Objectives: Working memory (WM) deficits are among the core cognitive abnormalities in schizophrenia. WM is subserved by widely distributed fronto-parietal networks and is undergoing robust development during adolescence. Studying the neural correlates of WM dysfunction in early-onset schizophrenia (EOS) will advance our understanding of aberrant neurodevelopmental processes in the disorder.

Method: Nineteen patients with EOS aged 13-19 and 20 matched healthy participants underwent functional Magnetic Resonance Imaging (fMRI) as they performed a N-back verbal WM task with 3 levels of difficulty (1-back, 2-back, 3-back). Following matching for task performance, 14 patients were compared to 20 controls, using non-parametric whole brain and region of interest approaches followed by psycho-physiological interaction analysis (PPI) with seed voxel from the left parietal cluster.

Results: Regions within the left prefrontal cortex, the left insula and bilateral anterior cingulate cortex showed reduced activation in EOS patients compared to healthy participants at the 2-back condition. In addition, ROI analysis at the same condition revealed hypoactivation in the EOS group with large effect sizes for left prefrontal and parietal regions. The PPI results revealed negative functional connectivity in the healthy participants’ group but not in EOS between left parietal and right parietal and bilateral frontal regions.

Conclusions: Our results support compromised function within the left prefrontal-cingulate network and left insula during the N-Back verbal WM task in patients with EOS compared to healthy participants. They also indicate the possibility of more widespread fronto-parietal network dysfunction, most noted in the left hemisphere in the disorder.