



Figure 1 | To recede or to challenge. Salay *et al.*³ report that a region of the brain known as the ventral midline thalamus (vMT) controls how a mouse responds to a threatening visual stimulus, such as an expanding dark circle in a ceiling display that looms overhead. **a**, The authors provide evidence that signalling from the vMT to the prefrontal cortex (PFC) promotes an active defence strategy, such as making an aggressive tail-rattling motion. **b**, By contrast, when levels of vMT activation are lower, mice respond to the looming stimulus by hiding.

In vivo recordings of neuronal activity revealed that vMT cells are most active when the animals are responding actively to looming stimuli by running and tail rattling. Salay *et al.* therefore asked whether vMT activity is sufficient to guide an animal's defence strategy. The authors injected the vMT with a viral construct carrying a receptor protein that, when activated, excites neurons. The receptor is activated on binding to a small ligand, which the authors administered systemically weeks after injection of the virus. Strikingly, when Salay and colleagues artificially activated vMT cells, the mice no longer hid from the looming stimuli, but instead rattled their tails frequently and ran around the open space. Conversely, when vMT cells were suppressed using a similar approach, the animals spent more time freezing and never rattled their tails in response to looming stimuli.

To investigate how vMT activation affects responses to looming in more detail, the authors genetically modified cells such that they could be activated by a laser, giving millisecond-level control of cell activity. They found that activating vMT cells either in tandem with or 30 seconds before the presentation of looming stimuli promoted the same active defence behaviours, such as tail rattling. This behavioural shift could outlast the stimulation itself, which makes it likely that activating the vMT causes a shift in internal state, instead of eliciting acute motor actions. Consistent with this hypothesis, the researchers showed that vMT activation induces strong and long-lasting autonomic responses indicative of

increased arousal, such as pupil dilation, but does not induce changes in motor activity in the absence of looming stimuli.

Next, Salay *et al.* investigated which projections from the vMT are relevant for guiding defence behaviours. They found that distinct regions of the vMT project to the prefrontal cortex and basolateral amygdala, both of which are implicated in many complex functions, including fear and anxiety. The authors again used a viral technique, this time to manipulate specific vMT outputs, and found that activating vMT projections to the prefrontal cortex pathway promoted an active threat-coping strategy (tail rattling) and increased arousal (Fig. 1). By contrast, activating the vMT–basolateral amygdala projection favoured a different behaviour, freezing. Taken together, the authors conclude that distinct vMT outputs control opposing threat-coping strategies.

Escaping and hiding are basic survival instincts when an animal is faced with a powerful predator. However, from time to time, prey animals need to stand their ground. For instance, adult ground squirrels protect pups in a burrow fiercely — after detecting a nearby snake, the squirrel flags its tail and aggressively harasses the snake by biting and kicking dirt towards it. As a result, the snake typically abandons its hunting effort and moves away⁵. When a weak animal challenges a stronger predator in this way, the animal might be considered 'brave'. Does it stand to reason, then, that the vMT drives a 'courageous' state?

Answers to this question remain unclear,



50 Years Ago

Britain's first heart transplant operation, performed last week at the National Heart Hospital, has been received with the usual gush of publicity which accompanies such events. But less acclaim has been given to the liver transplantation operation carried out at Addenbrooke's Hospital, Cambridge, on May 2, although this is technically by far the trickier of the two operations ... Several attempts at liver transplants have been made in the United States, but met with little success until June of last year. Since then advances in immunosuppression and organ storage have enabled the livers of deceased persons to be maintained in a form acceptable to the recipient's body for several hours ... The heart surgery team at the National Heart Hospital says that the heart transplant operation is the first of a series of operations leading to a combined heart–lung transplant before the end of the year.

From *Nature* 11 May 1968

100 Years Ago

The Gas Traction Committee, appointed in November last to consider the employment of coal-gas as a substitute for petrol and petroleum products in motors, its general safety, and conditions for use, has issued an interim report ... This deals chiefly with the present use of gas, mainly at low pressures, in suitable fabric bags; the work is to be continued to cover its use under higher compressions when the necessary appliances and plant are obtainable. The Committee is satisfied that gas can be efficiently, safely, and promptly substituted for motor spirit (only two minor accidents have been reported). Two hundred and fifty cubic feet are considered equivalent to one gallon of petrol, so that gas at 4s. per 1000 cub. ft. is equivalent in cost to petrol at 1s. per gallon.

From *Nature* 9 May 1918