Fetal Nerve Grafts Show Promise in Parkinson's

Implanting dopamine-secreting nerve cells in the brain of a Parkinson's patient markedly alleviated his symptoms

SWEDISH RESEARCHERS have taken a step toward developing what may be an effective new treatment for Parkinson's disease. On page 574 of this issue, Olle Lindvall, Anders Björklund, and their colleagues report that transplanting fetal nerve tissue into the brain of a man with severe Parkinson's disease produced a clinically significant improvement in the patient's condition.

It's the "first verified" demonstration that the procedure works in humans, says neuroscientist John Sladek of the University of Rochester School of Medicine, who has had similar successes in his own research, albeit with monkeys. The new results indicate that the Swedish group has made significant advances since 1987 when it first tried the transplant procedure and obtained only marginal improvements in two patients.

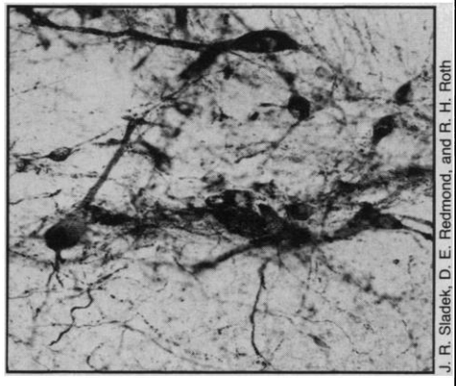
But in spite of these encouraging results, fetal tissue transplants are not about to become standard therapy for Parkinson's disease. "This does not represent an established therapy," Lindvall says, "but a further step forward."

Moreover, even if the therapy eventually proves out scientifically, it is likely to remain controversial on political and ethical grounds because it requires the use of fetal tissue obtained from induced abortions. The U.S. government has banned the expenditure of federal funds for research involving the transplantation of fetal tissue into human patients. In addition, research involving fetal tissue is prohibited in some states even if it is paid for by private funds.

Nevertheless, says neurologist Christopher Goetz of Rush–Presbyterian–St. Luke's Medical Center in Chicago, there is "absolutely" a need for better Parkinson's therapies, and the fetal nerve grafting procedure is considered one of the most promising approaches currently under study.

The idea behind the procedure is simple enough. The symptoms of Parkinson's disease—tremors and muscular rigidity that can eventually bring voluntary movements to a halt—are caused by the degeneration of nerve cells in a brain region called the substantia nigra. These neurons transmit their signals by releasing a chemical called dopamine. In its early stages, the disease can be treated by giving patients the amino acid levodopa, which is transported into the brain and converted to dopamine, making up for what the brain itself is incapable of producing. But the treatment loses its effectiveness after a few years, possibly because of continued nerve degeneration, and the patients begin experiencing periodic "off" times when their symptoms abruptly return.

Implanting dopamine-secreting neurons directly into the brain might, neurologists reasoned, provide a more physiological and more permanent source of the neurotransmitter. This seems to have worked in the current patient, a man who developed Parkinson's disease in 1977 and was severely impaired. In the 11 months before the surgery, he had an average of four to five off periods per day and spent nearly 50% of his time in that state, despite receiving optimal levodopa therapy. But after receiving a brain graft of fetal dopamine-secreting cells, he underwent a gradual improvement. By 3 months after the surgery, he was having at most one to two brief off periods a day, with very mild symptoms. His condition has remained stable now for an additional 5 months. "The improvement clearly has been of value to him," Lindvall says.



J. R. Sladek, D. E. Redmond, and R. H. Roth

Nerve network. *Embryonic dopamine neurons engrafted in a monkey brain make connections.*

Moreover, by using positron emission tomography to image the patient's brain, the Lund group, with their collaborators at Hammersmith and National Hospitals in London, showed that the engrafted neurons have survived. Poor graft survival may have been the reason why the two previous recipients of fetal nerve transplants were only marginally aided.

The marked improvement the Lund workers find now may be due to some relatively simple changes they made in the grafting procedures. For example, they used a solution with a composition more like that of biological fluids to prepare and store the nerve tissue. And they also injected the cells through a smaller tube to minimize the brain damage caused by the surgery itself. "I think all that resulted in a significant [graft] survival," Sladek says.

Meanwhile, an alternate grafting procedure that does not use fetal tissue may be falling by the wayside. That procedure, in which dopamine-secreting cells from the patient's own adrenal gland are implanted in the brain, attracted a great deal of attention in 1987 when physicians at the Hospital de Especialidades Centro Medico "La Raza" in Mexico City reported what appeared to be very dramatic improvements in patients who received the grafts. That was surprising. The Lund team, which is considered by U.S. neuroscientists to be very rigorous in its methods, had tried adrenal implants in a few patients at the beginning of the 1980s and had seen only slight improvements.

In the wake of the Mexican report approximately 180 Parkinson's patients in the United States and Canada were given the adrenal implants. But they experienced only modest benefits, says Goetz, who coordinated a multicenter study in this country and is also in charge of a registry maintained by the United Parkinson Foundation to track what is happening to the patients. They also had serious complications, most of which, such as pneumonia and bladder infections, were related to the surgery to remove the adrenal gland. "The pluses may not outweigh the minuses," Goetz says. "Most groups are in fact following their patients long-term and are not continuing to do the procedure."

The researchers agree that more experience with fetal nerve grafts is needed to establish whether they are superior to the adrenal implants. Still to be determined, Lindvall points out, is whether a fetal graft will permit a patient to reduce his or her levodopa intake or do without it completely. Also unknown is whether the grafts can survive permanently.

The Lund group has given the fetal grafts to an additional three patients, although none has been followed long enough to determine whether the grafts were successful. But at least the result with the first patient in this series was encouraging. "It indicates," Lindvall says, "that you can transplant neurons to human brain and get survival of the cells." ■ JEAN MARX