Medical Xpress

Switching learning on

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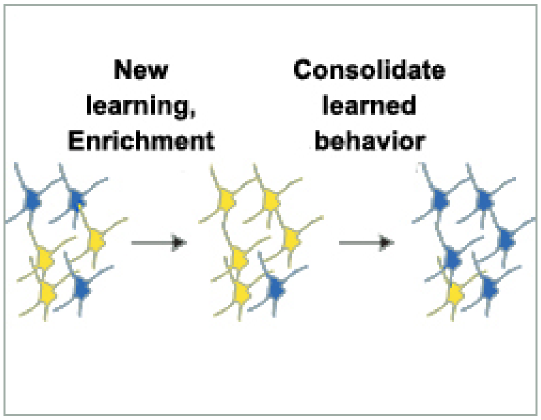

Learning in basket cells

Neurobiologist from the Friedrich Miescher Institute for Biomedical Research show how a network of neurons in hippocampus and cortex switches states to turn on and off learning in the adult. They further show how a stimulating environment promotes this switch, and thus learning. Their findings are published today in the renowned journal *Nature* and have far reaching implications also for diseases where learning and memory is impaired, such as Alzheimer's or dementia.

Learning to ride a bike, to ski or swim: After many days and weeks of practice, trial and error, we usually master a skill and never forget how to do it. What is also common knowledge is that motivation and a supportive environment usually help: learning how to ski in the extreme cold will take much longer than on a sunny day with an understanding teacher. While we can observe these phenomena over and over again with many tasks at hand, we still don't understand fully, what mechanisms in the brain first enable learning and then allow the switch to the state where "we just know", and hardly forget.

Pico Caroni and his team at the Friedrich Miescher Institute for Biomedical Research in Basel could now show that networks of specific cells in the brain regions relevant for each particular type of learning, switch first to a "learning state" and then to a "learnt state", and how the environment and experience modulate these processes.

In a study published today in the renowned scientific journal *Nature*, they could show that so called basked cells, inhibitory neurons assembled in a network to modulate the function of excitatory neurons in brain regions such as the hippocampus, switch between three states during a learning experience. From a neutral state, many basket cells de-differentiate as the learning experience starts. This facilitates local formation and remodeling of new connections, new synapses; the network is plastic and conducive to learning and memory of new relationships potentially important to master the task at hand.

As soon as the task has been successfully learned, this initial switch is reversed, and many basket cells switch to a highly differentiated state. The local network loses its ability to form new synapses, but at the same time enhances the function of strong synapses involved in the newly learned skill; the network loses its plasticity, but consolidates its gains. Learning is complete, the ability to perform the task stable.

Finally, the cells revert to the neutral state again, ready for the next task to learn.

Caroni and his team further showed that the learning environment influences the state of the basket cells. In an environment rich in stimuli and diverse experiences, a large fraction of the basket cells are in a low differentiation state, ready for learning. Importantly, the scientists show that they can pharmacogenetically switch the different basket cells, thereby inducing the predicted outcomes in the ability to learn. Inhibition of basket cells decreased their differentiation and increased the ability to learn, whereas activation of basket cells increased their differentiation state and reduced learning and memory skills.

These findings are ground-breaking in several ways. First, for a long time the scientific community believed that plasticity of neuronal connections in brain regions such as the hippocampus is permanently reduced in the adult. Caroni and his team now show that the same cells that ease learning and plasticity of neuronal connections in the young are involved in the same processes at an older age. Second, the scientists could show how the environment and experience influence plasticity and learning. "In dementia and Alzheimer's disease, stimulating activities have been proposed as therapeutic approaches to slow down the disease," comments Caroni, "our results provide now a scientific rational for such a therapeutic tactic. Being able to reversibly induce basket cell network states that modulate learning and memory formation might be harnessed for therapeutic strategies in these diseases."

More information: "Parvalbumin-expressing basket-cell network plasticity induced by experience regulates adult learning." Flavio Donato, Santiago Belluco Rompani & Pico Caroni. *Nature* 504, 272–276 (12 December 2013) DOI: 10.1038/nature12866 . Received 03 May 2013 Accepted 05 November 2013 Published online 11 December 2013

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