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**First theme choice:** Clinical/Behavioral/Intervention

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**Multivariate Associations between Dimensions of Psychopathology and Brain Volume in Children**

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**Introduction:** The comorbid, dimensional nature of psychopathology seems to be mirrored in related neural substrates, as studies have found similar neural mechanisms to be shared across multiple mental health disorders (1). While the traditional approach to studying psychopathology involves a categorical, case-control approach, there is a growing body of literature proposing that psychopathology can be conceptualized as a hierarchy of dimensional symptom domains (2,3). Further, these symptom dimensions can be related to neurostructural measures to identify common and unique neural substrates across domains of psychopathology. Previous studies using such a dimensional approach have shown inverse associations between psychopathology dimensions and gray matter volume (GMV) (4,5). For example, we recently investigated associations between regional GMVs and dimensions of psychopathology in a large sample of children and found that greater general psychopathology is associated with smaller volume throughout the brain (6). Additionally, we found that specific conduct problems and ADHD symptoms dimensions are also negatively associated with GMV in many regions. However, each brain region was examined independently, which does not allow for identifying which regions cluster together with which symptoms. A multivariate examination of both brain regions and psychopathology symptoms is a pivotal next step in understanding the multifaceted relationships between psychopathology and neurostructural variation during development.

**Methods:** We used data from 8,218 9- to 10-year-old children collected as part of the Adolescent Brain and Cognitive Development (ABCD) Study. Psychopathology was measured with the Childhood Behavior Checklist (CBCL) for school-aged children. Brain volume was acquired using 3T MRI. Partial Least Squares (PLS) analysis was utilized to determine which combination of GMVs maximize their covariance with the psychopathology dimensions. PLS analysis is a data-driven approach that allows for mutual examination of associations among multiple variable sets, which can facilitate the delineation of complex relationships between two different dimensional datasets. Age, sex, and race were included as covariates.

**Results:** PLS analysis yielded one stable latent variable, which explained 97% of the covariance across variable sets. Results suggest that children with higher scores on the general psychopathology factor, but also with scores on the ADHD and conduct problems factors, show smaller volumes across the brain.

**Discussion:** Here we replicate the finding that general psychopathology is associated with globally smaller brains in a large sample of 9- to 10-year-old children. These results suggest that globally smaller GMVs may be a nonspecific risk factor for general psychopathology, and possibly for conduct problems and ADHD. This study demonstrates the usefulness of data-driven approaches for uncovering brain-behavior relationships in children.

**References, if any:**
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**Keywords:**
Psychopathology, Neurostructure, Development