Neuroimaging Biomarkers at Baseline Predict Electroconvulsive Therapy Overall Clinical Response in Depression

A Systematic Review

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Objective: Major depressive disorder is a frequent and disabling disease and can be treated with antidepressant drugs. When faced with severe or resistant major depressive disorder, however, psychiatrists may resort to electroconvulsive therapy (ECT). Although very effective, the response falls short of 100%. A recent meta-analysis established clinical and biological predictive factors of the response to ECT. We decided to explore neuroimaging biomarkers that could be predictors of the ECT response.

Methods: We performed a systematic literature review up to January 1, 2018, using a Boolean combination of MeSH terms. We included 19 studies matching our inclusion criteria.

Results: Lower hippocampal, increased amygdala, and subgenual cingulate gyrus volumes were predictive for a better ECT response. Functional magnetic resonance imaging also found that the connectivity between the dorsolateral prefrontal cortex and posterior default-mode network is predictive of increased efficacy. Conversely, deep white matter hyperintensities in basal ganglia and Virchow-Robin spaces, medial temporal atrophy, ratio of left superior frontal to left rostral middle frontal cortical thickness, cingulate isthmus thickness asymmetry, and a wide range of gray and white matter anomalies were predictive for a poorer response.

Conclusions: Our review addresses the positive or negative predictive value of neuroimaging biomarkers for the ECT response, indispensable in a personalized medicine dynamic. These data could reduce the risk of nonresponders or resistance with earlier effective management. It might also help researchers elucidate the complex pathophysiology of depressive disorders and the functioning of ECT.

Key Words: MRI, DTI, functional MRI, neuroimaging, depression, ECT, treatment resistance, predictors

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With more than 300 million people affected and an 18% increase between 2005 and 2015, major depressive disorder (MDD) is an increasingly widespread illness and the leading cause of disability worldwide.[1] Beyond its social costs and economic burden,[2] MDD induces both the psychological and physical suffering of individuals through a broad range of health consequences[3] (ie, increased risks for suicidal behavior or cardiovascular death). Unlike common mood fluctuations, MDD requires a proper diagnosis, based on a semiological record with sadness or anhedonia, plus a combination of clinical manifestations including significant weight loss or gain, insomnia or hypersomnia, psychomotor agitation or retardation, asthenia, feelings of worthlessness or guilt, diminished concentration or indecisiveness, as well as recurrent thoughts of death. These manifestations should be observed for at least 2 weeks to determine whether they induce significant distress that breaks from usual functioning or that impair the patient's quality of life.[4]

Remarkably, the number of criteria determines the severity (mild, moderate, or severe) and their combination added to specifiers elicits the distinction of clusters, whereas "resistance" cannot be labeled before acknowledging treatment outcome. Imprecise assessment, a lack of resources, and social stigma associated with mental disorders are still hindrances for more than 50% of depressed patients (up to 90% in impoverished countries) for receiving appropriate treatment.[1] For others, despite a lack of international consensus defining treatment-resistant depression, 60% will not reach remission after first-line pharmacotherapy, and 30% will be considered as such[5–7] after 2 successive regimens of different classes of antidepressants in appropriate dose and duration.[8]

To date, electroconvulsive therapy (ECT) is the most effective treatment option, with response rates exceeding 50% to 60%[9] for resistant depression,[10,11] as well as an efficacy 3 to 6 times higher than with conventional drugs.[12,13] Electroconvulsive therapy is even recommended as first-line treatment in certain clinical situations (melancholic, catatonic, or psychotic features).[14]

First developed in 1938, this brain stimulation technique fell into disuse before rejoining the modern therapeutic arsenal: generalized seizure is now induced using a transcranial brief or ultrabrief pulse electrical stimulus above the titrated threshold, under general anesthesia, muscle relaxation, and continuous ventilation support when required.[14] Its mechanisms still remain putative. The main hypothesis proposed for its efficacy is based on its effect on the modulation of neurotransmitters.[15] There is an alternative model that remains controversial and only occasionally associated with behavioral changes[16] and may not even be related to ECT-induced neuroplasticity in humans (as suggested by the lack of a relationship between peripheral serum levels and real gray matter (GM) volume[17]). This model could, however, involve neurogenesis factors, such as brain-derived neurotrophic factor, as shown in in animals.[18,19]

On one hand, high power neuroimaging studies have identified consistent widespread anatomical brain abnormalities[20] and dynamic functional modifications in patients diagnosed with MDD,

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leading to the identification of a large corticolimbic network including the hippocampus,[21,22] the amygdala,[22,23] the dorsolateral, ventrolateral, and ventromedial prefrontal cortices (PFC), the inferior frontal cortex,[24] the anterior cingulate cortex (ACC), and the basal ganglia,[25] whose qualitative impairment seems to be closely linked to the severity,[26] age of onset,[27] and symptomatic cluster of depression.[28] On the other hand, ECT also induces volume increases in frontolimbic areas among other cerebral changes, as discussed in a recent meta-analysis[29,30] in which some findings proved to be predictive of the subsequent therapeutic response.[31] Structural imaging data have shown an expansion in white matter (WM) (amygdala, hippocampus, subgenual ACC, right anterior cingulate gyrus) and GM volumes (insular and postsuperior GM of temporal cortices).[29] Functional acquisitions have revealed an increased fractional anisotropy in dorsal frontal limbic circuits and a switch from negative to positive correlation between 2 pairs of networks: the posterior default mode and the dorsomedial PFC, and the posterior default mode and the dorsolateral PFC, respectively.[29] In between, additional neuroimaging data seem to show a prognostic value in response to ECT.[32,33]

Although described as a rapid, safe, and effective treatment,[34] a possible lack of efficacy or side effects[10] should be considered in a benefit-risk balance assessment for the patient.[35]

For the past decades, several studies have investigated biological and clinical response predictors, recently summarized in a review[36] and meta-analysis,[37] to identify patients more likely to benefit from ECT. According to this recent meta-analysis, psychotic features and older age are positive predictors for both response and remission, whereas the severity of the episode predicts only the response. To our knowledge, there is no published review specifically focused on noninvasive imaging predictors. The purpose of the present review is therefore to determine whether neuroimaging biomarkers at baseline could predict the overall clinical outcome of ECT.

MATERIAL AND METHODS

A systematic review of the international literature was conducted using the bibliographic search engine PubMed and the following medical subject headings (MeSH): (electroconvulsive therapy OR ECT) AND (depression OR MDD) AND (response OR outcome OR efficacy) AND (predict OR predictive OR prediction OR predictor) AND (imaging OR structural OR functional OR resting state OR CT OR MRI OR Diffusion Weighted Imagery [DWI]). We similarly tested a variation of Boolean combinations and manually examined the reference lists of the previously included articles to broaden the set of results.

Our inclusion criteria were the following: studies published in English from 1990 to January 1, 2018, involving clinically depressed patients with MDD according to *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) criteria, who had undergone brain imaging before the course of ECT regardless the acquisition protocol.

We searched the database using a predefined approach to identify potentially eligible studies. We first independently and then jointly selected studies based on their summaries. All online abstracts were reviewed and full-text papers were retrieved when relevant. This procedure followed the preferred reporting items for systematic reviews and meta-analysis criteria (PRISMA).[38]

RESULTS

We identified 19 studies (Fig. 1) dealing with the prediction of electroconvulsive treatment outcomes that focused on neuroimaging markers (13 with PubMed results as described previously, 5 more articles reviewing their reference lists, and 1 extra publication) among which one was conducted on computed tomography (CT) scans and 18 on magnetic resonance imaging (MRI) acquisitions, including 16 with structural (sMRI) and 2 with functional (fMRI) imaging data. The studies were conducted on a majority of

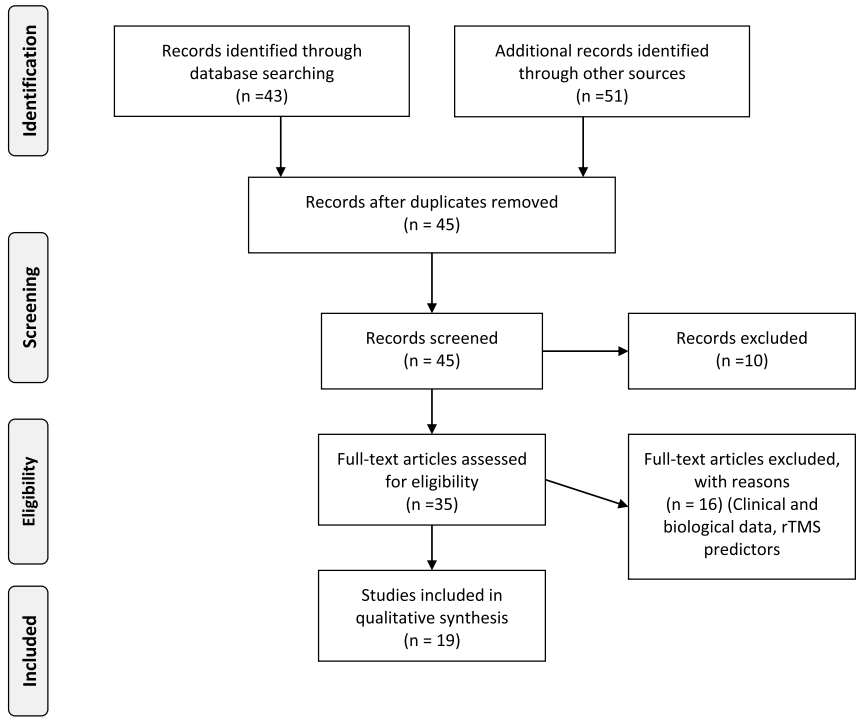

FIGURE 1. Flowchart.

either Americans or European adults (≥18 years old), divided into groups of 16[39] to 110[40] subjects, with available median ages from 41 ± 13.5[41] to 73.0 ± 8.45[40] years, 6 of them specifically focusing on geriatric depressed patients.[32,40,42–45]

Supplementary Table 1 (Supplemental Digital Content 1, http://links.lww.com/JECT/A80) summarizes the methodological aspects of the studies, including patient characteristics, ECT, and MRI parameters. The results emphasize treatment-predictive regions of interest (ROIs) and a dichotomous classification between markers of better and poorer response to electroconvulsive therapy.

Neuroimaging Markers of Better Response to Electroconvulsive Therapy

Hippocampus

Joshi et al[50] found that smaller hippocampal volumes (Fig. 2) at baseline in patients compared with controls indicated greater treatment-related changes in scores of the Hamilton Depression Rating Scale[55] (HDRS). In this study, total hippocampal volume at baseline or only left volume when examined separately predicted the subsequent clinical response. In a naturalistic treatment milieu, Lekwauwa et al[43] showed that a smaller right normalized hippocampal volume was associated with lower post-ECT Montgomery-Åsberg Depression Rating Scale (MADRS) (better response) in older patients with depression. In addition, Jiang et al[56] identified the right hippocampus and parahippocampus (Brodmann area [BA] 30) as one of the 6 ROIs referred to as "predictive network" of clinical targets, with baseline differences between remitters and nonremitters (except for the parahippocampus) and increases in longitudinal GM density using multisite data, thereby contributing to an unbiased prediction framework, specifically for MDD patients 50 years and older. Three structural MRI studies have therefore identified the hippocampus as a key region for predicting responses to ECT, while disagreeing on the hemisphere of interest.[43,50,56] In contrast, in only 1 study, Ten Doesschate et al[33] found no significant predictive value of the hippocampus for treatment outcome.

Amygdala

Two of the previously mentioned studies also focused on pretreatment amygdala volume (Fig. 2). Ten Doesschate et al[33] showed that a larger pretreatment normalized amygdala volume significantly predicted lower post-ECT MADRS scores and remission after treatment, with a greater predictive value of the normalized left relative to the right amygdala volume. Even though a structural plasticity of the amygdala induced by electroconvulsive therapy was noted, Joshi et al[50] found no significant relation between variations in its volume at baseline and overall clinical response.

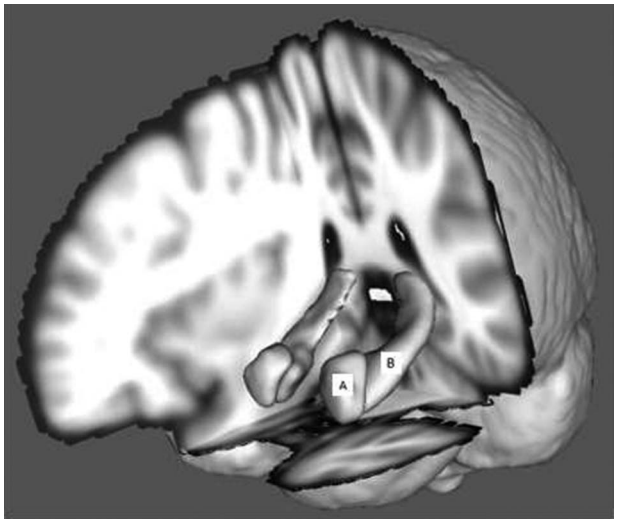

FIGURE 2. Hippocampus (B) and amygdala (A) as biomarkers of ECT response.

Prefrontal Cortex

Argylean et al[39] conducted one of the 2 resting-state fMRI (rs-fMRI) studies included in this review proposed identifying changes in regional neural activity reflecting ECT-induced improvements in mood. Regarding the PFC, analysis using fractional amplitude of low frequency fluctuations (fALFF) did not reveal any predictive value of pretreatment data collected. Dorsolateral PFC fALFF values, however, began in the normal range and descended much farther after ECT, suggesting that ECT decreased PFC activity. In the second study, Van Waarde et al[51] discovered 2 resting-state networks that predicted recovery from depression. One network centered in the dorsomedial prefrontal cortex (including the dorsolateral prefrontal cortex, orbitofrontal cortex, and posterior cingulate cortex) showed a significant classification accuracy, with 84% sensitivity, 85% specificity, and 88% predictive positive value (PPV). It is to noted that the orbitofrontal cortex is also one of the brain areas that provides the largest contribution to the classification of remitters versus nonremitters.

In addition, an sMRI study by Oudega et al[32] distinguished 2 outcome features that were significantly related to PFC imaging data. A more rapid response correlated with a larger pretreatment regional GM volume of the premotor cortex GM volume, consistent with increased motor activity in agitated geriatric depression, whereas a larger response magnitude was significantly associated with smaller ventrolateral PFC.

Frontal Cortex

Patients with a smaller pretreatment right inferior frontal gyrus (IFG) GM volume presented a more rapid response to ECT. While patients with psychotic symptoms (PSs), compared with those without PS, showed both smaller GM volumes of the left IFG and higher remission rates after ECT, geriatric depression with PS seemed related to smaller volumes of the IFG, involved in a strongly seizure-activated brain network.[32] In addition, the 6 ROIs predictive network identified in the older population by Jiang et al[56] also included the left superior frontal gyrus, the supplementary area (BA 6), and the right middle frontal gyrus (BA 10, 11), the latter being the only one without increased GM density throughout the longitudinal acquisition.

Limbic Lobe and Cingulate Gyrus

In the study of Van Waarde et al[51] on rs-fMRI, the cingulate cortex was the second area that distinguished responsive versus nonresponsive patients, as well as the center of the second brain network emerging from the multivariate pattern analysis (including the dorsolateral prefrontal cortex, sensorimotor cortex, parahippocampal gyrus, and midbrain) with 80% sensitivity, 75% specificity, and 80% PPV for remission. Although the prediction accuracy based on structural images was not significant, not all brain areas were located within the network analyzed, which could be interpreted either as relative decoupling of these regions with the network of interest or resulting from the multivariate analysis that did not overlap with the univariate connectivity maps, indicating that the regions are part of a wider multidimensional brain network. Moreover, the whole brain voxel-wise activity analysis of Argyelan et al[39] showed a significant change in fALFF from

pre- to post-ECT in the subgenual cingulate cortex (SCC) with a significantly higher blood oxygen level dependent signal fluctuations at baseline in patients compared with controls in post hoc analysis, which even decreased until normalization during the course of ECT. Thus, the higher baseline fALFF in SCC predicted the better response to electroconvulsive therapy, probably mediated by a decrease of regional activity.

With regard to structural acquisitions, the subgenual cingulate gyrus (SCG) was the area contributing the most to the discriminative maps of the dichotomous outcome classification established by Redlich et al,[48] with higher SCG GM volumes and relatively small degrees of structural impairment before ECT associated with successful treatment (84% accuracy and yet not included in Jiang et al's results,[56] perhaps because of different age ranges). Lastly, Pirnia et al[41] explored the widespread neuroplasticity induced by ECT across both dorsal and ventral corticolimbic circuits but failed to identify pretreatment predictive biomarkers. Variations in dorsal ACC thickness at baseline (T1) only trended toward predicting outcome, achieving significance in the early course of treatment (T2) in relation to the overall clinical response 1 week after completing the index series (T3). No predictive effect was observed for any other cortical ROI.

Basal Ganglia

Wade et al[49] investigated whether striatal and paleostriatal morphological changes were related to or predictive of response to electroconvulsive therapy. Indeed, patients showed smaller baseline accumbens and pallidal volumes compared with healthy controls, as well as a significant association with ECT for total putamen volume and left putamen increase, global accumbens increase, plus pallidum, and caudate variations in treatment responders, without morphometric changes over time compared with controls. The entire combined set of baseline volume features and shape metrics using the combined mood scale ratings predicted overall response to ECT with up to 89% accuracy and response for individual mood scale yielding a 45% area under the receiver operator characteristic curve for HDRS, 59% for MADRS, and 84% for Quick Inventory of Depressive Symptomatology: machine learning based solely on imaging features of limbic-cortical-striatal-pallidal-thalamic circuitry indicated patients likely to benefit from treatment.

Other Regions of Interest

In addition to focusing on patients with PS, Oudega et al[32] also dealt with the age of onset of depression. Patient with late-onset depression (LOD) had smaller bilateral lateral temporal (BA 21) GM volumes compared with those with early onset disease (EOD), and a higher response was significantly associated with a smaller pretreatment regional GM of right BA 21 that could not be explained by the age of onset: geriatric depression with LOD seemed associated with smaller volumes of the temporal cortex, related to a higher response. Interestingly, the authors noted that this 2014 study[32] showed neither smaller volumes of medial temporal lobes in patients compared with controls nor an association between medial temporal lobe atrophy (MTA) and magnitude of response after ECT, whereas their 2011[42] study did so with part of the same cohort. The difference was possibly due to the present exclusion of elderly patients with a higher MTA score, as MTA accelerates in the older old.[32,57]

In addition, Dols et al[40] re-examined differences in structural brain abnormalities in elderly patients with EOD or LOD to identify response predictors in terms of age of onset. They found opposing trends toward higher odds of response in EOD patients with more MTA and LOD with less MTA. Nevertheless, they were not able to conclude on any significant association between MRI characteristics at baseline, including MTA, and response to ECT in the separate subsets (EOD and LOD).

Lastly, the right inferior temporal gyrus (BA 37), left postcentral gyrus/precuneus (BA 1, 2, 3, 7), and left lingual gyrus/precuneus (BA 19, 39) also contributed to the 6 ROIs predictive network of clinical targets, with baseline differences between remitters and nonremitters along with increased longitudinal GM density, but smaller change magnitude in treatment-predictive than treatment-responsive regions.[56]

Neuroimaging Markers of Poorer Response to Electroconvulsive Therapy

Hippocampus

Based on the premise that ECT increased hippocampal neurogenesis in animal models,[19] Lekwauwa et al[43] presumed that this brain region contributed substantially to its underlying mechanisms of action. Therefore, patients with a larger hippocampal volume ratio (normalized for total cerebral volume) would show greater biological vulnerability and poorer acute ECT outcome. Post-ECT MADRS scores, however, were associated with right normalized hippocampal volume, whereas smaller total or left hippocampus volume analysis did not cross the threshold of significance.

Basal Ganglia and Reticular Formation

In the 2 groups compared by Simpson et al,[45] a poorer response was significantly associated with basal ganglia or Virchow-Robin spaces (VRS) hyperintensities in patients receiving pharmacotherapy but only tended to be associated with hyperintensities in the pontine reticular formation, with no connection to VRS in patients undergoing ECT.

Temporal Lobe

An analysis of the elderly cohort that later contributed to discovering predictors of a better response to ECT first led Oudega et al[42] to assess the influence of MTA (already proved to delay the response to pharmacotherapy[58]) on ECT outcome. Reasonably, patients with increased strata of MTA showed a concomitant diminished mean percentage decrease of MADRS score after ECT. In comparison with undamaged temporal lobes, moderate or severe MTA was significantly associated with a 3-fold lower chance of recovering from depression, after a longer interval for initial response and remission. Similar findings were confirmed in post hoc subgroups analysis, in early or late-onset nonpsychotic depressed patients with moderate or severe MTA compared with those without MTA. Although requiring a significantly higher number of sessions, patients with PS and MTA achieved a similar decrease in MADRS score compared with those with PS and no MTA, and thus, the presence of MTA seemed of no influence on the response to ECT in psychotic-depressed patients.

Frontal Lobe

Wade et al[47] also conducted a study on predictors of poor prognosis but chose to test relapse prediction within 6 months after treatment, based on pre- and post-ECT structural imaging data in retrospectively responsive patients. Pooling cohorts and analyzing posttreatment measurements provided the best classification performance, and 2 predictors at baseline were valuable for prognosis, including the ratio of left superior frontal to left rostral middle frontal cortical thickness.

Cingulate Gyrus

In the previous study,[47] cingulate isthmus thickness asymmetry was the second informative feature for predicting relapse emerging from pretreatment structural acquisitions as a result of a robust and normalized pairwise ratio.

Other Contributing Abnormalities

In addition to exceeding the limits of a strictly regional classification, several studies have questioned the relationships between wider cerebral abnormalities and clinical outcome after ECT. For example, Dequardo et al[53] examined the hypothesis that patients with greater structural impairment would present a poorer response to ECT. Although this pathology did not significantly alter posttreatment change in the HDRS score, enlargement of a third ventricle, itself considered an index of generalized brain pathology or regional brain stem abnormalities, was significantly associated with a greater number of sessions required for a maximum benefit from ECT. It is to be noted that a contradiction arose from the examination of Van Waarde et al[52] of interhemispheric and intrahemispheric structural imaging markers, in which none of the baseline MRI characteristics, including partial volumes of cerebrospinal fluid, were individually predictive of post-ECT MADRS scores and therefore excluded from the multivariate analysis.

Gray Matter

Similarly, Steffens et al[44] focused on subcortical gray and WM lesions, prompting the hypothesis of a vascular etiology of depression in the older population, so as to clarify diverging speculations about their effects on response to ECT. Concerning GM hyperintensities, higher severity scores were significantly associated with smaller improvements in Clinical Global Impression (CGI) severity scores, whereas larger areas of lesions, regardless of their severity, were marginally associated with a larger number of treatments required. In contrast, total GM characteristics were also part of the baseline noncontributory data that Van Waarde et al[52] decided not to use for their analysis.

White Matter

Hickie et al[54] reported an association between a poorer response to treatments (with correlations of the same order in patients receiving ECT or pharmacotherapy alone) and WM hyperintensities, which were also the only significant outcome predictor in a multiple regression analysis, explaining one fifth of the variance. On the contrary, Oudega et al[42] hypothesized that patients with WMH would have a poorer response to ECT, but there would be an association between the mean change in MADRS scores and overall cortical atrophy or WM hyperintensities, again excluded from the analysis of Van Waarde et al.[52] Finally, these results were consistent with the findings of Simpson et al[45] that deep WMHs (DWMHs) did not lead to a poorer outcome after ECT, as well as the conclusion of Steffens et al[44] that periventricular hyperintensity or DWMH was neither associated with the acute response nor with the number of treatments required to achieve remission.

DISCUSSION

To our knowledge, this review is the first to assess predictive factors of neuroimaging on the outcome of ECT. We have identified discrepancies in several publications and some remained inconclusive.[52] There are 2 main and opposing groups: baseline neuroimaging markers predict either a better or worse response after electroconvulsive therapy.

On the one hand, we found that lower hippocampal and higher amygdala volumes at baseline were associated with a greater improvement of patients, as did a higher volume of SCG GM. Resting-state fMRI studies suggest that the connectivity between posterior DMN and left dorso lateral prefrontal cortex might be a possible marker for an ECT response. On the other hand, we identified several factors predictive of a poorer response to ECT, such as deep WM hyperintensities in basal ganglia and VRS, medial temporal atrophy, the ratio of left superior frontal to left rostral middle frontal cortical thickness, cingulate isthmus thickness asymmetry, and a wide range of gray and WM anomalies.

Next to clinical predictive markers identified by van Diermen[37] whose meta-analysis emphasize that advanced age, PSs, and more severe depression are good predictive markers for the ECT response, neuroimaging data can be of additional predictive value. A previous study found that the hippocampus of patients with MDD associated with PSs was significantly smaller,[59] but there is no significant correlation between the severity of depression and smaller hippocampal volumes.[60] Among the articles included in this review, our findings concerning the hippocampus are not consistent with published results. A previous study showed that larger hippocampal volumes were associated with a better outcome for treatment response when using antidepressants.[61] This difference could be due to the specificity of the population of the studies in our review: among the 3 studies reporting that a smaller hippocampus is related to a better outcome of ECT, 2 focused on patients of elevated mean age.[43,56] Recent findings suggest that late-onset depression could be a prodromal stage of neurodegenerative conditions such as Alzheimer disease.[62] Moreover, although not substantiated in all human studies,[17] the theory of ECT-induced neurogenesis resulting from the increase of neurotrophic factors such as brain-derived neurotrophic factor[63] in preclinical findings[16] might therefore be a conceivable explanation for this difference observed for positive predictive factors between ECT and antidepressants. The fact that a longer duration or medical history of MDD is linked to a decrease of hippocampal volume is another indicator, which could explain this difference.[60,64]

Our review has several limitations. First, it includes studies with relatively heterogeneous populations, such as recurrent depressive disorders, treatment-resistant depression, late-onset depressions, or even isolated severe MDDs.[33,43,49–51] Several authors have hypothesized that these different clusters of patients might experience different diseases, with different etiologies leading to a common phenotype.[59] This may explain the variability observed among the results of the treatment and even resistance occasionally observed. The delay between pretreatment and posttreatment neuroimaging is not a confusing factor in our review because of our inclusion criteria (ie, pretreatment neuroimaging predictive factors of the efficacy of ECT). The link between predictive factors and brain changes after ECT treatment should be analyzed in future studies. Preliminary studies, however, must first assess early brain changes (structural and functional) (after 1 or 2 ECT treatments).

Another limitation is the lack of scientific data using alternative MRI sequences such as diffusion tensor imaging or diffusion-weighted imaging, specifically sought in our review procedure. A growing body of evidence using these specific MRI sequences has recently emerged, showing several brain alterations in fractional anisotropy in widespread structures such as the corpus callosum, bilateral superior longitudinal fasciculi III, right anterior thalamic projections, and the arcuate fascicle.[46] Moreover, a recent meta-analysis focused on the emergent role of tractography as a predictive factor of outcomes of deep brain stimulation treatment for depression, among other diseases.[65] We believe that the analysis of microstructural brain abnormalities is a promising new path for psychiatric researchers and neuroscientists. These important limitations preclude drawing generalizable conclusions on the general population. Cohort-based studies with integrative data, including neuroimaging, might help define those clusters of patients

who will benefit from ECT treatment more than others. This type of research has been published for rTMS,[28] based on clinical and neuroimaging features, and has helped define responder clusters.

Another growing body of evidence in depressive disorders is the immune/inflammatory approach. Biological,[66,67] genetic,[68,69] and cerebral nuclear imaging[67,70,71] methods have correlated cerebral and systemic inflammation and microglial activation with depressive disorders, notably disease duration and untreated periods.[71] The regions implicated by positron-emission tomography studies are consistent with regions of interest in depression such as PFC, ACC, and insula.[71] These data concern regions we identified as predictors for the ECT response, as well as areas modified by this treatment[29] (amygdala, hippocampus, dorsolateral PFC). The convergence of these results not only leads to better management of patients with MDD but also indicates future pathways for elucidating the complex pathophysiology of depression. The integration of immune data in parallel to clinical and classical neuroimaging features could help better define clusters of patients responding and resistant to ECT and even determine whether they will or will not respond rapidly. We hope that this will lead future generations of psychiatrists to a clearer path toward personalized psychiatry.

CONCLUSIONS

Our review addresses the positive or negative predictive value of neuroimaging biomarkers for the ECT response. This pretherapeutic approach seems indispensable in a personalized medicine dynamic. Subsequent studies combining clinical, biological, and neuroimaging data could reduce the risk of nonresponders. This might ultimately reduce the risk of resistance with earlier effective management.

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