A Low-Energy Cause for Huntington's

Biochemical defects that prevent brain cells from generating enough energy to function properly may prompt the brain-tissue death responsible for Huntington's disease, according to two new reports. A third report suggests that a reduction in the brain cells' capacity to take up a growth factor may contribute to the disease by leaving the cells especially vulnerable to low energy levels.

The findings suggest new strategies for treating people with Huntington's disease, which currently affects 25,000 individuals in the United States. Another 125,000 relatives of these patients are at risk of developing this genetic disorder.

Individuals with the mutation that causes Huntington's disease do not begin to show symptoms until their late thirties or forties. At first, they may experience only mild difficulty in muscle coordination. However, as the disease progresses — and more brain cells die — patients experience involuntary jerking movements, depression, impaired reasoning, and memory problems. Most die of natural causes after years of confinement to bed or a wheelchair.

In 1983, researchers found a genetic marker on chromosome 4 that medical laboratories now use to determine whether an individual has inherited the Huntington's disease mutation. Although scientists know that the gene mutated in Huntington's disease must lie near this chromosome 4 marker, they have yet to identify and isolate the gene.

In the first of the new studies — all reported this week at the Society for Neuroscience's annual meeting in Anaheim, Calif. — a group led by Walter J. Koroshetz of the Massachusetts General Hospital in Boston used magnetic resonance imaging (MRI) to measure lactic acid concentrations in the brains of 18 patients with Huntington's disease symptoms. The researchers found that the patients' brains contained roughly three times as much lactic acid — a by-product of cell metabolism — as healthy individuals' brains. They are now testing whether lactic-acid-lowering drugs can reverse Huntington's symptoms.

Koroshetz says the high lactic acid concentrations "are a red flag" indicating that energy-producing cellular organelles called mitochondria are not functioning normally within the brain cells of Huntington's disease patients. Although mitochondria possess their own genetic material, they do require some proteins encoded by genes in the cell's nucleus. Koroshetz suggests that the long-sought Huntington's disease gene may encode a mitochondrial protein, but he cautions that no gene involved in energy production has yet been discovered near the Huntington's disease marker on chromosome 4.

A second research group, led by M. Flint Beal of the Massachusetts General Hospital, has generated supporting evidence for this hypothesis with an animal model of Huntington's disease. Beal's group reported at the neuroscience meeting that the brains of rodents given a mitochondria-damaging substance showed patterns of cell death similar to those seen in the brains of Huntington's patients.

In the third study reported at the meeting, a research team led by Andrew Baird of the Whittier Institute for Diabetes and Endocrinology in La Jolla, Calif., has found that the brain cells of Huntington's disease patients contain fewer receptors for basic fibroblast growth factor (bFGF) than do the brain cells of normal persons used as controls. Baird suggests that this paucity of receptors might prevent patients' brain cells from absorbing enough bFGF, which is known to help nerve cells cope with high energy requirements. This could present a double whammy to cells already suffering from impaired mitochondria, he says, hastening the cells' demise.

The new studies "are very compelling," comments Huntington's researcher Nancy Wexler of Columbia University in New York City. She says the energy-deficiency theory could explain why Huntington's patients often lose weight despite eating twice the number of calories required by healthy individuals. — *C. Ezzell*

Big sparks create glowing porous silicon

A century-old device used to demonstrate sparking has helped shed new light on the mechanism of photoluminescence in porous silicon.

Hummel & Chang/Univ. Florida

Spark-eroded porous silicon.

Since first reported almost two years ago, the discovery that light causes acid-etched silicon to glow red has created much debate about the reason for this luminescence. Some researchers attribute the glow to quantum confinement effects in microscopic silicon "wires" left behind after etching: Electrons confined by these wires recombine with positive charges to produce light. Other evidence suggests that etching modifies silicon chemically and that either a silicon compound called siloxene or bonds between hydrogen — or perhaps oxygen — and silicon play a key role in luminescence (SN: 5/16/92, p.324).

Now physicist Rolf E. Hummel and graduate student Sung-Sik Chang of the University of Florida in Gainesville have discovered an acid-free way to make silicon porous. Their approach limits the chances that silicon will undergo the chemical changes of etching, Hummel says.

He and Chang place two silicon wafers in a Tesla transformer and generate sparks between the wafers for several hours. "You can make very, very intense, large sparks, like lightning in a thunderstorm," says Hummel.

The porous wafers then emit red light when subjected to a laser, they report in the Oct. 19 APPLIED PHYSICS LETTERS. "The longer you spark, the more porous the silicon and the better the photoluminescence," Hummel notes.

To guard against possible reactions between the wafers and the humid Florida air, they eroded a few silicon wafers in pure, dry nitrogen. "There was no difference" in luminescence between the resulting wafers, Hummel says. "In our case, the siloxene, the impurity, and the hydrogen theories can be ruled out [as the cause of photoluminescence]."

These results, coupled with others reported during the past few months, "cast a lot of doubt on models that attribute luminescence to specific [chemical] species," says Leigh T. Canham of the Defense Research Agency in Malvern, England. He, Hummel, and Chang caution that some contamination could occur as the scientists transfer the very reactive silicon from the nitrogen atmosphere to the instrument that measures light emitted.

But Canham also cites work in which German and Japanese researchers heated porous silicon to high temperatures and then exposed it to oxygen. Their results support his idea that quantum confinement may be responsible for this luminescence, Canham says. — *E. Pennisi*