Scientists show how a neuron gets its shape

April 2 2009

(PhysOrg.com) -- Ask a simple question, get a simple answer: When Abraham Lincoln was asked how long a man's legs should be, he absurdly replied, "Long enough to reach the ground." Now, by using a new microscopy technique to watch the growth of individual neurons in the microscopic roundworm Caenorhabditis elegans, Rockefeller University researchers are turning another deceptively simple question on its head. They asked, "How long should a worm's neurons be?" And the worms fired back, "Long enough to reach their targets."

The researchers' surprising result: Rather than growing like the branches of a tree — extending outward — certain neurons work backward from their destination, dropping anchor and stretching their dendrites behind them as they crawl away. The work, led by Shai Shaham, head of the Laboratory of Developmental Genetics, and Maxwell Heiman, a research associate in the lab, not only addresses an age-old question of how neurons get their shape, but is also changing the way scientists think about the genetic program that wires the brain and allows it to grow throughout development.

"When I came to the lab, I thought that you would build a brain just like you would a house," says Heiman. "The cell would measure the distance between its cell body and its target and then specify a dendrite of that length. Now, I'm not thinking about that kind of physical map at all. I think of a connectivity map, where what's programmed are these connections among neurons and between neurons and their anchoring points."

Since they were interested in how neurons get their shapes, Heiman and Shaham used a chemical to randomly mutate genes and then screened through thousands of animals for ones whose neurons were shaped abnormally. They specifically looked at a group of 12 sensory neurons whose dendritic tips converge at the worm's nose in a sensory organ called the amphid. These dendritic tips collect information from the outside environment and give the worm cues on how to react to it.

Two genes, called dex-1 and dyf-7, caught their attention. If the animals had a mutation in either one of these genes, Heiman and Shaham saw that even though the cell migrated normally away from the tip of the nose, the dendrite didn't stay anchored. Instead, it dragged along behind the cell body, resulting in an abnormally short dendrite. When they looked at the function of the proteins, the researchers found that they form a matrix to which the dendrites are anchored. Without the matrix to anchor the neuron, the dendrites didn't form properly.

The two proteins, it turns out, are very similar to proteins that anchor the hair cells that detect sound waves in the human ear. "That was our second surprise," says Heiman. "That there is this evolutionary relationship between a sensory organ in a worm and a sensory organ in humans. In the case of the worm, the anchor is being used to resist the force of cell migration. In our ear, it is the same anchor but it is being used for a completely different purpose."

The scientists' theory that the brain is wired based on connectivity (not absolute distance) provides an explanation of how the brain grows in proportion to the growth of an organism. "As the worm grows, its dendrites get longer and longer and the position of cell bodies change as they move farther away from a synapse," says Shaham. "But what stays the same are these connections."

More information: Cell 136(7)(April 3, 2009) DEX-1 and DYF-7 establish sensory dendrite length by anchoring dendritic tips during cell migration, Maxwell G. Heiman and Shai Shaham

Provided by Rockefeller University (news : web)