学位論文の要旨

Abstract of Thesis

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学位論文題目 Title of Thesis（学位論文題目が英語の場合は和訳を付記）

Studies on Electroencephalogram Oscillatory and Brain Connectional Abnormalities for Schizophrenia
（統合失調症の脳波振動と脳コネクションの異常に関する研究）

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Schizophrenia is a serious illness endangering human health, which is one of the most common and unexplained severe psychiatric diseases. According to the World Health Organization's April 2018 report, more than 23 million people worldwide suffer from schizophrenia disease. Most of the patients with schizophrenia are young and middle-aged, the neural mechanism underlying this deficit is unknown, and intervention of high-risk groups in the early stage of schizophrenia can have a better therapeutic effect, so the study on the difference between ultra high risk for psychosis criteria and first-episode schizophrenia is important for analyzing the pathogenesis and early intervention of schizophrenia.

In part 1, to investigate whether face-specific perceptual processes are influenced in schizophrenia patients, both face detection and configural analysis were assessed in normal individuals and schizophrenia patients by recording electroencephalogram (EEG) data. Here, a face processing model was built based on the frequency oscillations, and the evoked power (theta, alpha, and beta bands) and the induced power (gamma bands) were recorded while the subjects passively viewed face and nonface images presented in upright and inverted orientations. The healthy adults showed a significant face-specific effect in the alpha, beta, and gamma bands, and an inversion effect was observed in the gamma band in the occipital lobe and right temporal lobe. Importantly, the schizophrenia patients showed face-specific deficits in the low-frequency beta and gamma bands, and the face inversion effect in the gamma band was absent from the occipital lobe. All these results revealed face-specific processing in patients due to the disorder of high-frequency EEG, providing additional evidence to enrich future studies investigating neural mechanisms and serving as a marked diagnostic basis. In addition, this study constructed time-varying complex electrophysiological network to reveal brain mechanism. The first experiment revealed that schizophrenia patients showed decreased long-range connection and increased clustering coefficient only in upright faces condition in gamma (30-45 Hz) band, compared with healthy controls. This result showed that

disrupted holistic processing is the main cause of abnormal face processing in schizophrenia. The first experiment demonstrated that healthy old people showed increased long-range connectivity in audiovisual condition in beta (14-30 Hz) band, compared with healthy young people. This result suggested that old people need more cognitive resources to complete the task, especially in beta band.

In part 2, we investigate electrophysiological activities during resting-state in four groups (first-episode schizophrenia, FES, family-high risk for psychosis, FHR, ultra-high risk for psychosis, UHR, healthy controls, HC) by EEG. Abnormal functional connectivity is assumed to underlie neurocognitive deficits in patients with schizophrenia. As individuals with an ultra-high risk for psychosis have neurocognitive deficits that are mainly reflected in the alpha rhythm, the identification of neural networks is essential to our understanding of the disorder. We investigated the functional connectivity of the alpha rhythm during resting state EEG as a potential biomarker of ultra-high risk and schizophrenia and explored correlations between cognitive functioning and clinical symptoms. The participants included 28 patients with first- episode schizophrenia (FES), family-high risk for psychosis(FHR), ultra-high risk for psychosis (UHR), and 28 healthy controls (HC). The participants underwent a structured clinical interview to assess symptoms and completed a computerized battery to assess the major domains of neurocognitive functioning. Resting state EEG was recorded for 3 minutes under eyes-closed conditions. The data were segmented into 3second artefact-free epochs, and the functional connectivity of the alpha phase was estimated using the phase lag index (PLI), which captures the true synchronization of EEG signals. The FES and UHR groups displayed increased resting-state PLI connectivity compared with the HC group ($F(2,74) = 10.804$, $p < 0.001$). Significant increases in the global efficiency, the local efficiency and the path length of networks were found in the FES and UHR groups compared with those of the HC group. SZ and UHR showed an increased degree of connectivity compared with HC. The degree of the left occipital lobe area was higher in the UHR group than that in the FES group. The hypothesis of disconnection is confirmed. Furthermore, differences between the UHR and FES group were found, which is valuable for producing clinical significance before the onset of schizophrenia.

In part 3, we studied the self-referential memory (SRM) task was performed by 18 schizophrenia patients and 18 healthy controls. In the encoding stage of the SRM task, the behavioral experiment data and electroencephalogram (EEG) data were recorded in three experimental conditions (self-referential condition, other-referential condition, and physical condition). For data analysis, the electrophysiological performance of the time-frequency distribution, phase lag index (PLI) strengths, phase synchronization connectivity, and brainnetwork properties were assessed in schizophrenia patients compared to healthy controls. We found that schizophrenia patients exhibited abnormal alpha oscillation characteristics at the time of 100–300 ms poststimulus during the self-referential condition, which consisted of diminished time-frequency distributions over the prefrontal, parietal, and occipital regions; lower functional connectivity strengths of the PLI in the parietal and occipital areas; higher global efficiency and the lower characteristic path length; and nodal efficiency of local areas (increased nodal efficiency in temporal regions and decreased nodal efficiency in occipital

region) for dynamic network topology properties. Furthermore, the evoked power of the alpha band during the self-referential condition was significantly correlated with the SRM bias score in the patients ($r = 0.595$, $p = 0.009$). These results provided electrophysiological evidence and supported the hypothesis that an abnormal alpha rhythm might be the principal factor of dysfunctional self-referential processing in schizophrenia patients.

Through the above analysis, this study explores that the modulation frequency band of the characteristics of short face processing time and high energy, and the abnormal alpha Oscillatory might be the principal factor of dysfunctional self-referential processing in schizophrenia patients. The frequency modulation mechanism explains the advantages of schizophrenia neural mechanisms. In addiction, using two brain network construction methods, innovatively obtain abnormalities in the occipital region of patients with clinically high-risk population and first-episode schizophrenia, and support the hyper-connection of synaptic remission disorders in schizophrenia patients during brain development. The hypothesis provides the possibility of early detection and early intervention of schizophrenia. This paper explores the mechanism of face processing, self-referential processing and the characteristics of early brain electrical abnormalities in schizophrenia, and adds new factual evidence for the pathogenesis of schizophrenia. It also provides a direction for neurofeedback regulation to alleviate the psychological state of patients with schizophrenia.