Brains that learn not to fear

Extract from: Neural circuits underlying a psychotherapeutic regimen for fear disorders (Jinhee Baek, Sukchan lee, taesup cho, Seong-Wook Kim, Minsoo Kim, Yongwoo Yoon, Ko Keun Kim, Junweon Byun, Sang Jeong Kim, Jaeseung Jeong & Hee-Sup Shin, 2019)

Published on Nature: /doi.org/10.1038/ s41586-019-0931-y

EMDR and PTSD: recent evidences that helps to better understand the biological basis of this approach

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We live in stressful times. Epidemiological studies document a rise in the prevalence of 'classic' stressrelated illnesses, such as major depression, post-traumatic stress disorder (PTSD) and anxiety disorders, as well as addictions and other conditions that are often triggered by stress [1]. Fortunately, modern neuro science is coming up with new strategies to decipher how the brain deals with stress, with the ultimate goal of combating stress-related illness. Writing in Nature, Baek et al. [2] provide an example of the power of such strategies, using a combination of state-of-the-art neuro science techniques and a creative behavioural assay in mice. Experiencing the slow drip of chronic stress (caused, for example, by daily life in a war zone) is fundamentally different from going through a major traumatic event (for example, running over an improvised explosive device). Acute and intense stressors can become bound in memory with specific environmental stimuli, which serve as reminders of the original traumatic episode and alert us to potential dangers in the future. In PTSD, however, these stimuli become potent and pervasive anxiety triggers. Herein lies a therapeutic opportunity, because exposure to trauma reminders without resultant harm (for example, in the safety of a therapist's office) produces a new form of memory (called extinction memory) that reduces anxiety. This approach, known as extinction therapy, is a mainstay of PTSD treatment [3], but it doesn't work in all patients, and its effects often weaken over time. Therefore, major efforts are being made to identify ways to strengthen the process of extinction, for instance by delivering drugs that enhance the formation and consolidation of extinction memories [4]. The focus of Baek and colleagues' study is a psychological treatment called eye-movement desensitization and reprocessing (EMDR). In EMDR, the patient recalls a trauma while being shown visual stimuli designed to stimulate repetitive eye movements (a process known as alternating bilateral stimulation, or ABS) [5].

Baek and colleagues used mice that had developed fear behaviour (freezing) in response to a sound they had previously heard while receiving an unpleasant electric shock to their feet. The authors then led the mice to form an extinction memory by presenting the sound without an accompanying electric shock (an approach that mimics extinction therapy), while simultaneously exposing them to a set of light-emitting diodes (LEDs) that lit up in an alternating left–right sequence; this approach was intended to mimic ABS.

Note: generally the treatment of the traumatic memories happen some times later and in a safety situation as a therapeutic setting, without any risk that the event happens again; this procedure is very similar to the extincion procedure. In fact, during psychotherapy, access to the memory without the conditioned stimulus reproduces the extinction situation in the laboratory. As we know, this condition doesn't change the subjective disturbance or the PTSD or stress-related disorders's reaction.

Remarkably, nonetheless, the combined extinction and ABS approach led to a clear and persistent decrease in fear behaviour that was more pronounced than that produced by extinction alone. The authors observed that the combined extinction and ABS procedure stimulated the activity of the superior colliculus, an area of the brain that processes visual information and directs an individual's attention. The procedure also activated the mediodorsal thalamus, a region that receives neuronal projections from the superior colliculus. They found that communication between the two areas is needed for the reduction in fear behaviour and the level of activation of these two regions predicted the extent of the decrease in fear behaviour.

Baek et al. observed that the combined extinction and ABS procedure dampened the excitability of a population of neurons in the basolateral nucleus of the amygdala (BLA) — an area of the brain that calibrates fear responses [6] — that fired when mice exhibited fear behaviour. They then showed that there is a functional, two-step inhibitory connection between the mediodorsal thalamus and the 'fear-encoding' BLA neurons.

The reduced freezing was mainteined in a recall test without ABS, suggesting that the reduction was not due simply to visually evoked motor responses, but rather was based on long-lasting modification of brain circuitry.

These findings, put together, suggest a model in which the extinction and ABS procedures act in tandem to recruit the neuronal pathway that links the superior colliculus and the mediodorsal thalamus. This, in turn, reduces the fear response to the trauma-reminding stimulus that is generated by the BLA.

A broader question is how ABS, and by extension EMDR, works to aid memory extinction and reduce fear. One interpretation is that visual stimuli serve as distractors, drawing attention away from the fear-inducing stimulus to dampen anxiety and enable encoding of the extinction memory. But that does not explain the authors' observation that flashing LEDs in a non-sequential pattern fails to reduce fear behaviour. An explanation based on distraction would also sit uneasily with the current view that the process of extinction is enhanced by directing more, not less, attention to the fear-inducing stimulus, because this increased attention reinforces the new connection between the trauma reminder and safety [7]. Baek and colleagues propose that ABS shifts the balance between competing brain circuits, engaging one set of neural pathways that favour fear extinction to overshadow the influence of other pathways that favour the persistence of fear. Whether or not their model turns out to be correct, this study provides a plausible neurobiological explanation for the behavioural effects of ABS — and possibly, by extension, of EMDR.

Bibliograph

1. Kessler, R. C. et al. Arch. Gen. Psychiatry 62, 593–602 (2005).
2. Baek, J. et al. Nature http://doi.org/10.1038/ s41586-019-0931-y (2019).
3. Foa, E. B. & McLean, C. P. Annu. Rev. Clin. Psychol. 12, 1–28 (2016).
4. Bukalo, O., Pinard, C. R. & Holmes, A. Br. J. Pharmacol. 171, 4690–4718 (2014).
5. Shapiro, F. J. Anxiety Disord. 13, 35–67 (1999).
6. Tovote, P., Fadok, J. P. & Luthi, A. Nature Rev. Neurosci. 16, 317–331 (2015).
7. Pearce, J. M. & Hall, G. Psychol. Rev. 87, 532–552 (1980).

https://doi.org/10.1038/d41586-019-00294-8