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Structural abnormalities revealed by a finer cortical parcellation in schizophrenia

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Introduction: Schizophrenia is a major psychiatric disorder characterized by psychotic symptoms. Previous research has discovered important alterations in the brain of schizophrenia patients compared to that of healthy controls via neuroimaging. Neuroimaging approaches are useful for providing information about the organization of the brain cortex, which enables to map the topography of cortical regions, thus shedding light on how various brain regions are involved in certain activities and how they function as a system. Investigating the cortical structure with different structural measures leads to more information on the brain characteristics.

Aim of the study: Several brain atlases consisting of about 60 regions of interest (ROI) have been used in neuroimaging studies. However, analyzing the brain cortex at a finer level could enable more detailed analysis and provide a more advanced model of how the brain is differently organized in a target group. We aimed to utilize a modified brain atlas with a finer cortical parcellation (N=308) in analyzing the cortical structure of the brain.

Methods: We obtained T1 and diffusion-weighted images of 190 schizophrenia patients and 239 healthy controls from four study sites. We parcellated the brain cortex into 308 ROIs using the modified atlas based on the Desikan-Killiany atlas. Cortical thickness, surface area, gray matter volume, and curvature from T1-weighted images were calculated using FreeSurfer (ver 7.1). In addition, fractional anisotropy (FA) and mean diffusivities (MD) values were derived from diffusion-weighted images using DTIFIT in the FMRIB's Diffusion Toolbox. For adjusting the use of different image databases, we applied the ComBat harmonization to each structural measure. Linear regression was used to compare the differences in the structural measures between schizophrenia patients and healthy controls, including age, sex, and the interaction effect of age and sex as covariates. Between-group differences were adjusted using the Bonferroni correction, which accounted for the number of ROIs and structural measures.

Results: Significant differences in gray matter volume, cortical thickness, Gaussian curvature, FA, and MD were found between schizophrenia patients and healthy controls. Gray matter volume was lower in schizophrenia patients in the left lateral orbitofrontal, lingual, postcentral, supramarginal, and precuneus areas; and in right inferior-temporal, middle temporal, superior temporal, and supramarginal areas. Cortical thickness was decreased in schizophrenia patients in the left middle temporal, precentral, supramarginal areas; and right precentral and supramarginal areas. Gaussian curvature was larger in schizophrenia patients in the left paracentral and right fusiform cortex. The FA was lower in schizophrenia patients in the left middle temporal area and right lateral orbitofrontal, middle temporal, superior frontal, superior temporal, supramarginal areas. The MD was increased in schizophrenia patients in the left middle temporal, precentral, and pars orbitalis areas; and right caudal middle frontal, lateral orbitofrontal, rostral anterior cingulate, and pars triangularis areas.

Conclusion: There were significant structural abnormalities in the brain of schizophrenia patients compared with that of healthy controls, and with a finer level of cortical parcellation, it was possible to investigate the structural abnormalities in the brain of schizophrenia patients in more detail.

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Mapping functional connectivity in the visual target-detection network

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Background: Early visual information processing and higher-order cognitive processes like working memory and attention are considerably intertwined. This is exemplified by the interplay of visual areas with the bottom-up attention network during target detection. Hence, studying functional interactions between early visual areas and regions closely involved in higher order cognitive processes are of particular importance. However, the underlying functional connectivity patterns are not fully understood. Therefore, we aimed to investigate the interplay between early visual and higher-order brain areas during a target-detection task.

Methods: 50 healthy participants underwent fMRI in a 3 T Siemens Trio scanner. A target-detection task consisting of a series of flickering black-and-white-colored round shaped checkerboard stimuli subtending 0.3 degrees of visual angle was employed. Every two seconds, the checkerboards position switched among one of the possible quadrants. Each of the positions were located at equidistant points on an imaginary circle surrounding a central fixation cross. Thus, checkerboards appeared at homologous positions in each visual quadrant. The whole array subtended 2.4 degrees of visual angle. At random intervals, two centrally located squares of the checkerboards changed their color to yellow (target trials). Participants had to indicate by button press the detection of these targets. Throughout the task participants had to fixate a black, x-shaped fixation cross at the center of the screen. Overall, task duration was 5.5 minutes. Data analysis in BrainVoyager included standard data pre-processing. Additionally, we used a multiscale curvature driven cortex-based alignment procedure mitigating interindividual macro-anatomical correspondence. Functional data were analyzed using a random-effects multi-subject general linear model (GLM). We assessed functional connectivity using the instantaneous term of Granger causality mapping (GCM).

Results: Subjects' target detection rate was approximately 95%. For each visual quadrant, our GLM yielded clear circumscribed activations at the stimulus position across early visual areas. During target trials widespread activity was observed in a network comprising ventrolateral and dorsolateral prefrontal cortex (DLPFC), supplementary motor area and the lower right visual quadrant. In addition, GCM revealed consistent patterns of functional connectivity between bilateral anterior insula, somatosensory regions, right motor cortex and each visual quadrant during target presentation at that quadrant. Moreover, GCM revealed asymmetries regarding connectivity patterns in the form of a rightward bias. Here, the strongest connectivity pattern was observed between higher-order target detection networks like the DLPFC and temporoparietal junction and regions processing stimuli in the lower right visual quadrant.

Discussion: Our results confirm the central involvement of the insula in modulating attentional control and its close interactions with early visual areas. Furthermore, we found tentative evidence for differences regarding interactions between visual hemifields and higher-order cognitive areas in the form of a rightward bias. Our paradigm appears to be suitable to study interactions between early visual areas and regions supporting higher-order cognitive processes as well as disturbances of these interactions in neuropsychiatric disorders such as schizophrenia and autism spectrum disorder. Simultaneously, our paradigm functions as a time-efficient localizer to map regions in early visual areas for the analysis of more complex cognitive tasks using machine-learning algorithms.

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