

Transplant of stem-cell-derived dopamine neurons shows promise for Parkinson's disease

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Parkinson's disease is an incurable movement disorder that affects millions of people around the world, but current treatment options can cause severe side effects and lose effectiveness over time. In a study published by Cell Press November 6th in *Cell Stem Cell*, researchers showed that transplantation of neurons derived from human embryonic stem cells (hESCs) can restore motor function in a rat model of Parkinson's disease, paving the way for the use of cell replacement therapy in human clinical trials.

"Our study represents an important milestone in the preclinical assessment of hESC-derived dopamine neurons and provides essential support for their usefulness in treating Parkinson's disease," says senior study author Malin Parmar of Lund University.

Parkinson's disease is caused, in part, by the death of neurons that release a brain chemical called dopamine, leading to the progressive loss of control over dexterity and the speed of movement. Currently available drug and surgical treatment options can lose effectiveness over time and cause serious side effects such as involuntary movements and psychiatric problems. Meanwhile, another approach involving the transplantation of human fetal cells has produced long-lasting clinical benefits; however, the positive effects were only seen in some individuals and can also cause involuntary movements driven by the graft itself. Moreover, the use of tissue from aborted human fetuses presents logistical issues such as the limited availability of cells, hampering the effective translation of fetal tissue transplantation as a realistic therapeutic option.

To rigorously assess an alternative hESC-based treatment approach, Parmar and lead study author Shane Grealish of Lund University transplanted hESC-derived dopamine neurons into brain regions that control movement in a rat model of Parkinson's disease. The transplanted cells survived the procedure, restored dopamine levels back to normal within five months, and established the correct pattern of long-distance connections in the brain. As a result, this therapy restored normal motor function in the animals. Importantly, the hESC-derived neurons show efficacy and potency similar to fetal neurons when transplanted in the rat model of Parkinson's disease, suggesting that the hESC-based approach may be a viable alternative to the approaches that have already been established with fetal cells in Parkinson's patients.

In a related Forum article published in the same issue, Roger Barker of Addenbrooke's Hospital and the University of Cambridge laid out the roadmap for taking stem-cell-derived dopamine neurons to the clinic for treating Parkinson's disease. "This involves understanding the history of the whole field of cell-based therapies for Parkinson's disease and some of the mistakes that have happened," he says. "It also requires a knowledge of what the final product should look like and the need to get there in a collaborative way without being tempted to take shortcuts, because a premature clinical trial could impact negatively on the whole field of regenerative medicine."

Story Source:

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Journal Reference:

1. Shane Grealish, Elsa Diguët, Agnete Kirkeby, Bengt Mattsson, Andreas Heuer, Yann Bramouille, Nadja Van Camp, Anselme L. Perrier, Philippe Hantraye, Anders Björklund, Malin Parmar. **Human ESC-Derived Dopamine Neurons Show Similar Preclinical Efficacy and Potency to Fetal Neurons when Grafted in a Rat Model of Parkinson's Disease.** *Cell Stem Cell*, 2014; 15 (5): 653 DOI: [10.1016/j.stem.2014.09.017](https://doi.org/10.1016/j.stem.2014.09.017)

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