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Current progress in neuroimaging research for the treatment of major depression with electroconvulsive therapy

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Abstract

Electroconvulsive therapy (ECT) uses a certain amount of electric current to pass through the head of the patient, causing convulsions throughout the body, to relieve the symptoms of the disease and achieve the purpose of treatment. ECT can effectively improve the clinical symptoms of patients with major depression, but its therapeutic mechanism is still unclear. With the rapid development of neuroimaging technology, it is necessary to explore the neurobiological mechanism of major depression from the aspects of brain structure, brain function and brain metabolism, and to find that ECT can improve the brain function, metabolism and even brain structure of patients to a certain extent. Currently, an increasing number of neuroimaging studies adopt various neuroimaging techniques including functional magnetic resonance imaging (fMRI), positron emission tomography, magnetic resonance spectroscopy, structural MRI, and diffusion tensor imaging to reveal the neural effects of ECT. This article reviews the recent progress in neuroimaging research on ECT for major depression. The results suggest that the neurobiological mechanism of ECT may be to modulate the functional activity and connectivity or neural structural plasticity in specific brain regions to the normal level, to achieve the therapeutic effect.

Key Words: Neuroimaging; Major depression; Electroconvulsive therapy; Magnetic resonance imaging; Positron emission tomography; Magnetic resonance spectroscopy

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Core tip: Longitudinal neuroimaging studies in patients with major depression before

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and after electroconvulsive therapy (ECT) have shown that ECT has effects on specific brain areas. However, these ECT-regulated brain regions and their changes are uncertain. Based on recent studies with various neuroimaging techniques, this paper reviews longitudinal neuroimaging findings in recent years and discusses the relatively consistent results.

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INTRODUCTION

Major depressive disorder (MDD) has become a major public health problem throughout the world. Approximately 322 million people suffer from depression worldwide, with a prevalence rate of 4.4%. More than 1 million people commit suicide due to depression every year[1]. Neuroimaging studies have shown that the structural and functional alterations in frontal lobe, cingulate gyrus (CG), hippocampus, basal ganglia and other brain regions are closely related to the pathogenesis of depression [2].

Electroconvulsive therapy (ECT) is essentially a method of using electrical current to induce epileptiform discharges in the cortex, causing a systemic seizure to control mental symptoms. Since ECT was invented by Italian scientists Cerletti and Bini in 1938, it has been extensively applied to the treatment of mental disorders for > 80 years[3]. At present, ECT is an indispensable treatment in the field of psychiatry. It is still the first choice for patients with severe depression with stubborn suicidal thoughts, delusions, and food refusal, followed by schizophrenia and mania[4]. ECT has attracted increasing attention in neurologic diseases due to its rapid and high response rate in patients with depression[5,6].

Currently, the neural mechanisms underlying the clinical response to ECT for MDD remain uncertain, and there are no widely accepted biomarkers that can be used to assist in the diagnosis or treatment options for individual patients. It only relies on subjective judgments based on clinical features and lacks objective and reliable evidence[7]. To facilitate treatment development, a clearer understanding of the neural correlates of successful antidepressant responses is essential[8]. Neuroimaging technology has the potential to identify objective neurobiological markers that reflect the underlying pathophysiological process in a given mental illness, and it is a noninvasive research method for observing brain changes. Various neuroimaging techniques such as positron emission tomography (PET) and magnetic resonance imaging (MRI) have promoted research on neuropsychiatric diseases. At the same time, this provides a new window for the study of the therapeutic mechanism of ECT in depression.

Longitudinal studies of neuroimaging in patients with major depression before and after ECT have shown that ECT has effects on specific brain regions and circuits. Some studies in the late 1980s focused on refuting the hypothesis that ECT caused brain damage and found no overall evidence of structural changes or harmful effects[9-11]. After the first high-resolution (1 mm³) MRI study determined ECT-induced structural changes by detecting the increase in hippocampal volume[12], several subsequent studies confirmed that ECT can also induce alterations in hippocampal structure and other brain regions[13-16]. Recent research using machine learning and MRI can help patients and psychiatrists make more informed decisions about ECT as a treatment option[17,18]. These studies use machine learning algorithms to identify patients who are most likely to benefit from ECT at the individual level. Using these methods also helps to discover biomarkers in the brain that can predict the response to ECT treatment.

Although an increasing number of neuroimaging studies have attempted to reveal the neurological effects of ECT, these ECT-regulated brain regions and their changes are usually inconsistent. Therefore, based on recent longitudinal neuroimaging findings related to ECT treatment in depression, we investigated the progress made in these studies.

BRAIN FUNCTIONAL IMAGING STUDY FOR DEPRESSION WITH ECT

Functional MRI

Blood oxygenation level-dependent functional MRI (BOLD-fMRI) has been applied in the field of brain function research since the 1990s and has become the most rapidly developing functional detection technology. BOLD-fMRI has the advantages of being noninvasive, nonradioactive, repeatable, and having high temporal and spatial resolution. It also allows analysis on a single-subject basis to reflect the dynamic activity of neurons and the different patterns of response between adjacent cortices throughout the process. The spontaneous low-frequency activity information collected in the resting state is defined as the baseline brain function information, which reflects the spontaneous functional activities of the central nervous system in the basic state [19,20]. Therefore, fMRI in the resting state has obvious clinical advantages. Resting-state fMRI (rs-fMRI) is also particularly suitable for the study of patients with major depression because it does not require the patient to perform a specific task. Thus, rs-fMRI is increasingly widely used in the study of brain function in depression.

ECT can cause changes in the functional connectivity (FC) in specific brain regions in patients with depression. These changes may reveal that the clinical improvement of depression is related to the treatment effect of ECT through fMRI. Assessing changes in FC requires analyzing the differences before and after ECT. In recent years, different results have been reported [21]. In the voxel-analysis method, the CG is generally regarded as an important area related to ECT. There were significant changes in ECT, including a decrease in resting state FC (rsFC) in the left dorsal anterior cingulate cortex (dACC) and an increase in rsFC in the bilateral posterior cingulate cortex (PCC). Other important areas found in the rsFC after ECT are the frontal cortex, parietal cortex and temporal cortex, including the bilateral anterior central gyrus, dorsomedial prefrontal cortex, bilateral superior frontal gyrus (SFG), left angular gyrus (LAG), left precuneus, bilateral hippocampus, right superior temporal gyrus, right island, and cerebellum [21]. For instance, Wei *et al* [22] adopted FC strength (FCS) to identify brain hubs through resting-state fMRI at three time points, *i.e.*, prior to ECT, at the completion of ECT, and 1 mo after the completion of ECT. The results showed that the FCS of the LAG of patients with depression after ECT was significantly increased. Mo *et al* [23] found that the FC of the LAG with the bilateral inferior temporal gyrus (ITG), bilateral middle frontal gyrus, and other areas was significantly increased, accompanied by emotional improvement. Sun *et al* [24] used fMRI data to make preliminary predictions of individual response to ECT, and the results showed that the predictive areas were concentrated in the prefrontal and temporal cortices and the subcortical nuclei.

In seed-based analysis, CG is usually also selected as the seed region. After ECT, it was found that rsFC of the left subgenual anterior cingulate cortex (sgACC) with the left parahippocampal gyrus (PHG) increased, while rsFC of the contralateral temporal pole decreased [25]. During ECT treatment, rsFC of the subcallosal cingulate cortex with bilateral hippocampus, bilateral temporal poles, and ventral prefrontal cortex was significantly reduced [26]. Some studies also pointed out that rsFC of the sgACC with the amygdala and fusiform gyrus changed significantly after ECT treatment. Using fMRI data, Leaver *et al* [27] found that rsFC between the left dorsolateral prefrontal cortex (DLPFC) and sgACC was probably an important feature of the ECT response to depression. With regard to network-based and region-of-interest (ROI) analysis, the changes in rsFC in the left cerebellum, default mode network, ACC, and PCC were more frequent after ECT treatment.

ECT can also cause regional functional activity changes in patients with depression. It is an important method to study the regional functional activity changes in brain regions through fMRI. The indicators include amplitude of low frequency fluctuations (ALFF), fractional ALFF (fALFF), and regional homogeneity (ReHo). Qiu *et al* [28] found that ReHo of rs-fMRI showed significant differences in brain activity before and after ECT. MDD patients who received eight courses of ECT showed higher ReHo values in the bilateral frontal lobes, bilateral parietal lobes, and right caudate nucleus. Decreased ReHo values were observed in the left anterior cerebellar lobe, right CG, right superior temporal gyrus, and right medial temporal gyrus. Argyelan *et al* [29] used rs-fMRI to compare patients with treatment-resistant depression before ECT with normal controls and found that the fALFF of the right cingulate cortex increased significantly in patients, suggesting that local brain functional activity is hyperactive. The fALFF in the cingulate cortex in patients after ECT was significantly lower than that before ECT, and there was no significant difference compared with normal controls, indicating that ECT can significantly improve abnormal brain function activities. In addition, ReHo of the LAG [23] and ALFF of the dorsal medial prefrontal

cortex[30] in MDD patients increased significantly after ECT treatment. In a sham-controlled fMRI study, Miskowiak *et al*[31] found that the regulation of medial prefrontal hyperactivity during the encoding of negative affective information may be a common mechanism for different biological depression treatments. In response to negative emotional stimulation for depression, the activity in the amygdala increases abnormally. Redlich *et al*[32] used fMRI data to find that the patient's amygdala function normalized after ECT.

PET

PET is a modern imaging technology to detect and identify metabolic changes that occur prior to structural changes in tissues and organs under disease conditions at the molecular level. It measures and displays the biological activities of cells and molecules by injecting radioisotope drugs with appropriate half-life into the body. According to the concentration of the tracer, cerebral blood perfusion and glucose and neurotransmitter metabolism levels can be inferred, and it has the advantages of high sensitivity and accurate quantitative analysis.

PET is currently used to study changes in specific neurotransmitter receptors after ECT. Masuoka *et al*[33] used [¹⁸F]FE-PE2I PET to examine MDD patients before, during and after treatment and found that all patients had a reduced striatal dopamine transporter-binding potential (BP_{ND}). Combined with the patient's clinical response, it has been proven that the dopamine nervous system is part of the mechanism of ECT. Tiger *et al*[34] used PET and [¹¹C]raclopride to examine patients with severe MDD before and after ECT, and healthy controls. Compared with the control group, the [¹¹C]raclopride binding rate in all three parts of the striatum decreased significantly in the patients. However, there was no significant effect of ECT on D₂/D₃ binding in the patients. Baldinger-Melich *et al*[35] used PET and radioligand [¹¹C]harmine to evaluate cerebral monoamine oxidase A (MAO-A) distribution volumes (V_T). The results showed no significant difference in MAO-A V_T between patients with post-ECT treatment-resistant depression and healthy controls at baseline. This suggested that MAO-A V_T is not related to the clinically relevant mechanism of action of ECT. Using [¹⁸F]Setoperone PET, Yatham *et al*[36] found that serotonin₂ (5-HT₂) receptor binding was extensively reduced in all cortical regions of MDD patients after ECT. Furthermore, the reduction in the 5-HT₂ receptor in the right PHG, right lingual gyrus and right medial frontal gyrus was correlated with the improvement of depressive symptoms. These results were consistent with research on antidepressants[37-39]. Lanzenberger *et al*[40] used highly selective radioligand [carbonyl-¹¹C] WY100635-PET scans and compared the voxels of serotonin-1A (5-HT_{1A}) receptor binding (BP_{ND}) before and after ECT. The results showed extensive decreases in cortical and subcortical areas, except for the cerebellum and the occipital cortex. This PET study proposed the whole-brain involvement of postsynaptic 5-HT_{1A} receptor binding in ECT effects.

PET is utilized to evaluate ECT-related changes in [¹⁸F]-fluorodeoxyglucose (FDG) to measure the rate of local brain metabolism of glucose. The most consistent finding in pre- and post-ECT comparisons was decreased glucose metabolism in the bilateral frontal medial and inferior frontal areas and right frontal operculum[41]. The areas with increased glucose metabolism included the hippocampus, middle temporal lobe, left occipital lobe, parietal lobe and pons. Bak *et al*[42] used [¹⁸F]-FDG PET to study the efficacy of ECT in a 55-year-old woman with late-onset depression. ¹⁸F-FDG PET/computed tomography (CT) images of the patient's brain showed a diffuse decrease in brain metabolism. After the patient's symptoms were improved by ECT, her PET imaging showed her brain metabolism was normal. After improving the patient's symptoms through ECT, PET imaging showed that her brain metabolism was normal. Hassamal *et al*[43] adopted ¹⁸F-FDG-PET/CT before ECT to show extensive hypometabolism in the frontal, parietal and temporal cortices. After eight sessions of ECT, symptoms of psychosis and anxiety symptoms as well as cognitive impairment were resolved. ¹⁸F-FDG-PET/CT showed improvement in hypometabolism of the cerebral cortex, especially in the left parietal cortex, left temporal/occipital cortex, and bilateral frontal areas. The improvement of brain glucose hypometabolism may represent the neurophysiological mechanism of ECT for the treatment of psychotic episodes. However, Reininghaus *et al*[6] reported inconsistent results. They employed FDG-PET scans to measure the effects of a series of ECT treatments on brain glucose metabolism in depressed subjects before and after treatment. They found that there was almost no change in brain glucose metabolism. Therefore, they did not think that FDG-PET can evaluate the functional brain changes that may occur after ECT.

Magnetic resonance spectroscopy

Magnetic resonance spectroscopy (MRS) is used to determine abnormal metabolic conditions in tissues by measuring changes in the concentration of metabolites in the human body and observing different peaks and ratios of the spectrum curve. MRS is a noninvasive detection technology that can measure neurobiochemical information in specific brain functional areas and analyze the content of neurobiochemical substances. These compounds include γ -aminobutyric acid (GABA), glutamate (Glu), choline-containing compounds, N-acetyl-L-aspartic acid (NAA), glutamine (Gln), myoinositol, and creatine (Cr).

Glu plays a key role in the pathophysiology of depression[44]. There was evidence that the levels of Glu and Gln in pgACC were reduced[45,46], while the concentration of Glu in the DLPFC was unchanged[47,48]. ECT caused changes in glutamatergic neurotransmission that seem to be closely related to its antidepressant effects[49,50]. Njau *et al*[51] reported that Glx (Glu and Gln) increased in sgACC but decreased in the left hippocampus in patients with depression after ECT treatment, and these changes were related to the improvement of mood. Glx disorders in MDD patients and the regulation of Glx levels by ECT vary from region to region. Although some studies reported increased Glx levels in the DLPFC and ACC after ECT[49,52], one study was unable to replicate these findings[48]. There were similar contradictory reports for the hippocampus. A recent study reported the correlation between elevated hippocampal Glx and ECT response in patients with medication-resistant depression[53], while another report was unable to confirm these results[54]. In general, brain metabolism of Glu has been an important component of ECT efficacy, but there are differences in the exact mechanism.

In addition, reduced levels of GABA in cerebrospinal fluid and plasma, as well as in the frontal cortex, were reported in patients with depression[55]. Thus, increased serum levels and occipital GABA concentrations were observed after ECT[56,57]. However, Knudsen *et al*[58] used MRS to measure GABA changes in the prefrontal and occipital cortex in patients before and after ECT. There were no significant differences in GABA/Cr levels in the prefrontal cortex or occipital lobe between baseline patients and healthy subjects, and there was no statistically significant difference in GABA, Glu, glutamine, choline or GSH before and after ECT. They concluded that GABA should not be considered a key factor in the treatment of major depression with ECT.

NAA is a marker of neurons and axons, and its concentration can reflect the number and functional status of neurons. Proton MRS (H-MRS) showed that ECT can increase the content of NAA in the anterior CG and amygdala, suggesting that ECT has a nerve-promoting effect. Njau *et al*[51] detected MDD patients with ECT through ¹H-MRS and found that compared with the control group, the content of NAA in the left hippocampus of the patients was reduced before treatment. Meanwhile, the NAA levels of the dACC and right hippocampus also decreased significantly after ECT treatment.

Tosun *et al*[59] observed the metabolic changes of ACC in MDD patients after ECT through ¹H-MRS. There was no significant difference in the levels of ACC metabolites between the patients and the control group at baseline. ECT was associated with a statistically significant decrease in the NAA/Cr ratio in ACC. All patients responded to ECT treatment as measured by the clinical scale. These results suggest that a relative increase in Cr levels after ECT in MDD appears to be associated with an improvement in clinical severity. However, Ende *et al*[60] found that hippocampal NAA did not change after ECT, and the choline content increased, indicating that ECT may be related to increased membrane transformation and may reflect neurogenesis.

Because the different neurotransmitter systems involved in the antidepressant effect of ECT are connected to each other through a complex signal transduction network and the changes in the content of neurobiochemical substances are also complicated, the above findings based on MRS have presented inconsistent results.

BRAIN STRUCTURAL IMAGING STUDY FOR DEPRESSION WITH ECT

Structural MRI

ECT can improve brain function and change the brain structure in patients with depression. Many MRI structural studies in patients with MDD have shown morphological abnormalities, mainly manifested as cortical thickness, gray matter volume, and white matter integrity[61]. Longitudinal structural neuroimaging studies have proven that ECT increases the volume of the hippocampus, amygdala, caudate

nucleus, and temporal lobe. Some studies have found that ECT increases the volume of the hippocampus and amygdala in the temporal lobe system in patients with depression[62-64]. The strongest evidence of structural changes in the brain after ECT was an increase in the volume of the temporal lobe and subcortical structures, such as the hippocampal-amygdala complex, anterior cingulate cortex and striatum[65].

Voxel-based morphology (VBM) is a powerful and objective method for studying brain structural changes in patients with depression before and after ECT through MRI. Due to its simplicity of use, VBM has inspired many neuroscientists to characterize specific abnormalities in brain gray matter volume in MDD[66,67].

Some studies have used ROI methods to analyze brain regions closely associated with depression. Tendolkar *et al*[62] took the bilateral hippocampus and amygdala as regions of interest and found that ECT could increase the gray matter volume of the bilateral hippocampus and amygdala in patients with refractory depression. Accordingly, the Hamilton Depression Scale score was significantly reduced after ECT, and the severity of depressive symptoms was reduced. Gryglewski *et al*[68] found that structural changes were observed in the hippocampal subregions and amygdala after ECT. These structural changes are particularly involved in the pathophysiology of depression and stress-related diseases and still have high neuroplasticity in adulthood. Cao *et al*[69] used the latest hippocampal segmentation method and found that ECT induced cornu ammonis subfields, granule cell layer, molecular layer, and hypothalamic volume increases. It also accurately predicted the quantitative efficacy of ECT for each patient. Joshi *et al*[70] used FreeSurfer to segment the hippocampus and amygdala and found that ECT induced neuroplasticity processes related to clinical responses, which can correct the reduction in the structure of the hippocampus and amygdala associated with MDD. Patients with small hippocampal volumes were most likely to show an increase in volume and improve clinical response. Therefore, changes in the structure of the hippocampus and amygdala could serve as potential biomarkers for the development of other rapidly effective therapies. Jorgensen *et al*[54] used structural MRI (sMRI) of the hippocampus, amygdala, DLPFC, orbitofrontal cortex, and hypothalamus and found that the hippocampus and amygdala volume increased in patients with major depression after ECT, while the volume of the DLPFC decreased slightly. However, due to the lack of correlation between these changes and the antidepressant effect, this remodeling of the brain structure does not appear to directly affect the antidepressant effect of ECT. Wade *et al*[8] conducted a longitudinal study on the cortical volume, cortical thickness and cortical surface area of the caudate nucleus, putamen, pallidum, and nucleus accumbens through surface-based morphometry. Compared with the control group, the volume of the nucleus accumbens and nucleus pallidum were smaller in MDD patients. ECT caused an increase in the volume of the left putamen. In patients defined as responders to treatment, there was an increase in overall nucleus accumbens volume and local changes in globus pallidus and caudate nucleus volume. Thus, ECT induces structural plasticity in the dorsal and ventral striatum/pallidum.

In some studies, VBM has been effectively used to evaluate anatomical abnormalities in the whole brain. Ota *et al*[71] found that the volume of the bilateral medial temporal cortex, inferior temporal cortex and right anterior CG increased significantly after ECT. In addition, the rate of increase was associated with clinical improvement as measured by the Hamilton Depression Scale. Van Eijndhoven *et al*[72] compared the brain images of treatment-resistant MDD patients before and after ECT with normal controls and found that there was no significant difference in the thickness of the whole cerebral cortex between patients before ECT and normal controls. After ECT, the patients had increased cerebral cortex thickness in the left temporal pole, left middle temporal gyrus, and right insula compared with the control group. Meanwhile, the Hamilton Depression Scale score was significantly lower than before treatment, with an average decrease of 57%. Sartorius *et al*[16] analyzed sMRI before and after ECT and found that the gray matter volume of the whole brain increased in most patients after ECT, while the white matter volume of the brain did not significantly change. Further voxel-based morphological analysis showed that the volume of gray matter in the bilateral temporal lobe, the middle CG, the insular lobe and the putamen increased after treatment. Jiang *et al*[73] adopted six GM areas including the right hippocampus/parahippocampus, the right orbitofrontal gyrus, the right ITG, the left posterior middle gyrus/anterior process, the left auxiliary motor area and the left lingual gyrus to be identified as predictors of ECT response. They revealed that GM density only increased in the left auxiliary motor cortex and the left middle posterior gyrus/protrusion after ECT. The results indicate that the treatment prediction area and the treatment response area may be anatomically different. Pirnia *et al*[74] found that the thickness increased in the bilateral anterior cingulate cortex,

superior temporal cortex *etc.* ECT resulted in extensive neuroplasticity in the neocortex, limbic and paralimbic areas. Moreover, changes in ACC thickness can distinguish treatment responders and predict early responses during ECT.

Gbyl and Videbech[75] concluded that current MRI studies do not support the hypothesis that ECT causes brain damage. They confirmed that ECT causes an increase in the volume of the limbic area of the frontal lobe, and further research should explore the relationship between these increases and treatment effects and cognitive side effects. Many studies have shown an increase in hippocampal volume following ECT, but there are conflicting results as to whether the increase in hippocampal volume is associated with clinical response. Other studies have found increased GMV or cortical thickness in areas such as the amygdala, frontotemporal cortex, lingual gyrus, thalamus, and striatum.

Diffusion tensor imaging

Diffusion tensor imaging (DTI) is a derivative technique of diffusion-weighted imaging that can noninvasively detect the direction and integrity of white matter tracts by evaluating the diffusion of water molecules in nerve tissue. It has important applications in neuroimaging research.

Chen *et al*[76] performed a meta-analysis of microstructural brain abnormalities in drug-naïve patients with major depression through DTI. They observed that the main areas of fractional anisotropy reduction included the bilateral anterior limb of the internal capsule, body of the corpus callosum, right SFG, and right ITC. Gbyl and Videbech[74] found that an ECT-induced increase in the integrity of the white matter pathways in the frontal and temporal lobes through a meta-analysis of DTI, but the correlation between the increase in volume and the treatment effect and the mechanism of action of ECT are still uncertain. Yroni *et al*[77] found a reduction in the hippocampus and left amygdala during ECT in patients with treatment-resistant depression using mean diffusivity (MD) measure. They concluded that ECT can correct the microstructural integrity of these structures. Gryglewski *et al*[78] conducted a DTI study on patients with treatment-resistant depression using unilateral ECT and found that axial diffusivity was increased in the posterior limb of the internal capsule in the right hemisphere. Compared with the left hemisphere, the increase in this region was higher on the right. However, no correlation between this effect and treatment response was found. Repple *et al*[79] used DTI to analyze the alterations in the white matter structure in patients with depression before and after ECT and found that MD of the right hemisphere increased after ECT, which was a specific effect in the ECT group. Kubicki *et al*[80] revealed alterations in the structural connections of the hippocampal neural circuits after ECT. It also means that glial, neurotrophic or inflammatory response mechanisms affect the integrity of the axons. Lyden *et al*[81] observed a significant increase in fractional anisotropy in the dorsal frontolimbic circuits including the anterior cingulate, forceps, and left superior longitudinal fasciculus between baseline and transition to maintenance therapy. Radial and MD in overlapping regions and anterior thalamic radiation were reduced. Changes in DTI indicators related to treatment response indicated that ECT effects significantly differed between MDD and control groups. Alterations in white matter microstructure in the pathways connecting the frontal and limbic regions that occur in MDD are regulated by ECT and are associated with treatment response.

CONCLUSION

In recent years, the rapid development of neuroimaging technologies represented by MRI has played a major role in promoting the study of neurological mechanisms of mental diseases. With the continuous emergence of new technologies, they have been able to provide different levels of physiological and pathological information from macroscopic tissue morphology to microscopic subcellular structure, and from blood flow and energy metabolism to high-level brain functional networks, which embodies the characteristics of multidimensional and multimodal information. Research on the neural effects of ECT needs to consider the physical and mental state of patients with major depression to adopt appropriate neuroimaging technology. At present, MRI is the most commonly used method, and there are very few studies using single-photon emission CT.

In general, the findings of current neuroimaging studies are inconsistent. The main reasons are as follows: (1) The operating methods of ECT such as electrode position, electric dose, and treatment times are different; (2) Data collection and analysis

Table 1 Consistent findings in neuroimaging research on electroconvulsive therapy effects

Neuroimaging technologies	Methods/measures	Relatively consistent findings
fMRI	Functional connectivity strength	Changes in cingulate cortex, frontal cortex, and left angel gyrus
	Functional activity of local brain regions	Changes in cingulate cortex and prefrontal cortex
PET	Neurotransmitters	Downregulation of brain serotonin receptors
	Glucose metabolism	Reduction in glucose metabolism after ECT in bilateral anterior and posterior frontal areas
MRS	Gln/Glx, GABA, NAA, Cho, mI, Cr	None
sMRI	Gray matter volumn	Increase in hippocampus and amygdala
DTI	White matter	Alterations in microstructure and pathways

fMRI: Functional magnetic resonance imaging; PET: Positron emission tomography; MRS: Magnetic resonance spectroscopy; sMRI: Structural magnetic resonance imaging; DTI: Diffusion tensor imaging; Gln: Glutamine; Glx: Glutamate and Gln; GABA: γ -aminobutyric acid; NAA: N-acetyl-L-aspartic acid; Cho: Choline-containing compounds; mI: Myoinositol; Cr: Creatine; ECT: Electroconvulsive therapy.

methods are different; (3) Sample size collected for research is too small; and (4) Physiological disorders of patients with depression are heterogeneous. Despite these shortcomings, it is not possible to fully understand how ECT works, and there are still some encouraging findings. Table 1 gives a summary of relatively consistent findings. In the fMRI study of ECT treatment, the significant changes in the functional connection strength of the cingulate cortex, frontal cortex, and left angel gyrus were relatively consistent. Significant changes in the functional activity of the cingulate cortex and frontal cortex are also response markers for ECT treatment. For PET studies, consistent conclusions include a reduction in glucose metabolism after ECT in the bilateral anterior and posterior frontal areas and downregulation of brain serotonin receptors. Due to the complex neurobiochemical alterations in the brain, no consistent results have been obtained in the current studies on the treatment of depression with ECT based on MRS. Many sMRI studies have found that the increased volumes of the hippocampus and amygdala are the most important imaging markers for improving depression after ECT. Among white matter DTI studies, much evidence supports an increase in white matter pathway integrity after ECT.

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