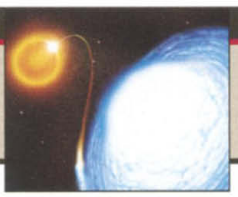
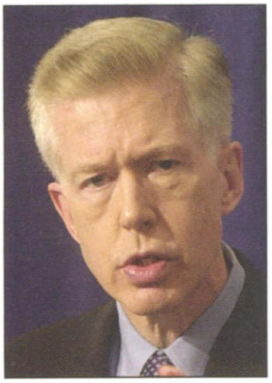


STEM CELL RESEARCH

California Flashes A Green Light



Golden opportunity. California Governor Gray Davis signs stem cell research bill.

On 22 September, California Governor Gray Davis signed the nation's first state law explicitly allowing scientists to derive human embryonic stem cell lines as well as to clone embryos to study and treat diseases in what is known as nuclear transfer research. The measure, sponsored by state Senator Deborah Ortiz (D–Sacramento), "is going to make a huge difference" in directing state resources toward such research and luring scientists to California, says stem cell researcher Irving Weissman of Stanford University, who helped draft the legislation. National regulations currently prohibit the use of federal funds, but not state or private money, for such research.

The measure permits "research involving the derivation and use of human embryonic stem cells, human embryonic germ cells, and human adult stem cells from any source, including somatic cell nuclear transplantation," with regulation by institutional review boards. The bill might also boost the supply of embryos available for research by calling on fertility doctors to inform patients of this option. Davis also signed a second bill making permanent a temporary ban on reproductive cloning.

The nuclear transfer bill does not provide new funds for stem cell research, but an aide to Ortiz says it is expected to "open up" existing state research funding programs by signaling the importance of stem cell research. The national debate has had an "enormously chilling effect" on the research, says Susanne Huttner, associate vice provost for research in the University of California (UC) system and head of the Industry-University Cooperative Research Program. She plans a mailing to alert scientists to the new measure.

The bill's greatest value, says Weissman, is its support for nuclear transfer. "There's a whole area of research that's been sitting there, and people have been afraid to do it," he says. Scientists want to be able to both create a cell line using a nucleus from a cell of a person with a genetically transmitted disease and distribute the cells to other researchers. "Under this law," he notes, "it'll be done in California."

Fittingly enough, UC San Francisco last week sent out its first batch of long-awaited stem cells to nine U.S. investigators. A U.K. shipment is next, says spokesperson Jennifer O'Brien. **–CONSTANCE HOLDEN**

NEUROSCIENCE

Drug Find Could Give Ravers the Jitters

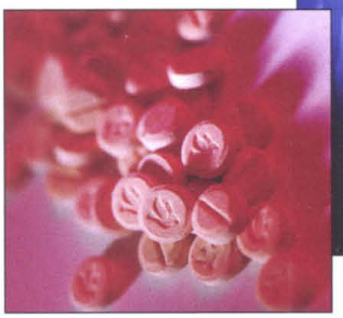
"Ecstasy" is a cruel misnomer for the party drug (±)3,4-methylenedioxymethamphetamine (MDMA). Long known to disrupt neurons that communicate via the neurotransmitter serotonin, the controversial drug now appears to have even more potential for roughing up the dopamine system.

A quintessential social drug, ecstasy heightens sensations, gives a euphoric rush, and creates feelings of warmth and empathy. It ostensibly achieves this effect by causing neurons to spurt huge quantities of serotonin. In the immediate aftermath, the partier is temporarily drained of serotonin, often depressed and unable to concentrate. Some researchers see strong evidence from both brain and behavioral research that permanent brain damage also can result from MDMA use, but others are skeptical and suggest that the drug might be useful for certain types of psychotherapy.

Now George Ricaurte and colleagues at Johns Hopkins University School of Medicine in Baltimore report on page 2260 that ecstasy can cause "profound dopaminergic toxicity," possibly explaining some of the drug's reported negative short- and long-term effects. Researchers administered the equivalent of a heavy party night's worth of MDMA to monkeys. The damage they observed suggests that one all-night "rave" might be enough to induce permanent brain damage and make a person more vulnerable to Parkinson's disease, which is caused by a loss of dopamine-producing neurons.

The researchers injected three doses of MDMA into five monkeys over a period of 9 hours. One monkey died of hyperthermia within hours: Overheating is one of the main side effects of ecstasy. Another grew shaky after the second dose and was not given the third. After 2 weeks, the three other animals were killed and found to have lasting reductions in systems that process serotonin and, even more markedly, dopamine. These neurotransmitters were depleted, and neurons that use them showed damage to their axons, projections that send signals to other cells. The two-dose monkey, killed after 6 weeks, showed similar symptoms. The researchers repeated the regimen with five baboons and, even 8 weeks after exposure, recorded a "profound loss" of markers seen in healthy dopaminergic axons.

Ricaurte says that other studies might have missed such dopamine system damage because they spaced the doses farther apart; protracted MDMA exposure, in contrast, might make dopamine neurons more vulnerable to the drug's toxic effects. The researchers go on to speculate that damage to the dopamine system might be responsible for cognitive deficits, such as memory loss, seen in some MDMA users. They assert that one reason no one has associated MDMA



Rave. Emergency room personnel call the hyperthermic effect of ecstasy (*inset*) "Saturday night fever."

CREDITS: (TOP TO BOTTOM) RICH PEDRONCELLI/AP; LAWRENCE MANNING/CORBIS; ANDREW BROOKES/CORBIS

with parkinsonism might be because the disease does not manifest itself until 70% to 80% of brain dopamine has been depleted.

Andy Parrott, head of the Recreational Drugs Research Group at the University of East London, calls the findings "very worrying." He points out that some ecstasy takers—even "novice" users—have motor symptoms such as tremors and twitches, "which may be best explained in these dopaminergic terms," because dopamine-dependent neurons are one of the major lines of communication in the motor system.

Other researchers are continuing to withhold judgment about the perils of MDMA, pointing to methodological difficulties in this kind of research and evidence that the damage might be only temporary. Cognitive neuroscientist Jon Cole of the University of Liverpool, for example, is skeptical about the Parkinson's risk. So far, he says, "there is only a single case report of parkinsonism related to the use of ecstasy. The sheer number of ecstasy users indicates that there would be millions of these patients presenting for treatment." Nonetheless, he says the study might call for a major revision of the existing view of MDMA: "The entire human literature ... relies on the notion that MDMA is a selective serotonergic neurotoxin."

The Johns Hopkins finding is thus unlikely to put an end to the ongoing debate over MDMA. Criminalized in the United States in 1985, MDMA is still a subject of intense controversy, because some psychologists believe it can be a useful adjunct to psychotherapy—helping people open up emotionally, especially those suffering from posttraumatic stress disorder. Indeed, trials are ongoing in Israel and Spain, and the U.S. Food and Drug Administration approved a new one last November to be conducted in North Carolina. –CONSTANCE HOLDEN

U.S. SCIENCE POLICY

NSF Fights Changes in Oversight Bill

Two Senate committees have approved a bill supporting a 5-year doubling of the National Science Foundation's (NSF's) budget, one of the highest priorities of NSF Director Rita Colwell and lobbyists for the scientific community. But the legislation also contains some bitter pills—involving science and math education, major research equipment, and NSF's relation with its oversight board—that Colwell hopes to avoid swallowing.

Lobbyists see this month's votes, which set NSF policies but don't provide any money, as a sign of the growing strength of their doubling campaign. "It's symbolic, but at least it puts both panels on record in favor of doubling," says Samuel Rankin, head of the Coalition for National Science Funding. The reauthorization bill, S. 2817, is a variation on one (H.R. 4664) passed in June by the full House, and the two versions must now be reconciled. The NSF spending bill goes through a different set of committees, which will miss a 1 October deadline to complete their work.

HOW TO DOUBLE THE NSF BUDGET

Current budget is $4.8 billion

Year	House plan	Senate plan
2003	$5.5b	$5.5b
2004	$6.3b	$6.4b
2005	$7.3b	$7.4b
2006	–	$8.5b
2007	–	$9.8b

SOURCE: (TOP) H.R. 4664, S. 2817

Double or nothing? Congress has endorsed bills that would double NSF's budget in 5 years, but its spending panels have yet to weigh in.

At the same time, those lobbyists are quite unhappy with provisions that would merge a Department of Education program that gives states money to improve science and math education with a new NSF program that awards grants through a national competition to achieve the same end (*Science*, 11 January, p. 265). The hybrid, proposed by senators who felt that NSF was more likely to run a high-quality program involving university scientists, would allow NSF to continue its national competition for 3 years before converting to a block grant program in 2006.

The compromise leaves both sides unhappy. The lobbyists fear that local jurisdictions could be left out in the cold if NSF makes grants on a competitive basis. "Moving the program to NSF effectively reduces vital resources and programs at a time when local education agencies need them the most," a coalition of professional societies wrote to Senator Ron Wyden (D–OR), chair of the science subcommittee of the Senate Commerce, Science, and Transportation Committee, shortly before a vote last week by the full committee. And NSF doesn't like being tied to a predetermined formula. The use of block grants, Colwell wrote Wyden the day before the vote, "is inconsistent with the Foundation's exemplary merit review process and conflicts with competitive processes that promote excellence." House members are also unhappy with the Senate language, which had been drafted and approved a week earlier by another Senate panel with jurisdiction over NSF's education programs, and they hope to remove it before the bill moves forward in the Senate.

On another contentious issue, the Senate panels and the House have adopted identical language requiring NSF to rank the impor-

ScienceScope

Blue Laser Blues A Japanese engineer out to gain more respect—and cash—for Japanese inventors suffered a setback last week when the Tokyo District Court ruled against his attempt to reclaim patent rights to a groundbreaking discovery.

Shuji Nakamura was working for Nichia Corp. in 1997 when he developed a blue light–emitting diode and later a blue semiconductor laser (*Science*, 21 March 1997, p. 1734). The devices have extremely promising commercial applications, with current annual sales topping $400 million. Now a professor of materials science at the University of California, Santa Barbara, Nakamura sought to reclaim the rights to a key manufacturing process, for which the company paid him $170. He also asked for $16 million in compensation.

On 19 September the court sided with Nichia, noting that Nakamura had used the company's facilities and staff for the research. It delayed a decision on the compensation issue. Nakamura, who hoped his suit would boost the status of Japan's corporate researchers, plans to appeal once the ruling becomes final.

Britain Shifts Space Cash Imagine this: The U.S. government suddenly decides that scientists need a more direct hand in running space missions and moves NASA's space science budget to the National Science Foundation. Although an unlikely scenario in the United States, the British government has decided to do something similar.

Following a review of the British National Space Centre (BNSC), the government announced this week that the agency's science budget will now be managed by the Particle Physics and Astronomy Research Council (PPARC). And its Earth-observing research funding will go to the Natural Environment Research Council. Most of the money—about $78 million annually—will still go straight into the coffers of the European Space Agency, but the researchers will now have a bigger say in how it is allocated.

Researchers are divided over the shifts. "It's a good idea," says Paul Murdin of Cambridge University's Institute of Astronomy, a former director of science at BNSC. "There's nothing like owning a budget to make you really care about it." But Birmingham University's Mike Cruise, chair of PPARC's space science advisory committee, thinks it is "regrettable." Although BNSC still coordinates the government's overall space activities, he says, it will be further removed from the scientists who can help craft long-range strategy.