More than a nice coating

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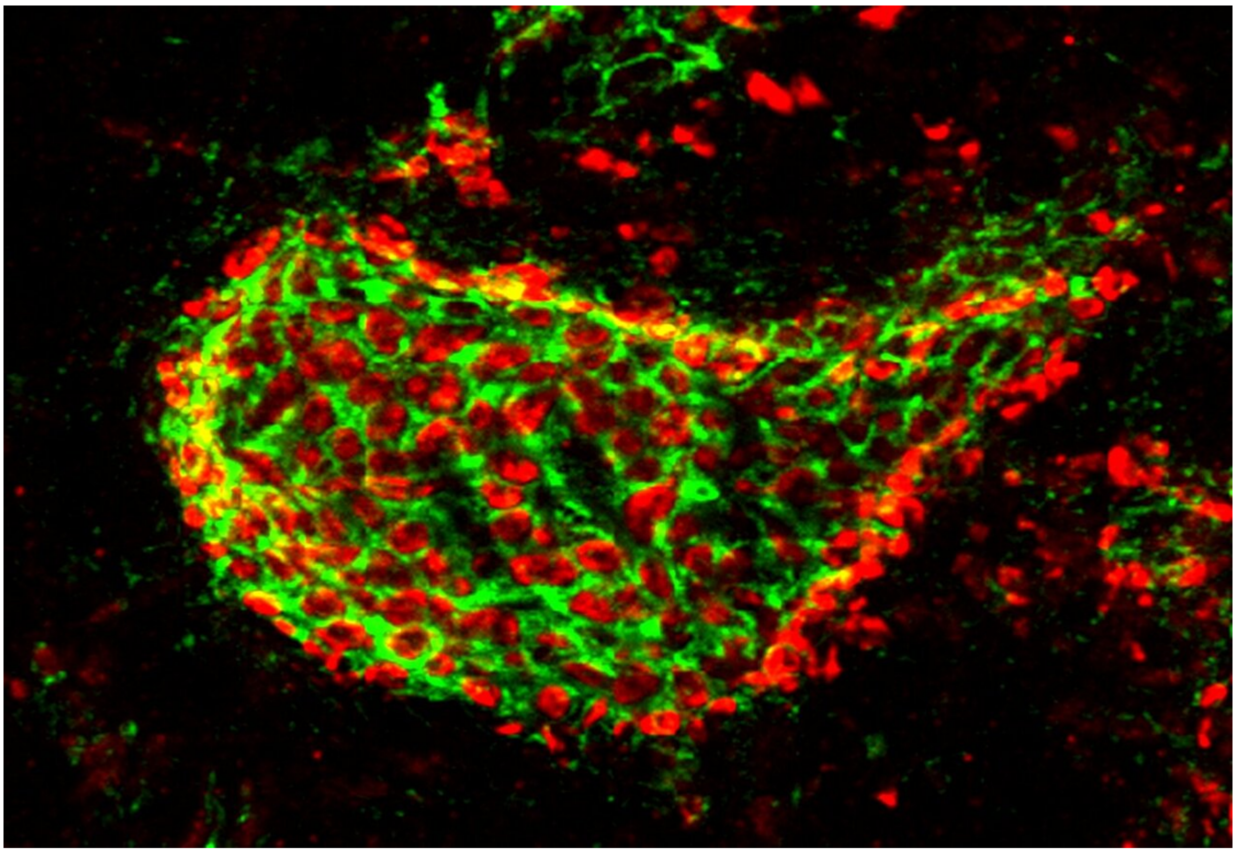

A perineuronal net (in green) with synapses embedded in it (in red) Credit: Daniela Carulli

Researchers at the Netherlands Institute for Neuroscience (NIN) have shown that specialized aggregates of molecules enwrapping nerve cells in the brain, the perineuronal nets, are crucial for regulating the connections between nerve cells that control motor memories. The discovery, published in the *Proceedings of the National Academy of Sciences* (*PNAS*), provide novel insight into how memories are formed and stored in the brain.

Perineuronal Nets Influence Learning

As the brain becomes older, the contacts between nerve cells (synapses) become less flexible, because they are encased in a meshwork of proteins and carbohydrates called a perineuronal net. In the current study, researchers of the NIN (Verhaagen group and De Zeeuw group), in collaboration with the University of Turin and the University of Cambridge, induced a remarkable remodeling of cerebral synapses. They improved the learning abilities of mice by using a powerful molecular tool to degrade the perineuronal nets. However, the capability of the mice to remember what they had learned was disturbed, indicating that the storage of acquired information requires intact perineuronal nets. "This is the first time that it has been shown that changes in perineuronal nets are instrumental for motor learning and memory," says Daniela Carulli, researcher at the NIN and first author of this study.

Changing Of Perineuronal Nets

Children have the capability to learn much better than adults, from mastering a new language to playing a musical instrument. This is possible thanks to the flexibility (or "plasticity") of the connections between nerve cells in young brains. Plasticity also allows a faster recovery from brain injury. "We discovered that perineuronal nets exert tight control on learning and memory in the adult brain," explains Carulli. The researchers investigated a well-characterized type of learning, called eyeblink conditioning, that depends on the cerebellum, a brain region involved in motor functions. "Our results indicate that perineuronal nets are diminished during the learning phase of eyeblink conditioning, but are restored at later stages, when memories are consolidated," Carulli continues.

Much still needs to be known as to how exactly perineuronal nets regulate plasticity, and, thereby cognitive functions. This is crucial in view of finding therapeutic strategies to tackle cognitive decline in the elderly or in patients with neurological disorders.

More information: Daniela Carulli et al, Cerebellar plasticity and associative memories are controlled by perineuronal nets, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.1916163117

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