Biology

Julie Ann Miller reports from Dallas at the meeting of the Society for Neuroscience

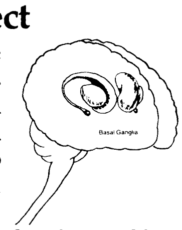
Beyond brain circuitry

The intricate maze of connections among nerve cells in the brain, although awe-inspiring, does not provide the whole story behind animal behavior. Recent evidence indicates that a hard-wired electrical circuit is not an adequate model for the brain. Characteristics invariant in an electrical circuit are flexible in nervous systems, so that fixed connections can vary their output during an animal's performance of different behaviors. The best-described nerve cell circuits are those of invertebrates, whose relatively few nerve cells can be identified. The specific connections among nerve cells have been determined in a variety of invertebrates. Now novel principles are emerging from what the scientists call "the second generation" of study of small neuronal circuits.

"Cells can dramatically change their own properties," says Peter A. Getting of the University of Iowa in Iowa City. "They show personal bias." Getting studies a circuit used in walking and swimming by a sea slug called *Tritonia*. The nerve cells he has examined form an anatomically fixed circuit, but at one synapse in that circuit the same neurotransmitter can have opposite effects. Normally, when the animal is "cruising" along the sea bottom, this neurotransmitter, serotonin, stimulates the next cell in the circuit. But in a situation where the animal needs to make a rapid escape, the serotonin causes inhibition. Getting and his colleagues have demonstrated that input from other cells reorganizes the interactions within the network and alters its function. He suggests that interactions among nerve cells in the spinal cord of vertebrates might also have variable patterns of "who talks to whom."

A nerve cell circuit that excites stomach muscles and generates motor patterns in crabs provides another example of variability in the functioning of neural circuitry. Eve Marder of Brandeis University in Waltham, Mass., reports that the output of this circuit is influenced by many different neurotransmitters and other substances, called neuromodulators, present in the group of nerve cells. These chemicals can change the strength, frequency or timing of nerve cell activity. Marder says, "Each substance reconfigures the circuit."

Deep core of brain gains respect



The cerebral cortex, the outer shell of the brain, has long been considered the nervous system's crowning achievement. What could compare to the sophistication of our speech and thought centers? Certainly not the deep "reptilian" brain structures known as the basal ganglia.

This view of the brain is all wrong, says Ann Graybiel of Massachusetts Institute of Technology. The deep brain structures have a sophistication all their own that rivals that of the cerebral cortex.

The basal ganglia have been considered primitive despite what is already known about their important functions. They play a role in the control of movement, influencing not just how an animal moves but also its decision whether or not to move. They also seem to be required for spatial memory. The basal ganglia receive input from almost all areas of the cortex. Some cells in this area have quite sophisticated characteristics; for example, in trained monkeys one type of cell responds to a click only when the sound signals a reward.

Part of the basal ganglion's underappreciation may stem from the much more homogeneous appearance of its cellular architecture compared with the dramatic layers of the cerebral cortex. "The basal ganglia structure looks more like liver," Graybiel says. But in her recent experiments she has distinguished cells by their neurotransmitters. The regions of the basal ganglia called the striatum are very rich in neurotransmitter chemicals. Almost all neurotransmitters and neuromodulators found anywhere in the nervous system are present in the striatum. Graybiel reports there is a clear pattern of organization in the striatum when the cells are distinguished by these signal chemicals.

"There is a logic to it," Graybiel says. Instead of layers as in the cortex, there are patches of cells, which Graybiel calls striasomes. Each neurotransmitter is especially dense either within or outside the striasomes. The striasomes also delineate areas that innervate different brain areas.

Graybiel finds evidence also for other patches within the striatum that represent input from different regions of the cortex. "Think of a whole mosaic of input compartments interleaving among the striasomes," she says. This mosaic resembles the organization of the cortex where interdigitating sets of columns handle different functions. Graybiel says, "The basal ganglion brings together different modalities, associated in a special chemical environment."

Carving out the nervous system

An important aspect of development is the whittling down of the brain: A newborn has far more nerve cells and nerve cell connections than does an adult. Recent research gives an indication of the magnitude and modes of this whittling. Pasko Rakic of Yale University School of Medicine reports that in some brain areas during the first weeks of life an infant loses as many as two nerve cells each second. He suggests that which cells are eliminated is influenced by the cells' activity and environment. His observations help explain the versatility of the primate brain, including its ability to compensate for physical abnormalities.

The overproduction of nerve cells has been demonstrated in several brain areas. For example, in the corpus callosum, a bundle of fibers connecting the right and left hemispheres, a newborn has 200 million axons (nerve cell output fibers) and the adult only 50 million. In a smaller connecting bundle, the hippocampal commisure, the newborn has 1.2 million axons and the adult 200,000, Rakic reports. Competition between fibers connecting to the same target appears to be the key to the selective elimination of connections and then of cells.

Several groups of scientists have demonstrated that if one eye of a monkey fetus is removed, axons from the remaining eye spread over the surface normally innervated by both eyes. Fewer axons from the lone eye are eliminated than would have been eliminated if both eyes were present. In recent work Rakic demonstrated a drop in nerve cell elimination following the loss of a competing area within the brain. Two years after removing part of the visual cortex of a fetal monkey, he finds that the area of the brain that normally shares target cells with the visual cortex is twice the normal size.

When the overabundance of fibers is not eliminated, can the extra fibers function? Would they be beneficial or detrimental to the brain's activities? To investigate these questions, Yale scientists removed one eye of a monkey fetus and asked whether the remaining eye, with its extra connections, would perform better or worse than one eye of a normal monkey. They found that on an acuity test — in which the monkey determines whether lines are close on a TV screen — the lone eye of the experimental animal did slightly better than the better eye of a normal monkey. Therefore the extra fibers do not hinder brain processing of visual information. Rakic reports that the extra input is not suppressed by the normal input; the extra cells are metabolically active as indicated by uptake of 2-deoxyglucose.

These findings suggest that the extra-keen sensitivity a blind or a deaf person seems to have in the remaining senses may reflect extra input and connections in the relevant brain areas. "The mammalian brain," Rakic concludes, "is more malleable than we had thought."