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.

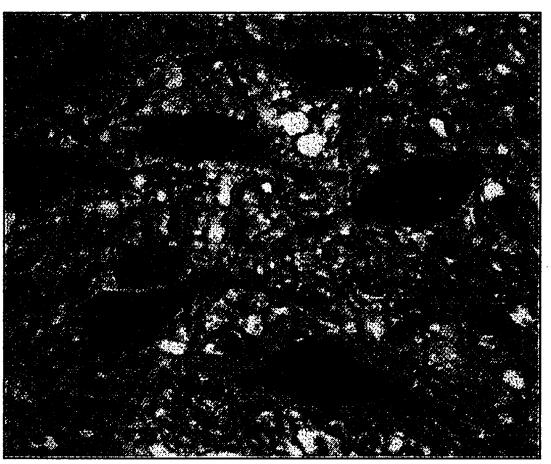
Researchers quickly figured out what had happened to the addicts: MPTP is metabolized to MPP+, which slips through the blood-brain barrier. Most neurons ignore the metabolite, but those carrying receptors for the neurotransmitter dopamine suck it up. Once inside these neurons, MPP+ interferes with electron 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.

CREDIT: MICHAEL ABBEY/PHOTO RESEARCHERS

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-

School daze. Last-minute doubts foiled a plan by Representative Vern Ehlers to hire master teachers in science and math.

state entanglement here,' " says one Democratic aide. Lobbyists for the National Education Association (NEA), casting a fresh eye on a bill that they hadn't expected to be voted on this year, noticed the same thing. Shrugging off the lapse, NEA's Joel Packard says: "It's a busy time of year."

Opponents say the language appears to violate a 1971 Supreme Court ruling (*Lemon* v. *Kurtzman*) that overturned two state programs that had subsidized teachers of secular subjects in private schools. The court's concern, says David Ackerman of the Congressional Research Service, is that subsidized teachers "might inculcate religion," in violation of the First Amendment separation of church and state. The prohibition might not apply to programs that pay for professional development or educational materials, Ackerman noted in an analysis of the issue that was prepared quickly on the day of the vote. Private schools currently receive such services under a variety of Department of Education programs. "The key is that public schools [must] maintain control of the money," says Packard, and the money may not be used to hire teachers.

Ehlers, who says that no member ever raised this point with him before the Tuesday vote, rejects that interpretation. "I don't see the distinction here," he says, noting that NSF has long included teachers at private schools in training and curriculum development programs. An NSF spokesperson says that the agency is not precluded from funding activities at private elementary and secondary schools but that most of its money goes to higher education.

Once the issue had been raised, however, opponents mobilized quickly. Packard enlisted his counterparts at the American Federation of Teachers and the National Parent Teacher Association, and together the groups placed phone calls to a handful of Democratic lawmakers. The word spread like wildfire. Even key legislators who had supported the bill in committee turned against it. Says a spokesperson for Representative Eddie Bernice Johnson (D–TX), a co-sponsor who wrote into the bill a program fostering partnerships with industry: "It really hurt her to vote 'No.' "

The rapid erosion of support surprised Republican leaders, who brought the bill to the floor under a "suspension of the rules" provision normally used for noncontroversial legislation. Although the bill actually attracted a majority, 215 to 156, it fell 33 votes short of the two-thirds margin required by the rules. Only 44 of 184 Democrats voted for it. Even Packard admits that the bill's downfall was unexpected. "To be honest, we thought it would pass and we'd have to take our case to the Senate," he says.

Ehlers says that he plans to reintroduce the bill in the next Congress, but it's not clear how much room there is for compromise. "I don't see any reason to modify my position, and I resent the last-minute effort to dismantle [the bill]," he says. Science education groups are disheartened. "We put a lot of work into it," says Gerry Wheeler, executive director of the National Science Teachers Association, part of a coalition of supporters that includes the American Physical Society and the American Astronomical Society. "It's scary that somebody could turn around all those Democrats." —JEFFREY MERVIS

ACADEMIC COMMUNITY

Ruling Allows Unions At Private Colleges

The National Labor Relations Board (NLRB) last week gave a nod to the first graduate students' union at a private university. The board's ruling that graduate teaching and research assistants at New York University (NYU) qualify as "employees" potentially puts them on equal footing with colleagues at publicly funded campuses in more than 20 states.

University administrators deplored the ruling, which thrilled labor organizers. "We're deeply disappointed," says NYU dean for science Peter Lennie. Unionization "will change dramatically the way in which faculty relate to students," adds vice president Robert Berne. But union supporters are "ecstatic," says Antony Dugdale, a spokesperson for the Graduate Employees and Students Organization at Yale University in New Haven, Connecticut, which has been leading efforts to unionize graduate students (*Science*, 29 November 1996, p. 1461).

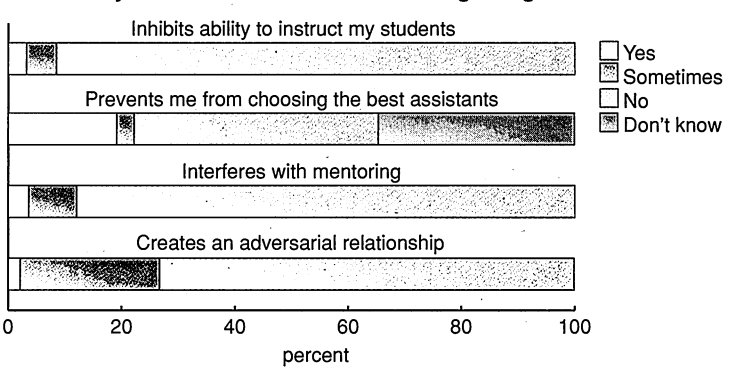
The 2 November ruling upheld an earlier decision by a regional NLRB official that teaching assistants are paid employees and therefore eligible for collective bargaining. The university appealed that decision to the full NLRB, but the three-person panel rejected NYU's argument that graduate assistants get "financial aid," not salaries. Responding to concerns about academic freedom, it noted that the history of faculty labor unions suggests that all parties will "confront any issues of academic freedom as they would any other issue in collective bargaining."

There is scant information on the effects of student unionization. A recent survey of 300 public university professors by Gordon Hewitt of Tufts University in Medford, Massachusetts, found that more than 90% did not feel unions harmed their relations with students (see chart). Similarly, an unpublished study by Daniel Julius of the University of San Francisco and Patricia Gumport of Stanford University found "no conclusive evidence" of problems.

But NYU officials said that labor relations at state universities—where about 20% of assistants are unionized—can't be compared with those at private schools, because federal law gives private employees broader organizing rights than it gives their colleagues at state-run schools. And Julius and Gumport predict that unionization "heralds yet another breakdown in the internal organizational fabric of higher education." Schools, they write, may hire temporary help rather than subsidize a "permanent class of unionized graduate students."

NYU officials also say the board made "artificial distinctions" between groups, excluding assistants subsidized by nonuniversity money and those doing research on their own dissertations. "This distinction is completely capricious" and will create tensions on campus, says Lennie. Some private university leaders, including Yale president Richard Levin and Boston University chancellor John Silber, are urging NYU to chal-

Faculty views on student collective bargaining



Happy union? A 1999 survey at five state universities found that collective bargaining has little effect on most faculty practices.

GRAPH: G. HEWITT