Abstract Title: Posterior Parietal Cortex Dysfunction is Central to Working Memory Storage and Broad Cognitive Deficits in Schizophrenia

Prefrontal cortex (PFC) dysfunction is widely believed to underlie working memory (WM) deficits in people with schizophrenia (PSZ), but few studies have focused on measures of WM storage devoid of manipulation. Research in neurotypical individuals has shown that storage capacity is more closely related to posterior parietal cortex (PPC) than PFC, suggesting that reductions in WM storage capacity in schizophrenia that are associated with broad cognitive deficits may be related to neural activity in PPC. In the present human neuroimaging study, 37 PSZ and 37 matched healthy control subjects (HCS) of either sex completed a change detection task with varying set sizes while undergoing functional Magnetic Resonance Imaging. The task was designed to emphasize WM storage with minimal top-down control demands. Whole-brain analysis identified areas in which BOLD activity covaried with the number of items maintained in WM (K), as derived from task performance at a given set size. Across groups, K values independent of set size predicted BOLD activity in PPC, including superior and inferior parietal lobules and intraparietal sulcus, and middle occipital gyrus. Whole-brain interaction analysis found significantly less K-dependent signal modulation in PSZ than HCS in left PPC, a phenomenon that could not be explained by a narrower K-value range. The slope between K and PPC activation statistically accounted for 43.4% of the between-group differences in broad cognitive function. These results indicate that PPC dysfunction is central to WM storage deficits in PSZ and may play a key role in the broad cognitive deficits associated with schizophrenia.