PUBLISHED: 21 NOVEMBER 2016 | VOLUME: 1 | ARTICLE NUMBER: 0010

NEUROSCIENCE

Hacking the brain to overcome fear

Confronting fears is a core component of cognitive behavioural therapies for anxiety disorders, but also a major hurdle for patients. A new study introduces a method for reducing defensive responses without consciously confronting the threatening cues, paving the way for fear-reducing therapies via unconscious processing.

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What if instead of struggling up a mountain of fear there was a simple way around it? Exposure therapy is the most successful treatment we have right now for alleviating fear and anxiety disorders[1]. During exposure sessions, patients have to recall and describe their traumatic event again and again, until it blunts their emotional reactions. For some, this could be an excruciating process; one they will choose to evade. In this first issue of *Nature Human Behaviour*, Koizumi and colleagues[2] introduce a technique to reduce defensive responses that avoids consciously recalling the threatening memory. This may pave the way for fear-reducing therapies by way of unconscious processing.

Koizumi *et al.*[2] took advantage of a simple learning phenomenon called classical, or Pavlovian, threat conditioning, the process by which we learn to associate neutral stimuli in the environment with dangerous outcomes. The entire study consisted of five sessions, run on consecutive days, that were conducted during functional magnetic resonance imaging (fMRI). On the first day, the participants experienced threat conditioning, during which they learned to associate a mild electric shock with two different images (vertical gratings of red and green circles, for example), but not two other images (vertical gratings of blue and yellow circles). Electrodes placed on the participants' fingers measured their skin conductance response, indicating their level of physiological arousal, one of the markers of fear. By the end of this procedure, the participants showed heightened physiological arousal in response to the red and green circles compared with the non-reinforced blue and yellow circles. This meant they were now 'afraid' of the images that predicted an upcoming electric shock.

The next three days were dedicated to accessing the brain's representation of one of the conditioned stimuli, without participants' awareness, and associating it with a positive outcome. During these 'neural reinforcement' sessions, the participants saw achromatic visual gratings. Using any mental technique, they were asked to increase the diameter of a disc on the monitor in order to gain monetary rewards. Unbeknownst to the participants, the experimenters monitored their brain responses and reinforced them, in real time, if the responses corresponded to the conditioned stimulus. In order to do this, an initial fMRI session preceded the experiment, in which the experimenters presented the visual stimuli to the participants, and, in the fMRI signal of the visual cortex, identified a unique multi-voxel pattern for each stimulus[3]. Then, during the neural reinforcement sessions, they decoded the fMRI signal for each participant and estimated how likely it was that the observed patterns corresponded to the target stimulus (the red circle, for example, while the green circle served as the control). As the likelihood that the target stimulus pattern was activated in the visual cortex increased, so did the size of the disc and the participants' monetary gains.

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Put simply, from their perspective, the participants did something that somehow enlarged the disc on the monitor and made them richer. This 'something' corresponded to the neural expression of the target stimulus pattern in the visual cortex. In this way, participants were rewarded by Koizumi *et al.*[2] for unconsciously producing neural responses representing a threatening visual stimulus, without actually seeing it. Indeed, the participants gave no indication of arousal responses during these sessions, they had no knowledge of the actual purpose of the study, nor were they able to guess the identity of the target stimulus.

The crucial test came on the fifth day, when the participants again saw all the stimuli. The session started with a few unsignalled electric shocks; a stressful exposure that effectively brings up threat memories. When later confronted with the stimuli, participants' conditioned defensive reaction to the target stimulus was significantly lower than their reaction to the control stimulus. Koizumi *et al.*[2] observed a similar pattern of results in the amygdala; the brain region that mediates classical conditioning and induces conditioned defensive reactions[4]. The amygdala showed similarly heightened responses to the target and control stimuli on day 1; but lower responses to the target compared with the control stimulus on day 5. Neural reinforcement, therefore, was effective in diminishing behavioural and neural reactions to the targeted threatening cue.

The ability to reduce threat learning via extinction training, the laboratory model of exposure therapy, depends on the integrity of the ventral medial prefrontal cortex[5] (VMPFC). Would this region engage in diminishing threat responses via unconscious processing? To address this, the authors searched the entire brain for the occurrence of target stimulus multi-voxel patterns that correlated with the likelihood of pattern occurrence in the visual cortex.

This form of 'information transmission' was mostly confined to the visual cortex and did not extend to the VMPFC. In fact, less information transmission between the visual cortex and VMPFC during neural reinforcement related to greater reduction in defensive reactions to the target stimulus on day 5. This suggests that during neural reinforcement, unlike extinction methods, VMPFC disengagement rather than engagement allows for threat reduction[6].

The results of Koizumi *et al.*[2] are the first demonstration that reduction of defensive reactions may be possible not only without consciously confronting the threatening cues[7] but even without physiological arousal. Changing fear may simply require 'neurohacking' — decoding the neural identity of threatening stimuli in the visual cortex and counter-conditioning them with rewards. To translate this into clinical treatment, the next steps should assess the efficacy of the technique for real-life memories, especially those that are old, strong and complex, as well as the stability of the change.

When facing the mountain of fear, then, which path would you choose? Will you take the uphill battle of confronting your fears or the unconscious way around it? This may not be a matter of choice but rather a question of compatibility. When we use the term 'fear', we interchangeably refer to the defensive behavioural and physiological responses to immediate threats, as well as the conscious feelings of fear. The 'two-system' framework[8] posits that separate neural circuits control these two consequences of threat detection. Malfunction of the circuits may affect either system and require differential treatment. For those with aberrant cortical circuits that underlie cognitive functions and feelings states, behavioural therapy and direct confrontation may work best. Those with abnormal defensive circuits may benefit from unconscious processing. It is also possible that treatment in one system would affect the other. The gateway for unconscious threat processing that Koizumi *et al.*[2] have opened up is an important step forward in understanding how the two systems interact. ❐

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