

Functional Connectivity Signatures of Polygenic Depression Risk in Youth

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Abstract : Background: Risks for depression are myriad and include both genetic and brain-based factors. However, relationships between these systems are poorly understood, limiting understanding of disease etiology, particularly at the developmental level. Methods: We use a data-driven machine learning approach connectome-based predictive modeling (CPM) to identify functional connectivity signatures associated with polygenic risk scores for depression (DEP-PRS) among youth from the Adolescent Brain and Cognitive Development (ABCD) study across diverse brain states, i.e., during resting state, during affective working memory, during response inhibition, during reward processing. Results: Using 10-fold cross-validation with 100 iterations and permutation testing, CPM identified connectivity signatures of DEP-PRS across all examined brain states (ρ 's=0.20-0.27, p 's<.001). Across brain states, DEP-PRS was positively predicted by increased connectivity between frontoparietal and salience networks, increased motor-sensory network connectivity, decreased salience to subcortical connectivity, and decreased subcortical to motor-sensory connectivity. Subsampling analyses demonstrated that model accuracies were robust across random subsamples of N 's=1,000, N 's=500, and N 's=250 but became unstable at N 's=100. Conclusions: These data, for the first time, identify neural networks of polygenic depression risk in a large sample of youth before the onset of significant clinical impairment. Identified networks may be considered potential treatment targets or vulnerability markers for depression risk.

Keywords : genetics, functional connectivity, pre-adolescents, depression

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