Abnormalities in the effective connectivity of thalamocortical circuitry in schizophrenia

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Background: Abnormalities in both the structure and function of key sensory regions may underlie some of the symptoms defining schizophrenia. Notably, recent work has identified structural abnormalities in visual processing regions in schizophrenia. Similarly, reductions in regional homogeneity (ReHo) and fractional amplitude of low frequency fluctuations (fALFF) have also been observed in the occipital regions. Furthermore, a recent large-scale study highlighted the thalamus as the major hub for network abnormalities in schizophrenia. In the current study, we sought to identify specific abnormalities in sensory and thalamic circuits that may underlie the myriad of symptoms and impairments characterized by the disorder, and whether these patterns discriminate patients from healthy controls.

Methods: We used resting fMRI data of 70 controls and 62 schizophrenia patients from the Centre for Biomedical Research Excellence (COBRE) dataset. Following standard preprocessing, data were subjected to ReHo and fALFF analyses to identify regions showing differences between patients and controls. We then used the region of ReHo and FALFF reduction overlap as a seed region for Granger causality analysis (GCA) to identify group differences in the effective connectivity between the cuneus and corresponding visual thalamic nuclei (according to the Oxford thalamic probability atlas). A second GCA was seeded from the thalamus to explore for bidirectional effective connectivity differences within the thalamocortical loop. Using a multiple kernel learning (MKL) approach, we explored whether patterns of local and effective connectivity can accurately differentiate controls from patients.

Results: The cuneus of the occipital lobe (and a portion of precuneus) showed significant concomitant reduction of ReHo and fALFF in patients. The effective connectivity between this region and the thalamus was significantly reduced in patients in both directions. These results suggest an abnormally low signal amplitude, local dysconnectivity as well as reduced thalamic connectivity of this sensory region in schizophrenia. The MKL classifier showed that patterns of ReHo discriminated patients from controls with the highest level of accuracy of 80.32% compared to the other measures. Furthermore, combining modalities of ReHo and GCA in the classifier provided similar accuracy of 78.99%.

Conclusions: Our results corroborate previous findings of aberrant connectivity of the thalamocortical circuitry in patients with schizophrenia. Moreover, our data suggests that the abnormally reduced inflow and outflow of visual information toward the corresponding thalamic nuclei, may have underlying local dysconnectivity as indexed by ReHo and fALFF. Investigating both regional as well as long-range connectivity may offer insight into the complex pathophysiology of schizophrenia that gives rise to the diverse symptomatology. Further, there is potential for classification approaches in revealing neurobiological markers for schizophrenia from resting state data.