Animal Brain Grafts Survive

An international team of scientists reports it has successfully grafted a functioning part of the brain of one animal onto the damaged brain of another. The transplant represents "the first demonstration [of] the grafting of mammalian brain tissue from one animal to another" where the brain-damaged animal appears to benefit, say the scientists. The experiments — limited thus far to rats — could ultimately have important implications in the treatment of Parkinson's disease and other motor disorders of the central nervous system.

Grafts in all nine of the implanted animals have not only survived without rejection for nine months, but have grown within their "new" brains and even extended their nerve fibers into nearby brain tissue. Perhaps most important, the Parkinson-like tremors induced in the rats by the experimental destruction of brain tissue have been significantly reduced in the majority of the nine animals since they received the implants.

"This opens up a new area of investigation, both because of its potential clinical applications and its meaning to basic science," National Institute of Mental Health psychopharmacologist Richard Jed Wyatt told SCIENCE NEWS. The team's findings are reported in the May 11 SCIENCE by Wyatt, Mark J. Perlow and William J. Freed, all of NIMH's Unit on Geriatric Psychiatry, Barry J. Hoffer of the University of Colorado pharmacology department and Ake Seiger and Lars Olson of the Karolinska Institute in Stockholm, Sweden.

Scientists believe that Parkinson's disease, characterized by uncontrollable, jerky movements, is caused primarily by the loss of cells in the brain's substantia nigra (SN) — one of several areas that normally produce the key brain chemical dopamine. Current treatment of Parkinson's involves administration of L-dopa, a drug that appears to stimulate dopamine production in the brain. But "despite some dramatic improvements," the scientists note, L-dopa is "not completely effective" and may produce "severe, untoward side effects."

But Wyatt and his colleagues were also inspired by the revolutionary concept of a brain graft itself. "No other attempts had been made to alter behavior with a graft," Wyatt said in an interview. Researchers in Sweden have attempted other types of brain implants, but those have "not taken well," he said. Mainly, though, the field is a virgin area because few researchers in the past have thought of attempting such a transplant, according to Wyatt.

In the current experiments, the dopamine-producing cells in the substantia nigra of a dozen male rats were chemically destroyed without damaging the remaining brain tissue. Previous studies have shown that when such SN-depleted rats are given the drug apomorphine, which behaves somewhat like dopamine in the brain, the animals involuntarily rotate — a reaction scientists say is equivalent to the tremors of human Parkinson sufferers. Using this method, Wyatt and his colleagues induced rotation in the rats.

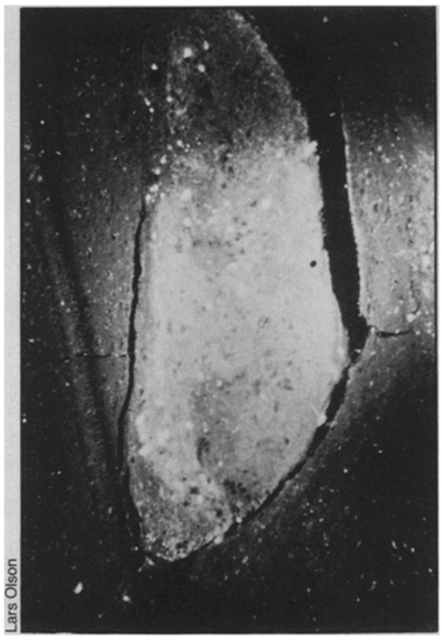
Nine of the adult rats received tissue containing healthy SN cells from the brains of rat fetuses. The transplanted tissue was injected not into the destroyed areas of the host brains but into a ventricle, or cavity, just above the caudate, a region involved in the brain's control of motor activity. Normally functioning SN nerve fibers infiltrate the caudate, but must travel "a substantial distance" to do so, Wyatt says. To give the graft a better chance to survive and "to find its home in the caudate," the researchers placed it on top of the caudate, where the implant's dopamine-producing nerve cells would have to travel only a short distance to take root. The three other rats were used as a control group and injected with adult sciatic nerve cells instead of fetal SN.

Beginning four weeks after the grafting, the rats again received apomorphine. All of those with brain implants showed reduced Parkinson-related rotation — including five rats that exhibited at least a 70 percent reduction in such movements. The control animals showed some lessening of rotation, but significantly less than that of the SN-brain-grafted group.

Moreover, the dopamine-containing fibers not only flourished within the grafts, but they grew and extended into the adjacent caudate of the host brain in all nine rats. The transplants have continued to function intact for nine months, with "little or no evidence of any scarring or pathological disturbances."

Because rejection has been a major problem with transplanting organs elsewhere in the body, the researchers are somewhat mystified as to why not even one of the rats has biologically rejected its brain graft. "We don't know," says Wyatt. "It may be that the brain is a privileged area — it may not be as subject to antibodies."

Wyatt cautions that the findings, while exciting and encouraging, represent just a first step in an almost uncharted psychopharmacological procedure. "There is a big gap between rats and humans," he says. In addition, four of the SN-grafted rats exhibited less than a 10 percent reduction of Parkinson-like symptoms. Problems in each of those four seem to stem from two factors: The scientists were unable to initially destroy *all* the dopamine-producing SN cells and left a small residual prior to the implant; these rats were grafted toward the rear portion of the ventricle, while the more successfully treated animals received implants toward the front. The researchers are currently investigating these and other factors in brain implants with monkeys, but have no results to report as yet.



Fluorescent, dopamine-containing graft is seen thriving in its host rat brain nine months after transplant. Grafted nerve fibers have grown into the caudate (right), which controls motor behavior.

Despite such hurdles, Wyatt is willing, if cautious, to speculate about the hypothetical applications to human victims of Parkinson's disease and possibly other motor abnormalities such as Huntington's disease. "The mechanisms [of grafting] in the human would actually be easier," he says, primarily because the human brain — particularly the caudate — is so much larger than that of the rat.

"The major issue [in a human brain graft] would be the source of the graft," Wyatt says. For obvious medical and ethical reasons, use of fetal brain material does not appear feasible. Wyatt suggests that perhaps dopamine-producing cells from a person's own adrenal gland or certain ganglia (nerve masses) in the central nervous system might provide alternative transplant material. Rat studies using this procedure have already begun, he says.

The scientists stress that much remains to be learned about the safety and long-term stability of brain grafts. Possible behavioral implications, for example, are not addressed in these first studies (although no observable side effects were apparent in the rats). But these results, they say, give hope to the possibility that brain implants "could offer the patient with Parkinson's disease . . . [and] other neurological disorders . . . a more physiological treatment than is presently available." □