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New study shows that fetal cells to treat Parkinson's disease may not function long term

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Neurons grafted into the brain of a patient with Parkinson's disease fourteen years ago have developed Lewy body pathology, the defining pathology for the disease, according to research by Jeffrey H. Kordower, PhD, and associates and published in the April 6 issue of *Nature Medicine*.

The finding suggest that Parkinson's disease is an ongoing process that can affect cells grafted into the brain in the same way the disease affects host dopamine neurons in the substantia nigra of the brain, according to Kordower, who is the lead author of the study and a neuroscientist at Rush University Medical Center.

"These findings give us a bit of pause for the value of cell replacement strategy for Parkinson's disease," said Kordower. "We still need to vigorously investigate this approach among the full armament of surgically-delivered Parkinson's disease therapies. While it is not clear to us whether the same fate would befall stem cell grafts, the next generation of cell replacement procedures, this study does suggest that grafted cells can be affected by the disease process."

The collaborative research study described in the article involves Rush, Mt. Sinai School of Medicine, New York, and the University of South Florida, Tampa, In it, individuals with Parkinson's disease received fetal cell transplants to reverse the loss in the brain of striatal dopamine.

The individual described in this article was a woman with a 22-year history of Parkinson's disease who underwent transplantation in 1993. After transplantation she experienced improvements in disease symptoms as measured by the Unified Parkinson Disease Rating Scale (UPDRS) and required substantially lower doses of antiparkinsonian medications. Her UPDRS scores remained improved into1997, but by 2004, she experienced progressive worsening of Parkinson's disease symptoms. She died in 2007 and her brain and that of two other patients in the study were comprehensively processed and analyzed. She had the longest survival after transplantation that had been reported to date among this study's participants.

Double-blind, sham-controlled studies that followed did not establish clinical benefit although significant improvement was observed in a subpopulation of patients. Post mortem studies of individuals in these studies showed a robust survival of grafted neurons, suggesting that the cells were not affected by Parkinson's disease as Kordower explains "Because Parkinson's disease pathology progresses over decades, we think that the individuals did not live long enough for the Parkinson's disease pathology to develop in the grafted cells."

Scientists have long debated whether Parkinson's disease results from an acute insult or event, or whether it is an ongoing pathological process that continues to affect healthy neurons, according to Kordower. This research indicates that mechanisms and molecules responsible for initiating the degenerative process are still present at a late stage and are capable of affecting grafted neurons. In addition, the processes that destroy dopamine neurons are not restricted to the midbrain.

"The findings also suggest that there may be either a pathogenic factor in the brain that affects dopamine producing neurons or a pathological process that can spread from one cellular system to another," said Kordower. "These findings have striking implications for understanding

what causes PD and the potential for cell replacement strategies to reverse the motor symptoms."

Source: Rush University Medical Center