Multivariate Associations between Dimensions of Psychopathology and Brain Volume in Children

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Background

- Childhood is important for brain development (Giedd et al., 1999).
- Mental disorders have high comorbidity, with many symptoms being dimensional, overlapping disorders, and hierarchically organized (Conway et al., 2019; Caspi & Moffitt, 2018; Lahey et al., 2017).
- Despite the dimensional nature of psychopathology, most research surrounding the neural mechanisms of psychopathology has employed case-control designs with a focus on categorically-defined disorders.
- Prior research has shown negative associations between dimensional factors of psychopathology and brain volume (Durham et al., 2021; Kaczkurkin, Park, et al., 2019; Romer et al., 2019; Snyder et al., 2017; Moore et al., 2019).
- However, the majority of these prior studies have used samples with large age ranges, which may obscure developmental changes, and used univariate statistical approaches, which do not allow for identifying which regions cluster together with which symptoms.
- The current research builds upon prior work through the investigation of multivariable associations between brain volume and psychopathology dimensions in a large sample of 9-10 year old children.
- Hypotheses: General psychopathology (as defined by a bifactor model) will be associated with smaller regional gray matter volume (GMV) throughout the brain.

Methods

Participants: Participants included the 9-10 year old children from Wave 1 (release 3.0) of the Adolescent Brain Cognitive Development (ABCD) Study (ABCD Study) (Volkow et al., 2018), which provides a publicly available and fully de-identified dataset.

Psychopathology measure: Psychopathology was measured with the Childhood Behavior Checklist (CBCL) for school-aged children (Achenbach, 2009).

Brain volume measure: Regional gray matter volume (GMV) was defined by automated atlases for cortical (Desikan et al., 2006) and subcortical (Fisch et al., 2002) regions.

Procedure: Parents completed the CBCL to assess for psychopathology symptoms experienced by their children. The child participants completed MRI scanning sessions. Imaging data was acquired at 21 sites using Siemens (Prisma VE118-C), Philips ( Achieva dStream, Ingenia), and GE (MR750, DV25-26) MRI scanners. Image processing was performed by the ABCD Data Analysis and Informatics Center using centralized protocols.

Bifactor analysis: Using 68 items from the Childhood Behavior Checklist (CBCL), an exploratory factor analysis identified three dimensions of psychopathology: internalizing, conduct problems, and ADHD. A confirmatory bifactor analysis was used to model these three factors plus a general factor of psychopathology (Moore et al., 2020).

Brain volume analyses: Partial Least Squares (PLS) analysis, a data-driven multivariate approach, was utilized to determine which combination of GMVs maximize their covariance with the psychopathology dimensions. Age, sex, race/ethnicity, and MRI serial number were included as covariates. One family member from twin or sibling pairs was randomly selected to be excluded from the data prior to conducting the PLS analysis. The final sample size used for the PLS analysis was N = 4,362. This sample was split into a training sample (N = 4,196) and a test sample (N = 4,166) that had similar demographics (i.e. age, education level, income, race/ethnicity).

Results

- General psychopathology was associated with smaller cortical and subcortical gray matter volumes, which is consistent with previous work (Durham et al., 2021; Kaczkurkin, Park, et al., 2019; Romer et al., 2017; Snyder et al., 2017).
- Conduct problems and ADHD symptoms were also associated with smaller cortical and subcortical gray matter volumes, but the relationships were weaker than that of the general factor.
- The current study extends prior work by showing that the association between smaller volumes and greater general psychopathology, conduct problems, and ADHD is apparent at a young age (9-10 years), and also when accounting for multivariate relationships across the datasets.
- This may suggest that reduced gray matter volume is a transdiagnostic risk factor across psychopathology domains.
- These findings can be related to prior research that found a general factor in childhood to be associated with an array of deficits, including deficits in self-control, emotion regulation, and executive functions (Caspi & Moffitt, 2018).
- These findings may serve as a baseline for future longitudinal analyses.

Conclusions

- Consistent with the emerging notion that the general factor may relate to non-specific variation in the brain, the present analyses provide support that the combined effect of general psychopathology, ADHD, and conduct problems (with general psychopathology contributing the most) in childhood is associated with globally smaller brain volumes.
- No evidence of an association between internalizing symptoms and brain volume was observed.
- While limited by a cross-sectional design, this study extends prior work by suggesting that the relationship between reduced gray matter volume and psychopathology is evident at an early age and by demonstrating the merits of taking a multivariate approach to the delineation of brain-behavior relationships.

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