Structural and Functional Alterations in Brains of Patients with Schizophrenia following Electroconvulsive Therapy

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To the Editor: Treatment-refractory schizophrenia (TRS) indicates that patients’ positive schizophrenia symptoms have proven resistant, even to adequate treatment with at least two different categories of antipsychotic drugs (adequate dose, duration, and adherence) and constitutes ~15–30% of cases of schizophrenia. According to schizophrenia treatment guidelines, modified electroconvulsive therapy (mECT) is the main method usually adopted to treat TRS and other treatment-resistant symptoms such as obstinate auditory hallucinations, severe delusions, stupor, and high excitation. However, there are rare studies that have reported brain alterations induced by mECT.

After systematically searching the PubMed database, we identified four studies reporting the brain features of patients with TRS and potential alterations, including structural, functional, and brain-network alterations following mECT treatment.

Huang et al.[1] reported that increased global functional connectivity density (gFCD) within the default mode network might be an important neural mechanism of mECT in schizophrenia. In these researchers’ sample, they observed mECT-induced gFCD increases in the left precuneus, the ventral medial prefrontal cortex, and the dorsal medial prefrontal cortex. Thus, these effects may be the neural mechanisms underlying the effect of mECT on TRS. Increases in gFCD reflect greater connectivity and thus communication between these regions and the entire brain. The findings of Huang et al. suggest that mECT can normalize otherwise aberrant communication between brain regions in patients with TRS.

Thomann et al.[2] reported that increased functional connectivity and decreased functional activity co-existed in the brains of patients with TRS.

Wolf et al.[3] reported that increased structural connectivity was not associated with clinical improvement in schizophrenia. Notably, in the subgroup analysis, schizophrenic patients demonstrated that increased volume in the lateral prefrontal/cingulate cortical network subsequent to mECT was associated with clinical improvement. This study investigated structural network alterations among TRS patients who received mECT treatment. This study provides strong evidence that mECT can cause alterations to the brain’s structure.

Another study conducted 24 years ago by Devanand et al.[4] observed that the passage of electricity, thermal effects, and the transient disruption of the blood-brain barrier during mECT did not cause structural damage to the brain. However, these researchers did not report structural alterations to the brain in their study. In the aforementioned three studies, all reported structural increases or decreases in the brains of TRS patients following mECT. Unfortunately, all the clinical information of the aforementioned studies had high heterogeneity.

Collectively, the available research indicates that mECT can induce increased grey matter in certain brain regions. However, mECT-induced functional connectivity adhered to a more complex pattern with coexisting increases and decreases. Decreased functional connectivity was observed in the cortical cortex, and increased functional connectivity was observed in the subcortical regions.

Currently, a more widely accepted hypothesis is that schizophrenia is accompanied by diffuse impairment of functional connectivity, with circumscribed hyperconnectivity superimposed over hypoconnectivity and with inter- and intra-regional dysfunction coexisting.[9] Moreover, topological alterations of brain networks in schizophrenia are presented as reduced local network connectivity and modular structure. Although functional alterations may have an anatomical basis, functional and structural alterations are not necessarily coupled.[5] The aforementioned studies, which have aimed to investigate brain network alterations induced by mECT, can also provide some clues for exploring brain network alterations in TRS, although the number of studies is small and the heterogeneity higher.

To the best of our knowledge, we have reviewed the available literature regarding the brain features of TRS. However, because the associated studies are rare and the heterogeneity among these studies is higher, we cannot draw a convincing conclusion. Therefore, in the future, we propose to conduct a well-designed follow-up study to

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dynamically characterize the trajectory of brain features in patients with TRS receiving different mECT treatment regimes.

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**Conflicts of interest**
There are no conflicts of interest.

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