New neural pathway for fear found in mice

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(Medical Xpress)—A team of researchers with the Chinese Academy of Sciences has found that there is a previously unknown neural pathway in the mouse brain that leads from the lateral amygdala to the auditory cortex. In their paper published in the journal *Nature Neuroscience*, the team describes testing they conducted on mice that showed that the pathway was required for mice to react to trained fear stimuli. Bo Li with the Cold Spring Harbor Laboratory in New York offers a News & Views piece on the work done by the team in the same journal issue.

Prior research has shown that there is a pathway in the mouse brain from the auditory cortex to the lateral amygdala—it is the mechanism that detects something that might be a threat and then sends it to the part of the brain that helps in formulating a response, such as freezing. In this new effort, the researchers discovered that there is a similar pathway that allows for sending signals in the opposite direction.

After noting more axons present than should be expected between the auditory cortex and lateral amygdala that didn't appear to be associated with a recognized pathway, the researchers conducted two experiments designed to prove that a new one existed. The first consisted of using optogenetics to shut down the part of the auditory cortex in mice that they believed might be responsible for signaling—the mice had been trained to respond to a noise associated with an electric shock. Afterward, they sounded the specific noise to see if the mice would freeze in response. They did not. The team then repeated the experiment by going another route, using a virus to disable to the pathway source. They found the same result—the trained mice 'forgot' to freeze when hearing the sound that was supposed to induce fear. Convinced they were on to something, the team then used two-photon imaging to watch what happened along the suspected pathway before, during and after a mouse had been trained to respond to a sound indicating a threat. They report that that they witnessed the formation of lateral amygdala axon boutons, dendritic spines and increases in synapses between the two brain regions.

The work done by the team offers strong evidence for the presence of a previously unknown neural pathway in the mouse brain, though they cannot explain why it exists. Future experiments will seek to find the reason and likely to see if there is a similar pathway in the human brain—though as Li notes, if there is, it is likely to be associated with vision, rather than hearing.

More information: Yang Yang et al. Selective synaptic remodeling of amygdalocortical connections associated with fear memory, *Nature Neuroscience* (2016). DOI: 10.1038/nn.4370

Abstract

Neural circuits underlying auditory fear conditioning have been extensively studied. Here we identified a previously unexplored pathway from the lateral amygdala (LA) to the auditory cortex (ACx) and found that selective silencing of this pathway using chemo- and optogenetic approaches impaired fear memory retrieval. Dual-color in vivo two-photon

imaging of mouse ACx showed pathway-specific increases in the formation of LA axon boutons, dendritic spines of ACx layer 5 pyramidal cells, and putative LA–ACx synaptic pairs after auditory fear conditioning. Furthermore, joint imaging of pre- and postsynaptic structures showed that essentially all new synaptic contacts were made by adding new partners to existing synaptic elements. Together, these findings identify an amygdalocortical projection that is important to fear memory expression and is selectively modified by associative fear learning, and unravel a distinct architectural rule for synapse formation in the adult brain.

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