Stabilizing neuronal branching for healthy brain circuitry

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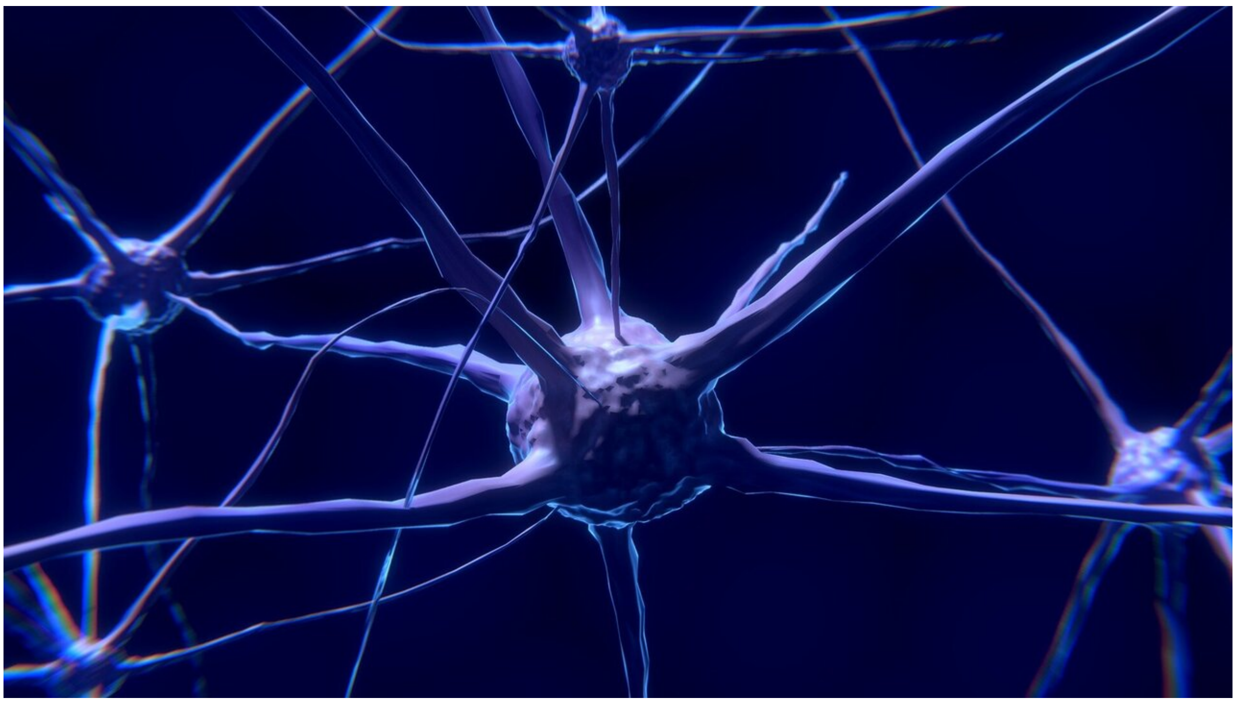

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Neurons form circuits in our brain by creating tree-like branches to connect with each other. Newly forming branches rely on the stability of microtubules, a railway-like system important for the transport of materials in cells. The mechanisms that regulate the stability of microtubules in branches are largely unknown. New research from the Vickie & Jack Farber Institute for Neuroscience—Jefferson Health has identified a key molecule that stabilizes microtubules and reinforces new neuronal branches.

"Like the railways to a new city, stable microtubules transport valuable material to newly formed branches so that they can grow and mature," explains Dr. Le Ma, associate professor in the department of Neuroscience and senior author of the study. Microtubule stability is regulated by proteins called microtubule-associated proteins (MAPs), which include many subtypes. Previous work from Dr. Ma and Stephen Tymanskyj, a postdoctoral fellow in the lab, had identified a subtype called MAP7, and found that it was localized at sites where new branches are formed. This made it a good candidate for regulating microtubule stability.

In the new study, published August 7 in *Journal of Neuroscience*, Dr. Tymanskyj and Dr. Ma used genetic tools to remove MAP7 from developing rodent sensory neurons and found that without MAP7, branches can still grow but they retract more frequently. This means that the branches cannot make complete and lasting connections without MAP7. The researchers also introduced more MAP7 protein to branches that had been cut by a laser and found that it could slow down or even prevent retraction that usually happens in response to injury. This suggests that manipulation of MAP7 could potentially rescue injured neuronal branches.

A key finding of the study demonstrated a unique property of MAP7 when it interacts with microtubules. The researchers found that in cells, MAP7 binds to specific regions of microtubules and makes them very stable but avoids the microtubule ends, where individual building blocks are rapidly added or removed. This valuable binding property prevents microtubules, or the cellular railway, from completely disassembling when branches retract. It also promotes steady re-assembly of microtubules to extend the cellular railway for subsequent branch growth. Moreover, the study is the first to demonstrate this new feature, which has not been observed for other MAPs.

Neuronal branches can be damaged by physical injury or toxicity. Understanding the role of MAP7 suggests new ways to reduce or avert that damage. "Our research has identified a new molecular mechanism of microtubule regulation in branch formation and has suggested a new target to potentially treat nerve injury," concludes Dr. Ma, who has already initiated new studies exploring this.

More information: Stephen R. Tymanskyj et al, MAP7 Prevents Axonal Branch Retraction by Creating a Stable Microtubule Boundary to Rescue Polymerization, *The Journal of Neuroscience* (2019). DOI: 10.1523/JNEUROSCI.0775-19.2019

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