Nature Reviews Neuroscience | AOP, published online 11 December 2013; doi:10.1038/nrn3658

LEARNING AND MEMORY

Synapse remodelling extinguishes fear

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An individual who experiences an aversive event or stimulus within a particular context may develop a fear of the context itself through a process known as fear conditioning. Controlled re-exposure to the same context (without the aversive stimulus) can sometimes eliminate the learned fear response in a process termed fear extinction; however, the neural changes that underlie fear extinction have not been established. Trouche *et al.* now show that fear extinction induces structural changes at specific synapses in the amygdala to suppress activity in the fear circuit.

Some neurons in the basolateral amygdala (BLA) are activated during fear conditioning and are subsequently reactivated during the expression of learned fear. To determine the effects of fear extinction on these 'fear neurons', the authors used transgenic mice in which excitatory neurons that were active during fear conditioning were fluorescently tagged and examined the effects of subsequent extinction training on the activity of the tagged fear neurons. They identified a population of fear neurons that were no longer active when the animals were re-exposed to the conditioning context after extinction training (termed 'silent fear neurons'), which confirmed that fear extinction silences neurons that are normally active in the fear circuit.

Inhibitory interneurons in the BLA have been implicated in fear extinction. Here, the authors observed an extinction-meditated increase in the expression of 67 kDa glutamic acid decarboxylase (also known as GAD1), an enzyme that is involved in GABA synthesis, and parvalbumin (PV), a protein that is expressed in most BLA interneurons, within perisomatic boutons that are located around the silent fear neurons. These changes indicated that there was an increase in the number of inhibitory synapses around these neurons. Thus, fear extinction can silence fear neurons by increasing the perisomatic inhibition of these neurons.

By contrast, the subset of fear neurons that remained active after extinction training exhibited an increase in the perisomatic expression of cannabinoid 1 receptor (CB1R), a receptor that is expressed by a separate, non-PV-expressing population of interneurons after extinction. CB1R activation suppresses GABA release. Thus, the authors suggest that increased CB1R expression might prevent extinction-mediated silencing of a subset of fear neurons.

These results suggest that perisomatic inhibitory synapses in the BLA undergo structural changes in response to contextual fear extinction. These synapses might be a viable target for strategies that are being designed to improve the effectiveness of exposure therapies to treat fear disorders in humans.

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ORIGINAL RESEARCH PAPER Trouche, S. *et al.* Fear extinction causes target-specific remodeling of perisomatic inhibitory synapses. *Neuron* **80**, 1054–1065 (2013)

> “perisomatic inhibitory synapses in the BLA undergo structural changes in response to contextual fear extinction”