



# Dimensions of Psychopathology Associated with Distinctive Patterns of Cortical Thickness in Youth

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## Background

Psychiatric symptoms emerge early in life and are associated with variations in brain structure. Cortical thickness is influenced by early life stressors and relates to early symptoms of psychopathology. Here, we investigated the association between cortical thickness and psychopathology. We used a bifactor model to derive dimensional factors of psychopathology. Furthermore, we examined the mediating effect of early life stress (trauma exposure) on the relationship between cortical thickness and dimensional factors of psychopathology.

## Methods

**Participants:** Participants included the 9-10 year old children from Wave 1 (release 2.0.1) of the Adolescent Brain and Cognitive Development (ABCD) Study ( $N = 9,672$ , 51% male, 53% White).

**Psychopathology measure:** Using 66 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.

**Trauma measure:** A latent factor of trauma was derived using 13 items from the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) assessing trauma experiences.

**Imaging data:** Imaging data was acquired at 21 sites using Siemens (Prisma VE11B-C), Phillips (Achieva dStream, Ingenia), and GE (MR750, DV25-26) MRI scanners. Imaging processing was performed by the ABCD Data Analysis and Informatics Center using centralized protocols.

**Statistical Analysis:** All analyses were performed using structural equation modeling (SEM) in Mplus with psychopathology and trauma as latent factors. Post-stratification weights were applied to account for stratification of the sample in the data sites. Data was clustered by family since the ABCD study includes twins and siblings. Correction for multiple comparisons was performed using FDR correction.

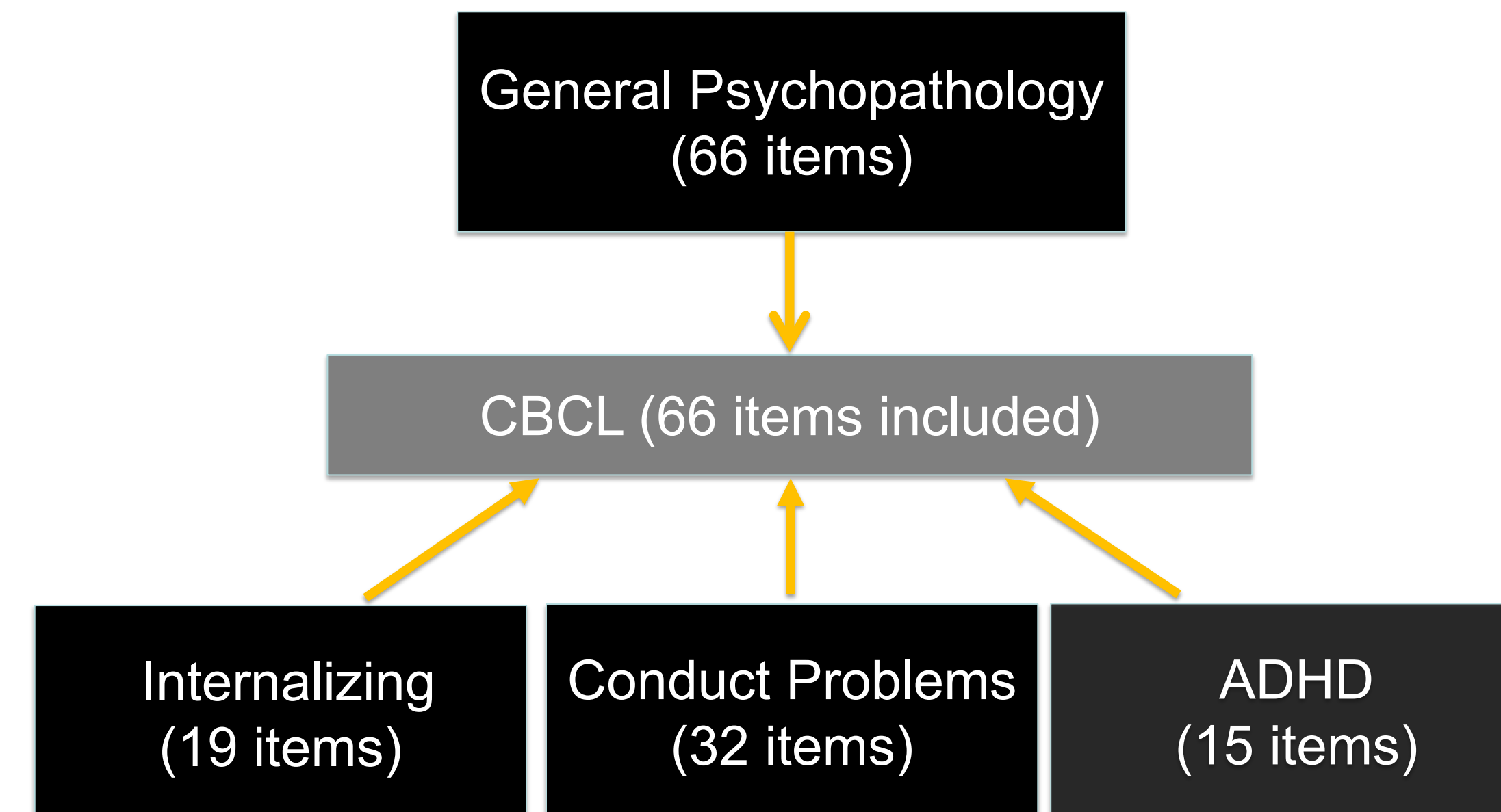
**SEM:** SEM analyses were performed using regional cortical thickness based on the Destrieux atlas with psychopathology factors and covariates of no interest.

regional cortical thickness = age + sex + race/ethnicity + MRI manufacturer + whole brain cortical thickness + general psychopathology + conduct problems + internalizing + ADHD

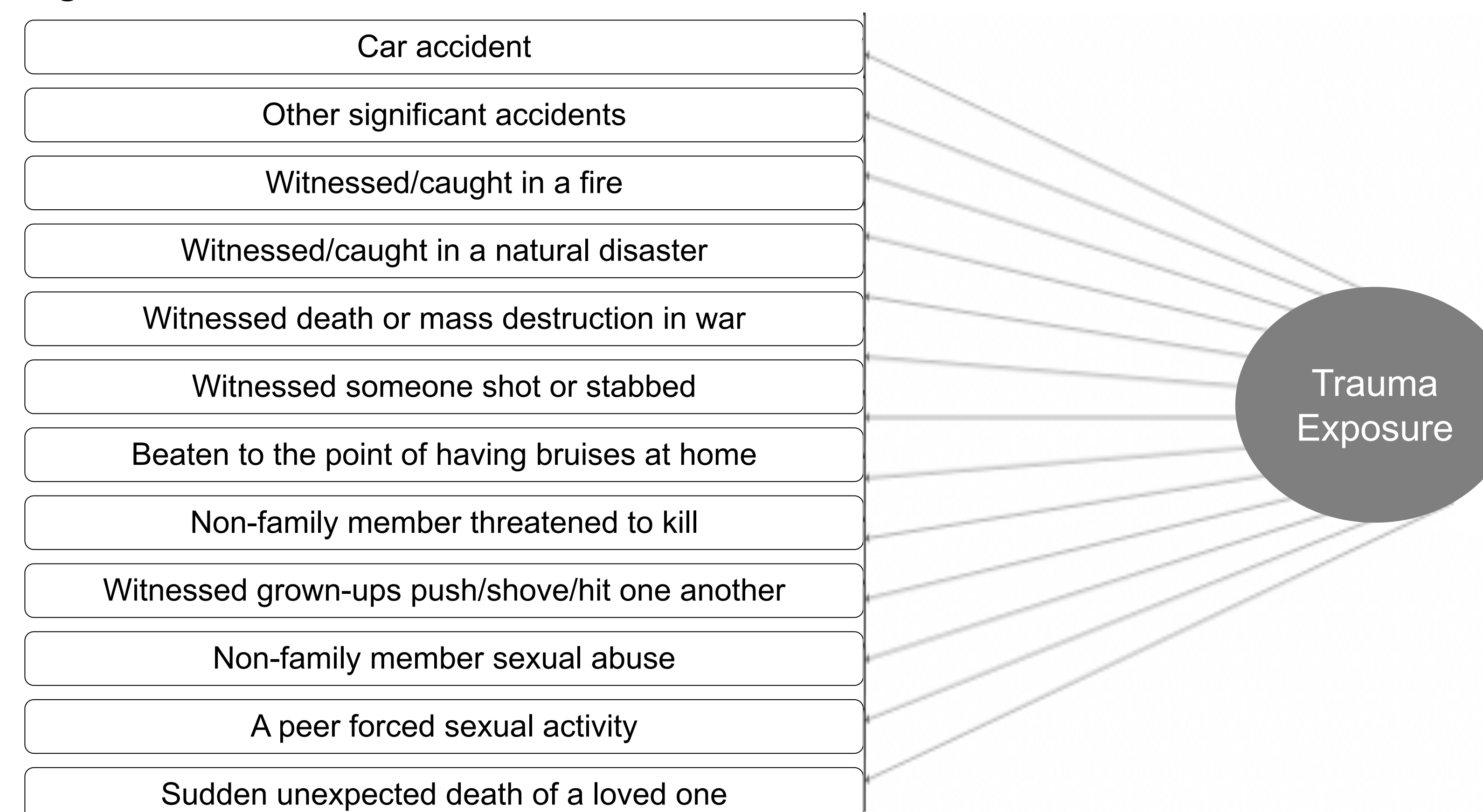
**Mediation:** Mediation analyses were performed using the cortical thickness regions significantly associated with the psychopathology factors identified from the SEM analysis. Trauma was tested as a mediator of the relationship between cortical thickness and psychopathology. The indirect effect was tested with the Mplus INDIRECT command using the delta method, which is similar to a Sobel test in large samples.

## Results

**Figure 1. Schematic of the bifactor model.** A bifactor model identified 4 dimensional factors of psychopathology (general, internalizing, conduct problems, and ADHD). General psychopathology reflects the symptoms shared across all domains. All factors are orthogonal to one another and thus were included in the same model.



**Figure 2.** Items included in the latent trauma variable



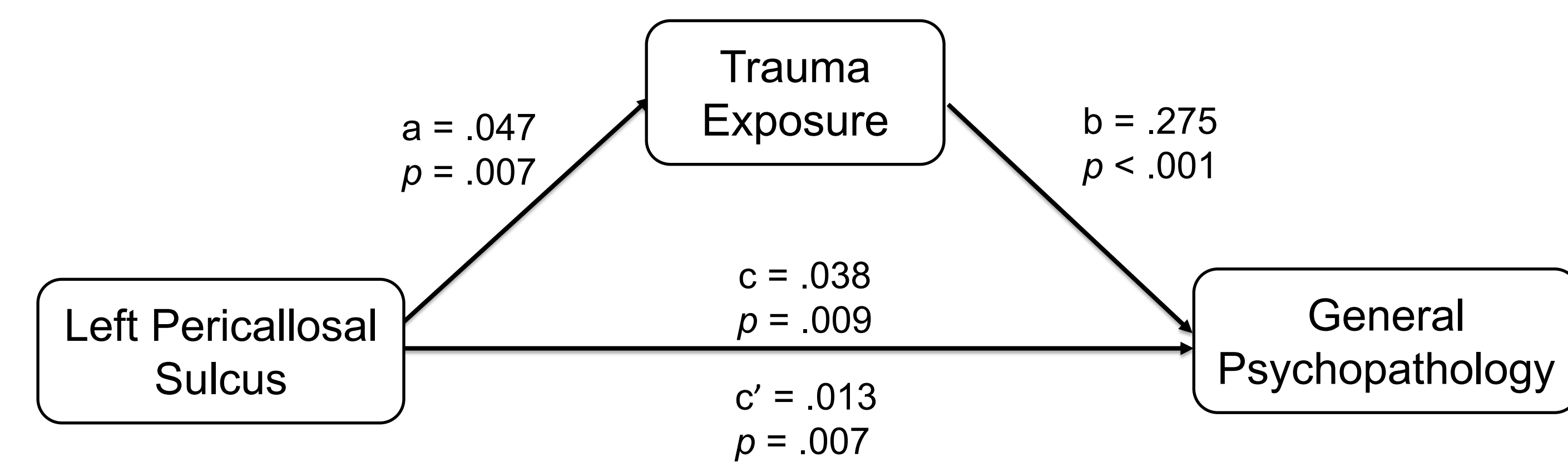
**Table 1.** Results of SEM analyses of the association between dimensional psychopathology factors and regional cortical thickness based on the Destrieux atlas

Region	Factor	$\beta$	SE	Effect Size (t)	p
Left central sulcus	General	-0.049	0.012	-4.25	<.001
Left parahippocampal gyrus	General	-0.040	0.012	-3.39	.025
Left pericallosal sulcus	General	0.038	0.011	3.35	.025
Left postcentral sulcus	General	0.030	0.010	3.20	.025
Right calcarine sulcus	General	0.045	0.014	3.11	.042
Left calcarine sulcus	General	0.047	0.016	3.00	.049
Right anterior segment of the circular sulcus of the insula	General	-0.037	0.013	-2.92	.049
Right pericallosal sulcus	ADHD	-0.068	0.019	-3.54	<.001

Multiple comparison error was corrected using False Discovery Rate ( $p < .05$ )

## Results

**Figure 3.** Mediation of left pericallosal sulcus on general psychopathology by trauma exposure



## Discussion

- Increased general symptoms of psychopathology were associated with reduced cortical thickness in the left central sulcus, left parahippocampal gyrus, and right anterior segment of the circular sulcus of the insula.
- Increased general symptoms of psychopathology were associated with increased cortical thickness in the left pericallosal sulcus, left postcentral sulcus, and bilateral calcarine sulci.
- Trauma exposure was positively associated with general symptoms of psychopathology, supporting the implication that trauma may contribute to non-specific symptoms of psychopathology.<sup>1</sup>
- A mediation analysis indicates that trauma exposure may explain part of the variance in the association between left pericallosal sulcus, which demarcates the inner boundary of the anterior cingulate cortex, and general psychopathology.
- Increased cortical thickness in the left pericallosal sulcus associated with general psychopathology in the early developmental stage may indicate:
  - Slow maturation of cortical thickness characterized by protracted myelination and pruning.<sup>2</sup>
  - Enhanced activation of the region leading to synaptogenesis, which may result in an increase in cortical thickness.<sup>3,4</sup>

## Support & Disclosures

**Disclosure** All authors report no competing interests

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