Nerve-cell transplants help brain-damaged rats fully recover lost ability to learn

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Nerve cells transplanted into brain-damaged rats helped them to fully recover their ability to learn and remember, probably by promoting nurturing, protective growth factors, according to a new study.

Building on previous investigation of transplants in the nervous system, this critical study confirms that cell transplants can help the brain to heal itself. Ultimately, it may lead to new therapies to help dementia patients. More generally, scientists can now develop and test new ways to help repair an injured nervous system -- whether through new drugs, genetically modified cells, transplanted neural (nerve) and non-neural brain cells, or other means.

The discovery was announced in the December issue of *Behavioral Neuroscience*, published by the American Psychological Association. The findings, according to the authors, confirm the potential of cell grafts to stimulate the release of growth factors for neurons, regenerate or reorganize a part of the brain, and restore cognitive function, in a process called neural plasticity.

This study focused on the hippocampus, considered to be the seat of learning and memory, whose shrinkage in Alzheimer's disease causes steadily worsening symptoms. The study's authors targeted a key player in the hippocampal "learning system," which includes the hippocampus itself, the subiculum (the major output structure connected to the cortex, the self-aware "thinking" part of the brain), and the adjacent entorhinal cortex.

Previously, these scientists had demonstrated that damage to the subiculum in rats led to deterioration of the hippocampus, and problems with learning. The next question was obvious: Could researchers do the opposite, repair the hippocampus and restore the memory functions?

They sought the answer at India's National Institute for Mental Health and Neuro Sciences and National Centre for Biological Sciences (Tata Institute for Fundamental Research), both in Bangalore. First, the scientists injected a neuron-destroying chemical into the subiculum area of 48 adult rats.

Next, again using precise micro-injections, the scientists transplanted hippocampal cells that had been taken from newborn transgenic mice and cultured in an incubator into the hippocampi of about half the rats. These special cells had a green fluorescent protein used to "label" and track them after transplantation. (Transgenic mice are bred with a little extra DNA that allows their cells to be grown in glass plates in incubators.)

Two months later, the scientists measured how well both the transplant and non-transplant rats learned and remembered, using two well-established maze tests of spatial learning. The rats given cell transplants had recovered completely: On both mazes, they performed as well as those rats which had not had their subiculums damaged. The rats without transplants did not recover: They had many problems learning their way through the mazes.

After studying behavior, the scientists examined what happened in the brain. Under the microscope, it appeared that the transplanted cells had settled mainly in a sub-area of the hippocampus called the dentate gyrus. There, the transplants appeared to promote the secretion of two types of growth factors, namely brain-derived neurotrophic factor and fibroblast growth factor, which boost the growth and survival of the cells that give rise to neurons. In the hippocampi of rats with cell transplants, the expression of brain-derived growth factor went up threefold.

It is significant that transplants can provide more neural growth factors in the hippocampus, because the formation of new neurons there may be critical for cognitive function.

Neural growth factors, also called neurotrophic factors, hold great promise for treating neurological problems. These specialized chemicals "provide an ideal micro-environment for making new neurons," said co-author Bindu Kutty, PhD. "They also protect existing brain cells, especially following an injury or other neurological insult."

Further study is needed, especially to understand the underlying repair mechanism and the apparent starring role of growth factor in brain health. Although the current study shows in the lab that brain-cell transplants can restore function, "more studies along these lines using appropriate animal models are required to find definitive answers about the safety and efficacy of such approaches," said Kutty. "We are still some way from achieving a new therapy based on these findings."

More information: "Transplantation of Hippocampal Cell Lines Improves Spatial Learning in Rats with Ventral Subicular Lesions," J. Rekha et al., Behavioral Neuroscience, Vol. 123, No. 6.

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