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TITLE:

Genetic and environmental influences, risk and subcortical brain volume mediation of traumatic stress on posttraumatic stress disorder symptoms in children

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ABSTRACT:

Volumes of subcortical brain regions of interest (ROIs) have been linked to posttraumatic stress disorder (PTSD). The variation for these phenotypes is heritable; although, most of prior research have assessed adults. Using ABCD data (N=11,875, M<sub>age</sub>=9.92) we extend this work to children to test if subcortical brain ROIs mediate the relationship between traumatic events (TEs) and PTSD symptoms (PTSDsx), and to determine the genetic variation and risk for these phenotypes. Volumes of 42 subcortical ROIs based on structural MRI, were modeled as mediators using machine learning methods (e.g., regularization) to reduce overfitting bias, and evaluate the role of numerous mediators using an agnostic approach, to select more parsimonious models. Most of the variance in subcortical volumes (41.73-57.40%) was explained by additive genetic factors. Whereas, environmental factors notably explained most of the variability in TEs (C=.62, E=.15) and PTSDsx (resC=.19, resE=.22). The direct effects of TEs on PTSDsx were high (.92).

However, the indirect effects through the subcortical ROIs with the highest mediation effects (e.g., caudate, lateral ventricles, cerebellum cortex) were small to non-influential (0.001-0.002). Using genome-wide structural equation modeling (gwsem) and polygenic scores, we assess the multivariate architecture, variation, and unique and shared risk, for PTSD and volumes of subcortical ROIs.

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