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Memorable debate: Do old brain cells die?

Why do so many people become more forgetful as they age? For 2 decades, scientists have held to a simple, and therefore appealing, hypothesis: Age-related memory difficulties result from a gradual loss of cells in the hippocampus, a brain area long associated with memory formation and recall.

This notion first arose when rat studies showed that cell density in the hippocampus dropped dramatically during the late stages of a rodent's life. Human studies seemed to confirm a similar age-related loss of brain cells.

In the last year, however, a small group of researchers has contested this view. "It's just plain not correct," says Peter R. Rapp of the State University of New York at Stony Brook.

This blunt challenge to dogma stems from a novel way of counting cells. While past studies tallied the number of brain cells in a thin slice of hippocampal tissue, the new method estimates the total number of hippocampal cells from counts of the cells in thick sections taken throughout the region.

A group headed by Mark J. West of the University of Aarhus in Denmark pioneered this technique and recently reported that the number of brain cells in the hippocampus differs little among young rats, old rats with good memory, and old rats with poor memory. Those results were criticized, however, because the group examined only a small number of animals and used a strain of rats different from that examined in most memory studies.

Rapp and Michela Gallagher of the University of North Carolina at Chapel Hill have now largely corroborated West's results in a study with a much larger number of rats. Moreover, they tested a rodent strain that's frequently used in age-related memory research.

Old rats, including ones that perform poorly in a memory-testing maze, have as many hippocampal brain cells as young rats, the two researchers report in the Sept. 3 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

"In aged rats, we see dramatic changes in learning and memory skills that depend on the hippocampus, but we see no evidence for an association between [brain] cell loss and the cognitive impairment we document," says Rapp, who asserts that he has collected similar data in studies of monkeys.

"I'm puzzled by the whole thing," says Philip W. Landfield, whose work over the last 20 years has provided much of the support for the idea that an aging hippocampus suffers cell loss.

Among other concerns, Landfield, a researcher at the University of Kentucky Medical Center in Lexington, questions whether the statistical methods used in the new counting technique are as accurate as its proponents attest. "I feel you can't estimate all the neurons in the hippocampus, some 1 million or so, by counting a few hundred," he says.

Dahlia Zaidel of the University of California, Los Angeles stresses that the human brain differs significantly from the rat brain and that the new results will be useful only if similar data are found in human brains available for autopsy.

If hippocampal brain cells are not dying, what causes the age-related memory woes?

Landfield notes that even if aging brain cells stay alive, they probably change in ways that alter their overall performance. For example, they may make different proteins.

The issue of hippocampal brain cell loss is more than an academic debate. If cells in the aging brain do not die, it may be possible to fix them, contend some investigators. "From a clinical perspective, it's extraordinarily good news," asserts Rapp. "It's a much easier task to restore normal function to existing [cells] than to try to build new brain cells."

Still, memory researchers do not uniformly embrace Rapp's optimism. "Counting cells is a very tricky business," notes Landfield.

— J. Travis