

A Brain-wide Risk Score for Psychiatric Disorder Evaluated in a Large Adolescent Population Reveals Increased Divergence Among Higher-Risk Groups Relative to Control Participants

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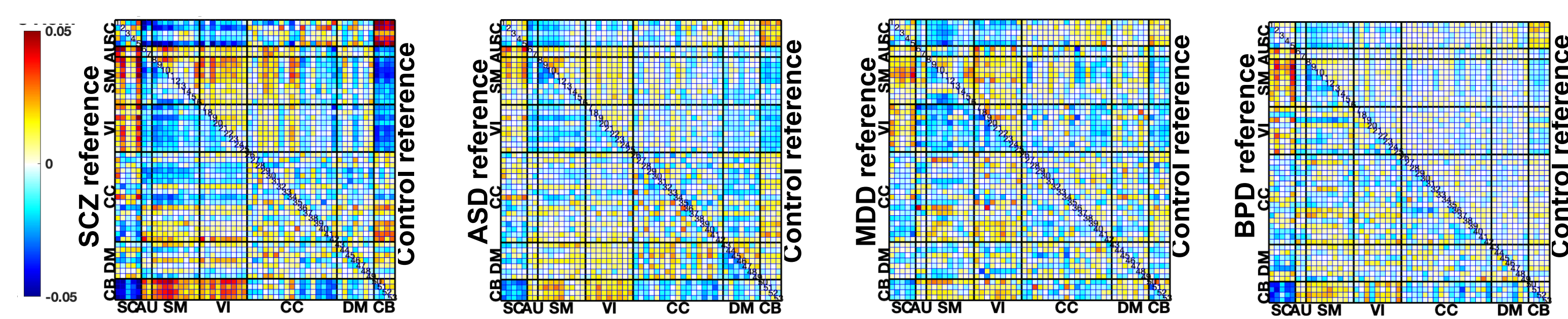
Backgrounds

Accurate psychiatric risk assessment requires biomarkers that are both stable and adaptable to development. Functional network connectivity (FNC), which steadily reconfigures over time, potentially contains abundant information to assess psychiatric risks. However, the absence of suitable analytical methodologies has constrained this area of investigation.

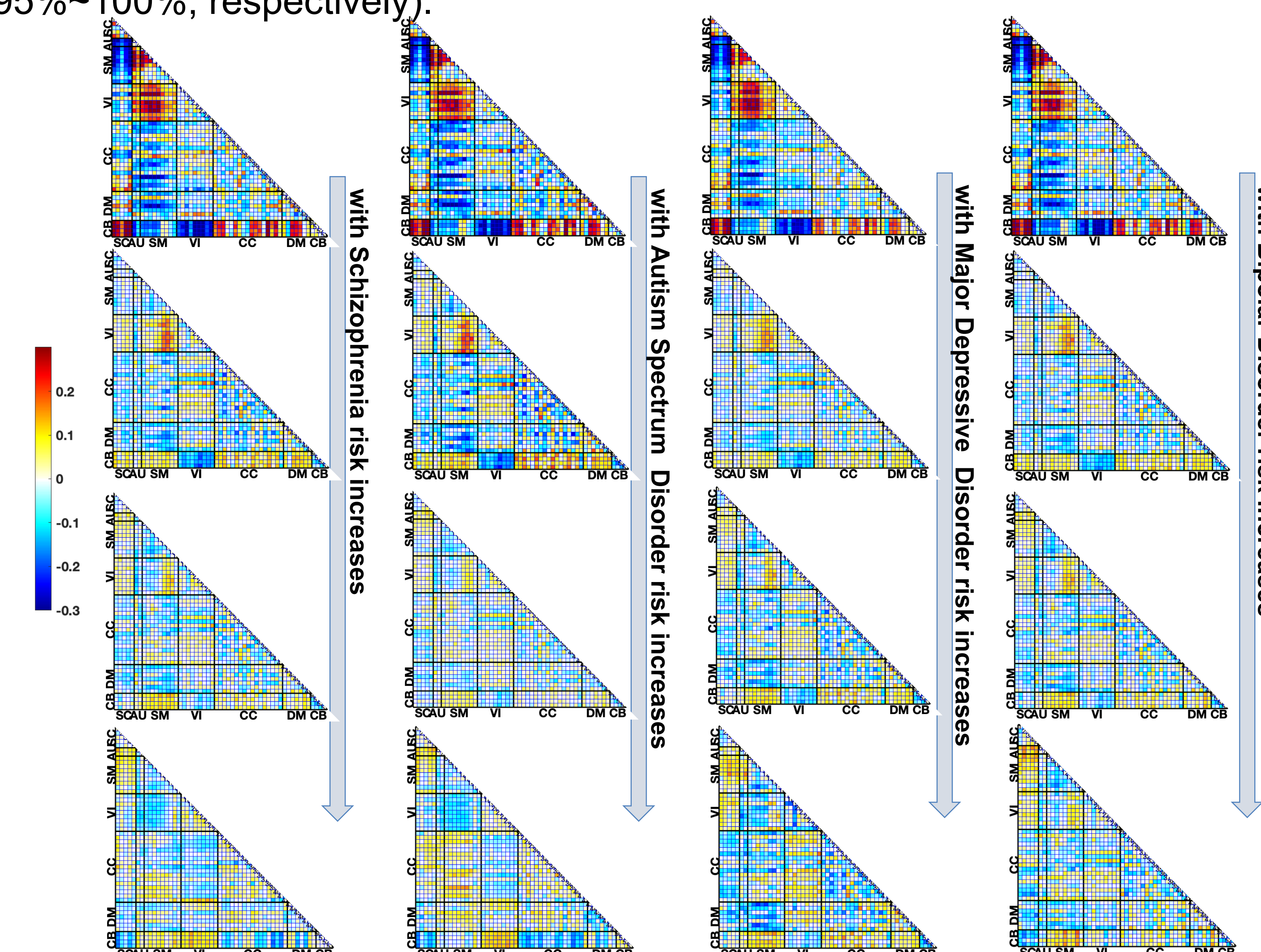
Results

The BRS revealed a clear, reproducible gradient of FNC patterns from low to high risk for each psychiatric disorder in unaffected adolescents. We found that low-risk ABCD Study adolescent FNC patterns for each disorder were strongly present in over 25% of the ABCD Study participants and homogeneous, whereas high-risk patterns of each psychiatric disorder were strongly present in about 1% of ABCD Study participants and heterogeneous. The BRS also showed its effectiveness in predicting psychosis scores and distinguishing individuals with early psychosis from healthy control individuals.

Result 1A. Functional network connectivity (FNC) references generated for each psychiatric disorder. Each figure displays the FNC of a psychiatric disorder in the lower triangle and the FNC of the control group in the upper triangle.



Result 1B. The FNC of ABCD Study baseline quartile, arranged from low risk (top) to high risk (down). All participants are ranked according to their scores for psychiatric risk. Each FNC represents the averaged FNC of 5% of the ABCD Study samples (from top to down, 0%~5%, 20%~25%, 70%~75%, and 95%~100%, respectively).



Materials and Methods

We investigated the brain-wide risk score (BRS), a novel FNC-based metric that contrasts the relative distances of an individual's FNC to that of psychiatric disorders versus healthy control references. To generate group-level disorder and healthy control references, we utilized a large brain imaging dataset containing 5231 total individuals diagnosed with schizophrenia, autism spectrum disorder, major depressive disorder, and bipolar disorder and their corresponding healthy control individuals. The BRS metric was employed to assess the psychiatric risk in 2 new datasets: Adolescent Brain Cognitive Development (ABCD) Study (n = 8191) and Human Connectome Project Early Psychosis (n = 170).

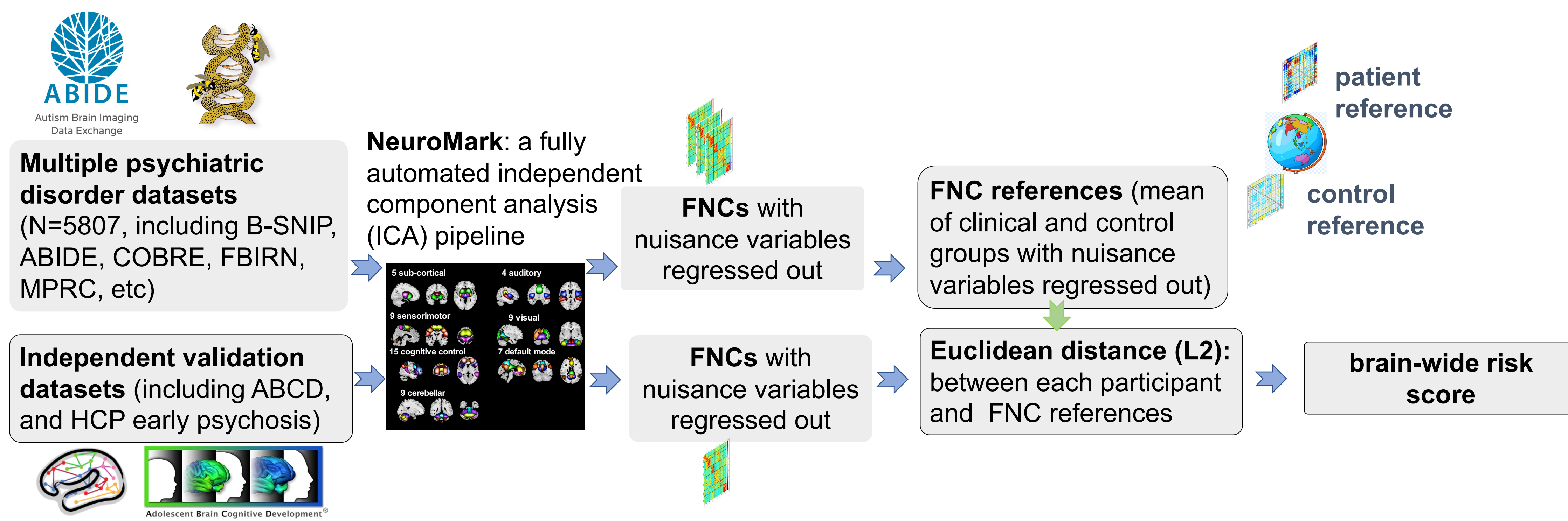
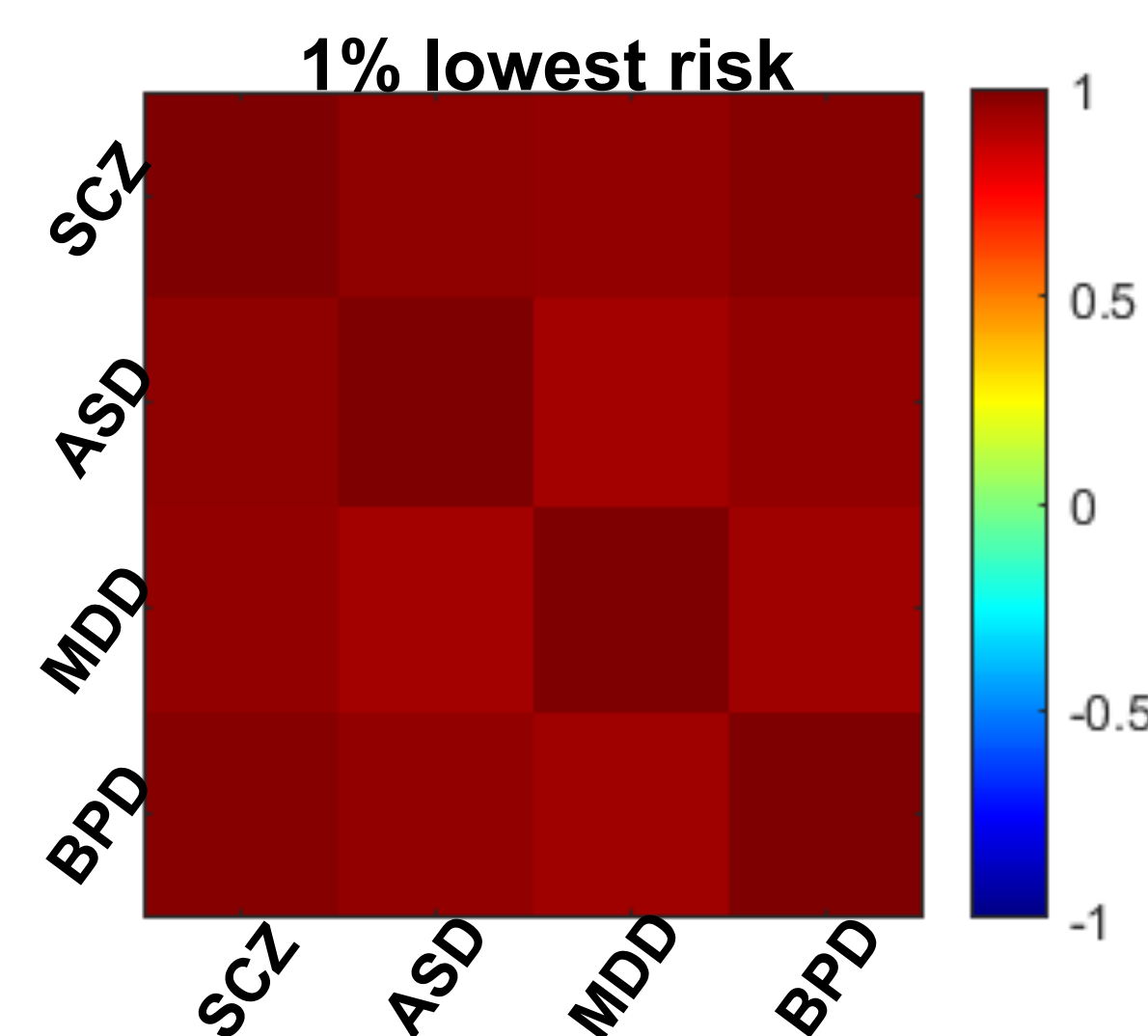
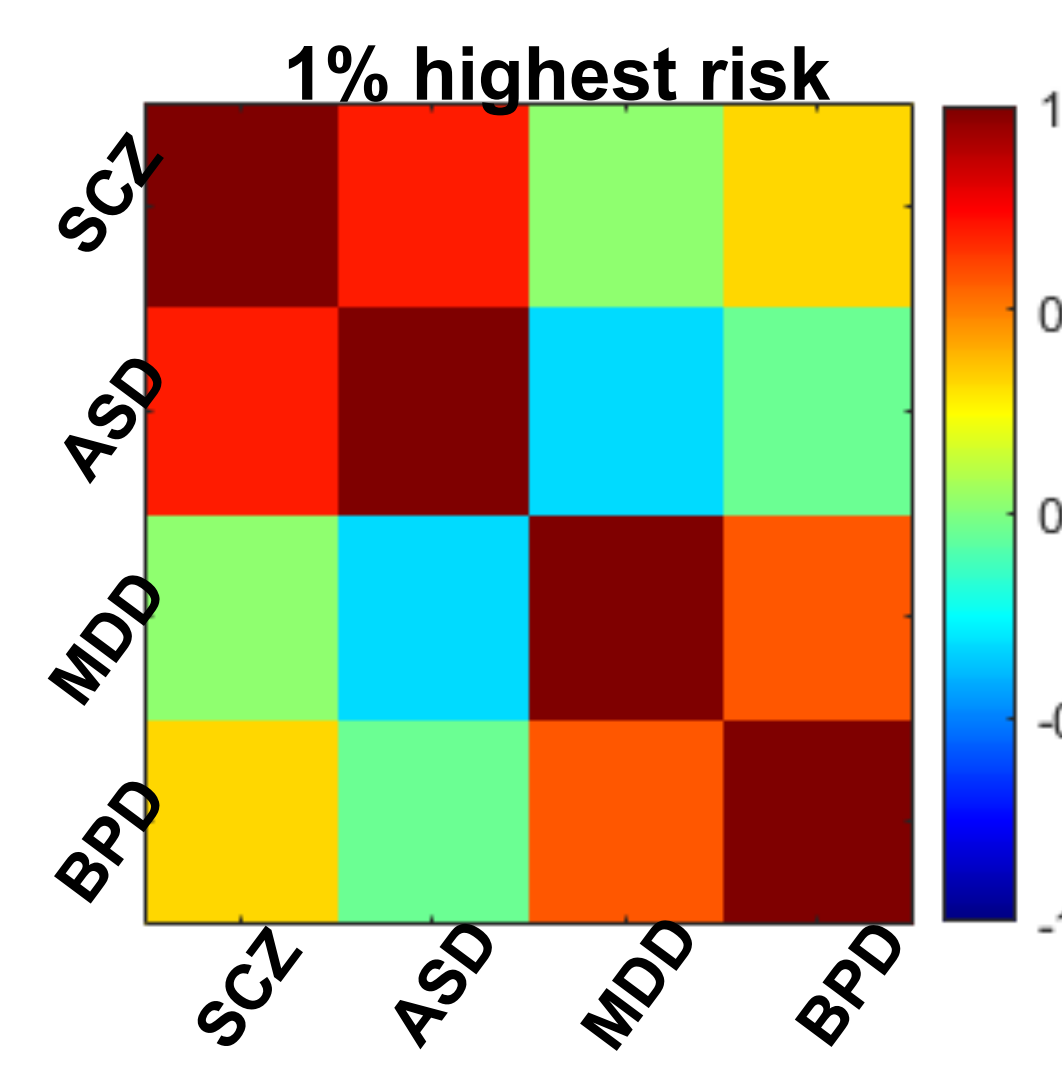


Figure 1. Pipeline for calculating the brainwide risk score. Psychiatric disorder references were constructed using 7 clinical studies. All functional magnetic resonance images (fMRIs) were processed using NeuroMark to obtain comparable functional network connectivities (FNCs). The FNCs were categorized according to diagnosis and were averaged to build references. After preprocessing, the Adolescent Brain Cognitive Development (ABCD) Study and Human Connectome Project (HCP) Early Psychosis FNCs from individual participants were compared with references to obtain brainwide risk scores.

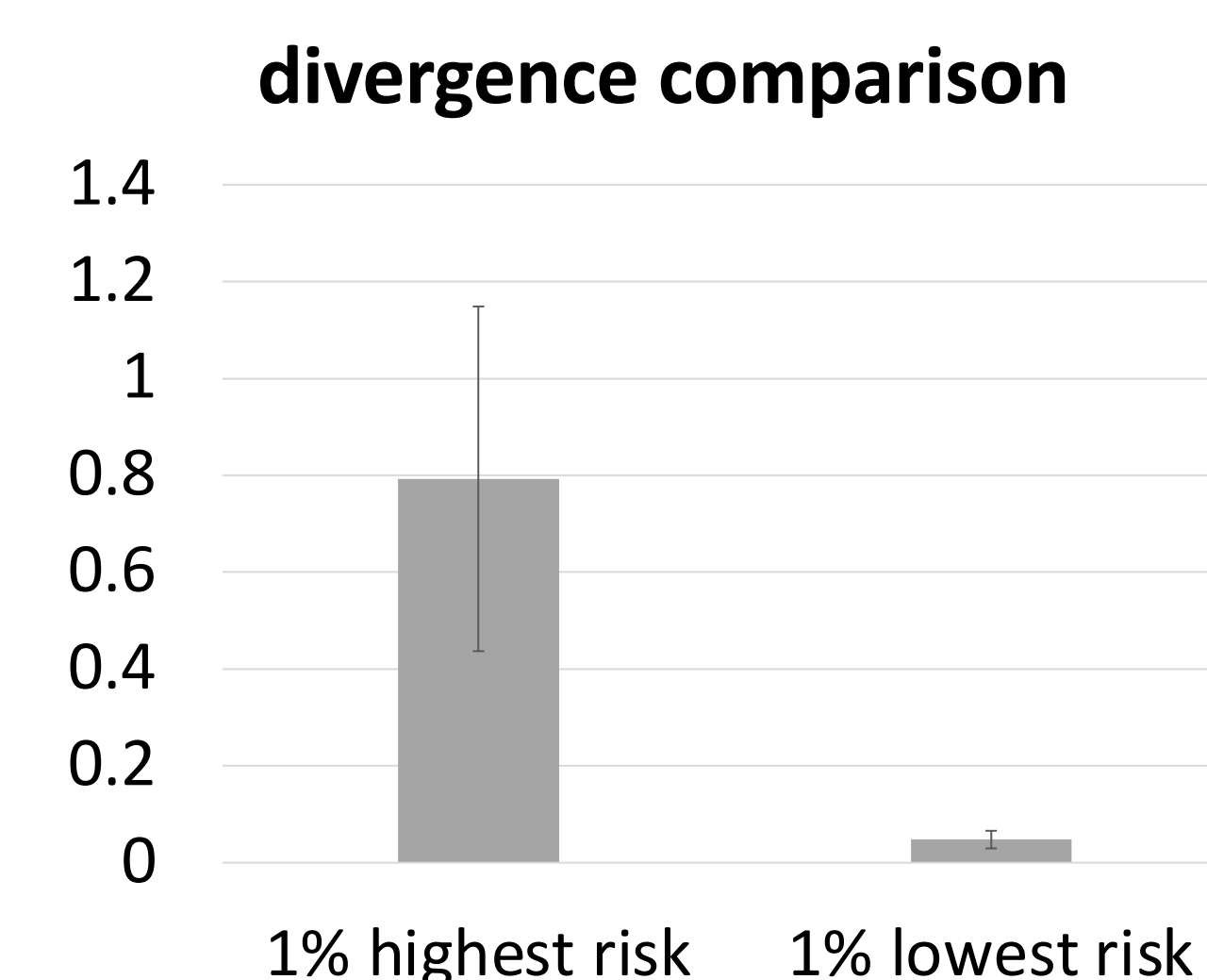
Result 2A. Cross-correlation among 4 psychiatric risk groups within the 1% lowest-risk ABCD Study participants



Result 2B. Cross-correlation among 4 psychiatric-risk groups within the 1% highest-risk ABCD Study participants;



Result 2C. Divergence comparison between the high-risk level and low-risk level.



Conclusions

The BRS could be a new image-based tool for assessing psychiatric vulnerability over time and in unaffected individuals, and it could also serve as a potential biomarker, facilitating early screening and monitoring interventions.

Reference

Yan, W., Pearlson, G. D., Fu, Z., Li, X., Iraj, A., Chen, J., Sui, J., Volkow, N. D., & Calhoun, V. D. (2023). A Brainwide Risk Score for Psychiatric Disorder Evaluated in a Large Adolescent Population Reveals Increased Divergence Among Higher-Risk Groups Relative to Control Participants. *Biological Psychiatry*.

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