Retina transplant restores rat reflex

For the first time, researchers have evoked reflex responses in laboratory rats with midbrain neural transplants, demonstrating that such transplants are capable of transmitting specific information in response to natural stimuli. The work, reported in the October PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (Vol.84, No.19), is the latest in a series of experiments that may lead to the use of nerve transplants to repair damaged neural circuitry.

Previous research had already shown that under proper conditions transplanted nerves are capable of surviving and even growing (SN: 2/28/87, p.135). Other research has shown that certain tissues, if transplanted to the brain, can secrete chemicals that will significantly influence neural function there (SN: 7/11/87, p.22). But in none of these cases have neuroscientists been able to show that direct, site-specific communication can be reestablished between a transplanted neuron and its target cell.

In the most recent effort to prove that capability, Henry Klassen and Raymond D. Lund of the University of Pittsburgh School of Medicine looked at one of the simplest neural pathways in rats — the visual reflex, whereby the eye's pupil constricts in response to light. In that reflex, information is transmitted from the light-detecting retina to the brain via the optic nerve. If a pupillary response is necessary, a command is transmitted from the brain to the pupil along a separate, oculomotor nerve.

"The pupillary reflex is very simple-minded, but it seems rather important to show that a transplant can relay a bit of specific, simple-minded behavior," Lund told SCIENCE NEWS. "In this case we relay some information that effectively says, 'The light's gone on,' and the output system responds appropriately to the stimulus."

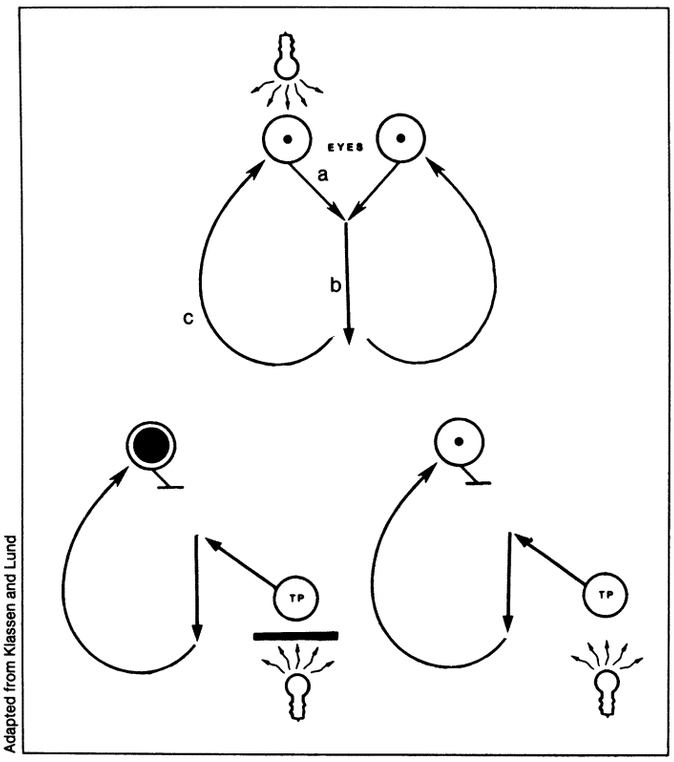
To test the ability of transplanted neuronal tissue to relay such a message, the researchers transplanted embryonic retinas directly onto the midbrains of newborn rats. Retinal tissue is neuronal in nature, and the transplants proceeded to make neuronal connections to the pupillary reflex-processing area of the brain. After five months, each rat was anesthetized and its optic nerve severed so that no information could be relayed from the eye to the brain. The oculomotor nerve from the brain to the pupil was left intact. Finally, the retinal transplant was bared by the removal of overlying bone. The researchers found that when the transplant was exposed to light, the pupil constricted, and that it dilated again when the light source was removed.

The experiment goes a step beyond other embryonic tissue transplants that have been shown, for example, to boost the production of the neurochemical dopamine in the brain.

"The dopamine system is like a mini-pump of a chemical which you're blasting off into the right general area," Lund says. "It tunes things up; it changes the excitability level to make things function more efficiently.

"In this case, though, we're taking some signal from the outside world and turning it into a response, so the requirement is that it has to make a very specific connection with the right group of cells that are actually dictating this response. It's not just a case of squirting a chemical across a gap or a synapse, but more that it's got to do something in exactly the right place, because there are other cells that would produce a very different response if it connected with the wrong ones."

Ultimately, researchers envision using transplants to restore lost neural functions, such as damaged optic nerves. "This is fantasy at the moment, and one wouldn't want to put out false hopes and say that we're going to cure blindness," Lund says. However, he adds, "I remember saying five or six years ago that it may take 20 years before [dopamine-producing transplants] get applied to humans, and of course I had to eat my words." — *R. Weiss*



Adapted from Klassen and Lund

Nerve pathway for pupil constriction in rats. Top: Light is detected by retina, and information is transmitted by optic nerve (a) to midbrain (b). Midbrain transmits pupillary response via oculomotor nerve (c). Bottom left: Optic nerve is severed. Retinal transplant (TP) on midbrain is shielded from light, resulting in pupil dilation. Bottom right: Transplant is exposed to light, and pupil constricts. In experimental procedures, one eye was removed at birth to ensure maximum growth of nerves by remaining eye.

First human genome map completed

Researchers have successfully mapped the relative positions of more than 400 genetic "markers" on all 46 human chromosomes, completing the first genetic linkage map of the entire human genome. The linkage map is an important first stage in the development of a more detailed gene-sequence map. Scientists hope that such a map may someday pinpoint all 100,000 or so genes that contain the human complement of hereditary material.

Even before such a detailed map is completed — a project expected to take many years and billions of dollars — the new linkage map is expected to help researchers identify and devise prenatal tests for a number of inherited diseases. In particular, the map will make it possible to identify diseases that are the result of two or more genes. Scientists suspect that heart disease, some cancers, certain mental illnesses and other common disorders may have such multiple genetic roots. Until now, however, it has been impossible to unravel the complicated inheritance patterns of these diseases.

"What strikes me is how rapidly this whole thing has come together," says Helen Donis-Keller, senior researcher with Collaborative Research, the Bedford, Mass.-based biotechnology company that spearheaded the four-year mapping effort. "A few months ago we had a whole lot of little islands, specks. All of a sudden, the whole thing converged. Suddenly we have good maps."

The research is to appear in the Oct. 23 CELL. — *R. Weiss*