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Researchers visualize formation of a new synapse

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A protein called neuroligin that is implicated in some forms of autism is critical to the construction of a working synapse, locking neurons together like "molecular Velcro," a study lead by a team of UC Davis researchers has found.

Published online in the June issue of the journal *Neural Development*, the study is accompanied by groundbreaking images that are the first to show two neurons coming together using neuroligin to construct a new synapse.

"Previous research has suggested that neuroligin is critical for the formation and stabilization of synapses," said Kimberley McAllister, an associate professor of neurology in the UC Davis School of Medicine and a researcher at the UC Davis Center for Neuroscience. "Our work suggests that neuroligin is one of the first molecules to be recruited to new synapses and that it also acts as Velcro to strengthen those new connections."

Neuroligin is a member of a family of four protein molecules that bind to another family of proteins, the β-neurexins, across synapses. During the past decade, scientists have observed that neuroligin is critical for synapse formation and function, but it is only recently that a link between the two synapse-forming molecules and autism has been recognized, McAllister said.

Lead study author and UC Davis postdoctoral fellow Stephanie Barrow

said that researchers had hypothesized that neuroligin could facilitate the recruitment of other proteins important in building synapses, but no one had been able to directly visualize the process. That's because synapses are less than 1 micron wide — 100 times narrower than a strand of human hair. To view the process, the researchers cultured neurons taken from newly born rats and flourescently labled the proteins —neuroligin, PSD-95 and NMDA — which are critical to synapse formation.

"We are the first to observe that neuroligin zips around dendrites (the branched projections of neurons) before synapses form and can accumulate very soon after contact between cells," Barrow said.

Barrow described what the team was able to visualize:

"Axons of one neuron grow toward the dendrites of neighboring neurons . As they do so, finger-like structures called filopodia extend and retract rapidly from the tip of the axons and eventually make a stable contact with the dendrite. We can then see neuroligin accumulate at these new contact sites very rapidly, possibly stabilizing adhesion between the two cells. After a few minutes, more neuroligin accumulates at this contact site, bringing NMDA receptors in with it, which is then followed by a much slower recruitment of PSD-95."

The images that accompany the study show that, indeed, the two synaptic receptor proteins, PSD-95 and NMDA, are independently recruited to the site of synapse formation once the connections are locked in place by neuroligin.

"Synapses are basically specialized sites of cell adhesion that are initially formed during development of the nervous system. Formation of viable synapses is crucial for establishing neuronal circuits that underlie behavior and cognition," said study senior author Philip Washbourne, a UC Davis postdoctoral fellow when the study was initiated and now an

assistant professor of biology at the University of Oregon.

McAllister and Barrow are continuing to capture images of the dynamics of other important molecules during synapse formation. Their goal is to create a virtual cinematic representation that includes many of the molecules that play important roles in the formation of a normal, working synapse.

"Many people think that improper synapse formation leads to the symptoms of autism," McAllister said. "This research will allow us to learn more about how synapses form to better understand what aspects of synapse formation might be altered in the disorder."

Source: University of California - Davis - Health System (news : web)