world evidence of age-independent electroconvulsive therapy efficacy: a retrospective cohort study. Acta Psychiatr Scand. 2022;145(1):100–8.
20. Blanken MAJT, Oudega ML, Hoogendoorn AW, Sonnenberg CS, Rhebergen D, Klumpers UMH, et al. Sex-specifics of ECT outcome. J Affect Disord. 2023;326:243–8.
21. Carstens L, Hartling C, Stippl A, Domke AK, Herrera-Mendelez AL, Aust S, et al. A symptom-based approach in predicting ECT outcome in depressed patients employing MADRS single items. Eur Arch Psychiatry Clin Neurosci. 2021;271(7):1275–84.
22. Oka F, Weischedel K, Bakian A, Mickey BJ. Treatment-resistant Mood disorders in LGBTQ people. J Clin Psychiatry. 2022;83(4).
23. Takamiya A, Liang K, ching, Nishikata S, Tarumi R, Sawada K, Kurokawa S, et al. Predicting Individual Remission after Electroconvulsive Therapy based on structural magnetic resonance imaging. J ECT. 2020;36(3):205–10.
24. van Diermen L, Versyck P, van den Ameele S, Madani Y, Vermeulen T, Fransen E, et al. Performance of the psychotic Depression Assessment Scale as a predictor of ECT Outcome. J ECT. 2019;35(4):238–44.
25. Mickey BJ, Ginsburg Y, Jensen E, Maixner DF. Distinct predictors of short- versus long-term depression outcomes following electroconvulsive therapy. J Psychiatr Res. 2022;145:159–66.
26. van Diermen L, Vanmarcke S, Walther S, Moens H, Veltman E, Fransen E, et al. Can psychomotor disturbance predict ect outcome in depression? J Psychiatr Res. 2019;117:122–8.
27. Veltman EM, de Boer A, Dols A, van Exel E, Stek ML, Sienaert P, et al. Melancholia as Predictor of Electroconvulsive Therapy Outcome in later life. J ECT. 2019;35(4):231–7.
28. Nakajima K, Takamiya A, Uchida T, Kudo S, Nishida H, Minami F et al. Individual prediction of Remission based on clinical features following electroconvulsive therapy. J Clin Psychiatry. 2022;83(5).
29. Ma Y, Rosenheck R, Ye B, Fan N, He H. Effectiveness of electroconvulsive therapy in patients with less treatment-resistant depression by the Maudsley Staging Model. Brain Behav. 2020;10(7).
30. Rovers JJE, Vissers P, Loef D, van Waarde JA, Verdijk JPAJ, Broekman BFP, et al. The impact of treatment resistance on outcome and course of electroconvulsive therapy in major depressive disorder. Acta Psychiatr Scand. 2023;147(6):570–80.
31. Steinholtz L, Reutfors J, Brandt L, Nordanskog P, Thörnblom E, Persson J, et al. Response rate and subjective memory after electroconvulsive therapy in depressive disorders with psychiatric comorbidity. J Affect Disord. 2021;292:276–83.
32. Nicolini AP, Sienaert P. Borderline Personality Disorder and Outcome of Electroconvulsive Therapy in patients with Depression. J ECT. 2023;39(2):74–80.
33. Opel N, Narr KL, Abbott C, Argyelan M, Espinoza R, Emsell L, et al. Elevated body weight modulates subcortical volume change and associated clinical response following electroconvulsive therapy. J Psychiatry Neurosci. 2021;46(4):E418–26.
34. Wade BSC, Hellemann G, Espinoza RT, Woods RP, Joshi SH, Redlich R, et al. Depressive symptom dimensions in treatment-resistant Major Depression and their modulation with Electroconvulsive Therapy. J ECT. 2020;36(2):123–9.
35. Aksay SS, Hambsch M, Janke C, Bumb JM, Kranaster L, Sartorius A. Alcohol Use Disorder as a possible predictor of Electroconvulsive Therapy Response. J ECT. 2017;33(2):117–21.
36. Copersino ML, Long MP, Bolton P, Ressler KJ, Seiner SJ, Yip AG. First Acute-Course Electroconvulsive Therapy for Moderate-to-severe Depression benefits patients with or without Accompanying Baseline Cognitive Impairment. J ECT. 2022;38(2):74–80.
37. Pathak P, Mehra A, Ram S, Pal A, Grover S. Association of serum BDNF level and Val66Met polymorphism with response to treatment in patients of major depressive disease: a step towards personalized therapy. Behav Brain Res. 2022;430:113931.
38. Ryan KM, Dunne R, McLoughlin DM. BDNF plasma levels and genotype in depression and the response to electroconvulsive therapy. Brain Stimul. 2018;11(5):1123–31.
39. Maffioletti E, Gennarelli M, Gainelli G, Bocchio-Chiavetto L, Bortolomasi M, Minelli A. BDNF genotype and baseline serum levels in relation to Electroconvulsive Therapy effectiveness in treatment-resistant depressed patients. J ECT. 2019;35(3):189–94.
40. Maffioletti E, Gennarelli M, Magri C, Bocchio-Chiavetto L, Bortolomasi M, Bonvicini C, et al. Genetic determinants of circulating VEGF levels in major depressive disorder and electroconvulsive therapy response. Drug Dev Res. 2020;81(5):593–9.
41. Pisanu C, Vitali E, Meloni A, Congiu D, Severino G, Ardau R, et al. Investigating the role of leukocyte telomere length in treatment-resistant depression and in response to Electroconvulsive Therapy. J Pers Med. 2021;11(11):1100.
42. Ryan KM, McLoughlin DM. Telomere length in depression and association with therapeutic response to electroconvulsive therapy and cognitive side-effects. Psychol Med. 2020;50(12):2096–106.
43. Sigström R, Kowalec K, Jonsson L, Clements CC, Karlsson R, Nordenskjöld A, et al. Association between Polygenic Risk scores and Outcome of ECT. Am J Psychiatry. 2022;179(11):844–52.
44. Luykx JJ, Loef D, Lin B, van Diermen L, Nuninga JO, van Exel E, et al. Interrogating associations between Polygenic liabilities and Electroconvulsive Therapy Effectiveness. Biol Psychiatry. 2022;91(6):531–9.
45. Neyazi A, Theilmann W, Brandt C, Rantamäki T, Matsui N, Rhein M, et al. P11 promoter methylation predicts the antidepressant effect of electroconvulsive therapy. Transl Psychiatry. 2018;8(1):25.
46. Moschny N, Jahn K, Bajbouj M, Maier HB, Ballmaier M, Khan AQ et al. DNA methylation of the t-PA gene differs between various Immune Cell subtypes isolated from depressed patients receiving Electroconvulsive Therapy. Front Psychiatry. 2020;11.
47. Maier HB, Moschny N, Eberle F, Jahn K, Folsche T, Schülke R, et al. DNA methylation of POMC and NR3C1-1F and its implication in Major Depressive Disorder and Electroconvulsive Therapy. Pharmacopsychiatry. 2023;56(02):64–72.
48. Moschny N, Zindler T, Jahn K, Dorda M, Davenport CF, Wiehlmann L, et al. Novel candidate genes for ECT response prediction—a pilot study analyzing the DNA methylome of depressed patients receiving electroconvulsive therapy. Clin Epigenetics. 2020;12(1):114.
49. Sirignano L, Frank J, Kranaster L, Witt SH, Streit F, Zillich L, et al. Methylome-wide change associated with response to electroconvulsive therapy in depressed patients. Transl Psychiatry. 2021;11(1):347.
50. Kaurani L, Besse M, Methfessel I, Methi A, Zhou J, Pradhan R, et al. Baseline levels of mir-223-3p correlate with the effectiveness

of electroconvulsive therapy in patients with major depression. Transl Psychiatry. 2023;13(1):294.
51. McGrory CL, Ryan KM, Kolshus E, McLoughlin DM. Peripheral blood E2F1 mRNA in depression and following electroconvulsive therapy. Prog Neuropsychopharmacol Biol Psychiatry. 2019;89:380–5.
52. Kolshus E, Ryan KM, Blackshields G, Smyth P, Sheils O, McLoughlin DM. Peripheral blood microRNA and VEGFA mRNA changes following electroconvulsive therapy: implications for psychotic depression. Acta Psychiatr Scand. 2017;136(6):594–606.
53. van Zutphen EM, Rhebergen D, van Exel E, Oudega ML, Bouckaert F, Sienaert P, et al. Brain-derived neurotrophic factor as a possible predictor of electroconvulsive therapy outcome. Transl Psychiatry. 2019;9(1):155.
54. Loef D, Vansteelandt K, Oudega ML, van Eijndhoven P, Carlier A, van Exel E, et al. The ratio and interaction between neurotrophin and immune signaling during electroconvulsive therapy in late-life depression. Brain Behav Immun Health. 2021;18:100389.
55. Psomiades M, Mondino M, Galvão F, Mandairon N, Nourredine M, Suaud-Chagny MF, et al. Serum mature BDNF level is Associated with Remission following ECT in Treatment-Resistant Depression. Brain Sci. 2022;12(2):126.
56. Mindt S, Neumaier M, Hoyer C, Sartorius A, Kranaster L. Cytokine-mediated cellular immune activation in electroconvulsive therapy: a CSF study in patients with treatment-resistant depression. World J Biol Psychiatry. 2020;21(2):139–47.
57. Yrondi A, Sporer M, Péran P, Schmitt L, Arbus C, Sauvaget A. Electroconvulsive therapy, depression, the immune system and inflammation: a systematic review. Brain Stimul. 2018;11(1):29–51.
58. Kruse JL, Congdon E, Olmstead R, Njau S, Breen EC, Narr KL, et al. Inflammation and improvement of Depression following electroconvulsive therapy in treatment-resistant depression. J Clin Psychiatry. 2018;79(2):17m11597.
59. Carlier A, Rhebergen D, Schilder F, Bouckaert F, Sienaert P, Veerhuis R, et al. The pattern of inflammatory markers during electroconvulsive therapy in older depressed patients. World J Biol Psychiatry. 2021;22(10):770–7.
60. Carlier A, Berkhof JG, Rozing M, Bouckaert F, Sienaert P, Eikelenboom P, et al. Inflammation and remission in older patients with depression treated with electroconvulsive therapy; findings from the MODECT study. J Affect Disord. 2019;256:509–16.
61. Kruse JL, Olmstead R, Hellemann G, Wade B, Jiang J, Vasavada MM, et al. Inflammation and depression treatment response to electroconvulsive therapy: sex-specific role of interleukin-8. Brain Behav Immun. 2020;89:59–66.
62. Yilmaz NS, Sen B, Karadag RF, Aslan S, Ekmekci Ertek I, Bozkurt A, et al. A kynurenine pathway enzyme aminocarboxymuconate-semialdehyde decarboxylase may be involved in treatment-resistant depression, and baseline inflammation status of patients predicts treatment response: a pilot study. J Neural Transm. 2022;129(12):1513–26.
63. Sorri A, Jarventausta K, Kampman O, Lehtimaki K, Bjorkqvist M, Tuohimaa K et al. Low tumor necrosis factor-alpha levels predict symptom reduction during electroconvulsive therapy in major depressive disorder. Brain Behav. 2018;8(4).
64. Kranaster L, Hoyer C, Aksay SS, Bumb JM, Müller N, Zill P, et al. Biomarkers for antidepressant efficacy of Electroconvulsive Therapy: an exploratory Cerebrospinal Fluid Study. Neuropsychobiology. 2019;77(1):13–22.
65. Pariante CM, Lightman SL. The HPA axis in major depression: classical theories and new developments. Trends Neurosci. 2008;31(9):464–8.
66. Suijk DLS, Dols A, van Exel E, Stek ML, Veltman E, Bouckaert F, et al. Salivary cortisol as predictor for depression characteristics and remission in electroconvulsive therapy in older persons. World J Biol Psychiatry. 2019;20(9):683–90.
67. Baeten RF, Van Rossum EFC, De Rijke YB, Sabbe BGC, Van Der Mast RC, Belge J, et al. Hair cortisol in patients with a depressive episode treated with electroconvulsive therapy. J Affect Disord. 2020;274:784–91.
68. Jiang R, Abbott CC, Jiang T, Du Y, Espinoza R, Narr KL, et al. SMRI biomarkers predict Electroconvulsive Treatment outcomes: Accuracy with Independent Data sets. Neuropsychopharmacology. 2018;43(5):1078–87.
69. Gärtner M, Ghisu E, Herrera-Melendez AL, Koslowski M, Aust S, Asbach P, et al. Using routine MRI data of depressed patients to predict individual responses to electroconvulsive therapy. Exp Neurol. 2021;335:113505.
70. Xu J, Li W, Bai T, Li J, Zhang J, Hu Q, et al. Volume of hippocampus-amygdala transition area predicts outcomes of electroconvulsive therapy in major depressive disorder: high accuracy validated in two independent cohorts. Psychol Med. 2023;53(10):4464–73.
71. Cao B, Luo Q, Fu Y, Du L, Qiu T, Yang X, et al. Predicting individual responses to the electroconvulsive therapy with hippocampal subfield volumes in major depression disorder. Sci Rep. 2018;8(1):5434.
72. Nuninga JO, Mandl RCW, Boks MP, Bakker S, Somers M, Heringa SM, et al. Volume increase in the dentate gyrus after electroconvulsive therapy in depressed patients as measured with 7T. Mol Psychiatry. 2020;25(7):1559–68.
73. Schmitgen MM, Kubera KM, Depping MS, Nolte HM, Hirjak D, Hofer S, et al. Exploring cortical predictors of clinical response to electroconvulsive therapy in major depression. Eur Arch Psychiatry Clin Neurosci. 2020;270(2):253–61.
74. Redlich R, Opel N, Grotegerd D, Dohm K, Zaremba D, Bürger C, et al. Prediction of Individual Response to Electroconvulsive Therapy via Machine Learning on Structural Magnetic Resonance Imaging Data. JAMA Psychiatry. 2016;73(6):557.
75. Bruin WB, Oltedal L, Bartsch H, Abbott C, Argyelan M, Barbour T, et al. Development and validation of a multimodal neuroimaging biomarker for electroconvulsive therapy outcome in depression: a multicenter machine learning analysis. Psychol Med. 2024;54(3):495–506.
76. Takamiya A, Kishimoto T, Liang K, ching, Terasawa Y, Nishikata S, Tarumi R, et al. Thalamic volume, resting-state activity, and their association with the efficacy of electroconvulsive therapy. J Psychiatr Res. 2019;117:135–41.
77. Repple J, Meinert S, Bollettini I, Grotegerd D, Redlich R, Zaremba D, et al. Influence of electroconvulsive therapy on white matter structure in a diffusion tensor imaging study. Psychol Med. 2020;50(5):849–56.
78. Kubicki A, Leaver AM, Vasavada M, Njau S, Wade B, Joshi SH, et al. Variations in hippocampal White Matter Diffusivity Differentiate response to Electroconvulsive Therapy in Major Depression. Biol Psychiatry Cogn Neurosci Neuroimaging. 2019;4(3):300–9.
79. Tsolaki E, Narr KL, Espinoza R, Wade B, Hellemann G, Kubicki A, et al. Subcallosal Cingulate Structural Connectivity Differs in responders and nonresponders to Electroconvulsive Therapy. Biol Psychiatry Cogn Neurosci Neuroimaging. 2021;6(1):10–9.
80. Leaver AM, Vasavada M, Joshi SH, Wade B, Woods RP, Espinoza R, et al. Mechanisms of antidepressant response to Electroconvulsive Therapy studied with perfusion magnetic resonance imaging. Biol Psychiatry. 2019;85(6):466–76.
81. Pang Y, Wei Q, Zhao S, Li N, Li Z, Lu F, et al. Enhanced default mode network functional connectivity links with electroconvulsive therapy response in major depressive disorder. J Affect Disord. 2022;306:47–54.
82. Dini H, Sendi MSE, Sui J, Fu Z, Espinoza R, Narr KL et al. Dynamic functional connectivity predicts treatment response to

Electroconvulsive Therapy in Major Depressive Disorder. Front Hum Neurosci. 2021;15.
83. Li Y, Yu X, Ma Y, Su J, Li Y, Zhu S, et al. Neural signatures of default mode network in major depression disorder after electroconvulsive therapy. Cereb Cortex. 2023;33(7):3840–52.
84. Moreno-Ortega M, Prudic J, Rowny S, Patel GH, Kangarlu A, Lee S, et al. Resting state functional connectivity predictors of treatment response to electroconvulsive therapy in depression. Sci Rep. 2019;9(1):5071.
85. Leaver AM, Wade B, Vasavada M, Hellemann G, Joshi SH, Espinoza R et al. Fronto-temporal connectivity predicts ECT Outcome in Major Depression. Front Psychiatry. 2018;9.
86. ten Doesschate F, Bruin W, Zeidman P, Abbott CC, Argyelan M, Dols A, et al. Effective resting-state connectivity in severe unipolar depression before and after electroconvulsive therapy. Brain Stimul. 2023;16(4):1128–34.
87. Domke AK, Hempel M, Hartling C, Stippl A, Carstens L, Gruzman R, et al. Functional connectivity changes between amygdala and prefrontal cortex after ECT are associated with improvement in distinct depressive symptoms. Eur Arch Psychiatry Clin Neurosci. 2023;273(7):1489–99.
88. Sun H, Jiang R, Qi S, Narr KL, Wade BS, Upston J, et al. Preliminary prediction of individual response to electroconvulsive therapy using whole-brain functional magnetic resonance imaging data. Neuroimage Clin. 2020;26:102080.
89. Li X, Guo J, Chen X, Yu R, Chen W, Zheng A, et al. Predicting responses to Electroconvulsive Therapy in adolescents with Treatment-Refractory Depression based on resting-state fMRI. J Clin Med. 2023;12(10):3556.
90. Li X, Yu R, Huang Q, Chen X, Ai M, Zhou Y et al. Alteration of whole brain ALFF/fALFF and degree centrality in adolescents with depression and suicidal ideation after Electroconvulsive Therapy: a resting-state fMRI study. Front Hum Neurosci. 2021;15.
91. Enneking V, Dzvonyar F, Dück K, Dohm K, Grotegerd D, Förster K, et al. Brain functional effects of electroconvulsive therapy during emotional processing in major depressive disorder. Brain Stimul. 2020;13(4):1051–8.
92. Gruzman R, Hartling C, Domke AK, Stippl A, Carstens L, Bajbouj M, et al. Investigation of Neurofunctional Changes over the Course of Electroconvulsive Therapy. Int J Neuropsychopharmacol. 2023;26(1):20–31.
93. Ermis C, Aydin B, Kucukguclu S, Yurt A, Renshaw PF, Yildiz A. Association between Anterior Cingulate Cortex Neurochemical Profile and Clinical Remission after Electroconvulsive Treatment in Major Depressive Disorder. J ECT. 2021;37(4):263–9.
94. Njau S, Joshi SH, Espinoza R, Leaver AM, Vasavada M, Marquina A, et al. Neurochemical correlates of rapid treatment response to electroconvulsive therapy in patients with major depression. J Psychiatry Neurosci. 2017;42(1):6–16.
95. Erchinger VJ, Miller J, Jones T, Kessler U, Bustillo J, Haavik J et al. Anterior cingulate gamma-aminobutyric acid concentrations and electroconvulsive therapy. Brain Behav. 2020;10(11).
96. Scangos KW, Weiner RD, Coffey EC, Krystal AD. An electrophysiological biomarker that May Predict Treatment response to ECT. J ECT. 2019;35(2):95–102.
97. Tsai HJ, Yang WC, Tsai SJ, Lin CH, Yang AC. Right-side frontal-central cortical hyperactivation before the treatment predicts outcomes of antidepressant and electroconvulsive therapy responsivity in major depressive disorder. J Psychiatr Res. 2023;161:377–85.
98. Kirsten A, Seifritz E, Olbrich S. Electroencephalogram Source Connectivity in the prediction of Electroconvulsive Therapy Outcome in Major Depressive Disorder. Clin EEG Neurosci. 2020;51(1):10–8.
99. Francis-Taylor R, Ophel G, Martin D, Loo C. The ictal EEG in ECT: a systematic review of the relationships between ictal features, ECT technique, seizure threshold and outcomes. Brain Stimul. 2020;13(6):1644–54.
100. Langroudi ME, Shams-Alizadeh N, Maroufi A, Rahmani K, Rahchamani M. Association between postictal suppression and the therapeutic effects of electroconvulsive therapy: a systematic review. Asia-Pacific Psychiatry. 2023;15(4).
101. Fox CA, McLoughlin DM. Speed of electroconvulsive therapy for depression: effects of electrode placement. Acta Psychiatr Scand. 2021;143(5):444–52.
102. Saeed M, Sher Z, Khan F, Iqbal F, Siddiqui TA, Wahab A et al. Right Unilateral Versus Bilateral Electroconvulsive Therapy in Patients With Clinical Depression. Cureus. 2021.
103. Balint T, Nazim Khan R, Hooke G. The Relative Effectiveness of Bilateral and Unilateral Electrode Placement in Electroconvulsive Therapy (ECT) in Patients With Major Depressive Disorder: A Retrospective Cohort Study. Cureus. 2023.
104. Su L, Jia Y, Liang S, Shi S, Mellor D, Xu Y. Multicenter randomized controlled trial of bifrontal, bitemporal, and right unilateral electroconvulsive therapy in major depressive disorder. Psychiatry Clin Neurosci. 2019;73(10):636–41.
105. Gill S, Hussain S, Purushothaman S, Sarma S, Weiss A, Chamoli S, et al. Prescribing electroconvulsive therapy for depression: not as simple as it used to be. Australian New Z J Psychiatry. 2023;57(9):1202–7.
106. Tor PC, Bautovich A, Wang MJ, Martin D, Harvey SB, Loo C. A systematic review and Meta-analysis of brief Versus Ultrabrief Right Unilateral Electroconvulsive Therapy for Depression. J Clin Psychiatry. 2015;76(09):e1092–8.
107. Abbott CC, Quinn D, Miller J, Ye E, Iqbal S, Lloyd M, et al. Electroconvulsive therapy pulse amplitude and clinical outcomes. Am J Geriatric Psychiatry. 2021;29(2):166–78.
108. Park MJ, Kim H, Kim EJ, Yook V, Chung IW, Lee SM, et al. Recent updates on Electro-Convulsive Therapy in patients with Depression. Psychiatry Investig. 2021;18(1):1–10.
109. Gbyl K, Videbech P. Electroconvulsive therapy increases brain volume in major depression: a systematic review and meta-analysis. Acta Psychiatr Scand. 2018;138(3):180–95.
110. Takamiya A, Kishimoto T, Hirano J, Kikuchi T, Yamagata B, Mimura M. Association of electroconvulsive therapy-induced structural plasticity with clinical remission. Prog Neuropsychopharmacol Biol Psychiatry. 2021;110:110286.
111. Gudayol-Ferré E, Peró-Cebollero M, González-Garrido AA, Guàrdia-Olmos J. Changes in brain connectivity related to the treatment of depression measured through fMRI: a systematic review. Front Hum Neurosci. 2015;9.
112. Long Z, Du L, Zhao J, Wu S, Zheng Q, Lei X. Prediction on treatment improvement in depression with resting state connectivity: a coordinate-based meta-analysis. J Affect Disord. 2020;276:62–8.