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HOT TOPICS

Dimensional approaches to understanding threat conditioning and extinction in anxiety

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The model of threat conditioning and extinction has been used to disentangle the mechanisms underlying how threat is learned and then regulated, through extinction learning. Past studies have demonstrated impaired memory of fear extinction in PTSD and anxiety patients relative to healthy controls [1–3]. Recall of the fear extinction memory is clinically relevant given that exposure-based therapy, which is often used to treat anxiety and fear-related pathologies, relies on the principles of extinction learning. Failure to consolidate and later recall the extinction memory trace would result in elevated fear levels, which would contribute to maintain and/or exacerbate the clinical symptoms.

The Research Domain of Criteria (RDoC) aims to study dimensions of psychopathology across individuals irrespective of their diagnosis. The rationale for this approach is that some dimensions, such as acute threat, cut across diagnoses, suggesting shared mechanisms of psychopathology. Will the RDoC approach provide novel information about the mechanisms of psychopathology?

We exposed 84 individuals suffering from an anxiety disorder and 21 healthy controls to a threat conditioning and extinction protocol and recorded skin conductance responses (SCR) and BOLD signal as biological markers of fear [4]. On day 1, participants saw three stimuli, two (CS+) were paired with a shock and one was not (CS−). Extinction learning then took place, where participants were exposed multiple times to one of the CS+ and the CS−, without receiving shocks. The following day, participants were exposed to all CSs. SCR in response to shock delivery (i.e., the unconditioned response—UCR) was used as a biological metric to assess the dimension of acute threat across all individuals suffering from anxiety. That metric was positively correlated with activations in the somatosensory cortex, the dorsal anterior cingulate cortex (dACC), and the insular cortex, highlighting the involvement of fear-promoting brain regions during shock delivery. Based on the UCR, four groups were created. Individuals who had higher UCR during threat conditioning exhibited deficient extinction memory recall the next day, as indexed by higher SCR and greater activation in the dACC. Our results suggest that the immediate response to an unconditioned stimulus, which correlates with greater activations of the fear network, has a predictive value of extinction recall, both at a physiological and neural level. As suggested [4], multiple brain regions of the fear network are likely interacting to produce such effects. Future studies should investigate the connectivity within the fear network, which could inform about potential mechanisms.

These findings echo previous data from trauma-exposed populations, where higher physiological reactivity in the aftermath of trauma exposure has been associated with a worse clinical course [5, 6]. It now remains to be determined whether UCR, obtained from a laboratory-based threat conditioning protocol, could predict response to exposure-based therapy in individuals suffering from psychopathologies characterized, among other things, by elevated levels of fear. While the DSM-based approach remains useful and informative, the development and utilization of biologically based metrics could help identifying individual differences that are clinically relevant. An objective and reliable metric could complement the clinician's observations to better inform personalized medicine.

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AUTHOR CONTRIBUTIONS

Both authors have contributed to this work and approved the final version of this manuscript.

ADDITIONAL INFORMATION

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