One injured nerve fiber heals another

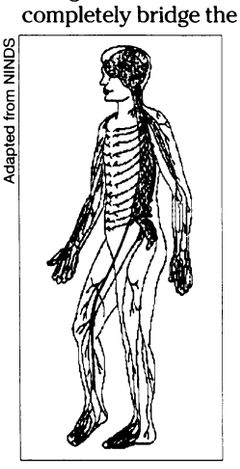
In an unusual finding that suggests a new strategy for healing damaged spinal cords, scientists have shown that severing nerve fibers in the body's periphery stimulates repair of related fibers within the cord. The counterintuitive research tackles the perplexing issue of why peripheral nerve fibers regenerate but those in the central nervous system—the brain and spinal cord—do not.

"The conventional explanation is that the environment of the peripheral nervous system is permissive [to regrowth], whereas in the central nervous system, the environment is hostile," says Clifford J. Woolf of Massachusetts General Hospital in Boston. Indeed, myelin, the insulating sheath around nerve cell fibers, inhibits regrowth in the spinal cord but not in the periphery.

Questioning the importance of environment, Woolf and his colleague Simona Neumann wondered if peripheral nerves simply respond better to damage. When such cells suffer an injury, they switch on many of the same genes employed during their original growth. "Maybe the problem of a lack of growth in the central nervous system is that [damaged] cells don't switch into an actively growing state," suggests Woolf.

The researchers found a perfect test bed for this idea: Some sensory nerve cells extend fibers, or axons, into both the peripheral and central nervous systems. In the cells studied by Woolf's group, the main body sits just outside the spinal cord. The peripheral axon—for example, one in the sciatic nerve running down the leg—reports sensory information. To carry that sensory data to the brain, each cell has a second axon that enters the spinal column and ascends the cord.

In their initial experiment, Neumann and Woolf simultaneously severed the peripheral and central axons of these nerve cells in rats. The peripheral damage stimulated the injured central axons to partially regenerate, they report in the May NEURON. The damaged axons extended new growth into the injury site but didn't completely bridge the gap.



Adapted from NINDS

Some sensory nerve cells extend fibers, or axons, both into the periphery (blue) and along the spinal cord (red). Curiously, damage to peripheral axons may help injured spinal cord axons regenerate.

The researchers then added a slight twist to their experiment. It takes the central body of a nerve cell some time to react to an injury along a lengthy axon. The damage signal has to travel down the axon, the cell has to switch genes on and manufacture proteins, and those proteins must then make the journey along the axon.

Recognizing the delay, the investigators decided to sever the peripheral axons of the nerve cells 1 week before the experiment damaged the axons in the spinal cord. "When we pre-injured the peripheral nerves, priming the cells into an actively growing state, and then cut the central axons, we got regrowth right across [the cut] and into the spinal cord above the lesion," says Woolf.

While such regeneration is impressive for spinal cord axons, the researchers have not yet shown that the axons reconnect appropriately and provide any functional recovery for the paralyzed rodents. Other researchers have partially healed spinal cord injuries in animals by blocking the inhibitory myelin proteins or engrafting peripheral nerve cells into the damaged areas (SN: 7/27/96, p. 52).

The approach employed by Neumann and Woolf may not support full recovery from a spinal cord injury, says Ira B. Black of the University of Medicine and Dentistry of New Jersey in Piscataway. Many of the spinal axons travel down from the brain and don't have a peripheral component. It's unclear how scientists could trick these descending fibers into assuming a growing state.

Woolf cautions that the strategy that his group applied to the rodents is not one that physicians would consider. "I don't think anyone would ever take someone with a spinal cord injury and start damaging their peripheral nerves," he says.

Instead, his group plans to isolate the molecular signals generated by injured peripheral axons and determine which ones trigger nerve cells to regenerate.—*J. Travis*

Depressed smokers ride immune downer

Depression and cigarette smoking may make for a particularly dangerous combination. Men suffering from major depression who smoke around a pack of cigarettes a day experience immune-cell changes that research has linked to cancer development, a new study finds.

These disruptions of immune function do not occur in depressed nonsmokers, report Waymond Jung and Michael Irwin, both psychiatrists at the San Diego Veterans Affairs Medical Center. People in good mental health don't exhibit the immune-system change either, whether or not they smoke up to a pack a day.

A prior independent study found that mentally healthy individuals who smoke two packs of cigarettes or more each day display immune changes comparable to those now observed in moderate smokers with depression.

Long-term data indicate that cigarette smokers who endure bouts of clinical depression exhibit elevated cancer rates, even for cancers not associated with cigarette use. This raises health concerns, since rates of cigarette use are high for people with major depression.

"Our findings are compatible with epidemiological data showing that a combination of depressed mood and [cigarette] smoking increases the risk of cancer development," Jung and Irwin contend. Their results appear in the May/June PSYCHOSOMATIC MEDICINE.

Jung and Irwin explored an immune pathway by which depression and smoking together might promote cancer. They collected blood samples from 127 nonsmokers who did not have any psychiatric disorders, 11 moderate smokers in good mental health, 46 nonsmokers diagnosed with major depression, and 61 moderate smokers also suffering from major depression.

Compared with the other three groups, depressed men who smoked cigarettes had substantially greater numbers of white blood cells—a general sign of compromised immunity—and their natural killer cells responded only weakly to foreign cells introduced in laboratory tests.

Natural killer cells play a surveillance role in the healthy immune system by destroying any cells that show early signs of cancerous growth.

Jung and Irwin's finding of low activity in depressed smokers' natural kill cells is "provocative and potentially important," remark psychologist Janice K. Kiecolt-Glaser and immunologist Ronald Glaser in an accompanying editorial.

Combined with moderate cigarette use, physiological effects of depression may boost susceptibility to tumor progression, suggest Kiecolt-Glaser and Glaser, both of the Ohio State University College of Medicine in Columbus.

They add that the results have broad implications for the burgeoning field of immunotoxicology, which examines how various substances undermine the immune system. Certain chemicals may disrupt immune functions only in the presence of psychological conditions such as depression or sustained mental stress, the Ohio scientists maintain.

Further studies should examine whether a mix of depression and cigarette smoking accompanies impaired immune function in women, note Jung and Irwin. Moreover, nobody knows yet whether immune function declines sharply in cigarette smokers who suffer from other psychiatric disorders, such as schizophrenia, they say.

—*B. Bower*