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Study Preregistration: Data-Driven Profiles of Youth Executive Function and Their Longitudinal Associations With Externalizing Problems

STUDY SYNOPSIS

Introduction Summary

Youth externalizing problems such as hyperactivity, impulsivity, and aggression often persist into adulthood and predict a range of other problems, evidencing critical need for early detection and intervention. Yet, efforts in these areas have relied almost exclusively on behavioral and clinical data. Recent initiatives, such as the Research Domain Criteria,[1] integrate external validators such as performance on neuropsychological tasks to identify biomarkers. One promising potential biomarker relates to executive function (EF), high-level cognitive skills needed to plan and perform goal-directed behaviors.[2]

Two domains of EF are inhibitory control (IC) and working memory (WM). IC is the ability to override prepotent responses, whereas WM is the ability to mentally manipulate information no longer perceptually present.[2] EF deficits manifest in in most externalizing disorders and symptom domains; however, much is still unknown about the specificity of these associations for both executive performance and externalizing psychopathology. Specifically, past work has focused primarily on externalizing diagnoses and their associations with specific forms of EF (eg, IC). However, there is evidence of both clinical and EF heterogeneity,[3,4] suggesting that externalizing problems are best studied dimensionally, and EF deficits may be better understood through profiles that cross-cut subdomains.

The current study applies exploratory machine learning methods (eg, clustering, data splitting) to identify EF profiles from performance on 2 WM and IC tasks, and their longitudinal associations with externalizing symptom dimensions across early adolescence. We will use 4 waves of data from the Adolescent Brain Cognitive Development℠ (ABCD) Study[5] to identify profiles of EF task performance at the baseline and 2-year follow-up appointments, to explore their characteristics and temporal stability, and to investigate their associations with externalizing psychopathology, both concurrently and longitudinally. Secondary analyses will explore associations between EF profiles and externalizing diagnoses.

Method Summary

Participants. We plan to include 5,501 youth (9-10 years of age at the baseline appointment) from the ABCD Study®, an ongoing prospective study of US youth mental health. Data will be obtained from the ABCD Study 5.1 data release. The ABCD Study was approved by the Institutional Review Board at University of California, San Diego, and all participants provided written informed consent prior to participating. Youth will be included in the current analyses if they have complete data for relevant EF measures at the baseline and 2-year follow-up appointments.

Measures. Externalizing symptoms were assessed with the caregiver-reported Child Behavior Checklist 6-18 (CBCL).[6] We will use narrow band syndrome *t* scores of aggressive behaviors, attention problems, and rule-breaking behaviors, along with the broad band *t* score of externalizing problems. Externalizing diagnoses were made with a caregiver-reported computerized version of the Kiddie Schedule for Affective Disorders and Schizophrenia for *DSM-5* (KSADS-COMP-PL).[7] We will use diagnoses of attention-deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder, and disruptive mood dysregulation disorder for secondary analyses. IC and WM were measured with the Stop Signal Task (SST) and Emotional N-Back (EN-Back), respectively.[8] For both tasks, we will use all condition-level accuracy and reaction time data.

Analytic Strategy. We will split the data into 2 roughly equal groups: a training and a testing set. Next, we will apply principal component analysis to the SST and EN-Back tasks and cluster on the components from both

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tasks to identify profiles of EF performance. These steps will be followed independently for the baseline and 2-year follow-up appointment task data. We will apply 5 common clustering algorithms: k-means, hierarchical agglomerative (Ward linkage), spectral (Cluster-QR), HDBSCAN, and DBSCAN.[9,10] To characterize and evaluate the temporal stability of the identified clusters, we will apply logistic regression with best subset selection and use a similarity metric. Finally, we will use the training set to explore concurrent and longitudinal relationships between the EF profiles and clinical data, which will be subsequently assessed in the testing set to determine their generalizability. All analyses will be performed in Python, with clustering algorithms sourced from the Scikit-learn package.[10]

Significance Summary

The current study will broaden scientific knowledge of how EF is organized and associates with externalizing symptom domains cross-sectionally and longitudinally. Findings may elucidate developmental phenotypes of psychopathology and enhance identification of cognitive mechanisms with the potential to inform future treatment development.

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CRediT authorship contribution statement

Zoë E. Laky: Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Daniel S. Pine:** Writing – review & editing, Conceptualization. **Charles Y. Zheng:** Writing – review & editing, Supervision, Formal analysis, Conceptualization. **Reut Naim:** Writing – review & editing, Supervision, Methodology, Data curation, Conceptualization.

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Code Availability Statement: All code will accompany the final Stage 2 manuscript and be publicly available on our GitHub repository (https://github.com/NIMH-SDAN) upon acceptance.

Data Sharing: Data from the ABCD Study are publicly available and must be requested through the National Institute of Mental Health Data Archive (NDA). Data used in the preparation of this article were obtained from the Adolescent Brain Cognitive Development[SM] (ABCD) Study (https://abcdstudy.org), held in the NIMH Data Archive (NDA). This is a multisite, longitudinal study designed to recruit more than 10,000 children aged 9-10 and follow them over 10 years into early adulthood. The ABCD Study® is supported by the National Institutes of Health and additional federal partners under award numbers U01DA041048, U01DA050989, U01DA051016, U01DA041022, U01DA051018, U01DA051037, U01DA050987, U01DA041174, U01DA041106, U01DA041117, U01DA041028, U01DA041134, U01DA050988, U01DA051039, U01DA041156, U01DA041025, U01DA041120, U01DA051038, U01DA041148, U01DA041093, U01DA041089, U24DA041123, U24DA041147. A full list of supporters is available at https://abcdstudy.org/federal-partners.html. A listing of participating sites and a complete listing of the study investigators can be found at https://abcdstudy.org/consortium_members/. ABCD consortium investigators designed and implemented the study and/or provided data but did not necessarily participate in the analysis or writing of this report. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or ABCD consortium investigators. The ABCD data repository grows and changes over time. The ABCD data used in this report came from NIMH Data Archive https://doi.org/10.15154/z563-zd24.

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