NEURAL CIRCUITS

A nucleus of fear

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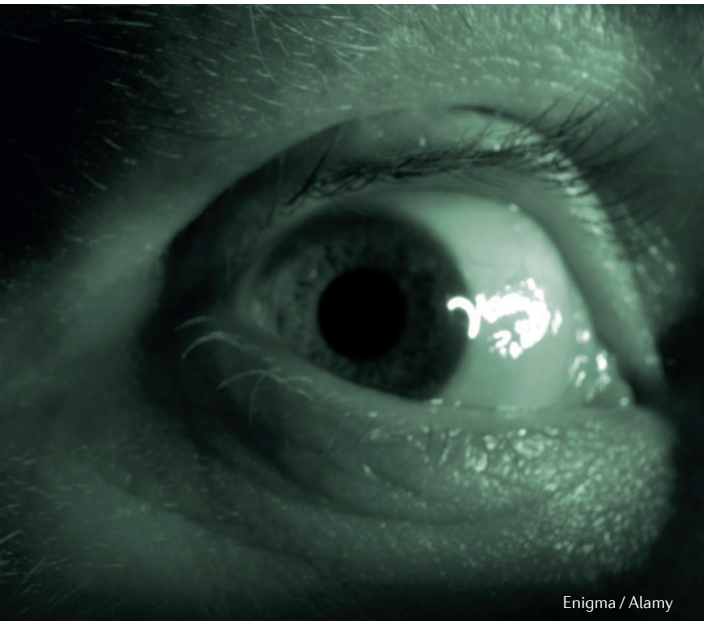
The paraventricular nucleus of the thalamus (PVT) shows activity following exposure to various stressors, but its role in governing threat-induced behavioural responses is unclear. Now, two studies show that the PVT has a role in the maintenance and retrieval of fear memories.

The central nucleus of the amygdala (CeA) and the basolateral amygdala (BLA) are involved in the storage of fear-conditioned memories, and the PVT sends projections to both of these structures.

Penzo *et al.* examined PVT responsiveness in mice just after fear conditioning — during which the animals were trained to associate a tone with an electric shock — or fear memory retrieval. Both tasks led to an increase in expression of c-FOS — a marker of neuronal activity — in the posterior PVT (pPVT), implicating this region in fear processing.



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The authors found that the pPVT preferentially innervated the lateral division of the CeA (CeL). Chemogenetic inactivation of pPVT–CeL projections before fear conditioning or fear memory retrieval attenuated fear responses (freezing), suggesting that the pPVT is involved in establishing and retrieving fear memories.

The storage of fear-conditioned memories is associated with potentiation of excitatory responses in somatostatin-expressing (SST^+) neurons in the CeL, which can be detected from 3 hours after fear conditioning. Selective blockade of pPVT neurons during fear conditioning inhibited this potentiation when measured 24 hours but not 3 hours post conditioning. Together, these data suggest that pPVT neurons, through action on SST^+ CeL neurons, are not required for the induction of fear memory but are required for the consolidation and retrieval of such memories.

Do-Monte, Quiñones-Laracuente, and Quirk had observed previously that the dorsal midline thalamus (dMT), which includes the PVT, is necessary for fear memory retrieval 24 hours after fear conditioning but not at earlier time points. This suggested that the circuits for such memories change with time; the focus of their new study.

The authors pharmacologically inhibited dMT activity in rats at various time points after fear conditioning. dMT inactivation 6 hours post conditioning had no effect on fear memory retrieval, whereas inactivation 24 hours post conditioning or later impaired retrieval. Interestingly, for the later time points, rats continued to show impairment of fear memory retrieval even when the inhibitor was removed. This suggests that the dMT is necessary for fear memory maintenance as well as retrieval.

Strikingly, the PVT showed activation (measured by c-FOS expression) at 24 hours and at 7 days but not at 6 hours post conditioning, and the CeA also showed activation at the later time point. By contrast, the BLA showed activation at 6 hours and at 24 hours but not at 7 days post conditioning, and the prelimbic frontal cortex (PL), which sends projections to the PVT and BLA, was activated at all three times. This suggests that over time there is a shift in the circuitry underlying fear memory retrieval, from a PL–BLA to a PL–PVT–CeA pathway.

In support of this hypothesis, optogenetic silencing of PL projections to the PVT at 7 days but not at 6 hours post conditioning blocked fear memory retrieval, whereas silencing PL projections to the BLA at 6 hours, but not at the later time point, blocked retrieval. Moreover, silencing PVT projections to the CeA at 7 days, but not earlier, persistently attenuated retrieval.

Together, these studies suggest that the PVT is a crucial component of fear-processing circuits, and that the nature of these circuits may change with time.

Darran Yates

ORIGINAL RESEARCH PAPERS Penzo, M. A. *et al.* The paraventricular thalamus controls a central amygdala fear circuit. *Nature* http://dx.doi.org/10.1038/nature13978 (2015) | Do-Monte, F. H., Quiñones-Laracuente, K. & Quirk, G. J. A temporal shift in the circuits mediating retrieval of fear memory. *Nature* http://dx.doi.org/10.1038/nature14030 (2015)