



## Extracellular barriers

The regulation of fear memory extinction differs between juvenile and adult mice; however, the molecular basis of this difference is not known. Herry and colleagues now show that the formation of perineuronal nets (PNNs) in the amygdala

prevents the permanent extinction of fear memories in adult mice.

Conditioned fear responses result from exposure to a neutral stimulus (the conditioned stimulus (CS)), such as a sound, paired with an aversive, unconditioned stimulus (US), such as a foot shock, and can be extinguished in rodents by repeated exposure to the CS without the US. In contrast to extinction in adults, extinction in juvenile animals is permanent, suggesting that the mechanisms that underlie extinction undergo a developmental switch.

PNNs, which consist of chondroitin sulphate proteoglycans, form postnatally around parvalbumin-positive GABA ( $\gamma$ -aminobutyric acid)-ergic interneurons and are known to accompany the closure of the critical period for plasticity in ocular dominance in the visual cortex. The authors investigated whether a similar principle underlies the switch in mechanisms of fear extinction.

They found that PNN formation in the basolateral amygdala (BLA) occurred during the first 4 postnatal weeks, with a marked increase after postnatal day 16 (P16). Interestingly, when mice were conditioned before P16 or after P23 and then, after extinction training, re-exposed to the CS in either the extinction or the

fear conditioning context, only those that had been conditioned after P23 exhibited fear renewal, suggesting that PNN formation correlates with the potential for renewal of extinguished fear responses.

Next, the authors tested whether PNN degradation with chondroitinase ABC (CHABC) could revert an adult extinction phenotype to a juvenile one. Twenty-four hours after local CHABC injection, PNNs could no longer be detected in the BLA of adult mice. This loss of PNNs re-enabled the permanent erasure of fear memories through the extinction paradigm, but only when the PNNs were degraded before fear conditioning, indicating that PNNs have a role in the representation and extinction of fear memories.

In summary, formation of PNNs in the BLA marks the end of a developmental period during which fear memories can be permanently erased by extinction. The mechanisms through which PNNs contribute to the developmental changes that bring about the closure of the critical period remain to be elucidated.

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