

PARKINSON'S DISEASE

Dopamine May Sustain Toxic Protein

ther rejected or didn't have enough money to fund. He plans to invite rejected researchers to post their ideas on a free electronic bulletin board. That way, he says, scientists can avoid being penalized by a peer-review system that is "inherently flawed, overly cautious, ... and unfriendly to real innovation."

Some researchers at the center of the storm say they don't see the release of their names as a threat. "Even the most successful researchers don't always get funded, but I can see why someone might feel embarrassed," says Mark Blumberg, a neuroscientist at the University of Iowa in Iowa City, who, like Vagell, is on the list but was eventually funded by the National Institute of Mental Health (NIMH). Vagell, who says he doesn't mind the attention, finds Kurzon's information-sharing plan "interesting, ... [but] I can't imagine that funders are facing a shortage of good applicants."

This is the second time that the 71-year-old Kurzon, a Harvard-trained physician who has worked in the pharmaceutical industry and as a venture capitalist, has forced NIH to cough up such a list. In 1980, he won a court order forcing the National Cancer Institute to reveal the names of its unfunded applicants after he learned that it had rejected a proposal from prominent biochemist Albert Szent-Gyorgyi. Kurzon turned the list over to a social scientist studying peer review.

Kurzon went to federal court again last year, after NIMH rejected a 1999 Freedom of Information Act request for a similar list. In July, a judge found that although neither NIH nor Kurzon had made a strong case, the law requires agencies to make records public whenever possible. So on 12 October NIH sent Kurzon a list of the 800-plus NIMH applicants who weren't funded in the spring of 1999, after informing everyone on the list and inviting them to contact Wendy Baldwin, head of the agency's extramural grants agency.

"I can't see how a list of names is ... the most effective way to advance science," says Baldwin. The agency already encourages researchers who don't get NIH funding to approach private donors, she says.

Kurzon thinks that NIH officials are missing the point. The exercise will have been worthwhile if it leads to the funding "of even one overlooked gem of an idea," he says, adding that he plans to ask every NIH institute to provide updated lists of its unfunded applicants. But scientists may cling to their anonymity a bit longer: Kurzon has yet to raise the money to mail out his invitations or set up his Web site.

—DAVID MALAKOFF

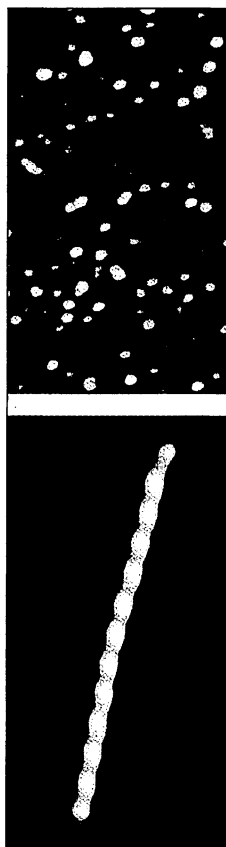
The tremors, stiffness, and slurred speech that accompany Parkinson's disease are rooted in the death of neurons that churn out the chemical messenger dopamine. But precisely what kills these brain cells has long stumped researchers. Now a provocative test tube study suggests that a surprising culprit—dopamine itself—may assist in the neurodegeneration that defines the disease. Parkinson's researchers say the findings are intriguing and worthy of follow-up experiments but caution that they must be confirmed in cell cultures and laboratory animals.

Neurons in parts of the brain stricken by Parkinson's disease are marked by tangled deposits called Lewy bodies. These clumps are made of the folded, or fibrillar, version of a protein called α -synuclein. Neuroscientists initially assumed that fibrillar α -synuclein—as opposed to the unfolded form common in healthy brains—is responsible for neural demise. Recently, however, researchers have pursued a version of α -synuclein that hovers between normal and fibrillar, called protofibrillar, which some consider far more toxic than fibrils.

On page 1346, Peter Lansbury of Harvard Medical School in Boston and his colleagues describe their search for compounds that either prevent or encourage protofibril accumulation. Lansbury's team used human α -synuclein produced by bacteria to screen 169 compounds. To the researchers' surprise, of the 15 compounds that inhibited the

transition from protofibril to fibril—thus, presumably, making protofibrils stick around in a cell longer—14 belonged to a set of neuromodulators called catecholamines, which includes dopamine.

The results appeared paradoxical; after all, Parkinson's disease is caused by a crippling loss of dopamine. How could dopamine be worsening the disease? "The whole thing led in a very unexpected direc-



Misfolding. Dopamine may keep α -synuclein in toxic protofibrils (top) by preventing it from forming fibrils (bottom).

ScienceScope

The fall of RISE In May 2000, an advisory committee to the National Science Foundation (NSF) proposed a big spending boost in mathematics and the physical sciences, citing their role in national security and economic development. Committee members hoped that the 20-page manifesto—the Reinvestment Initiative in Science and Engineering (RISE)—would inspire a doubling of the NSF budget, a goal of NSF director Rita Colwell.

But the campaign never took off. Last week the committee vented its anger at NSF's top management for failing to trumpet its message while a recent Defense Department commission led by former U.S. Senators Gary Hart and Warren Rudman attracted national attention by making many of the same points. "NSF had an opportunity to be at the forefront on the role of science in national security and economic development, and it dropped the ball," said chemist Ronald Brisbois of Macalaster College in St. Paul, Minnesota. "RISE could have been on everybody's lips [after 11 September] instead of Hart-Rudman."

NSF staffer Robert Eisenstein says he understands their frustration. But he also told the committee that Colwell *et al.* "are very supportive" of the RISE plan.

Arsenic Déjà Vu Ending one of the biggest scientific controversies of the young Bush Administration, the Environmental Protection Agency (EPA) last week issued a new standard for arsenic in drinking water. It chose exactly the same level of 10 parts per billion (ppb) set by the Clinton Administration.

In March, EPA administrator Christine Whitman suspended that standard and asked for more scientific review, noting that cleanup costs could be high. Her move provoked an uproar among environmentalists and some members of Congress and inspired countless jibes about the president's disregard for the public's health. But if more review was meant to block the standard, it backfired: A National Academy of Sciences panel found that the cancer risks of arsenic were greater than previously thought, suggesting that even 10 ppb might not be protective enough (*Science*, 21 September, p. 2189). The panel's chair, retired pathologist Robert Goyer, declined to comment on EPA's decision. But he said that it's in line with a World Health Organization guideline followed by many countries.

very thinnest ice thickness proposed," says Turtle, at least at the places and times Europa's several central-peak craters formed.

Another, stereoscopic analysis of surface forms is yielding even larger estimates of ice thickness. Planetary scientists Paul Schenk of the Lunar and Planetary Institute in Houston and William McKinnon of Washington University in St. Louis have calculated that ice more than 6 kilometers thick must underlie plateaus they have found to rise 0.5 to 1 kilometer in height and pits 0.5 kilometer deep. That "rules out the ultrathin case," says McKinnon, echoing Turtle.

Although the thicker ice thesis seems to be gaining ground, planetary geologist Robert Sullivan of Cornell University acknowledges that the real world is often not as simple as one extreme or the other. Planetary scientist Christopher Chyba of the SETI Institute in Mountain View, California, says he's also leaning in the direction of thick ice, but "we're not going to feel confident until we get there again."

That won't happen anytime soon, however. Budget-strapped NASA has yet to commit itself to a mission to send an orbiter to Europa, which could confirm an ocean from orbit by measuring the tidal squeeze on the satellite. But getting an ice thickness "won't be easy," says one possible participant.

—RICHARD A. KERR

U.S. DEPARTMENT OF ENERGY

Science Office Grows, Nonproliferation Stalls

It could have been worse. The new science budget for the U.S. Department of Energy (DOE) isn't flat, as the Bush Administration had requested. But Congress has spent much of the 2.5% increase it awarded the department on pet projects, and it squeezed programs in Russia that protect nuclear stockpiles and employ former weapons scientists.

The \$25 billion spending bill—ap-

proved on 1 November and expected to be signed shortly by the president—includes \$3.2 billion for DOE's Office of Science, which is the largest funder of basic physical science programs at U.S. universities and government laboratories. Although it follows the White House budget blueprint closely in most respects, lawmakers restored \$10 million for fusion studies and tacked on nearly 10% for DOE's Biological and Environmental Research (BER) program (see table). Legislators, however, earmarked nearly all of BER's \$84 million in new money for equipment and construction at specific universities—typically in the home states of senior members of the House and Senate spending panels. There is \$11 million, for instance, for the new Mental Illness and Neuroscience Discovery Institute at the University of New Mexico in Albuquerque; the state is the home of Senator Pete Domenici, a top Republican on the appropriations committee.

Given earlier fears of budget cuts, "the bite turned out to be nowhere [near as] bad as the bark," says Scott Sudduth, the Washington, D.C.-based director of government relations for the University of California. Still, researchers "got rather slim pickings if you consider the important role that science plays in national security," adds Michael Lubell, a lobbyist for the American Physical Society in Washington, D.C.

Arms control advocates, meanwhile, failed to increase funding for DOE's nuclear nonproliferation programs. The 2002 budget contains \$803 million for arms control programs, \$29 million more than the president's request but \$69 million less

than this year. It also lumps into a single \$42 million pot the budgets for two programs—the Initiatives for Proliferation Prevention (IPP) and the Nuclear Cities Initiative (NCI)—aimed at keeping weapons scientists from freelancing for U.S. enemies.

The decision disappointed IPP officials, who had been expecting a substantial increase from last year's budget of \$24.5 million, but buoyed NCI backers, who feared Congress would follow the Administration's wishes and practically kill the \$27 million



HOW DOE SCIENCE FARED (\$ MILLIONS)

	2002 Request	2002 Final	Change from 2001
Office of Science	3159	3233	2.5%
High-Energy Physics	721	716	0.6%
Nuclear Physics	361	361	—
Basic Energy Sciences	1005	1004	1.2%
Fusion Energy Sciences	239	249	—
Biol. & Envir. Research	443	527	9.3%
Advanced Scientific Computing Research	164	158	-4.6%
Other	226	218	-25%

ScienceScope

Geologic Rebound Things looked grim earlier this year for scientists in the water resources division of the U.S. Geological Survey (USGS). The Department of the Interior had requested a budget that would have cut funding for the National Water Quality Assessment (NAWQA) by 30%, slashed 71% from the Toxic Substances Hydrology Program, and completely eliminated a nationwide network of cooperative research institutes (*Science*, 11 May, p. 1040). Alarmed, groups that use USGS water data—from environmentalists to civil engineers—raised a ruckus.



Now they, and the USGS, can breathe a sigh of relief. When President George W. Bush signed the 2002 Interior appropriations bill into law this week, many of the proposed cuts had evaporated. The toxics and NAWQA programs got 2.3% and 1.6% raises, respectively, while the State Water Resources Research Institutes won a 10% boost. "Compared to the bleak scenario in the spring, things are much better," says David Blockstein, a senior scientist with the National Council for Science and the Environment in Washington, D.C. But he's not optimistic that the water programs will be spared next year, when the federal budget is expected to be even tighter.

Squeaky Wheels The newly signed Interior appropriations bill (see above) also contained mixed news for researchers upset with plans to ax two science centers at the Smithsonian Institution. Last spring, Smithsonian director Lawrence Small announced plans to eliminate the Conservation and Research Center in Front Royal, Virginia, and the Center for Materials Research and Education in Suitland, Maryland (*Science*, 13 April, p. 183). The proposed closures were part of a plan to reorganize Smithsonian science and free up funds for other projects.

After protests from researchers and local lawmakers, Small backpedaled, but warned that Congress would have to come up with more money to keep the units open. It did, giving the Smithsonian \$497 million in 2002, \$3 million more than the president's request. That's barely enough to cover all the costs of those units, says the Smithsonian's Paula DePriest. And the other science units will take a \$1.9 million hit. "It's actually very grim," she adds.

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