Differential functional network connectivity strength during rest in Williams syndrome.

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Background: Williams syndrome (WS) is a neurodevelopmental disorder arising from hemizygous microdeletion at 7q11.23 and characterized by hypersociability and impaired visuospatial cognition. Previous work has identified multiple loci of abnormal structural (Marenco et al., 2007) and functional (Sarpal et al., 2008) connectivity associated with WS, suggesting that coordinated intrinsic activity across key neural networks may also be impacted by this condition. To test this hypothesis, we compared network connectivity strength, measured with resting state fMRI (rs-fMRI), in children with WS and typically developing (TD) children.

Methods: Children with WS (n=18, age=12±4SD, males=10) and age- and sex-matched TD children were studied in a resting, eyes-open state over 12 minutes with 3T rs-fMRI (TR/TE=2000/24ms, 184 images). Data preprocessing included motion correction, normalization to MNI space, censoring of corrupted volumes, anatomic CompCor, and bandpass filtering (0.008<f<0.1 Hz). Generation of network maps for each individual was accomplished with the dual regression technique as described by Filippini et al. (2009). A concatenated, multi-subject time series was decomposed using ICA yielding 10 group-level network components (MELODIC software). A spatial regression for each component was conducted on each individual’s time series to generate a time course that was used in a second (temporal) regression to generate a participant-specific network map for each component of interest. Resulting participant network maps were masked by the group component map, and the mean value within this mask was extracted for each participant as a measure of the strength of network functional connectivity. These values were compared between groups with t-tests, and Bonferroni correction for multiple comparisons was applied.

Results: Relative to TD children, those with WS showed lower network strength in the default mode network (p<0.009, corrected), dorsal attention network (p<0.03, corrected), and right frontal-parietal network (p<0.05, corrected).

Conclusions: Here we extend past work in WS to show that overall connectivity strength of core neural networks is distinct in WS. These results suggest that the neuro-functional correlates of 7q11.23 microdeletion are not limited to isolated nodes in dorsal stream and social cognitive structures, and support the pursuit of further work to delineate the neurobehavioral corollaries of these findings.