Newly Discovered Proteins May Stimulate Nerve Regeneration

The ability of some nerves to regrow after injury, while others remain permanently severed, may be determined by specific proteins from surrounding cells, new studies indicate. The findings may have long-range implications for the treatment of central nervous system disorders and traumas. Neurobiologist Eric Shooter of Stanford University announced the discovery of the proteins at a symposium of neuroscientists held on Oct. 18 at the Johns Hopkins Medical Institutions in Baltimore.

Many of the body's "peripheral" nerves, such as nerves in skin and muscle, can grow back and regain function after they are cut or crushed. But the central nerves — those in the brain and spinal cord — don't regenerate, which accounts for the devastating and irreversible consequences of so many neck and head injuries. Experiments over the past few years indicate that this crucial difference in regenerative capacity may have less to do with the nerves themselves than with the company they keep — the various non-neuronal cells that ensheathe the nerves. These cells differ in the central and peripheral nervous systems, and scientists have been able to sprout new branches (axons) from central nerves by bringing the nerves into contact with peripheral sheath cells (SN: 12/5/81, p. 363).

Shooter, in collaboration with Pate Skene of Vanderbilt University, has taken this research a step further, to determine what signals might be stimulating the regeneration. Shooter and Skene studied crushed peripheral nerves in rats and found that nerve regrowth was always associated with the production of a specific protein (called "37K" because of its molecular weight of 37,000 daltons) by the cells surrounding the nerves. When growth was completed, production of the protein ceased. "The time course of protein production correlated beautifully with the regeneration of the nerve," Shooter says. He speculates that the protein may act as an "on" signal triggering growth in damaged nerve cells, possibly by altering their pattern of gene expression. Certain genes could be activated or repressed to initiate a growth program.

The researchers also discovered two other proteins, 51K and 54K, whose production diminished during regeneration, but returned to former levels when the process finished. "If it turns out that these are signals controlling the growth of the axon, then we have both the positive control [37K] and the negative controls [51K and 54K] in one experiment," Shooter says. The researchers have isolated the 37K protein and have begun to study its effects on individual, cultured nerve cells.

Skene says he is "fairly convinced" that the protein is manufactured in the body by Schwann cells. Such cells comprise a major portion of the cells in the sheaths of peripheral nerves, but aren't found in the central nervous system. Whether Schwann cells — or the proteins they appear to produce — are the key to nerve regeneration is a matter for further research. Some evidence comes from Skene's recent studies of injured optic nerves in toads. These central nerves, like those of many non-mammalian species, do regrow, and Skene has recently observed the production of a protein similar to 37K during their regeneration.

The next step, Shooter says, is to find out if the proteins are absent in the mammalian central nervous system. If they are, then providing the protein to injured central nerves may stimulate regeneration — the dream of many physicians and accident victims. But if the proteins are already present, Shooter explains, "it would tell us that there's something fundamental about the central neuron which makes it rather difficult to turn on regeneration."

—R. Pollie

Hungry mind: Tracking appetite in the brain

Hunger is a state of mind, but it is a complex state that scientists have had a difficult time in unraveling. Several different brain hormones seem to be implicated in appetite control, but just how the different neurotransmitters interact has remained unclear. New evidence from two laboratories is now converging on a possible explanation for how the brain regulates — or fails to regulate — hunger and satiety. The research could lead to the development of new appetite depressants that are free of the side effects of existing drugs.

Three neuroscientists — Steven M. Paul and Bridget Hulihan-Giblin of the National Institute of Mental Health and Phil Skolnick of the National Institutes of Health — report in the Oct. 29 SCIENCE that they have identified two binding sites for amphetamine, a known hunger killer, in the brains of rats. Although it is too early to tell conclusively, Paul says, the sites could turn out to be neuronal receptors through which diet drugs (and perhaps a natural brain hormone) convey their anorectic, or appetite killing, message. The findings suggest such a role: the sites tend to be concentrated in the nerve endings, so that they could conceivably be involved in a synaptic event such as neurotransmission; and one of the sites binds with amphetamines and related drugs in concentrations that are directly proportional to the drugs' potencies in killing appetite. Moreover, the sites do not appear to be involved in mediating the other behavioral effects of amphetamines, such as hyperactive, repetitive behavior — a finding that points to the possibility of drugs that specifically regulate appetite without side effects.

The researchers report that the highest concentrations are in the hypothalamus. And they suspect, according to Paul, that the amphetamine binding site may also be a release site for the neurotransmitters serotonin and norepinephrine, which have long been suspected of involvement in appetite.

This research is consistent — at least in part — with new research by two Rockefeller University neuroscientists who have been studying the biochemistry of appetite. Sarah Leibowitz and Meena Jhanwar-Uniyal report they have found that both epinephrine and dopamine receptor sites play a role in appetite — but a very complex role that depends on where in the hypothalamus the sites are located. Norepinephrine in the mid-hypothalamus stimulates appetite, Leibowitz told SCIENCE NEWS, but in the lateral hypothalamus it suppresses feeding (as do dopamine and amphetamine). And, as she will report next week at the meeting of the Society for Neuroscience in Minneapolis, the number of norepinephrine sites in the lateral hypothalamus increases dramatically in food-deprived animals, whereas the sites in the medial hypothalamus are almost totally lost. Because the concentration of sites increases when transmission is low and decreases when transmission is rapid, a hungry animal would logically be expected to have fewer binding sites in the region where appetite is stimulated. This is because appetite-stimulating neurotransmitters "are turning over like crazy," Leibowitz says. Paul and his co-workers have also found that the concentration of amphetamine binding sites varies as animals are starved or overfed, but they have not yet observed these changes in specific brain regions. It is unclear, Leibowitz says, whether both labs are studying the same sites.

"We believe that both dopamine and norepinephrine are mediating the effects of amphetamines," Leibowitz says. But she adds that, even though serotonin is clearly involved in some way in appetite regulation, she has found no evidence that amphetamines act through serotonin transmission, as the government scientists suggest.

—W. Herbert