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BEHAVIOURAL NEUROSCIENCE

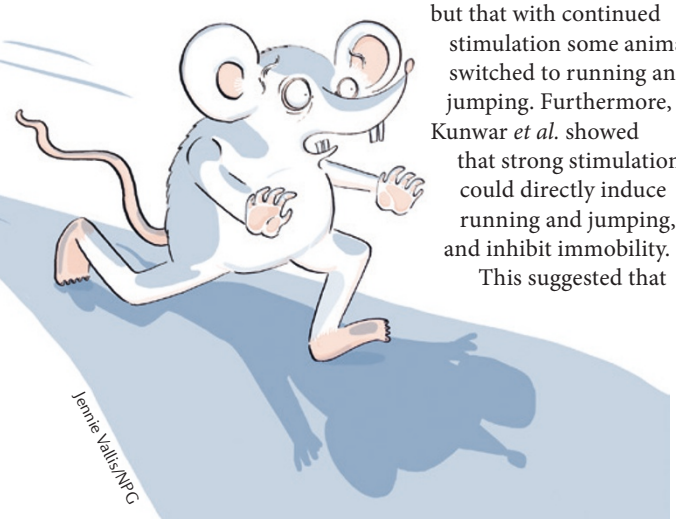
Going on the defensive

> these studies show that the VMH has a key role in mediating an array of defensive behaviours

The ventromedial hypothalamus (VMH) has been implicated in defensive behaviours, which animals adopt to avoid danger; however, its precise role and the underlying neural circuitry are unclear. Two new studies reveal the VMH to be a key orchestrator of multiple defensive behaviours in mice.

In the CNS, the expression of steroidogenic factor 1 (SF1) is largely restricted to the dorsomedial and central parts of the VMH (VMHdm/c). The authors of each of the studies virally expressed channelrhodopsin 2 (ChR2) in SF1-expressing ($SF1^+$) neurons in mice, allowing them to optogenetically manipulate neural activity in the VMHdm/c in behaving animals.

Wang *et al.* and Kunwar *et al.* found that activation of SF^+ neurons with a low-intensity or low-frequency light stimulus induced immobility in mice, but that with continued stimulation some animals switched to running and jumping. Furthermore, Kunwar *et al.* showed that strong stimulation could directly induce running and jumping, and inhibit immobility. This suggested that VMHdm/c activation could elicit various defensive behaviours, depending at least partly on its level of activation.



Jennie Vallis/NPG

Both studies examined the effect of VMHdm/c activation in place preference paradigms. Mice were placed in an arena with two compartments and received a light stimulus to the VMHdm/c for a limited period when they entered only one of these two compartments. Gradually, most of the tested animals spent less and less time in the stimulation chamber as a trial progressed, indicating that VMHdm/c activation promotes avoidance, another key defensive behaviour.

Kunwar *et al.* examined the longer-term effects of VMHdm/c activation on place preference, by using a modified version of the above assay, in which the two compartments differed in terms of design and odour. The authors determined which chamber the mice showed an initial preference for and found that they could train the animals to avoid this chamber by activating the VMHdm/c with an intense light stimulus. Strikingly, 24 hours later, mice still showed avoidance for their initially preferred chamber, indicating that activation of $SF1^+$ neurons can condition a learned defensive behaviour. Furthermore, targeted ablation of $SF1^+$ neurons reduced anxiety and defensive responses to predators, suggesting that these neurons control a generalized, fear-like emotional state.

Wang *et al.* probed the circuits through which VMHdm/c promoted defensive behaviours. The ChR2 expressed in the $SF1^+$ neurons was tagged with enhanced yellow fluorescent protein, enabling the authors to examine the terminal fields of these cells. They found that the VMHdm/c innervated various regions, notably the anterior hypothalamic nucleus (AHN) and the periaqueductal grey (PAG). Optogenetic activation of the VMH–AHN pathway induced various defensive behaviours, including avoidance, whereas light-induced activation of the VMH–PAG pathway mostly promoted immobility. Interestingly, retrograde labelling experiments revealed that more than one-half of the VMHdm/c neurons sent collateral projections to both the AHN and the PAG, suggesting that the VMH controls multiple defensive behaviours through neurons that may innervate multiple target areas.

Together, these studies show that the VMH has a key role in mediating an array of defensive behaviours. Furthermore, according to Kunwar *et al.*, the findings suggest that this hypothalamic structure is sufficient to induce an emotion-like state and thus argue against the view that the hypothalamus acts just to relay output from the amygdala.

Darran Yates

ORIGINAL RESEARCH PAPERS Wang, L., Chen, I. Z. & Lin, D. Collateral pathways from the ventromedial hypothalamus mediate defensive behaviors. *Neuron* **85**, 1344–1358 (2015) | Kunwar, P. S. *et al.* Ventromedial hypothalamic neurons control a defensive emotion state. *eLife* http://dx.doi.org/10.7554/eLife.06633 (2015)