Protein Protects, Restores Neurons

A naturally produced molecule may guard against neurodegenerative disorders such as Parkinson's disease and amyotrophic lateral sclerosis, according to a quartet of scientific papers published this week.

The shuffling gait, rigidity, and other symptoms of Parkinson's disease result from the deterioration of certain nerve cells that originate in an area of the brain known as the substantia nigra. These neurons produce a chemical messenger called dopamine that the body needs in order to move normally.

In 1993, a Colorado-based research team reported isolating a protein called glial-cell-line derived neurotrophic factor (GDNF). GDNF is one of a family of neurotrophic factors, molecules that maintain and nourish neurons. The 1993 paper suggested that GDNF specifically supports the neurons depleted in Parkinson's disease.

Now, Lars Olson of the Karolinska Institute in Stockholm, Sweden, and his colleagues provide tantalizing evidence that GDNF can protect against — even reverse — the progressive deterioration caused by Parkinson's disease.

The researchers discovered that injecting mice with GDNF seems to shield them from a later administration of MPTP, a compound that kills the same neurons destroyed in Parkinson's disease. A GDNF injection in the brain apparently spared about half of the dopamine-producing neurons that would have died under MPTP's toxic assault.

"There was marked, but not complete, protection," Olson says.

The Swedish team's findings also suggest that GDNF can restore dopamine production to MPTP-damaged neurons. In this experiment, the researchers gave the destructive MPTP to mice, then injected them 1 to 2 weeks later with GDNF.

The team found evidence that injecting GDNF directly into the brain helps spur a repair process. After the MPTP attack, the dopamine-producing neurons still alive start to branch out, sending more fibers to the striatum, the area of the brain where the nerve terminal releases its precious cargo of dopamine.

"Within a week or so we could see improvement," Olson says.

Researcher Ronald M. Lindsay of Regeneron Pharmaceuticals in Tarrytown, N.Y., called the findings "rather exciting." Lindsay wrote an editorial that accompanies the four papers, all of which appear in the Jan. 26 NATURE.

The Swedish team's results with GDNF are bolstered by another report, this one by Klaus D. Beck of Genentech in South San Francisco and his colleagues. Beck's group relied on a slightly different model of Parkinson's disease. The team cut the axons, or fiberlike extensions, of dopamine-producing neurons where they emerge from the substantia nigra on their way to the striatum. Once cut, about 50 percent of those neurons will die.

When Beck's team administered GDNF to rats immediately after snipping the animals' axons, they found that only about 15 percent of the dopamine-producing neurons degenerated.

Taken together, these findings hold out hope for the 1 million people in the United States afflicted with Parkinson's disease, Lindsay says. Such findings raise the possibility that doctors could administer a bolus of GDNF to Parkinson's patients to alleviate the rigidity of movement that characterizes this disease. Olson's results suggest that even after the damage has been done, GDNF may jump-start these crucial neurons.

Two separate papers add another twist to GDNF's potential. Both research teams report data hinting that this protein may protect motor neurons, the nerve cells attacked by amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease. People with ALS experience progressive weakness of the muscles in the hands, forearms, and legs as their motor neurons disintegrate. ALS afflicts about 20,000 people in the United States.

Both research groups showed that GDNF treatment helps motor neurons in developing animals survive an injury that usually results in nerve cell death.

Such results add to the belief that GDNF, or some other neurotrophic factor, might help reverse the crippling progress of ALS.

Regeneron and other companies are already testing some of these compounds on people suffering from this disease.

As for the future of such neurotrophic factors in the treatment of Parkinson's or ALS, "there's still lots to do before we know which of these will be potentially useful in the clinic," says Lindsay.

— K. Fackelmann

French cave yields Stone Age art gallery

A striking new addition to the ancient cave paintings that make up Western Europe's unofficial Museum of Prehistoric Art debuted last week, to the delight of archaeologists. French officials announced in Paris that explorers had discovered an underground cave displaying more than 300 well-preserved, expertly rendered wall paintings created by humans approximately 20,000 years ago.

The multichambered cave, found on Dec. 18, 1994, in southwestern France near the town of Vallon-Pont-d'Arc, boasts a Stone Age art collection that rivals that of Lascaux, the most famous site of prehistoric cave paintings, asserts Jean Clottes, an archaeologist who works for the French government. Clottes has inspected the new site.

"This is truly a great discovery," he told SCIENCE NEWS. "I was deeply moved when I saw the paintings. They're as good as any art made anywhere in the world."

Many scenes on the cave walls show animals running or engaged in some other activity. The most commonly portrayed creatures are woolly rhinoceroses, lions, and bears, as well as a smaller number of mammoths, oxen, horses, and wild cats. A rare prehistoric image of a hyena appears in one scene, and the only known cave paintings of a panther and several owls have also been noted.

Painting material included charcoal, yellow ochre, and a red pigment made from hematite.

AP

Newly discovered cave painting includes buffalo and horses.

Clottes calls the artistic technique used to represent the animals "exquisite." In a number of panels, animals are outlined to portray a larger group and to give the scene a sense of depth. A black pigment was sometimes spread by hand to shade