

Parkinson's Cell Transplant Shows Good Reinnervation at 24 Years

Sue Hughes | May 10, 2016

A postmortem examination of a patient with Parkinson's disease who underwent dopaminergic cell transplantation 24 years ago has shown that the transplanted neurons survived and had reinnervated the brain for all that time.

The findings provide "proof of concept" that cell transplantation may be a viable option for patients with Parkinson's disease, the researchers, from Lund University, Sweden, say.

In a paper [published online](#) in *Proceedings of the National Academy of Sciences of the United States of America* on May 2, the researchers report that the patient experienced major clinical benefits for at least a decade after transplantation.

The patient showed such marked improvement that medication with L-dopa was no longer necessary 3 years after the transplantation, they note. Imaging indicated that dopamine function was completely normal in the transplanted brain structure 10 years after the operation, and the latest postmortem findings show that the transplanted dopamine-producing cells and their normal neural connections are still present almost a quarter of a century after the operation.

However, the improvements in symptoms were gradually lost from 14 years after transplantation, "indicating that even extensive graft-derived dopaminergic reinnervation loses its efficacy in a severely degenerating brain," the researchers state.

One of the Most Successful Cases

Lead author, Professor Jia-Yi Li, explained to *Medscape Medical News* that this patient was 1 of 18 patients who received fetal cell transplants for Parkinson's in Lund, Sweden, in the late 1980s. Most have since died, and in 5 patients postmortem examination of the brain has been performed. This patient is one of the most successful cases.

"This patient represents the longest survivor at 24 years posttransplant, and we show that even at this long after the procedure the transplanted cells have completely reinnervated the putamen," Professor Li said. Because patients received the transplant on only one side of the brain, the researchers could compare the two sides of the brain on postmortem examination. "We found the transplanted side showed complete reinnervation whereas the nontransplanted side showed no dopaminergic profile."

Professor Li noted that the more than 10 years of symptom relief "is a very good result from one single procedure." He added: "But the eventual gradual return of symptoms shows that the degeneration of the brain does not occur just in the putamen — it spreads throughout the brain."

The patient also developed cognitive impairment at around the 14-year mark, and progressive dementia ensued.

"It was thought at the time of transplant that this patient was a typical Parkinson's patient, but he developed Parkinson's dementia later on and the patients who develop such dementia have a much heavier pathology in the brain with the presence of Lewy bodies," he said.

"This patient had more Lewy body pathology in the transplanted cells than previous patients we have reported," he said. Previously, about 1% to 5% of transplanted cells have been found to show Lewy body pathology, but this patient had 10% to 12% of transplanted cells affected in this way.

"This Lewy body pathology is associated with Parkinson's dementia, which only develops in certain patients," he added.

"Our results indicate that the Lewy body pathology propagates from the host brain into the transplanted cells."

Fetal cell transplantation fell out of favor in the 1990s after trials in the United States showed side-effect issues, including severe dyskinesias. While some of the Swedish patients also showed dyskinesias, Professor Li noted that this was less of an issue than in the United States.

"We used a different technique for transplantation which was more successful than the US trials," he said. "But the whole field stopped after the US experience."

New European Trial Underway

However, preclinical work continued to refine the techniques involved, and a new European clinical trial of fetal cell transplantation for Parkinson's is now underway.

"Our observations from postmortem examination of our patients may help patient selection for the current European trial of fetal cell transplant and future trials of stem cell therapy," Professor Li said. "The fact that Lewy body pathology still affected the transplanted tissue suggests that patients with heavy Lewy pathology may not be so suitable for cell transplantation."

Commenting on this case report for *Medscape Medical News*, James C. Beck, PhD, vice president, scientific affairs, Parkinson's Disease Foundation, New York, New York, agreed that the findings would be useful to guide future research.

"What is notable about this case is that it gives us an idea of what we could expect from a successful transplant," he said. "For example, it took 3 years from time of transplant to see the full effect. You hear stories about possible improvement just weeks after a stem cell transplant but this would appear to be unrealistic."

"But once the effects started to be seen this patient lived with minimal Parkinson's symptoms for 10-plus years," he said. "That is a fantastic achievement."

"However, this report also tells us that transplantation of cells is unlikely to be a cure for Parkinson's because the disease returned. It gave the brain a boost of dopamine, which produced some good relief of the motor symptoms for many years, but it did not prevent Lewy body dementia from developing."

Dr Beck said that while techniques may have now improved, fetal tissue transplant might be a possibility for a few selected patients, "but it is not going to be widescale treatment routinely available because there will be a limited supply of fetal tissue and the whole issue of using fetal tissue is ethically very difficult."

Stem cell therapy is much more viable as stem cells can be produced in large quantities in a standardized procedure, and clinical trials of stem cells in Parkinson's are expected to start soon.

"This current report of fetal cell transplant shows us what might be expected from stem cell transplants — a tremendous benefit may be possible but it unlikely to be a forever fix," Dr Beck added.

Roger Barker, MBBS, consultant neurologist at Addenbrookes Hospital, Cambridge, United Kingdom, who is coordinating the new European trial of fetal cell transplants, told *Medscape Medical News* the current report was "very interesting and important in that it shows that grafted dopamine cells can survive for so long in the brain of a Parkinson's disease patient."

But he agreed that this field will move toward stem cells in future for ethical and logistical reasons.

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