NEURAL CIRCUITS

Pain or pleasure?

To ensure survival, animals must distinguish between environmental stimuli associated with positive outcomes (such as food) and those associated with negative outcomes (such as predators). Synaptic plasticity within the basolateral amygdala complex (BLA) mediates these stimulus–outcome associations; however, the mechanisms by which positive-outcome (or appetitive) versus negative-outcome (or aversive) associations are formed have not been defined. A new paper by Tye and colleagues now begins to uncover the circuits that encode positive and negative associations in the BLA.

Distinct neuronal populations in the BLA have been proposed to drive behavioural responses to appetitive or aversive stimuli. Here, the authors compared two populations of BLA neurons: those that project to the nucleus accumbens (NAc), a region associated with reward-like behaviour, and those that project to the centromedial amygdala (CeM), a region associated with conditioned fear. Mice underwent either a fear-conditioning or a reward-conditioning training protocol, after which the strength of the synaptic input received by each population of BLA neurons was examined in a slice preparation. Fear conditioning resulted in an increase in the strength of synapses onto CeM-projecting neurons but a reduction in the strength of synapses onto NAc-projecting neurons. Reward conditioning had the opposite effect: it increased the strength of synapses onto NAc-projecting neurons but reduced it for CeM-projecting neurons.

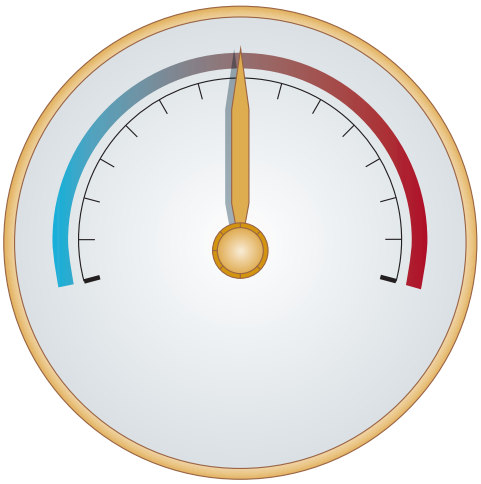
To determine whether the observed changes in synaptic strength are important for downstream behavioural responses, the authors asked whether enhancing or inhibiting the activity of each population of BLA neurons would affect the ability to establish avoidance or reward-seeking behavioural responses. The light-activated cation channel channelrhodopsin 2 was expressed in either NAc- or CeM-projecting neurons, which enabled the authors to use photostimulation to selectively enhance the activity of each population. In a place-avoidance assay, the delivery of photostimulation to CeM-projecting neurons induced avoidance of the part of the test chamber associated with the stimulation. By contrast, when the photostimulation of NAc-projecting neurons was coupled to nose-poke responses, the animals demonstrated increased self-stimulation. Furthermore, when the authors used the light-driven chloride pump halorhodopsin to impair synapse strengthening in CeM-projecting neurons, the ability of the animals to learn a conditioned freezing response in the fear-conditioning protocol was impaired, whereas reward-seeking behaviour was increased.

These findings suggest that the synaptic changes exhibited by NAc- and CeM-projecting neuron populations in response to learned associations between sensory stimuli and particular outcomes are distinct and differ according to the emotional valance of the association. The factors that mediate these differences remain unclear — although the authors did observe some distinctions in electrophysiology, morphology and gene expression between the two populations — and this remains an important open question for future research.

Katherine Whalley

ORIGINAL RESEARCH PAPER Namburi, P. *et al.* A circuit mechanism for differentiating positive and negative associations. *Nature* **520**, 675–678 (2015)

“Fear conditioning resulted in an increase in the strength of synapses onto CeM-projecting neurons but a reduction in the strength of synapses onto NAc-projecting neurons”



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