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Extinction of fear in the amygdala: Justification and development of a neuron model

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Anxiety disorders cause chronic reactions to a triggering event that disrupt pursuit of normal daily routines. Disorders such as post-traumatic stress disorder or specific phobia can be ameliorated through the process of fear extinction. By examining the studies published on fear extinction as well as ones on mechanisms of long-term depression (LTD) of neurons in rats, specific receptors and chemical messengers that inhibit easily excited neuronal fear connections have been found and used to provide justification and modification of a computational model of this extinction learning in the rat amygdala (where the mediation of fear memory is thought to occur). These mechanisms of fear inhibition can work by affecting both the presynaptic neuron and the neuron on which it acts (postsynaptic neuron). For example, depotentiation at lateral amygdala synapses did not depend on adenosine A1 or metabotropic glutamate receptor II (mGlurRII), but did require NMDA receptors, L-type voltage gated calcium channels (LVGCCs), and calcineurin; when calcium enters through NMDA receptors and LVGCCs to activate calcineurin, the calcineurin reduces the excitability of the neuron through inactivation of postsynaptic neurotransmitter receptors. Also, long-term depression of presynaptic release of neurotransmitters was found to be mediated by postsynaptic retrograde diffusion of nitric oxide back across the synapse. Although parameters that affect the acquisition and extinction of fear memories have yet to be well understood or quantified, the computational model using GENESIS (GEneral NEural SImulation System) incorporates the most up-to-date findings of neuronal studies. The program simulates the response of a pyramidal neuron in the lateral amygdala to sensitization, conditioning, and extinction of a tone and shock-induced fear. Through matching of experimental data, the model may help predict what cellular mechanisms should be further investigated in order to ultimately develop a way to better treat anxiety disorders.