Multiple axons and actions with PSD-95

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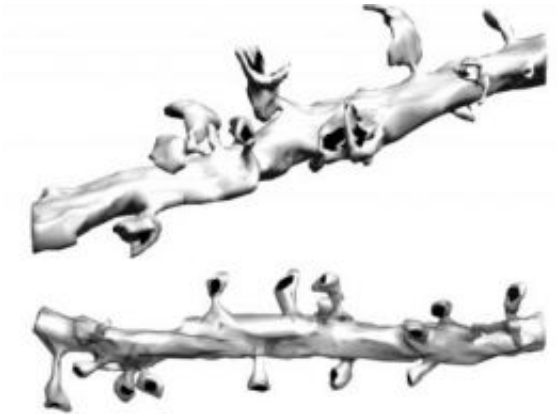

More PSD-95 means bigger spines (top), and multiple axon connections. Credit: Nikonenko, I., et al. 2008. J. Cell Biol. doi:10.1083/jcb.200805132.

Nitric oxide gets neurons together. And it seems to do it backward. Work by Nikonenko et al. suggests that a protein called PSD-95 prompts nitric oxide release from postsynaptic dendritic spines, prompting nearby presynaptic axons to lock on, and develop new synapses. The study will appear in the December 15, 2008 issue of *The Journal of Cell Biology (JCB).*

It is becoming increasingly clear that synaptogenesis is not solely axon driven. PSD-95 is a major component of postsynaptic densities—a conglomeration of scaffolding proteins, neurotransmitter receptors, and signaling proteins that are thought to shape dendritic spines—and reduced levels of PSD-95 impair synapse development. How PSD-95 works, however, was unknown.

Nikonenko et al. overexpressed PSD-95 in cultured hippocampal neurons and found that the cells' dendritic spines grew two to three times their normal size and were often contacted by multiple axons—a rare occurrence in the adult brain. By mutating different parts of PSD-95, the team discovered that the region responsible for prompting multi-axon connections was also required for binding nitrogen oxide synthase.

The team cut to the chase, bathed neurons in nitric oxide, and showed this was sufficient to promote the extra axon connections. Since bathing cells in nitric oxide and overexpressing proteins do not reflect normal physiological conditions, the team also inhibited nitric oxide synthase in wild-type neurons and confirmed that synapse density was reduced.

Overexpressing PSD-95 increased the amount of nitric oxide synthase at postsynaptic densities, suggesting PSD-95 recruits the synthase to its required locale. Interestingly, PSD-95 that lacked its synthase interaction domain still induced super-sized dendritic spines, suggesting PSD-95 wears more than one hat at the synapse construction site.

More info: Nikonenko, I., et al. 2008. J. Cell Biol. doi:10.1083/jcb.200805132. www.jcb.org

Source: Rockefeller University