NATIONAL SCIENCE FOUNDATION

Report: All's Fair in NSF Major Awards

For every winner in the high-stakes competition for multimillion-dollar science awards, there are always losers—and sometimes charges of unfairness. As it has dipped its toes more and more into big science in the last decade, the National Science Foundation (NSF) has been at the receiving end of a few such charges, but a new report* suggests that any unfairness at the agency is more a matter of perception than reality.

The report, written by a panel formed by the National Academy of Sciences (NAS), concludes that NSF's procedures for deciding major awards are generally sound, although it chastises the agency for at times having inconsistent or unclear criteria. NSF "will be subject to less criticism from the community, Congress, and other sources if they more clearly spell out the rules of the game," notes University of Texas at Dallas president Robert Rutford, who chaired the NAS panel.

A charge that such rules were flouted in 1990 prompted the academy's critique. That year, the Massachusetts Institute of Technology (MIT) had submitted a proposal to NSF to create a National High Magnetic Field Laboratory. The agency, however, awarded the $60-million contract to a consortium led by Florida State University (FSU). The coup by the southern school outraged MIT, which already had a well-respected magnet lab in place and had outpointed the FSU bid in outside peer reviews. Complaints to Congress followed, and Congress soon called on NAS to examine the decision process behind NSF's major awards: those totaling more than $1.5 million a year or $6 million over 5 years.

But if the Massachusetts delegation was hoping the academy would come down heavily on NSF for the magnet lab decision, it was disappointed. The report studiously avoids reevaluating past decisions, and though it suggests some changes in the award process, overall it is supportive of NSF. "We're offering tweaking to a reasonably good system. We're not fixing a broken machine," says Lyle Schwartz, director of the Materials Science and Engineering Laboratory at the National Institute of Standards and Technology.

One tweak the panel does strongly recommend is to standardize a two-phase review process for evaluating proposals, rather than relying on the one-shot review often used now. The first phase would rank proposals solely on technical merit, while the second phase could address other criteria, such as personnel development or geographical distribution of awards. This would be an improvement, says the panel, over reviews in which all the criteria are evaluated together to produce a staff recommendation for the National Science Board (NSB), NSF's governing body, which must explicitly approve all major awards. To ensure that technical merit is the most important factor in the final decision, only those proposals achieving the highest scores in the first evaluation would be passed on for this second-phase review.

The NAS panel also expresses concern that the NSB is hard-pressed for time to perform its duties carefully. Some 30% of NSF's research budget now qualifies as major awards and is thus under the board's direct authority. "These guys are incredibly overworked," notes Stanford University physicist Douglas Osheroof. One quick fix suggested by the NAS panel is to boost the funding threshold for NSB review to $2 million a year or $8 million over 5 years. The panel also addressed the back end of the award process, recommending that the NSB deliver a public rationale for all of its major decisions, something that is not now required.

NSF has pledged to take a close look at the recommendations. "We all recognize the system isn't perfect and can use improvements," says Alan Gaines, NSF's liaison officer for the study. But no modifications will fully inure the agency from criticism, admit some authors of the NAS report. Says panel member Clarence Allen, a Caltech geologist, "There are always going to be winners and losers and unhappy people. That's inevitable."

–John Travis

* "Major Award Decision-Making at the National Science Foundation," NAS Press, 1-800-624-6242.

NICOTINE RESEARCH

Key Study Unveiled—11 Years Late

In 1989, a Canadian research team published a critical piece of research—the development of a simple animal model for studying nicotine's effect on the brain. At the time, the model was considered a breakthrough in the drive to understand how nicotine exerts its addictive effects. Last week, however, it was claimed that Philip Morris, maker of Marlboro, had completed similar research 6 years earlier but had blocked publication of its findings. Researchers contend that Philip Morris' scientific censorship significantly delayed work by other groups on the addictiveness of nicotine.

Those charges were aired on 31 March, when Representative Henry Waxman (D–CA) claimed at a press conference that Philip Morris had deliberately suppressed studies showing that rats will self-administer nicotine by pressing levers to inject it into their veins. According to experts on drug abuse, self-administration of a substance by an animal is one of the hallmarks of an addictive drug.

The tobacco industry has always maintained that nicotine is not addictive, but Waxman charged at the press conference that Philip Morris' own research demonstrated for the first time that "without being susceptible to advertisements or peer-pressure...rats were willing to go to great lengths to get nicotine" and, indeed, that the rats "seem to be addicted to nicotine." Such a finding supports charges by Food and Drug Administration (FDA) Commissioner David Kessler that tobacco companies may intend cigarettes to provide nicotine to maintain, or even trigger, an addiction. If that contention is proved true, the FDA would have authority to regulate—conceivably even ban—cigarette sales (*Science*, 18 March, p. 1555).

The basis for Waxman's charge is a manuscript that was accepted for publication in *Psychopharmacology* in 1983 and then withdrawn by Philip Morris, according to letters between the journal's editor and Victor DeNoble, the first author on the study. Waxman released the manuscript and the letters at the press conference. In a written response to Waxman's allegations, Philip Morris denied withholding the results of its nicotine research from the scientific community, noting that while DeNoble was employed by Philip Morris he published five other articles on nicotine-related research. In one instance, wrote Philip Morris, DeNoble was told not to publish until he had completed an internal manuscript review. A Medline search by *Science* turned up several articles by DeNoble on nicotine's effect on behavior in rats, but it identified no articles reporting nicotine self-administration in rats. On the advice of his lawyer, DeNoble, a psychologist who now works with mentally-retarded people in Delaware, declined to comment.

In their still unpublished paper, DeNoble, Paul Mele, and Francis Ryan, then of the Philip Morris Research Center in Richmond, Virginia, report that rats will press a lever as many as seven times to trigger an infusion of about 30 μg of nicotine per kilogram of body weight directly into their veins. DeNoble's group found that the dose was critical: The number of times the rats

pushed the lever fell if the nicotine levels were much higher or lower than 30 μg per kilogram of body weight.

The research doesn't just provide political support for efforts to regulate tobacco, however. According to William Corrigall of the Addiction Research Foundation in Toronto, it contains scientific information that would have speeded up research on nicotine if it had been published in 1983. At the time the Philip Morris study was conducted, researchers had shown that monkeys and dogs will self-administer nicotine, but they had had little luck in getting rats to do so—a necessity if they were to develop a suitable model in which to study the neural pathways through which nicotine exerts its addictive effects. Critics say publication of DeNoble's study would have given other researchers the animal model they were seeking. "DeNoble had the experience with [animal models of addiction] to know to start at low doses of nicotine and to work up gradually," says Jack Henningfield of the National Institute on Drug Abuse in Baltimore.

By 1989, however, Corrigall and Kathleen Coen, also of Toronto's Addiction Research Foundation, had independently arrived at the same conclusions as the DeNoble team. Corrigall and Coen found rats pushed the lever most often when they received 30 μg of nicotine per kilogram of body weight. "The compelling thing is that the [rats in the two studies] seem to respond best to the same dose of nicotine," says Corrigall. Corrigall speculates that at lower doses nicotine is not addictive, and at higher doses its aversive properties cancel out its addictive ones.

Corrigall's work, published in *Psychopharmacology*, "supercharged medical research on nicotine addiction," says Henningfield. Within a few years, the Corrigall team had used its rat model to show how nicotine activates a neural pathway, called the mesolimbic system, that creates intense cravings.

Corrigall cautions that the rat model is not a complete model of human cigarette smoking, which probably also depends on factors such as nicotine's ability to alleviate tension and to improve concentration. Nonetheless, he says, nicotine "is clearly addictive in people. People [like rats] will increase their workload to get nicotine. They will pay more for cigarettes. They will smoke outside in snow storms and rainstorms."

To determine whether the tobacco companies intend nicotine to have an addictive effect, Waxman has called a hearing on 14 April of the subcommittee on Health and the Environment, which he chairs. The CEOs of seven American cigarette manufacturers have been summoned to attend.

–Rachel Nowak

FORENSIC MEDICINE

SIDS Paper Triggers a Murder Charge

ATLANTA—Twenty-two years ago, Alfred Steinschneider made a splash in the medical community with a landmark paper detailing multiple cases of sudden infant death syndrome (SIDS) in a single family. The paper became one of the most widely cited papers in SIDS research, providing support for a theory that some cases of the disorder may result from an inborn abnormality characterized by prolonged sleep apnea, or loss of breath. Now, the paper is making news again: as exhibit A in a murder case.

On 23 March, prosecutors brought murder charges against Waneta E. Hoyt of Newark Valley, New York, the 47-year-old mother of the children whose deaths Steinschneider described in his paper. The publication, in the October 1972 issue of *Pediatrics*, triggered the murder investigation when it was brought to prosecutors' attention in connection with a completely different case in the late 1980s. If the murder charge is upheld, it would demolish Steinschneider's theory that this family's tragedy suggests a link between SIDS and severe apneic episodes caused by an abnormality present at birth—a theory that SIDS researchers say is no longer widely accepted among scientists but still has some support in the medical profession. And it would raise a troubling question: Could Steinschneider have prevented the deaths of two of the Hoyt children? Steinschneider, who is now president of the American SIDS Institute, an Atlanta-based organization, stands by the conclusions of his paper and vehemently denies that he could have done anything more to prevent the deaths.

Stands by his conclusions. Alfred Steinschneider.

Steinschneider was an assistant professor of pediatrics at the Upstate Medical Center in Syracuse, New York, when he published his paper describing the fate of two siblings identified as M.H. and N.H., plus three children from other families. Steinschneider still declines to name his former patients, but M.H. and N.H. have been identified by prosecutors as Molly and Noah Hoyt. Steinschneider notes in the paper that because three siblings of M.H. and N.H. had previously died as infants, he monitored them closely, repeatedly admitting them to the hospital for observation.

Here is how he described Molly's death, which occurred soon after she was discharged from the hospital: "At 8:15 a.m., M.H. awoke, was disconnected from the [apnea] alarm, bathed, and fed without difficulty.... Mrs H. placed her in the crib and left the room for 'a minute to get something.' When she returned, M.H. was apneic and cyantic [sic]. She was given mouth-to-mouth resuscitation without success."

Noah Hoyt, born about 1 year after Molly's death, also made repeated visits to the hospital. Each time he was sent home, Steinschneider wrote, the infant reportedly suffered loss of breath. Finally, the paper says, "At about 8 a.m. on the morning after discharge and while asleep, N.H. had an apneic and cyanotic episode which failed to respond to resuscitative efforts." Steinschneider's paper also chronicles apneic episodes among two siblings from another family and a third, unrelated child. Of the five infants, only the Hoyt children died.

These tragic events led Steinschneider to conclude that some SIDS-prone babies may be born with abnormalities characterized by apneic episodes. If so, some SIDS deaths may be prevented by checking for abnormal respiration and using apnea monitors for infants in families that have already had one SIDS death. The paper, says Janice Ophoven of the Children's Hospital in St. Paul, Minnesota, "really was a seminal article," which influenced treatment for children in SIDS-afflicted families.

Over the years, the paper's influence has waned, however. Other researchers have found little support for the idea that SIDS is caused by apnea or that it runs in families, says Marie Valdes-Dapena, professor emeritus of pathology and pediatrics at the University of Miami, although some hospitals still provide apnea monitors for infants whose siblings have died of SIDS. Researchers have proposed more than 100 possible causes for SIDS ranging from suffocation, which may be more likely to occur when an infant sleeps on its stomach, to food allergies, to a developmental abnormality. The murder charges against Waneta Hoyt may be the final blow to the apnea-SIDS theory.

Steinschneider's paper was first brought to the attention of New York prosecutors in 1986, when William J. Fitzpatrick—then an assistant prosecutor in Onondaga County—called Linda Norton, a forensic pathologist and former medical examiner for Dallas County, Texas, for help with a different case involving the death of several children in one family. Norton, who had read Steinschneider's description of the deaths of M.H. and N.H.,