Neural alterations in threat reversal learning as mechanisms linking childhood trauma and transdiagnostic psychopathology in youth

Stephanie N. DeCross 1, Sahana Kribakaran 2, Paola Odriozola 2, Margaret A. Sheridan 3, Nim Tottenham 4, Dylan G. Gee 2, & Katie A. McLaughlin 1
1 Department of Psychology, Harvard University, Cambridge, MA; 2 Department of Psychology, Yale University, New Haven, CT; 3 Department of Psychology and Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill, NC; 4 Department of Psychology, Columbia University, New York, NY

BACKGROUND

Threat reversal learning is a vastly understudied threat learning process of particular clinical relevance, describing the ability to flexibly update associations of stimuli with threat and safety.

METHODS

Sample: 100 youth (9-19 years old), n=50 with exposure to childhood trauma (physical abuse, sexual abuse, and/or chronic exposure to domestic violence; assessed in a multi-informant, multi-method approach).

FUNCTIONAL CONNECTIVITY

The trauma group displayed elevated connectivity between right hippocampus and ACC and frontal areas during New CS+ > New CS− (new safety learning), driven by elevated connectivity specifically during New CS−. Additionally, greater connectivity between right hippocampus and amygdala during New CS+ > New CS− was associated with elevated PTSD symptoms (p<.01).

DISCUSSION

In default mode network regions, the trauma group displayed blunted discrimination between cues when contingencies were reversed during threat reversal learning, consistent with reduced flexibility in safety signal learning.

In right amygdala, the trauma group displayed elevated response to New CS+ > New CS− across the run. This might suggest increased sensitization to the threat cue and failure of habituation. Curiously, the associations between altered neural response and psychopathology, and related indirect effects in mediation models, were in the opposite direction as expected.

Examining alterations in threat learning processes such as threat reversal learning captures important aspects of real-world learning, like the need to flexibly update threat and safety associations based on environmental contingencies. These approaches hold great promise for translational research and practice, enabling opportunities for the development of novel interventions.

REFERENCES & FUNDING

How does childhood trauma alter neural patterns of activation and connectivity during threat reversal learning in youth in ways that are relevant to mental health?

Mixed effects models showed that trauma predicted patterns of neural response in vmPFC, right and left hippocampus, PHG, and right amygdala.

The group displayed greater activation in amygdala during New CS+ > New CS− (new threat learning).

The trauma group displayed reduced activation in hippocampus and PHG during New CS− > New CS+ (new safety learning) and greater activation in amygdala during New CS+ > New CS− (new threat learning) compared to controls.

Altered patterns of neural activation during threat reversal learning mediated the link between childhood trauma and transdiagnostic psychopathology.

Implicated forms of psychopathology included generalized anxiety, panic, PTSD, depression, and psychosis spectrum symptoms.