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New Method for Making Neurons Could Lead to Parkinson's Treatment

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A new method of synthesizing dopamine-producing neurons, the predominant type of brain cell destroyed in Parkinson's, offers hope for creating cell-replacement therapies that reverse the damage.

The method provides an efficient way of making functional cells. When transplanted into mice and rats with brain damage and movement problems similar to Parkinson's, the cells integrated into the brain and worked normally, reversing the animals' motor issues.

The finding brings researchers a step closer to testing a stem-cell-derived therapy in patients with this disorder. "We finally have a cell that seems to survive and function and a cell source that we can easily scale up," says [Lorenz Studer](#), a researcher at the Sloan Kettering Institute and senior author on the new study. "That makes us optimistic that this could potentially be used in patients in the future."

The research also highlights the challenges of generating cells for tissue-replacement therapy, showing that subtle differences in the way the cells are made can have a huge impact on how well they work once implanted.

Many of the symptoms of Parkinson's disease—which include tremor, muscle rigidity, and loss of balance—are linked to loss of dopamine in the brain. While medications exist to replace some of the lost chemical, they do not alleviate all of the symptoms and can lose their effectiveness over time. Scientists hope that replacing lost cells with new ones will provide a more complete and long-term solution.

In the new study, researchers started with human embryonic stem cells, which by definition can differentiate into any cell type. To make a specific type of cell in high numbers, scientists expose the stem cells to a cocktail of chemicals that mimic what they would experience during normal development.

While stem-cell researchers had previously been able to create dopamine-producing neurons from human stem cells, these cells did little to alleviate movement problems in animals engineered to mimic the symptoms of Parkinson's. In 2009, Studer and others developed a method of making the cells that more closely mimics the way they form during development. The resulting cells also carry more of the molecular markers that characterize dopamine-producing cells in the brain

In the new research, published Sunday in the journal *Nature*, Studer's team found a way to make these cells even more efficiently. This is significant in terms of ultimately testing the therapy in humans; many methods for making specific types of cells are complex and yield small amounts of the desired product.

They could scale up the process to make enough material to transplant into monkeys, whose larger brains are more akin to humans' than other animals used in testing.

In addition, the researchers demonstrated that transplants of the cells could correct Parkinson's-like problems in mice and rats. Three different tests of motor function "all very dramatically improved when you put the cells in," says Studer.

While the two monkeys in the study also had brain damage reminiscent of Parkinson's, not enough time has passed to determine whether the transplants will help, Studer says. It took five months post-transplant for the cells to have a visible effect in rodents.

The findings demonstrate the challenges of developing treatments based on living cells. "Previously, I think, many people thought of cell therapy [for Parkinson's] as a dopamine-producing biological pump," says [Ole Isacson](#), a neuroscientist at Harvard Medical School. But in reality, it requires a very specific replacement of nerve cells. Unless you have a specific differentiation protocol, you won't get functional recovery in rodent models." Isacson was not involved in the research but has collaborated with Studer on other projects.

Researchers mostly used embryonic stem cells in these experiments, because tissue derived from these cells is already being used in [human trials for treating spinal cord injury](#) and certain types of blindness. They also showed that the protocol works on induced pluripotent stem (iPS) cells, which are derived from adult cells that are turned back to an embryonic-like state using a combination of genetic or chemical factors. iPS cells are genetically matched to the cell donor, and might ultimately provide a preferable source of tissue for therapy. However, these cells are further from human testing because they are much less studied than embryonic cells.

Studer's team now plans to make the cells on an even larger scale in a facility that meets conditions set by the U.S. Food and Drug Administration for human therapies. "We need to be able make enough cells to graft 100 patients," says Studer. He predicts that will take a year or two, followed by extensive safety testing to make sure the differentiated cells do not behave in unexpected ways once implanted.