NEUROSCIENCE

Pesticide Causes Parkinson's in Rats

A widely used pesticide causes a syndrome in rats that looks, both behaviorally and neurologically, very much like Parkinson's disease. This new finding supports tentative epidemiological data suggesting that pesticide exposure increases a person's risk of developing the disease, which afflicts about 1 million people in the United States and is characterized by tremors, slowness, and a loss of balance. It also gives Parkinson's researchers their best model system yet for investigating how and why the disease strikes.

Although the research team, led by Timothy Greenamyre of Emory University in Atlanta, was intrigued by the epidemiologic clues, the study was designed instead to answer fundamental questions about the disease. They used the pesticide rotenone—the active ingredient in hundreds of products, from flea and tick powders to tomato sprays—because its structure and mode of action resemble those of a compound called MPTP. In the early 1980s, MPTP was found to cause a severe Parkinson's-like syndrome in young heroin addicts.

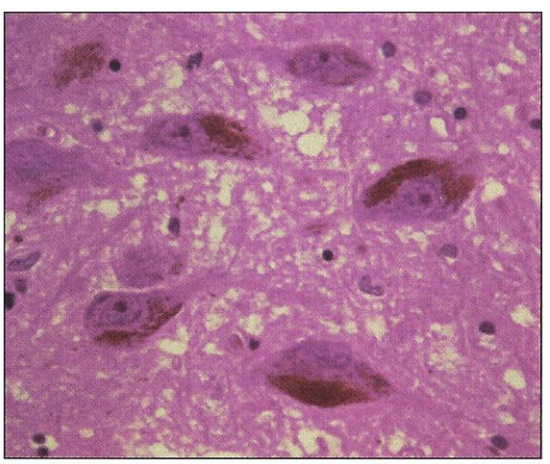
Researchers quickly figured out what had happened to the addicts: MPTP is metabolized to MPP+, which slips through the blood-brain barrier. Most neurons ignore the metabolite, but those carrying receptors for the neurotransmitter dopamine suck it up. Once inside these neurons, MPP+ interferes with electron transport in the cells' mitochondria, releasing free radicals that eventually kill the cells. This produces the same movement defects as those seen in Parkinson's disease, which is caused by the loss of dopamine-producing neurons in a brain region called the substantia nigra.

One of the more chilling aspects of the MPTP episode was the realization that many common pesticides are structurally similar to MPP+. What's more, both rotenone and MPP+ kill cells by interfering with part of the mitochondria's electron transport system called complex 1. Now, as described this week at the Society for Neuroscience meeting in New Orleans, Greenamyre's team has shown that rotenone produces Parkinson's-like symptoms in rats similar to those MPTP induced in humans. (The results will also appear in the December issue of *Nature Neuroscience*.) "I've been hoping someone would do the work that Tim is publishing," says neurologist Caroline Tanner of the Parkinson's Institute in Sunnyvale, California.

In the experiment, 25 rats injected with the pesticide for 1 to 5 weeks developed rigidity and unsteady movements. In the rat's brains, the dopamine-producing circuits deteriorated, and surviving cells had cellular deposits that looked a lot like Lewy bodies, another hallmark of Parkinson's. Other animal models mimic the dopamine circuit degeneration of the disease, but this is the first to show Lewy body–like deposits as well, making this an excellent model of Parkinson's, says Virginia Lee, a neuroscientist at the University of Pennsylvania in Philadelphia.

The researchers chose rotenone as a possible trigger of a Parkinson's-like syndrome to test the importance of one subtle symptom of the disease. In the last decade, other teams had found that mitochondrial complex 1 action is disrupted throughout the bodies of patients with Parkinson's—in blood cells and muscle cells, as well as in the dopaminergic circuits. No one knew how important this systematic complex 1 inhibition was. Could interfering with complex 1 throughout the body—not just in the dopaminergic cells that MPP+ infiltrates—cause the disease?

In Greenamyre's rats, at least, disrupting complex 1 systematically can produce what looks like Parkinson's disease. Rotenone, unlike MPP+, can slip through any cell's membranes. The researchers found that, as expected, complex 1 activity was inhibited throughout the brain, but only the dopaminergic cells degenerated, just as in Parkinson's. Lee suspects that dopaminergic neurons are more fragile than other cells and can't withstand the free radical damage caused by rotenone's disruption of complex 1.



No longer elusive. Lewy bodies typical of Parkinson's disease (above) can now be mimicked in a rat model.

As to whether rotenone or other pesticides contribute to Parkinson's in humans, the researchers urge caution. So far, more than 15 epidemiologic studies have linked Parkinson's to crude environmental risk factors, such as living in the countryside or working in the agricultural, chemical, or pharmaceutical industries. But no single chemical, including rotenone, has been reliably implicated as a risk factor. At this stage, Greenamyre suspects the risk of Parkinson's is a function of genetic predisposition—potentially related to how efficiently one metabolizes toxins—as well as of environmental exposures.

–LAURA HELMUTH

SCIENCE EDUCATION

Ehlers Bill Suffers Surprising Defeat

A popular, bipartisan bill to improve school science and math education derailed suddenly in Congress late last month after critics said that it might violate a constitutional ban on government support for religion. But the action involved more than scholarly debate. The House's 24 October vote also demonstrated the political clout of the country's two major teachers' unions—which disapproved of a provision for grants to private schools—and the relative weakness of scientific groups that lobbied for the bill.

The last-minute controversy over the National Science Education Act (H.R. 4271), the major legislative vehicle this year for federal intervention in science and math education, came as a shock to its chief sponsor, Representative Vern Ehlers (R–MI). Ehlers had spent months forging a bipartisan coalition to support his push to raise the quality of teachers in elementary and secondary schools (*Science*, 21 April, p. 419). The linchpin of that strategy was a novel, $50-million-a-year program to provide schools with master teachers—experienced educators who would help train new staff, develop curricula, and generally champion science and math. The House Science Committee passed the bill unanimously on 24 July (*Science*, 4 August, p. 713), and the education panel waved it through in September, clearing the way for a special fast-track vote in the waning days of the 106th Congress.

The day before the vote, however, legislators' offices suddenly began buzzing about a provision that would have created a program at the National Science Foundation (NSF) "to make grants to a state or local educational agency or to a private elementary or middle school for the purpose of hiring a master teacher." The language had been in the bill since July, but embarrassed Capitol Hill staff and education lobbyists admit that they hadn't noticed it until the bill was scheduled for a vote.

"We were sitting around during a lull in the negotiations over the Labor-HHS bill [a bitterly contested spending measure still awaiting resolution] when I saw the language and said, 'Whoa! There's a church-

CREDIT: MICHAEL ABBEY/PHOTO RESEARCHERS