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BRAIN MENDING

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By Kathleen McAuliffe

When a vital tissue or organ becomes defunct, cadavers and prosthetic devices are the logical places one would turn to for spare parts. Neither avenue is possible for victims of brain lesion. Their disability results from the death of tissue in a small, confined portion of the brain, often no larger than a grape. But some of these people could benefit from a novel, though controversial, type of organ bank.

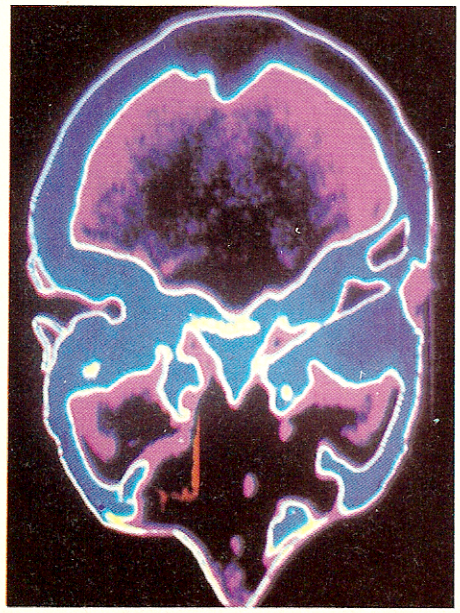
Embryos, including human embryos, might become an invaluable source of brain tissue for transplantations. This is the impact of research conducted by Barry Hoffer, of the University of Colorado; Richard Wyatt, of the National Institute of Mental Health (NIMH), in Bethesda, Maryland; and Lars Olson, of the Karolinska Institute, in Stockholm. While older animals' brain tissues rapidly degenerate when placed in foreign surroundings, embryonic cells have no trouble adapting to a new abode. The researchers extracted brain cells from a rat fetus and implanted them in a comparable region of an adult rat's lesioned brain. Instead of dying, the cells continued to develop normally and grew into the host's neural network.

But embryonic cells are more than good colonizers. They are skilled pathfinders, and this talent is crucial in repairing lesion damage. Confronted with millions of crossroads, called synapses, fetal cells seem to have no difficulty finding their way to the target area. Indeed, even when implanted off course, they have an uncanny way of reaching the destination that nature intended. The navigational feats of birds and fish are tame by comparison.

Already Hoffer and his colleagues are using embryonic grafts to alleviate the symptoms of lab-induced Parkinson's disease in rats. For both man and rodent, the disorder is caused by a lesion in that part of the brain responsible for producing dopamine, a substance essential for normal motor control. The scientists transplant tissue from an area of a fetal brain that corresponds to the site of the lesion in afflicted rats. Approximately two thirds of the cells survive and establish interconnecting links with a neighboring neural center. As dopamine levels begin to rise, the rats show a decrease in behavioral abnormalities associated with the disease.

"We've now examined the grafts for about a year, which is almost half the life span of a rat," Hoffer says, "and there appears to be no rejection." How do they escape detection by the host's arsenal against foreign invaders? The secret lies in the brain's blood barrier, which screens out antibodies and other lymphatic cells. As far as the body's immunological system is concerned, the brain is neutral territory where foreign grafted cells can coexist with the local inhabitants. The eyes, too, share the brain's special status of being "immunologically privileged," thereby raising hopes of someday grafting new eyes for the blind.

Much closer to realization, according to Hoffer, is the prospect of using fetal implantations to cure certain forms of brain impairment that involve a focal loss of neurons. Besides Parkinson's disease and Huntington's chorea, numerous disorders of the hypothalamus are subsumed in this category. Results from experiments now being done on primates will prove crucial in assessing the clinical utility of this procedure. Even if scientists are successful beyond their wildest dreams, however, the path from monkey to man may be strewn with moral obstacles.



Brain lesions may soon receive cell implants.

"Where are we going to get the embryonic tissue?" asks William Regelson, of the Medical College of Virginia. "You'll have to use a living human embryo. An aborted fetus won't do. Are women going to become impregnated to provide embryos? We're faced with a very serious problem, and we'll have to find ethical alternatives to it. For example, if we can develop the technology to grow embryonic cell lines in culture, that might provide one solution."

Likewise Hoffer, for ethical reasons, rules out using living embryos. But given no other options, he thinks aborted fetuses could indeed supply the donor material. To obtain the fetal tissue, he foresees no need to modify abortion techniques now being used in hundreds of clinics.

Still, abortion itself presents a moral dilemma for many people. Hoffer would much rather find a substitute for the embryonic donor altogether. In the case of Parkinson's disease, he may already have succeeded. The peripheral nervous tissue of an adult, he believes, could serve the same function as embryonic brain tissue.

"Luckily, nature has been parsimonious," Hoffer remarks. "Dopamine acts as a neurotransmitter in the brain, but it is also used in the peripheral nervous system, for example, in the adrenal glands." When adrenal cells are used as the graft material, Hoffer found that "they become more nervelike and send out branches that can actually grow into the recipient's brain." This strengthens the possibility that Parkinson's victims might supply their own grafts by donating a portion of their adrenals.

For other brain disorders, nature may not be so parsimonious. If vital neurochemicals are not present in the peripheral nervous tissue, the embryonic

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donor could be the only alternative. So far scientists have not had to confront this problem directly. But the science of embryonic implantation is rapidly expanding. The same principles that apply to the treatment of brain lesions may be used in restoring other organs, particularly eyes.

Two years ago Richard Wyatt received a strange phone call from two of his coworkers at NIMH. "We know that you, as a psychiatrist, are interested in introspection," they said. "What would you give to be able to peer around inside the mind?"

Wyatt couldn't imagine what they were up to. Yet colleagues William Freed and Mark Perlow were referring to an experiment Wyatt himself had dreamed up. As he soon discovered, they had transplanted a rat's embryonic eye, including the optic stalk, into the brain of an adult rat. Skin, muscle, and bone over the implantation site had been removed. There, sitting in the middle of the brain, was a tiny eye staring out at him. What's more, it appeared partially functional!

Freed had flashed light stimuli into the grafted eye and found its nerve impulses varied with the intensity of the light. How can an eye, so far astray from its home territory, still see?

One possibility is that the optical stalk had somehow managed to hook up with the lateral geniculate body, a relay station for visual signals in the brain. Wyatt and Freed are working together to determine exactly what happened. Instead of cutting open the rat's head, they are planning to insert fiber optics through a tiny hole in the skull to see whether the eye can be stimulated by an external source.

Even with fiber optics, an eye inside the brain would not seem useful either to rat or man. But if an eye can grow where it's not supposed to, then why not where nature saw fit?

"It is one thing to graft an eye and achieve some electrical activity," Hoffer says, "and quite another to get it to grow into the eye socket, with optical stalk wired up to the visual cortex." Nevertheless, he is greatly encouraged by the degree to which embryonic tissues are preprogrammed to recognize, and link up with, the proper targets in the host. To grow a functioning eye for a blind person, the fetal graft would have to establish interconnecting links with thousands of nerves arranged in a fantastically intricate network. But, according to Hoffer, the prospects of doing so may be no more farfetched "than if ten years ago you said we could treat Parkinson's disease by transplanting embryonic pieces of brain."

Should Hoffer's research or that of his colleagues reach fruition, "the right to life" may take on even more complex ethical overtones: the right to *whose* life—that of the unborn child or an adult suffering from severe physical impairment? ∞