

Stem cell activity deciphered in the aging brain

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Neurobiologists have discovered why the aging brain produces progressively fewer new nerve cells in its learning and memory center. The scientists said the finding, made in rodents, refutes current ideas on how long crucial "progenitor" stem cells persist in the aging brain.

The finding also suggests the possibility of treating various neurodegenerative disorders, including Alzheimer's disease, dementia and depression, by stimulating the brain's ability to produce new nerve cells, said senior study investigator Ashok K. Shetty, Ph.D., professor of neurosurgery at Duke University Medical Center and medical research scientist at Durham VA Medical Center.

Results of the study appear online in the journal *Neurobiology of Aging*. The research was funded by the National Institutes of Health and the U.S. Department of Veterans Affairs.

Previous studies by Shetty and others had demonstrated that as the brain ages, fewer new nerve cells, or neurons, are born in the hippocampus, the brain's learning and memory center. In one study, Shetty and colleagues showed that the production of new neurons in rats slows down dramatically by middle age -- the equivalent of 50 years in humans.

But scientists did not know what causes this decline.

The common assumption had been that the brain drain was due to a decreasing supply of neural stem cells in the aging hippocampus, said



lead study investigator Bharathi Hattiangady, Ph.D., research associate in neurosurgery. Neural stem cells are immature cells that have the ability to give rise to all types of nerve cells in the brain.

In the current study, however, the researchers found that the stem cells in aging brains are not reduced in number, but instead they divide less frequently, resulting in dramatic reductions in the addition of new neurons in the hippocampus.

To conduct their census, the researchers attached easy-to-spot fluorescent tags to the neuronal stem cells in the hippocampus in young, middle-aged and old rats.

They found that in young rats, the hippocampus contained 50,000 stem cells -- and, significantly, this number did not diminish with aging. This finding, the researchers said, suggested that the decreased production of new neurons in the aged brain was not due to a lack of starting material.

The researchers then used another fluorescent molecule to tag all stem cells that were undergoing division in the process of staying "fresh" in case they were recruited to become mature nerve cells.

They found that in young rats, approximately 25 percent of the neural stem cells were actively dividing, but only 8 percent of the cells in middle-aged rats and 4 percent in old rats were dividing. This decreased division of stem cells is what causes the decreased neurogenesis, or birth of nerve cells, seen with aging, the scientists said.

"This discovery provides a new avenue to pursue in trying to combat the cognitive decline associated with conditions such as Alzheimer"s disease and with aging in general," Hattiangady said.

The team now is searching for ways to stimulate the brain to replace its



own cells in order to improve learning and memory function in the elderly.

One approach being explored is to treat older rats with drugs designed to mimic the action of compounds called neurogenic factors, which encourage stem cells in the brain to divide, Shetty said. The researchers also are grafting neural stem cells grown in culture dishes into the hippocampus, to stimulate those already present. Additional approaches include using behavioral modification techniques, such as physical exercise and exposure to an enriching environment, that are known to stimulate proliferation of stem cells.

Source: Duke University Medical Center

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