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Functional Connectivity as a Biomarker for Treatment Response in Schizophrenia

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Abstract

BACKGROUND: Schizophrenia is a severe mental illness affecting about 1% of the population. Patients experience positive (hallucinations/delusions), negative (flat affect), and cognitive (memory deficits) symptoms that often lead to profound disability. The treatment of schizophrenia with antipsychotic drugs helps some of the symptoms, but these medications are associated with profound side effects and a high rate of treatment noncompliance. Currently, it is not possible to identify patients who will respond to antipsychotic drugs early in treatment; one way to do this would be to find a biomarker, or indicator, of early treatment response. Previous studies of the effects of antipsychotic drugs in schizophrenia suggest that changes in functional connectivity may be a biomarker for treatment response. We therefore sought to characterize differences in VTA FC between unmedicated patients with schizophrenia and matched healthy controls and to identify changes in VTA FC in patients with schizophrenia following one week of APD treatment to test the hypothesis that changes in VTA FC in the early stages of APD treatment would predict treatment response. METHODS: 21 unmedicated patients with schizophrenia (SZ0) and 21 matched healthy controls (HC) were scanned using resting-state fMRI. SZ0 were scanned while unmedicated and after 1 week of treatment with risperidone. After data preprocessing, FC maps were created for the VTA using the Pearson's correlation coefficient between the ROI time series and all other brain voxels. FC maps were compared using a factorial random effects model to assess changes in VTA FC between participant groups, and reported for a false discovery rate-corrected p-value less than 0.05. RESULTS: VTA FC was found to decrease in SZ0 compared to HC in the dorsal anterior / middle cingulate cortex, thalamus, precuneus, and fusiform gyrus. Following one week of APDs, VTA FC increased to the thalamus and fusiform gyrus. This pattern indicates that some of the FC abnormalities observed in SZ0 are reversed following one week of APD treatment. FC between the VTA and dorsal anterior cingulate cortex was correlated with good treatment response, while FC between the VTA and default mode network was correlated with poor treatment response. This suggests that previously reported changes in default mode network FC in schizophrenia may be mediated by the VTA.

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