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### **Functional connectivity in patients with schizophrenia and controls during working memory task performance**

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Individuals with schizophrenia reliably show abnormalities in appropriate task-related activation of a network of regions typically implicated in working memory. However, less is known about the degree to which these abnormalities reflect disturbed functional connectivity among the critical elements of the working memory network. The purpose of the study was to examine possible schizophrenia related differences in functional connectivity during performance of verbal and non-verbal working memory tasks using three approaches: 1) across participants, reflecting individual differences in the degree to which participants are able to co-activate regions involved in the working memory network; 2) within-subjects across time during task performance, reflecting the trial by trial fluctuations in the coordinated activity of regions involved in working memory; and 3) within-task based on group-averaged timeseries, examining subject-invariant characteristic of the timeseries. fMRI data during performance of word and face 2-back working memory tasks was acquired from 38 individuals with DSM-IV schizophrenia and 38 demographically similar healthy controls. A set of 11 regions (bilateral dorsal lateral PFC, inferior PFC, PPC, cerebellum, thalamus, and ACC) were selected that showed significant activity in both word and face working memory in both patients and controls. Between-subject connectivity analyses indicated reduced connectivity of cerebellar to cortical connections, as well as enhanced connectivity of left DLPFC region to thalamus and right PPC. In contrast, second-level analysis of within-subject correlations revealed reduced prefrontal to parietal connectivity. We also found an interaction for connections within the cerebellum and the cerebellar to right DLPFC connection, with connections being enhanced in words task and reduced in faces task. Group-averaging of timeseries produced similar results, but with added evidence for reduced inter-hemispheric connectivity, most pronounced in task with words. We hypothesize that the reduced within-subject connectivity demonstrated by individuals with schizophrenia reflects impairments in the trial-by-trial ability to appropriately coordinate activity between DLPFC regions and other cortical nodes of the working memory network. In contrast, the changed pattern of between-subject connectivity may reflect the differences in the overall ability to recruit working memory related regions.