# 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

an animal and throw it into relief.

Few other cave-painting sites contain depictions of woolly rhinoceroses, notes Randall White, an archaeologist at New York University who has seen a videotape made by investigators of many of the new cave paintings.

"Caves [with prehistoric paintings] tend to have one thematic animal, and it may be rhinos at this location," White suggests. "There's no indication that rhinos were hunted or eaten."

Other artwork at the new site includes tracings of human hands and various geometric signs, such as large dots and bars. One panel shows three horses' heads, two painted yellow and one red, next to red dots that form several semicircles and a number of bars.

The meanings attached to such symbols remain unknown, White says.

Three people, including a government official who helps guard prehistoric sites in the region, uncovered the art gallery while exploring gorges known for their ancient, decorated caves. They cleared rocks from an opening that emitted a telltale current of air and exposed a 21-foot-deep tunnel that led to the underground chambers. The tunnel had served as a chimney for the cave site, Clottes says. Natural processes have sealed off the cave's original entrance.

A network of art-bedecked chambers lay within. Some wings of this ancient art gallery cover the area of a living room, while others are as large as 70 yards long and 40 yards wide. The entire cave extends about 1,500 yards.

Investigators have found remnants of fires, pieces of flint, human footprints, and numerous bear bones on the floor of the cave. A bear skull had been deliberately placed on a thick rock in one chamber, although Clottes does not know whether this reflects a ritual practice.

Archaeologists will collect samples from the cave for radiocarbon analysis within the next few months, Clottes says. For now, he and White agree that the site is probably between 17,000 and 20,000 years old. — *B. Bower*

# New alloys: Mixing it up on metal surfaces

Normally, gold and nickel don't mix to create an alloy. The atoms of these two elements are sufficiently different in size that they tend to remain segregated.

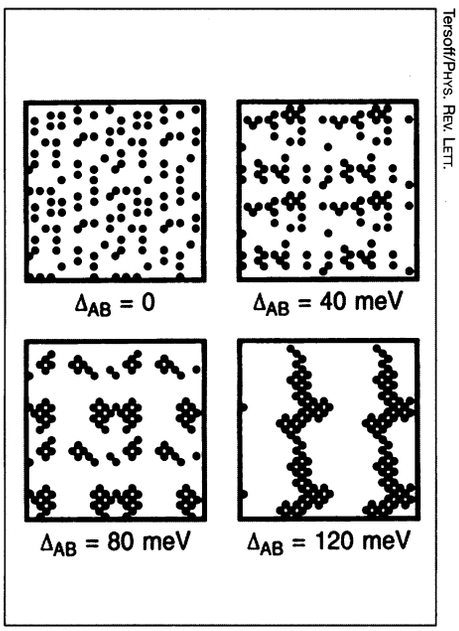
However, researchers have discovered recently that pairs of incompatible elements can readily mix to form an alloy — as long as the mixture is confined to a single layer of atoms on the surface of a crystal of one of the two metals. These novel, two-dimensional alloys include mixtures of gold and nickel on a nickel surface, silver and platinum, antimony and silver, and sodium or potassium and aluminum.

"The fact that you can form an alloy at a surface of something that won't form one in the bulk is interesting and striking," says Jerry D. Tersoff of the IBM Thomas J. Watson Research Center in Yorktown Heights, N.Y. "It gives you the opportunity for creating materials that couldn't otherwise exist."

Now, Tersoff proposes that such surface alloys are likely to form whenever a mismatch of atomic sizes is the main factor determining the behavior of a mixture of two elements. He describes his theoretical argument in the Jan. 16 PHYSICAL REVIEW LETTERS.

"This explains why the phenomenon is surprisingly common," Tersoff says. Remarkably, the same effect that suppresses intermingling within a crystal — atomic size mismatch — favors intermixing at its surface.

Mixing atoms of different sizes creates mechanical strains in the material, and the atoms tend to arrange themselves to minimize the strain energy. Tersoff's calculations and computer simulations show that on a surface, mixing represents a good strategy for reducing the strain.




Tersoff/PHYS. REV. LETT.

*Computed distribution of gold atoms (black dots) within a gold-nickel surface layer. When only atomic size differences matter, gold atoms disperse themselves as widely as possible (top left). As the tendency of gold atoms to segregate increases, they form larger clusters on the surface.*

For example, to minimize strain, gold atoms resting on a nickel surface tend to stay as far apart from each other as possible (see illustration). This allows nickel atoms to fill in the gaps to create a surface alloy.

These alloys may prove useful in processes such as catalysis. — *I. Peterson*

# Enzyme error behind neural tube defects

Women who supplement their diet with folic acid from the time they conceive through the first few months of pregnancy reduce the risk that their baby will develop a devastating neural tube defect. A new study shows why this B vitamin may work and suggests how to identify some of the women who need it most.

The brain and spinal cord develop from a single pancake of cells that first folds into a tube. If this neural tube does not fuse completely during the first 3 to 6 weeks of human life, the brain may fail to develop fully (anencephaly), certain protective structures may fail to shield the spinal cord (spina bifida) from paralyzing and potentially lethal injury, or both.

Recent studies have also linked neural tube defects to mothers deficient in another vitamin, $B_{12}$, notes James L. Mills of the National Institute of Child Health and Human Development in Bethesda, Md. Only one chemical reaction in the body requires both $B_{12}$ and folic acid. This reaction recycles an amino acid that does not go into proteins (homocysteine) into one that does (methionine). Mills and his coworkers reasoned that a defect in the enzyme driving this transformation might underlie neural tube defects.

They now offer confirmatory evidence of this from a study of pregnant women in Dublin, where the incidence of neural tube defects is nearly double that in the United States. Most of the 81 women whose babies suffered such defects had significantly higher concentrations of homocysteine in their blood than did mothers of 323 healthy babies born in the same hospitals.

Moreover, blood tests indicated that most women whose babies developed the neural tube defects were not deficient in either folic acid or $B_{12}$. The group published its findings in the Jan. 21 LANCET.

This study "is the first to really suggest a mechanism" for neural tube defects, notes Norman W. Klein of the University of Connecticut in Storrs. It also points out the value of someday screening women for a defect in homocysteine metabolism, he says.

Mills and his colleagues say their data reinforce the idea of supplementing women of childbearing age with folic acid and probably vitamin $B_{12}$. Klein argues instead that "what [women] need is methionine" — an essential amino acid most abundant in animal proteins. For now, the Food and Drug Administration is reviewing plans to ensure that women receive enough folic acid by requiring — perhaps as early as this year — that manufacturers add the vitamin to all "enriched" grain-based products. — *J. Raloff*