Cell Transplants into Monkey and Human Brains

Successful transplantation of brain cells from fetal to adult monkeys was reported by two research groups last week. The scientists announced that the transplanted cells reversed symptoms of Parkinson's disease, which had been chemically induced in the adult monkeys before the transplant.

"As far as we know, this is the first report of a [successful] brain cell transplant in primates," said D. Eugene Redmond of Yale University at the meeting in Dallas of the Society for Neuroscience. Because each study used only two or three animals, the results are considered very preliminary and far from clinical application. However, Swedish scientists at the same meeting reported some success in a recent clinical experiment using a related strategy. Adrenal gland cells transplanted into the brains of two human subjects with Parkinson's disease gave measurable, though temporary, improvement of symptoms.

In each of the monkey studies, the scientists used a chemical called MPTP (SN: 10/5/85, p. 213) to trigger symptoms of Parkinson's disease, a degenerative disorder that afflicts about 500,000 people in the United States. MTPT destroys the cells that produce the neurotransmitter called dopamine in one area of the brain. These cells are the same ones that degenerate in the human brain to cause Parkinson's disease. Most patients with this disease are treated with a drug called L-dopa that replaces the missing dopamine. But this therapy loses effectiveness over years of treatment.

Redmond, along with John R. Sladek of the University of Rochester (N.Y.) and Robert H. Roth of Yale, administered MPTP to African green monkeys, inducing the tremors, general inactivity, muscle rigidity and episodes of immobility characteristic of Parkinson's disease. They then removed dopamine-producing cells from the midbrains of fetal African green monkeys. These fetal cells were implanted into the brains of two MPTP-treated monkeys.

One monkey's behavior improved dramatically, while another showed a more moderate improvement, Redmond reports. In the most dramatic case, the monkey had lost its tremor and improved its movements by a week after the surgery. Two weeks later, the monkey's behavior appeared normal, Redmond says.

These behavioral observations were backed up by anatomical and chemical data. The scientists report that the implanted dopamine-producing cells survived for at least two months, during which there was an increase in the amount of a dopamine metabolite in the cerebral spinal fluid.

The other research group reporting a successful brain cell transfer was led by R.A.E. Bakay of Emory University in Atlanta. Bakay and his colleagues administered MPTP to rhesus monkeys. They did not observe tremors, but they report decreased activity and a characteristic bent-over posture in the MPTP-treated monkeys. After implantation of fetal dopamine-producing cells into two MPTP-treated monkeys, movement and activity improved, but the monkeys' movement repertoire remained "somewhat limited," Bakay says. He presented evidence of increased levels of dopamine metabolites and of survival of the transplanted cells.

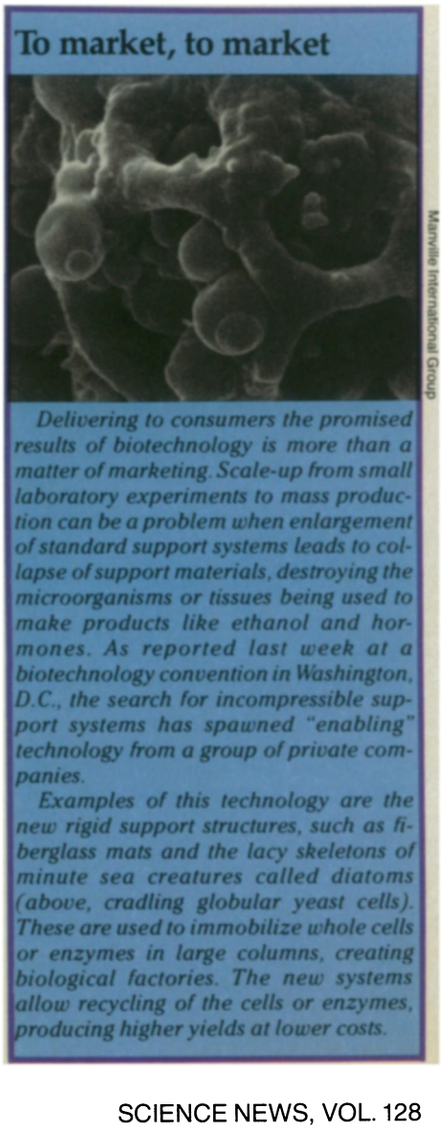
Neither group found any indication that the transferred brain cells were attacked by the host immune system. "We therefore feel that fetal tissue transplantation in primates can effectively reverse behavioral abnormalities and biochemical abnormalities induced by MPTP," Bakay and his colleagues say.

But other scientists at the meeting tended to be more cautious. "I think both reports are quite preliminary," says William J. Freed of the National Institute of Mental Health and St. Elizabeths Hospital in Washington, D.C. "I think it's very interesting, but there were too few animals to draw conclusions."

Scientists at the meeting also raised questions about whether the rhesus monkeys showed the specific Parkinsonian symptoms; whether the evidence of improvement is convincing; whether in either study enough fetal cells survived to explain the increased levels of dopamine metabolites reported; and whether the behaviorial improvements can be attributed to a spontaneous recovery or regrowth of the adult monkeys' own brain cells rather than to the influence of transplanted cells. The studies were criticized for not having sufficient control animals. In addition, immunologists suggested that cell rejection responses or the development of destructive allergies might arise only months after the transplant.

While implantation of nerve cells will not be performed on human subjects in the near future, Swedish scientists already report a limited success in transplanting cells from patients' adrenal glands into their brains. The adrenal gland cells produce dopamine, and thus can partially compensate for the dopamine deficiency of Parkinson's disease. Anders Björklund of the University of Lund told reporters that two patients who received this treatment last May showed dramatic improvement in their movements. But the improvement subsided over a two-month period, during which the implanted cells are presumed to have died. Björklund says that the observed improvement, although temporary, was greater than that seen in two patients similarly treated several years ago (SN: 11/20/82, p. 325). Björklund does not expect this procedure to reach clinical use for at least 10 to 30 years.

One hope behind the attempts to transplant nerve cells, rather than adrenal cells, is that the transplants will communicate with the host brain in a manner more sophisticated than by simply pumping out a required chemical. Evidence from rodent brain cell transplants, which have been successfully performed for about seven years, indicates that the transplants can establish synapses with host cells and both receive and transmit nerve signals. "We have all been quite pleasantly surprised," says Sladek, "at how well integrated transplanted cells are in the rodent brain, although they are still lacking in fine tuning." —*J.A. Miller*



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