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NEWS

Morphologic, Microstructural, and Connectomic Correlates of Attention Deficit/Hyperactivity Disorder in Adolescents

PURPOSE

To investigate microstructural, morphological, and functional connectivity correlates of ADHD on brain MRI of adolescents.

METHODS AND MATERIALS

We retrieved the imaging and clinical information of 1,830 subjects with ADHD and 6,067 without ADHD from the ABCD (https://abcdstudy.org/) database of 11,876 adolescents - participants' average (SD) age was 118.94 (7.46) months. We excluded those with incomplete clinical information, history of traumatic brain injury, and failure to pass image quality control. In multivariate logistic regression adjusted for age and sex, we examined the association of ADHD with different neuroimaging metrics. The neuroimaging metrics included fractional anisotropy (FA), neurite density (ND), mean-(MD), radial-(RD) and axial diffusivity (AD) of white matter (WM) tracts, cortical region thickness and surface areas from T1-MPRAGE series, and functional network connectivity correlations from resting-state fMRI. We applied False Discovery Rate (FDR) to correct for multiple comparisons. We also optimized, trained, tested, and validated different combinations of machine learning classifiers and feature selection algorithms for prediction of ADHD.

RESULTS

Individuals with ADHD had a significantly (adjusted $p<0.05$) lower FA and ND but higher MD and RD - predominantly in left hemispheric WM tracts compared to those without ADHD. Presence of ADHD was associated with reduced cortical regions, especially in the right middle temporal gyrus (adjusted $p<0.001$). The auditory-, cingulo-parietal, ventral-/dorsal-attention and default-network differed between those with and without ADHD. In repeated 10-fold cross-validation, a combination of elastic net logistic regression with hierarchical clustering feature selection yielded the highest and most stable performance, attaining an AUC of 0.6085, 95% CI [0,5757, 0,6414], in predicting ADHD in an independent validation set.

CONCLUSIONS

Abnormal functional connectivity, involving networks related to memory processing, tonic alertness, and the auditory process, thinning of brain cortex, and WM tract neural fiber loss and microarchitectural disintegrity are markers of adolescents' ADHD. Multimodal neuroimaging metrics can be used as input for machine learning models to support identification of at-risk children.

CLINICAL RELEVANCE/APPLICATIONS

Using a large population cohort, we elucidated the underlying neurobiology of adolescents' ADHD and suggest a possible role for neuroimage-based machine-learning models to assist with diagnosis.