Releasing the neuronal brakes for learning

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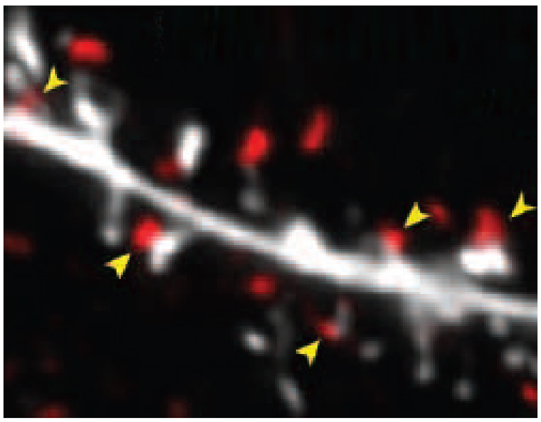

Example of a dendrite of a principal neuron (white) and synaptic contacts (yellow arrowheads) from SOM1 interneurons.

(Medical Xpress)—Learning can only occur if certain neuronal "brakes" are released. As the group led by Andreas Lüthi at the Friedrich Miescher Institute for Biomedical Research has now discovered, learning processes in the brain are dynamically regulated by various types of interneurons. The new connections essential for learning can only be established if inhibitory inputs from interneurons are reduced at the right moment. These findings have now been published in *Nature*.

For some years, most neurobiologists studying learning processes have assumed that the new connections required for learning can only be established and ultimately reinforced if certain neuronal "brakes" are released – a process known as disinhibition. It has also been supposed for some time that various types of interneurons could be involved in disinhibition. Interneurons are nerve cells that surround and – via their connections – inhibit the activity of principal neurons. It has not been clear, however, whether these cell types actually play a role in disinhibition and how they control learning.

Andreas Lüthi and his group at the Friedrich Miescher Institute for Biomedical Research have now demonstrated for the first time how a learning process is dynamically regulated by specific types of interneurons.

In Lüthi's experiments, mice were trained to associate a sound with an unpleasant stimulus, so that the animals subsequently knew what would happen when they heard the auditory cue. The researchers showed that, during the learning process, the sound stimulus released a brake in some of the principal neurons. More precisely, it induced the activation of parvalbumin-positive (PV+) interneurons, leading indirectly – via somatostatin-positive (SOM+) interneurons – to disinhibition of the principal neurons. The latter thus became receptive to further sensory inputs. If this was immediately followed by the unpleasant stimulus, then another brake was released. Once again, PV+ interneurons were involved, but this time the principal neurons were directly disinhibited. Steffen Wolff, a postdoc in Lüthi's group and first author of the publication, explains: "The principal neurons temporarily reached a level of activation enabling neuronal connections to be reinforced in such a way that the animal could learn the association between the sound and the unpleasant stimulus."

Lüthi comments: "This is the first time we've been able to identify so clearly the function of defined interneurons in a learning process, and to show how successive disinhibition can enable this process. We assume that interneurons disinhibit the principal neurons in a highly dynamic manner. They integrate, as it were, the state of numerous different neural networks, activated for example by sensory input, earlier experiences or emotional states, and thus permit or prevent learning. I think these findings are also of interest in the context of conditions where learning processes are impaired or dysfunctional, as in the case of anxiety disorders."

More information: Wolff SB, Gründemann J, Tovote P, Krabbe S, Jacobson GA, Müller C, Herry C, Ehrlich I, Friedrich RW, Letzkus JJ, Lüthi A (2014) "Amygdala interneuron subtypes control fear learning through disinhibition." *Nature*. 2014 May 11. DOI: 10.1038/nature13258 . [Epub ahead of print]

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