

chief sponsor, Senator Spencer Abraham (R-MI), are meant to increase the pool of technologically adept U.S. workers available to fill vacancies at domestic information technology companies. Many of those jobs now go to foreign workers. "We wanted to look beyond the immediate crunch and get at the long-term problem of training more Americans," says an Abraham staffer who follows the issue. "And NSF has a good reputation for running quality programs."

The legislation was a last-minute addition to the bill, which raises the cap on so-called H-1B visas from 65,000 to 115,000 this year and next before dropping back to 65,000 in 2002. The scholarship provision calls for NSF to run a competition that would award up to 10,000 \$2500-a-year scholarships to low-income students pursuing associate, undergraduate, or graduate degrees in mathematics, engineering, and computer sciences. The exact income level has yet to be determined. In addition, NSF would receive roughly \$6 million to be divided between systemic reform efforts in elementary and secondary schools (see p. 1800) and year-round enrichment courses in science, mathematics, and engineering. The money would be available annually through 2001.

Although they welcome the money, NSF officials are concerned about the administrative burden of a new program. They would prefer to make the scholarships part of NSF's existing stable of programs aimed at strengthening the U.S. scientific labor force, including a rapidly growing advanced technology education initiative at community colleges. "A national scholarship program is a huge undertaking," says Joseph Bordogna, acting deputy NSF director. "We haven't decided anything, but we're hoping to do something that is consistent with what we are already doing."

The closest thing to a scholarship program at NSF now is the agency's graduate research fellowships. But those awards are based on merit, not need, and they go to the institutions that students attend rather than to the students directly. "We're not geared up to run an individual scholarship program, including cutting thousands of checks," says one senior education official. NSF officials are also disappointed that the bill appears to exclude most of the natural sciences, noting that science is increasingly interdisciplinary and that graduates often take jobs outside their academic

specialty. Abraham's aide says those restrictions "were a deliberate attempt" to train people for the information technology industry.

Educators at institutions that serve large numbers of low-income students say that the scholarships should help those already planning careers in information technology. But they warn that efforts to increase the flow of students into the field must start much earlier. "They may be interested, but many of our students don't have the skills to pursue the degrees that offer the high-paying jobs," says William Edmonson, president of Panola College, a community college in east Texas with an NSF grant to reform undergraduate

science and math instruction. "The foreign students who come here are at a distinct advantage because they've already taken the necessary courses in high school."

—JEFFREY MERVIS

"[Our] foreign students are ... at a distinct advantage because they've already taken the necessary courses."

—William Edmonson

NEUROBIOLOGY

Drug May Suppress the Craving for Nicotine

They are tired of the scornful glances of strangers, of shivering in cold entranceways, of the fear they will die from their habit. For these reasons and more, each year 35 million smokers in the United States alone try to quit. But more than 90% start again within a year. Now, new evidence suggests that a drug used to treat epilepsy in Europe may one day help smokers kick the habit.

In the January 1999 issue of *Synapse*, neuroanatomist Stephen Dewey at Brookhaven National Laboratory in Upton, New York, and his colleagues report that in baboons and rats, an epilepsy drug called gamma vinyl-GABA (GVG) suppresses a neurochemical hallmark of nicotine and other addictive drugs: a rise of the neurotransmitter dopamine in the brain's "reward centers." It

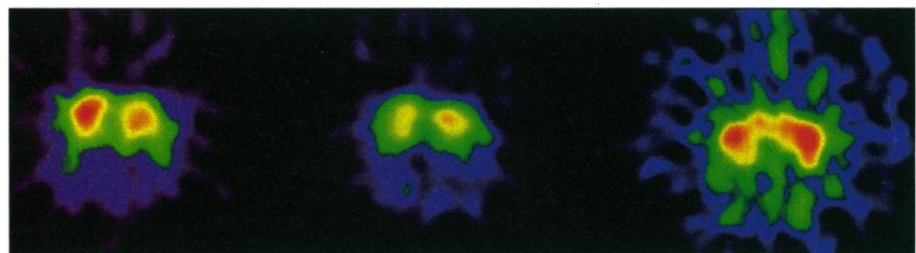
also stops behaviors in rats thought to mirror human cravings for nicotine.

Current smoking cessation aids either deliver nicotine more safely, via patches, gums, or sprays, or combat depression in former smokers. But the Dewey team's work, if confirmed in human studies, may lead to a drug that could help many people stop smoking in a different way: by suppressing their "need" for nicotine and possibly by reducing the "high" as well.

GVG may also have potential as a therapy for cocaine addiction, because the same team reported similar findings for that drug in the August issue of *Synapse*. "These pre-clinical data are tremendously interesting and provocative," says Alan Leschner, director of the National Institute on Drug Abuse, who nevertheless cautions that further study is needed to determine whether GVG will be a useful—and safe—treatment for addiction.

Dewey didn't originally set out to find an addiction drug. Although not approved in the United States, GVG has been used for years to treat epilepsy in 60 other countries. It works by irreversibly blocking a brain enzyme that breaks down the neurotransmitter γ -aminobutyric acid (GABA), which inhibits neural activity. Thus, brain GABA levels rise, dampening the excessive nerve firing that can lead to epileptic seizures. In 1990, Dewey, psychiatrist Jonathan Brodie at New York University School of Medicine, and their colleagues set out to see whether GVG could also treat schizophrenia. Some of this disease's symptoms have been linked to higher than normal levels of the neurotransmitter dopamine in certain brain areas, and the researchers reasoned that GVG might help by suppressing the dopamine-producing cells.

In 1992, Dewey and Brodie showed that GVG does lower dopamine in a region of the baboon brain. But before pursuing GVG as a schizophrenia treatment, Dewey became intrigued by a Brookhaven colleague's work on drug abuse that focused on dopamine. "I thought, 'I bet [GVG] will work'" to block the dopamine surge caused by addictive drugs, Dewey recalls. This surge is thought to underlie the "high" that keeps addicts coming back for more and



Craving suppressor? The PET images show the binding of a radioactive drug to dopamine receptors in the baboon brain. Compared to the control (left), nicotine (center) reduces the binding, indicating increased brain dopamine levels, while the drug GVG (right) prevents that effect.

perhaps also feelings that make them anticipate the arrival of a drug.

In the current study, Dewey, Brodie, and their colleagues have shown that GVG can block the dopamine rush produced by nicotine. The researchers found that whereas nicotine injections double the dopamine levels in the reward centers of the brains of control rats, GVG given 2.5 hours before the nicotine could completely block the dopamine rise. And in positron emission studies that infer dopamine levels by detecting how much of a radioactive tracer can bind to dopamine receptors—low binding indicates high endogenous dopamine—the scientists saw something similar in baboons.

To find out whether this change in brain chemistry has behavioral effects, team member Charles Ashby, a neuropharmacologist at St. John's University in Jamaica, New York, tested GVG's effects on a rat behavior called conditioned place preference, which is thought to reflect what happens in humans when particular environmental stimuli elicit drug cravings. First, Ashby and his colleagues gave rats repeated nicotine injections while they were in either of two connected boxes, one striped and the other plain, teaching them to associate nicotine with one of the boxes. Then, they let rats choose between the boxes after receiving a dose of either a control solution or GVG.

As expected, control rats stayed in the box where they had received nicotine, but the rats given GVG displayed no preference, suggesting that GVG erased their attraction to places associated with the drug. "We think GVG stabilizes dopamine levels such that animals don't get the dopamine rush when they go to the chamber associated with the drug," says Dewey. In humans, by extension, the treatment might dampen the intense drug cravings ex-smokers feel when they experience something—a sip of coffee, for example—that reminds them of cigarettes.

And GVG may help combat cocaine cravings as well. This past August, Dewey, Brodie, Ashby, and their colleagues showed that GVG can prevent a cocaine-induced burst of dopamine in baboon brains. They further demonstrated that the drug blocks conditioned place preference in rats that have learned to prefer environments associated with cocaine injections.

Of course, nobody can say whether GVG can help people stop smoking, or using cocaine, until it is tested in human smokers and cocaine users, something just now being considered by doctors at medical centers equipped to conduct such trials. And human tests may be delayed by concerns about the peripheral vision defects GVG causes in some epilepsy patients, which is why the U.S. Food and Drug Administration has not approved it. The much lower GVG doses

needed to combat nicotine cravings may not cause these problems, however. Indeed, says Dewey, if further testing pans out, "we might be able to help people on any of a number of addictive drugs."

—INGRID WICKELGREN

AIDS RESEARCH

New Czar Aims to Sharpen France's Effort

PARIS—France is second only to the United States in spending on AIDS research, but in recent years the payoff has seemed disproportionately modest. Although French clinicians have conducted major studies to evaluate anti-HIV drugs developed elsewhere, France has created few new therapies of its own (*Science*, 16 January, p. 312). But French officials are hoping that will change soon. At a press conference earlier this week, France's new AIDS czar, immunologist Michel Kazatchkine, unveiled plans to harness basic AIDS research more tightly to eventual therapeutic goals, as well as to beef up the nation's AIDS vaccine effort.

Kazatchkine—who in October replaced virologist Jean-Paul Lévy as director of the National Agency for AIDS Research (ANRS)—was joined at the press conference by Claude Allègre, France's minister of research, and Bernard Kouchner, the health minister. Both Allègre and Kouchner said that their presence was intended in part to scotch rumors, circulating over the past year, that the ANRS would be disbanded and its activities absorbed into other research agencies once Lévy stepped down. "We are not going to pull back or make a lesser effort in AIDS research," said Kouchner.

However, beginning next year, that effort will be much more tightly focused. For example, although about 25% of the ANRS's 1999 budget of \$42 million will be spent on basic HIV research, half of that sum will now be reserved for "coordinated actions" designed to lead to new therapies. The other half of the basic research allotment will be awarded to researchers on the basis of grant proposals, although these will now be much more stringently judged than in past years. "The barrier for funding these projects will be raised higher," Kazatchkine told *Science* in an earlier interview. "Basic [AIDS] research should not just bring one more piece to the puzzle but have the goal of identifying

new targets for therapy."

Vaccine research will also receive a boost next year, up 18% from the roughly \$6.4 million spent in 1998. Kazatchkine says that one key goal will be to involve new industrial partners in vaccine development. At the moment, only the Lyons-based pharmaceutical company Pasteur Mérieux Connaught (PMC) is working with ANRS on vaccines. "If PMC has been so dominant, it is because not many other [companies] have come in," Kazatchkine says. Indeed, at the press conference, both Allègre and Kouchner decried the general reluctance of French companies to get involved in HIV research. "There is a black hole there," said Kouchner. "The international companies developing new [anti-HIV] drugs are not French."

The new plans to focus more heavily on therapeutic goals drew mixed reviews from researchers who spoke to *Science*. "The way one develops a vaccine or finds a drug is not by going basic but through the most rigorous application of basic knowledge to research that is goal-oriented," says virologist Marc Girard of the Pasteur Institute in Paris. And

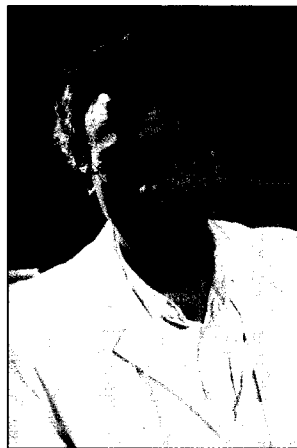
Françoise Brun-Vézinet, a virologist at the Bichat-Claude Bernard Hospital in Paris and a member of ANRS's scientific advisory council, says that focusing more effort on clinical AIDS research makes sense because "this is what has worked best" at the ANRS. Moreover, Brun-Vézinet adds, fundamental HIV research can still be accommodated in France's other research organizations, such as the giant biomedical agency INSERM.

But some question whether it makes sense to limit the focus of ANRS's research to

specific targets. An AIDS researcher who asked not to be identified says, "So far the other 'coordinated actions' of ANRS have not been impressive, and the vaccine effort has been groping in the dark. Raising the barrier is a good idea, but it should be on everything, not just basic research."

Despite the assurances from Allègre and Kouchner that the ANRS will continue to exist, the agency's mandate expires at the end of 2000, at which time the government will have to decide whether to renew it. That gives Kazatchkine 2 years to prove that French AIDS research can produce results. "I told the ministers it was absolutely premature to close down the ANRS," Kazatchkine says. "If they asked me to take over, I guess they agreed."

—MICHAEL BALTER



Focus on therapies. French AIDS czar Michel Kazatchkine.