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LEARNING AND MEMORY

Face-to-face with fear generalization

Our ability to generalize from previous experiences enables us to select appropriate behaviours when we encounter similar situations. However, over- or under-generalization could lead to the selection of inappropriate responses, making the regulation of this process essential. A new study by Onat and Büchel now provides insight into the neuronal operations that contribute to and regulate fear generalization in humans.

In fear generalization, an individual responds in a similar manner to a stimulus that is perceptually similar to one that has previously been associated with an aversive event (a conditioned stimulus (CS+)). A perceptual model of fear generalization suggests that the perceptual similarity between CS+ and a test stimulus drives the aversion-processing pathways that regulate behaviour. However, factors such as the ambiguity of the test stimulus (and thus uncertainty about the extent to which it relates to adversity or safety) may also be important. Here, the authors used functional MRI on subjects participating in a fear-generalization procedure to test these ideas.

During the baseline phase of the procedure, the subjects viewed eight faces that could be arranged in a circular continuum according to their perceptual similarity. During the fear-conditioning phase, one face was selected to be the CS+ and paired with a mild electric shock. The face that was the most perceptually dissimilar to CS+ was designated CS–. Finally, in the test phase, the subjects again viewed all eight faces. By measuring the subjects' post-conditioning autonomic (skin conductance) and behavioural (rating of shock expectancy) 'fear responses' to viewing each of the eight faces, the authors demonstrated that fear generalization had occurred. Furthermore, the amplitude of the fear response to each face positively correlated with its perceptual similarity to CS+.

In agreement with the perceptual model, blood oxygenation level-dependent signal measurements in several brain regions, including the ventromedial prefrontal cortex (vmPFC), exhibited response profiles similar to the behavioural and autonomic responses. However, the anterior insular cortex (aIC) and the inferotemporal cortex (ITC) exhibited different response profiles. Fear 'tuning' (a measure of the selectivity of the response to CS+) in the aIC was much sharper than it was in other regions or in the behavioural and autonomic responses. Furthermore, during conditioning, multivariate activity patterns in the aIC in response to the CS+ became less similar to those for the other faces and more similar to the pattern triggered by an electric shock alone. This led the authors to suggest that the aIC encodes 'threat identification'. Activity in the ITC, however, was similar for CS+ and CS– and could distinguish these faces from the intermediate (and thus more ambiguous) faces, implying that it encodes ambiguity-based uncertainty.

Regulation of fear tuning is crucial to ensure optimal behavioural responses. The authors showed that behavioural and autonomic fear tuning became sharper over the course of the test phase. This change in tuning was reflected in the response profile of the vmPFC and could best be predicted by a model that combined the responses of the aIC and the ITC and in which the contributions of the aIC and the ITC are associated with increased or decreased tuning selectivity, respectively.

These findings suggest that the brain regulates fear generalization by integrating (possibly in the vmPFC) activity related to the identification of a threat with information about its ambiguity.

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> Regulation of fear tuning is crucial to ensure optimal behavioural responses

ORIGINAL ARTICLE Onat, S. & Büchel, C. The neuronal basis of fear generalization in humans. *Nat. Neurosci.* **18**, 1811–1818 (2015)
FURTHER READING Tovote, P. *et al.* Neuronal circuits for fear and anxiety. *Nat. Rev. Neurosci.* **16**, 317–331 (2015)

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