7 tesla resting-state functional imaging reveals distinct patterns of circuitry underlying specific dimensions of functioning in adolescents with depression

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**Background**: Major depression (MDD) is prevalent in adolescents and the neural underpinnings are poorly understood. New initiatives in psychiatry have emphasized the importance of elucidating brain-behavior relationships underlying specific dimensions of illness. Functional neuroimaging at high magnetic fields offers the opportunity to collect high-resolution data to better characterize neural circuitry and elucidate these important brain-behavior relationships. The purpose of this study was to evaluate resting state functional connectivity (RSFC) under high-resolution conditions to identify anomalies in networks associated with depression. This study focused on amygdala-related networks given recent evidence for their role in being aberrant in MDD.

**Methods**: Adolescents with MDD and healthy controls underwent clinical assessment and 7T brain scanning. Resting-state functional imaging was collected using a multi-band sequence with parameters including 1.5 mm isotropic voxel, TR=1.4s, TE=19ms, MB=3, IPAT=3, 81 slices with 1.5mm isotropic voxel, 270 volumes, 6 minutes. Geometric distortion was corrected then ICA denoising was performed. Seed-based, whole-brain regression was conducted in each subject to measure amygdala RSFC. Higher-level analyses were performed to examine group differences and to measure correlations between whole-brain amygdala RSFC and clinical measures including depression severity, emotion regulation difficulties, temper problems, and social anxiety. Results were corrected for multiple comparisons using AFNI AlphaSim (corrected p < 0.05).

**Results**: Nineteen adolescents completed clinical assessment and neuroimaging; 4 subjects were excluded due to motion or other artifacts, leaving 15 adolescents (10 with MDD, 5 controls) for analysis. Group comparisons revealed amygdala RSFC abnormalities, replicating our earlier work showing impaired amygdala-parahippocampal RSFC and exaggerated amygdala-precuneus RSFC (Cullen et al JAMA Psychiatry 2014). Greater depression severity correlated with lower amygdala-subcallosal cingulate RSFC but higher amygdala-precuneus RSFC. Social anxiety and difficulties in emotion regulation correlated with low amygdala-caudate RSFC, and with greater amygdala RSFC with anterior and posterior cingulate. Emotion regulation difficulties correlated with lower amygdala-superior frontal RSFC. Greater temper problems correlated with lower amygdala-dorsolateral prefrontal RSFC, and greater amygdala-precuneus RSFC.

**Conclusions**: To our knowledge, this is the first study to examine functional networks using 7T fMRI in adolescents with depression. Our amygdala RSFC findings replicate our past work and additionally provide new information illuminating the specific networks implicated in different dimensions of illness. Results from this small study provide the framework for future research confirming the involvement of these specific neural circuits in the diverse dimensions of depression, which can serve as targets for interventions designed to alter these functional systems.