Cognitive disorders can be caused by too much of a key protein

February 3 2011, By Ken Branson

In this illustration, the microtubules on the left are lining up correctly. On the right, with the protein PSD-95 "overexpressed," things have gone wrong.

Too much of a necessary protein in the brain can thwart the normal growth of neurons and lead potentially to cognitive disorders, according to a recent study by Rutgers researchers, published in the Journal of Neuroscience.

The protein, PSD-95, is necessary for the growth of dendrites, the parts of neurons that reach out to, and help connect with, other cells.

To understand what's going on in our neurons in our brains, you can start by looking at your hand, says lead author Bonnie Firestein, professor of cell biology and neuroscience in Rutgers' School of Arts and Sciences. Imagine that the center of your hand is the body of a neuron – a nerve cell – and that the fingers are dendrites.

Dendrites reach almost, but not quite, to other neurons, separated from them by a tiny space called a synapse. The two cells on either side of a synapse use that space to send electrical and chemical signals to each

other. The reaching out of neurons to other cells – and, therefore, the ability of neurons to reach out at all – is essential to the functioning of the nervous system. Anything that interferes with that reaching out might lead to cognitive disorders, such as autism, Firestein says.

“If your hand is a cell and your fingers are dendrites, how would you add another finger?” Firestein asks. “You’d have to add bones and flesh, and what’s the cellular equivalent?”

The cellular equivalents are tiny, hollow structures called microtubules which, when a new dendrite is formed, line up in the right way to support the new structure. In a microscopic image, they look a little like a raft of freshly cut logs floating down a river. The protein PSD-95 has to be present in just the right amount for that to happen. Firestein and her co-authors report that, too much PSD-95 causes microtubule anarchy. The microtubules, instead of floating straight down the new structure to support it, turn back on themselves, twist themselves into odd shapes, and generally fail to do their job.

Firestein and her colleagues write that PSD-95 interacts with EB3, another protein located on the end of microtubules that serves as a binder. If the PSD-95 is “overexpressed” – that is, if there is too much of it – or if the EB3 is mutated, then the microtubules are “altered.” That is, they don’t line up as they should, and the physical structure of the dendrite is changed. Change may be the law of life, but this is one of those cases where any change is bad. Anything the microtubules do other than line up properly can only lead to trouble, Firestein says.

“We think this is a basic mechanism, and if you alter the amount of PSD 95 in a cell, you’ll alter the way the dendrites form,” she says. “And if you do that, you can end up with cognitive disorders like autism.”

Provided by Rutgers University