Adult Human Brains Add New Cells

Offering hope that brain cells slain by stroke, disease, or injury are replaceable, five cadavers have presented scientists with the first solid evidence that nerve cells continue to be born throughout life in the human brain.

The new study, described in the November NATURE MEDICINE, challenges the long-held doctrine that an adult human brain cannot form new nerve cells, or neurons, the information-processing cells of the brain. Scientists had crafted a plausible explanation for that dogma: Higher animals, especially people and other primates, might be so dependent upon learned skills and memories encoded in their neural circuits that their brains don't dare grow new neurons that might disrupt those imprints.

"You would have new cells that never went to elementary school," notes Pasko Rakic of Yale University School of Medicine in New Haven, Conn.

Yet, evidence that the brains of mature animals develop new neurons has gradually emerged. Most of the research has focused on the hippocampus, a brain region normally involved in learning and the processing of memories. In birds, mice, and other animals, scientists have clearly documented the birth of hippocampal neurons throughout life. Earlier this year, researchers finally extended that observation to primates, showing neuron birth in adult marmoset monkeys (SN: 3/21/98, p. 180).

Investigators have now used the tragedy of cancer to find similar evidence in people. Although the chemicals used to label newborn cells in the animal experiments are toxic, physicians administering chemotherapy to cancer patients occasionally use them to monitor tumor growth. The chemicals, such as bromodeoxyuridine, or BrdU, become part of newly formed DNA when dividing cells copy their genetic information. Researchers, for example, can then identify any cell with BrdU in its DNA as a recent arrival.

Peter S. Eriksson of Göteborg University in Sweden persuaded a physician using BrdU on people with cancer of the tongue or larynx to ask the family, whenever a patient died, if he could remove brain sections for study. Since 1996, Eriksson has received such permission five times and quickly obtained the needed brain material, before it deteriorated.

Working with a research team led by Fred H. Gage of the Salk Institute for Biological Studies in La Jolla, Calif., Eriksson's group examined slices of the hippocampus, focusing on an area called the dentate gyrus, where neuron birth occurs in other adult animals. The researchers identified BrdU-labeled cells and stained the brain region with antibodies that distinguish neurons from other kinds of brain cells. In the five people, whose ages at death ranged from 57 to 72, there were sometimes more than 200 new, healthy neurons per cubic millimeter of dentate gyrus, the scientists report. Gage estimates that 500 to 1,000 neurons are born in the gyrus each day—a small fraction of the many millions already there.

"It's wonderful. It lays to rest, finally, a controversy that I think has really blocked progress in understanding what these new neurons might be doing," says Elizabeth Gould of Princeton University, who led the marmoset work.

Some controversy lingers, however. Rakic maintains that neuron birth in adults is a limited phenomenon, perhaps occurring only in the dentate gyrus. Gould counters that the no-new-neurons dogma has stopped scientists from thoroughly testing whether neuron birth occurs elsewhere in the brain. "We need to find out how widespread this phenomenon is," she says.

Gage notes that scientists must now factor neuron birth in adults into their thoughts about plasticity, the ability of the brain to reshape its neural circuits throughout life. Potentially even more important—if investigators can understand why parts of the adult brain do or do not grow new neurons—is the possibility of inducing cell proliferation to replace dead neurons in people who have suffered strokes or who have neurodegenerative illnesses such as Alzheimer's or Huntington's diseases. —*J. Travis*

Cancer drug helps paralyzed mice walk

A bacterial toxin that can destroy the developing lungs of a newborn child has unexpectedly enabled mice paralyzed by spinal cord injuries to walk again.

The toxin, known as CM101, was originally considered as a cancer drug by a research group led by Carl G. Hellerqvist of Vanderbilt University in Nashville. Bacteria known as group B streptococci secrete this carbohydrate molecule, which binds to a cell-surface protein found on blood vessels in newborn infants' lungs, marking them for destruction by an immune response. Since growing tumors depend upon the formation of new blood vessels, which also bind the toxin, Hellerqvist and his colleagues are testing whether CM101 can similarly mark tumors for destruction.

Recently, the researchers started to wonder about spinal cord injuries. They noted that the scar that often forms at the site of such an injury may be a major impediment to the cord's recovery. Since this scarring depends on immune cells delivered by new blood vessels, they hypothesized that CM101 might have a therapeutic effect.

When given intravenously within several hours of a paralyzing spinal cord injury and for several days after, CM101 allowed 24 out of 26 mice to regain the ability to walk within 2 to 12 days, the scientists report in the Oct. 27 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. In contrast, none of 14 untreated mice suffering a similar injury recovered their mobility, and 8 died within 24 hours.

CarboMed, a firm founded in 1990 by Hellerqvist to commercialize CM101, is encouraged by both the new results and recent cancer trials that indicate the drug is safe. The company plans to test the compound on people immediately after they have suffered spinal cord injuries. "By the end of next year, we should be in clinical trials," says Hellerqvist.

While several investigators who study spinal cord injuries say that such a leap is premature until CM101 undergoes significantly more animal testing, some of them are nevertheless impressed by the apparent recovery of the mice. "The results are phenomenal," says Arlene Y. Chiu of the National Institute of Neurological Disorders and Stroke in Bethesda, Md., who recently heard Hellerqvist present his results and saw a video of the treated mice walking and climbing.

Chiu and other investigators caution that Hellerqvist's group didn't use an established model of spinal cord injury but developed its own method of damaging the cord, complicating comparisons with other treatments. Moreover, the large percentage of deaths in the untreated group is unusual for spinal cord injuries and makes evaluating CM101 a challenge, says Naomi Kleitman of the Miami Project to Cure Paralysis.

Further research is needed to explain how CM101 works. Some evidence collected by Hellerqvist suggests that it indeed eliminates scarring and so encourages new connections among cells. Other experiments suggest that CM101 may protect cells whose connections remained intact. "The drug appears to preserve the overall health and structure of the nerve cells," Kleitman says. —*J. Travis*