How neurons get their branching shapes

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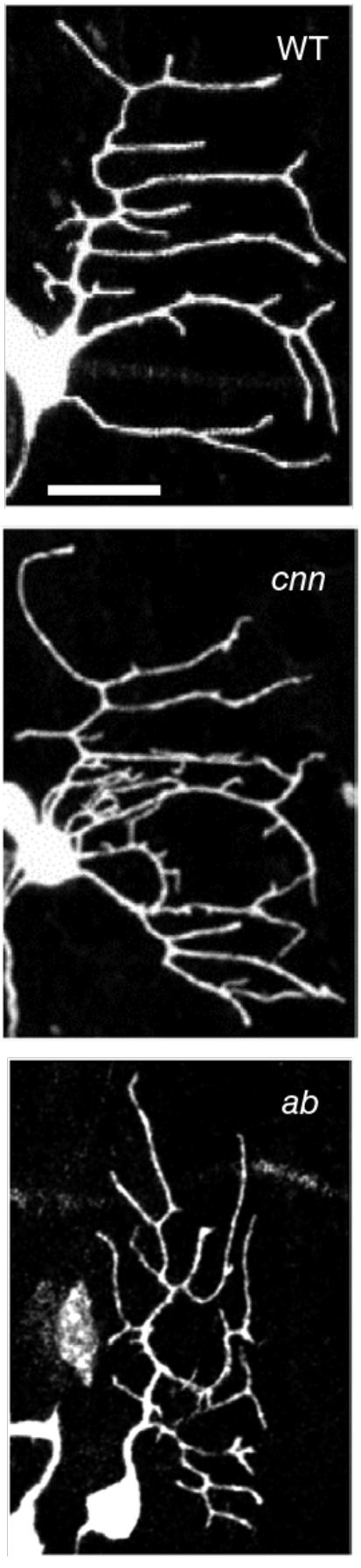
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Dendritic branching in wild type (top), centrosomin mutants (middle), and Abrupt mutants (bottom). Note the increased branching in the mutants. Credit: RIKEN

For more than a hundred years, people have known that dendritic arbors—the projections that neurons use to receive information from other neurons—differ in size and shape depending on neuron type. Now, researchers at the RIKEN Brain Science Institute in Japan have discovered a factor helps shape dendritic arbors. Published in *Nature Neuroscience*, the work reveals how the protein centrosomin prevents dendrites from branching out.

Dendrites grow and branch as structural elements called microtubules push the ends out in specific directions. Microtubules are often likened to cellular scaffolding, and are built on site by growing out from one end. To determine how microtubule growth and dendritic branching is regulated, the researchers examined sensory neurons from Drosophila fruit flies.

The scientists focused on a type of Drosophila sensory neuron that has very limited dendritic branching and expresses the transcription factor called Abrupt. Researchers began by determining that expression of Abrupt leads to reduced arbors, while its absence leads to more complex arbors. Next, they tested a group of candidate proteins from the pathway of molecular events initiated by Abrupt, looking for one that regulates microtubules. They found that loss of centrosomin—a protein that makes microtubule-based structures necessary for cell division—resulted in more extensive dendritic branching, and its addition could block the increase in branching caused by lack of Abrupt. The team then

discovered that by working with another protein called pericentrin, centrosomin could control where new microtubules form within the dendrites.

When one end of a microtubule is attached to something, it does not push out new dendritic branches as it grows. However, when microtubules form at no particular site, the opposite is true, and new branches are more likely to form as it grows. Further testing revealed that centrosomin acts as a glue that fixes microtubules, particularly to Golgi bodies, which is why its presence promotes less complex branching.

"The shape and complexity of neuronal dendrite arbors are often disrupted in neurological diseases," notes team leader Adrian Moore. "It turns out the two microtubule regulators we found in this study of Drosophila neurons—centrosomin and pericentrin—are encoded by genes mutated in some human brain disorders. As we learn more about how neurons control the growth of dendrites it will help us understand these diseases more completely, and we may learn how to initiate and direct neuron growth as therapy for diseases and after neuronal injury."

More information: Yalgin C, Ebrahimi S, Delandre C, Yoong LF, Akimoto S, Tran H, Amikura R, Spokony R, Torben-Nielsen B, White KP, and Moore AW (2015). Centrosomin represses dendrite branching by orienting microtubule nucleation. *Nature Neuroscience*. DOI: 10.1038/nn.4099

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