Myelination found to determine the nerve cell power of inhibition

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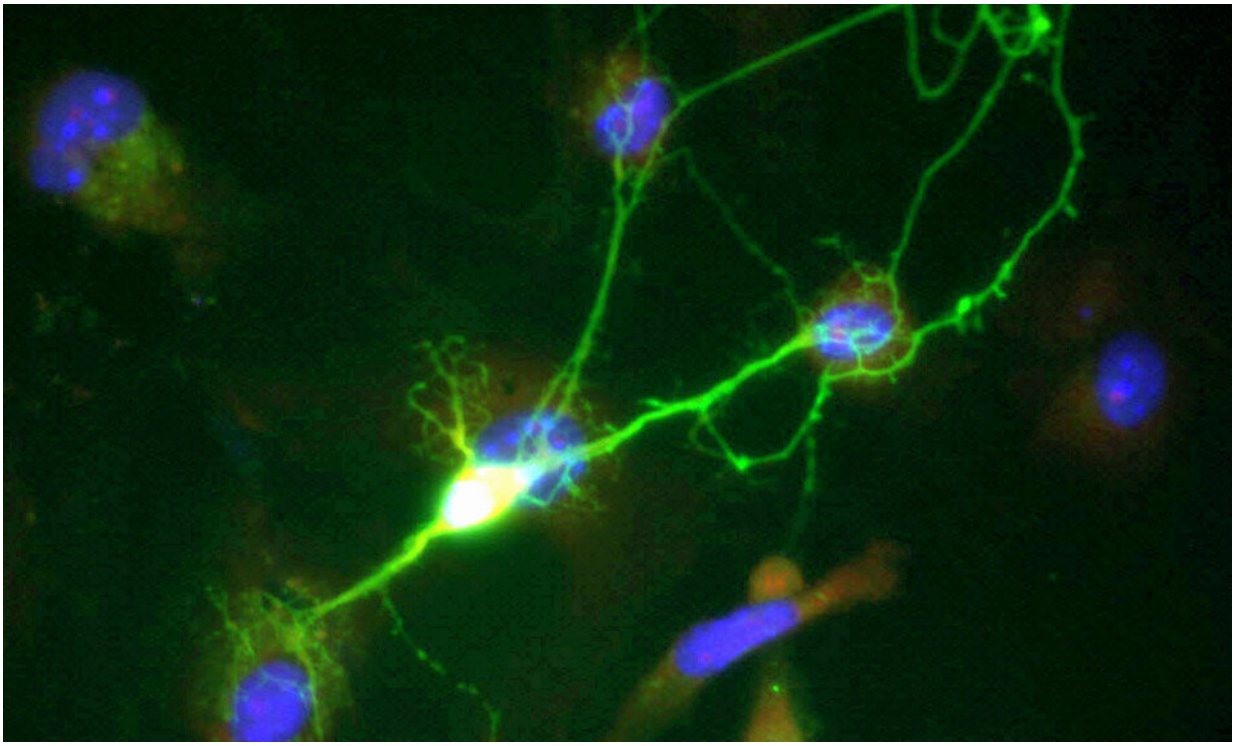

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Researchers from the Netherlands Institute for Neuroscience (NIN) shed new light on how myelin loss might underpin aberrant brain activity which have been observed in people with multiple sclerosis. This study, published in *eLife*, suggests that myelination, however patchy on specific interneurons, is required to reach their full inhibitory potential.

Impact of losing myelin

The brain contains billions of nerves that connect with each other via cable- like structures called axons. Axons transmit electrical impulses and are often wrapped in a fatty substance called myelin. This substance increases the speed of nerve impulses and reduces the energy lost over long distances. Loss or damage of the myelin layer—which is the case for multiple sclerosis– can cause serious disability. Although myelinated axons play pivotal roles in brain function, only little is understood about their role in the electrical architecture of local circuits where experiences are processed, and memories are stored.

However, a fast-firing neuron within the brain, called the PV+ interneuron, has short, sparsely myelinated axons. Even so, PV+ interneurons are powerful inhibitors that regulate important brain rhythms and cognitive processes in gray matter areas of the brain. Recent findings have shown that also axons of PV+ interneurons are insulated by myelin sheaths. Yet it remains unclear how the unusual, patchy myelination affects their function.

Epileptic spikes as indicator

To study the impact on interneurons and slow brain waves, researcher Mohit Dubey, from the NIN, together with colleagues from the Erasmus Medical Centre used genetically engineered mice either lacking or losing myelin. "As mice progressively lost myelin, the speed of inhibitory signals from PV+ interneuron did not change but their signal strength decreased" says Dubey. As a result of being no longer inhibited by PV+ interneurons, the power of slow brain waves dramatically increased. These waves also triggered brief spikes resembling signals seen in epilepsy, only when the mice were inactive and quiet. Restoring the activity of PV+ interneurons helped to reverse the epileptic spikes.

"These results expand our understanding of the importance of myelin in gray matter and its clinical relevance to demyelinating disorders such as multiple sclerosis" says Maarten Kole, group leader at the NIN. More research is needed to determine whether these brief epileptic spikes could be a biomarker of multiple sclerosis and/or a target for developing new therapeutic strategies to limit cognitive impairments.

More information: Mohit Dubey et al, Myelination synchronizes cortical oscillations by consolidating parvalbumin-mediated phasic inhibition, *eLife* (2022). DOI: 10.7554/eLife.73827

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