Neurons Regenerate Into Spinal Cord

Neuroscientists this week reported that they have coaxed damaged sensory nerves to grow directly into the spinal cord, and that the regenerated nerves made functional connections inside the spine. The research, performed on rats, shows for the first time that nerve damage in and around the spinal cord can be reversed. Neurosurgeons say the techniques may someday be used to repair a variety of spinal injuries that only a few years ago were considered irreparable.

The accomplishment is the latest in a series of successes through which scientists have become increasingly adept at inducing limited nerve regeneration in mammals. Regeneration has been most successful with peripheral nerves, which run from the spine to the muscles and sense organs. However, regeneration of central nervous system neurons – those found in the brain or spinal cord – has proved more difficult. Brain-cell regeneration has at times been successfully induced (SN: 10/17/87, p.245). But researchers have yet to find a way to stimulate regrowth of damaged nerves that are completely enclosed in the spinal cord. The current research, although done with peripheral nerves, demonstrates regrowth *into* the spinal cord with reconnection to central nervous system nerves inside the cord. It is, in a sense, only a half step away from the ultimate goal of inducing regeneration of central nervous system nerves within the spinal cord.

Jerry Silver of the Case Western Reserve University School of Medicine in Cleveland and Michel Kliot of Columbia University's Neurological Institute in New York City induced the nerve growth using tiny paper "bridges" coated with special cells taken from fetal rats. The cells, called astrocytes because of their star-like shape, provide the necessary physical and chemical environment to allow nerve regeneration and penetration into the spinal cord, the researchers say. They reported their results at a symposium on spinal cord injury preceding the annual meeting of the Society for Neuroscience in New Orleans.

"Astrocytes are the highway engineers of the embryo in terms of nerve formation," Silver says. "They can build little canals and bridges and all kinds of things." Not only do astrocytes provide a useful mechanical bridge to guide and support developing nerves, he says, but they also produce growth-promoting chemicals and make substances that nourish nerve cells as they grow.

Most important, however, astrocytes seem to prevent the scarring that otherwise occurs when a nerve cell gets ripped from or damaged near the spine. Such scarring is believed to be an important factor preventing damaged nerve cells from growing back into the cord, where they normally connect with other cells or reach directly to the brain.

In their experiments, the researchers first crushed – just outside the spinal cord – the sensory nerve that transmits sensations from a rat's foot to its spinal cord. They left intact the motor neuron running from the spine to the leg. Every two days they pinched the rats' toes and watched for leg movement as an indicator of regained sensation. Control rats, which were not given astrocyte bridge implants, did not regain toe-pinch responses.

But 15 rats were implanted at the crush site with tiny bridges made of porous paper covered with fetal-rat astrocytes. Seven of these regained sensation. Later, the nerves were completely severed and the toe-pinch response was again eliminated, proving that the regained response was not from some other neural route.

Postmortem studies showed that spinal scarring was absent, and that the nerve cells had indeed penetrated the spinal cord and made new connections with the proper cells in the spine. All told, the distance spanned was less than a millimeter. But while the step may have been a small one by neuronal standards, it represents a leap forward for neurobiologists. By disproving the assumption that spinal penetration and functional repair are impossible, Kliot says, the real significance of the research is in the crossing of "a psychological barrier almost more than anything else."

Similar experiments on humans are probably years away, and may have to be done elsewhere, the researchers say. Ohio, where the rat tests were done, is one of five states that prohibit research using cells from human fetuses, and human fetal astrocytes would be required if the procedure were to be done on humans. The researchers are now developing techniques for growing fetal-rat astrocytes in culture, in hopes of eliminating the need for fresh fetal cells.

Someday, the researchers add, the fetal cells themselves may be unnecessary. "Right now we're using astrocytes because astrocytes are smarter than we are," Kliot says. "Eventually we'd like to isolate the [cellular] proteins involved. Then we may be able to make a bridge not of living cells, but of molecules that will allow us to do the same thing." – *R. Weiss*

Reactions to alcohol: Cortisol clues

The natural sons of alcoholic fathers are thought to be a group at great risk for developing alcoholism later in life. Recent studies indicate that a substantial portion of this group shares a brain wave deficiency with chronic alcoholics and reports feeling less drunk after a few drinks compared with controls who have no alcoholic relatives (SN: 9/29/84, p.196).

To these potential "markers" of a predisposition to alcoholism, researchers now add a hormonal measure: levels of cortisol in the bloodstream. Marc A. Schuckit of the San Diego Veterans Administration Hospital and his colleagues find that this indirect measure of biological responsiveness to alcohol is lower after drinking among young adult sons of alcoholics than among sons of nonalcoholics.

The data suggest that sons of alcoholics have a less intense biological reaction to alcohol that promotes greater use of the substance, report the investigators in the November ARCHIVES OF GENERAL PSYCHIATRY. It is not yet clear, they say, whether differences in cortisol response to alcohol are genetically controlled or directly tied to an alcoholic predisposition.

The researchers chose cortisol as a biological measure because a number of human and animal studies have shown that blood levels of the hormone increase after fairly large doses of alcohol are ingested. Also, as tolerance to alcohol develops with continued drinking, cortisol levels do not drop off.

Schuckit and his co-workers tested 30 healthy, young adult sons of alcoholic fathers and 30 sons of nonalcoholics. Subjects in the two groups were matched for age, race, religion and educational level. Each received three types of drinks in random order: a placebo with no alcohol, a moderate dose of alcohol mixed in a sugar-free, noncaffeinated, carbonated beverage, and a heavy dose of alcohol in the same mixer.

Blood cortisol levels, measured every 30 minutes for four hours after each test, were significantly lower for sons of alcoholics in the two alcohol conditions, particularly following the heavy dose. A similar difference was observed 30 minutes after the placebo was administered, note the scientists, suggesting that, at least in the early going, reactions to lab procedures may have affected cortisol levels. But, they add, the largest group differences occurred about two hours after drinking alcohol, well past the 30-minute point. – *B. Bower*