Insular Dysfunction Reflects Altered Between-Network Connectivity and Severity of Negative Symptoms in Schizophrenia during Psychotic Remission.

Abstract:
Schizophrenia is characterized by aberrant intrinsic functional connectivity (iFC) within and between intrinsic connectivity networks (ICNs), including the Default Mode- (DMN), Salience- (SN), and Central Executive Network (CEN). The anterior insula (AI) of the SN has been demonstrated to modulate DMN/CEN interactions. Recently, we found that the dependence of DMN/CEN interactions on SN's right AI activity is altered in patients with schizophrenia in acute psychosis and related to psychotic symptoms, indicating a link between aberrant AI, DMN, CEN, and psychosis. However, since structural alterations of the insula are also present during psychotic remission and associated with negative symptoms, impaired AI interaction might be relevant even for psychotic remission and corresponding symptoms. Twelve patients with schizophrenia during psychotic remission (SR) and 12 healthy controls were assessed using resting-state fMRI and psychometric examination. High-model-order independent component analysis of fMRI data revealed ICNs including DMN, SN, and CEN. Scores of iFC within (intra-iFC) and between (inter-iFC) distinct subsystems of the DMN, SN, and CEN were calculated, compared between groups and
correlated with the severity of symptoms. Intra-iFC was altered in patients' SN, DMN, and CEN, including decreased intra-iFC in the left AI within the SN. Patients' inter-iFC between SN and CEN was increased and correlated with the severity of negative symptoms. Furthermore, decreased intra-iFC of the left AI correlated with both severity of negative symptoms and increased inter-iFC between SN and CEN. Our result provides first evidence for a relationship between AI dysfunction and altered between-network interactions in schizophrenia during psychotic remission, which is related to the severity of negative symptoms. Together with our previous results, data suggest specific SN/DMN/CEN reorganization in schizophrenia with distinct insular pathways for distinct symptom dimensions.

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