Eyeing uninhibited nerve regeneration

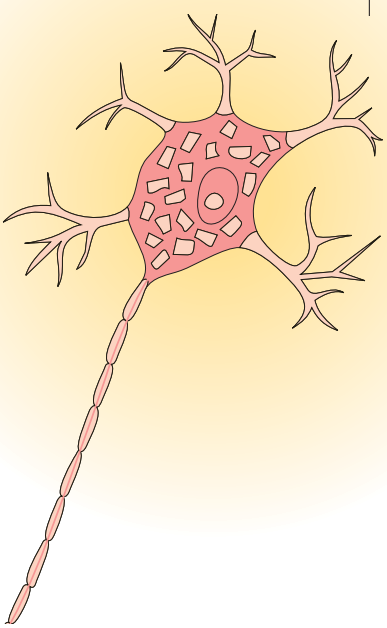
Captured most symbolically today in the wheelchair image of ex-"Superman" Christopher Reeve—and lingering in the greatest fears of most healthy adults—is the paralysis due to damaged and destroyed nerves. Whether the damage arises through accident, stroke, or degenerative disease, nerves of the brain and spinal cord (the central nervous system, CNS) do not naturally regenerate, unlike those elsewhere in the body. Molecular biology, in all its power, has yet to crack the problem of regeneration, but continuing studies are providing greater knowledge of the processes involved.

The CNS is a naturally inhibitory region for nerve regrowth, partly because of the presence of myelin-associated glycoprotein (MAG), a potent inhibitor of regeneration. MAG is one of the sialic acid-binding lectins (carbohydrate-binding proteins) previously shown in vitro to bind to specific glycans present in certain gangliosides. In a recent paper, Alka A. Vyas and colleagues at Johns Hopkins University (Baltimore) and the University of Hamburg (Germany) reported in vivo evidence that two of the major brain gangliosides, GD1a and GT1b, act as surface receptors for MAG (*Proc. Natl. Acad. Sci. U.S.A.* **2002,** *99* (12), 8412–8417). The presumption of the study was that the binding of MAG to these specific ligands prevents nerve regeneration in mammalian systems.

To demonstrate that these gangliosides were in fact the MAG targets, the researchers used four different techniques. They treated the nerves with neuraminidase to degrade the glycoproteins; they blocked ganglioside biosynthesis; they genetically modified the terminal structure of the surface gangliosides to alter their binding capabilities; and they used ganglioside-specific monoclonal antibodies to block the presumptive target sites. In all four cases, some nerve regeneration took place.

The long-term promise of this research is that nerve-surface gangliosides may provide valuable targets for CNS therapeutics. It is far too early to predict whether this discovery will lead to the remediation of such catastrophic damage as that suffered by Reeve and others, but it is a further step to a greater understanding of a critical aspect of the process of nerve growth control.

—MARK S. LESNEY



Examining the sweet tooth

Irresistible cravings for sweets, often referred to as "sugar addiction", might share some of the same physiological characteristics as drug dependence, according to Princeton University (New Jersey) researchers.

In a study, neuroscientist Bart Hoebel and his colleagues hypothesized that intermittent, excessive sugar intake would cause rats to show signs of opioid dependence (*Obesity Res.* **2002,** *10,* 478–488). They also predicted that if the sugar intake were blocked, the rats would show withdrawal signs such as shaking. By establishing an animal model of sugar dependency, they say, scientists will be able to further explore the relationship between addictions, brain physiology, and food cravings.

According to Hoebel, sugar stimulates the brain to produce natural opioids. "We think that is a key to the addiction process," he explains. "The brain is getting addicted to its own opioids as it would to morphine or heroin. Drugs give a bigger effect, but it is essentially the same process."

The rats in this study were kept from food for 12 h while they slept and until their breakfast meal. Then they were given a nutritionally balanced meal in addition to sugar water. Gradually, the rats increased their sugar intake to twice their normal daily amount and began consuming most of the sugar within the first hour. When the sugar was removed from the rats' diet, they exhibited teeth chattering—a common withdrawal sign—within 24 h.

Some of the rats were also given a drug midway through the study that blocks opioid receptors in the brain, thus removing the sugar's effect on the brain. Not only did these rats display teeth chattering, they also showed anxiety and a shift in the brain's normal balance of neurochemicals.

Hoebel points out that these rats should be considered "sugar-dependent" rather than "sugar-addicted", because it is not yet known whether the rats have exhibited signs of craving and relapse once withdrawal is over, two important behavior elements that define addiction. Further studies will examine the rats to see how they behave after withdrawal.

Although these results might give insight into the addictive properties of sugar, it is unclear what the results mean for those who feel powerless in the face of their own cravings for sweet confections. "The implication," says Hoebel, "is that some animals, and some people, can become overly dependent on sweet food, particularly if they periodically stop eating and then binge."

—JULIE L. McDOWELL

Advertiser

PALL LIFE SCIENCES
600 South Wagner Road, Ann Arbor, MI 48103, 800-521-1520, 734-913-6114, www.pall.com