NEUROSCIENCE QUARTERLY

SPRING 2003

"The new strategy of the animal rights activists is to de-emphasize federal agency regulation, bridge the human-nonhuman divide, use courts to shape social attitudes and be species-specific."

– Michael Socarras

IN THIS ISSUE

Latest Animal Rights Strategy: Animals as Persons

Defining animals as persons is the latest strategy of animal rights activists to interfere with research and other activities that rely on animals, a leading expert told a meeting held in Washington, DC. He suggested that only one approach will prove to be an effective response.

Michael Socarras

"The new strategy of the animal rights activists is to de-emphasize federal agency regulation, bridge the human-non-human divide, use courts to shape social attitudes and be species-specific," lawyer Michael Socarras told a gathering of the National Association for Biomedical Research (NABR).

NABR is the only national, nonprofit organization dedicated solely to advocating sound public policy that recognizes the vital role of humane animal use in biomedical research, higher education and product safety testing. The Society for Neuroscience is a NABR member.

Socarras said key activists are shifting to incremental steps and are already drawing support from prominent legal theorists like Harvard law professor Lawrence Tribe who argued for Al Gore against George W. Bush in the Supreme Court.

A partner in the firm Greenberg Traurig, LLP in Washington, DC, Socarras has represented NABR in several animal rights cases and has worked with researchers for more than 14 years. He spoke as a panelist in a discussion on legal rights for animals which could have long and short term implications for the way animals are viewed by society and how the trend might affect animal research.

Socarras cited the work of several legal theorists who support the animal-as-person philosophy. He quoted Gary Francione of Rutgers as saying, "When I say that animals have rights, what I mean by that is that animals have an interest in not being regarded as things, and that interest can't be taken away from them simply because it will benefit us."

Another argument notes that the public certainly thinks that bacon that one buys at the supermarket is property, but it doesn't really think that chimpanzees are property in the same way. "To get beyond humans in terms of beings with legal rights seen as persons would be such a huge historic breakthrough that it would inevitably have an effect on, perhaps incrementally, a range of other species," according to Peter Singer of Princeton, who is among those associated with the animal activist agenda.

Steven Wise, an attorney and author, maintains that the idea that humans are above nonhumans is similar to the idea current at one time that men were above women or that whites were above blacks, or masters were above slaves.

These views and those of others, Socarras says, contain a common thread of domination. He said they attempt to link activities such as domestic violence and the struggle for women's rights with animal abuse, and also link animal rights with the civil rights movement.

Continued on page 2

SOCIETY FOR NEUROSCIENCE

Continued from page 1...

The initial focus of the new strategy is on great apes. For example, the Great Ape Project International, founded in 1993, seeks "to include the nonhuman great apes within the community of equals by granting them the basic moral and legal protection that only human beings currently enjoy."

Socarras noted the increased focus on establishing a theoretical basis for trustees, next-friends or guardians to speak for animals in court modeled on the idea of having people appointed by courts to act on behalf of children and the incompetent. Several jurisdictions already have pet guardian laws, including Boulder, Colorado; San Francisco, West Hollywood and Berkeley in California; and the state of Rhode Island.

Animal activists view the US Department of Agriculture (USDA), the government agency responsible for enforcing the Animal Welfare Act (AWA), as understaffed, ineffective and uninterested. Under the new legal standing for animals, Socarras says animals, guardians or citizens will be able to sue research facilities, dealers and exhibitors, citing the AWA. He noted that 266 requests were made during 2001 to the USDA's Animal, Plant and Health Inspection Service for access to animal care inspection reports, most likely from people who distrust researchers and the USDA to care properly for animals.

Socarras warned that legal precedents exist in several areas. Corporations are declared to be persons with full constitutional rights by state law. Inanimate objects – such as ships, oil rigs or cash – can sue or be sued. Guardians can routinely act in court for children and incompetents. Socarras cited several cases in which courts ruled that persons could sue on behalf of animals and in which animals were labeled not "mere property."

> *"Animals never do anything morally right or wrong, because moral right and wrong are not in their world. Morality is an essential feature of human life, but has no place whatever in the lives of rats and chickens."*
>
> – Carol Cohen

In reviewing the possible ways to respond to this argument, Socarras says that the only effective route is to use philosophical and religious arguments for the primacy of the human person. These arguments are fundamentally philosophical, religious, legal and ethical rather than scientific, according to Socarras. He says that rights are not scientifically measurable or empirically provable. According to this view, human beings are unique because they make moral judgments and have a responsibility for stewardship over animals.

"Animals never do anything morally right or wrong, because moral right and wrong are not in their world. Morality is an essential feature of human life, but has no place whatever in the lives of rats and chickens," says Carol Cohen, a philosopher at the University of Michigan. Socarras went on to quote Pope John Paul II: "God entrusted animals to the stewardship of those whom he created in his own image. Medical and scientific experimentation on animals, if it remains within reasonable limits, is a morally acceptable practice since it contributes to caring for or saving human lives."

Socarras explained that legal personhood is not about cognition, ability to communicate or autonomy because our society has decided that even a severely disabled human is a person with full rights. Although activists say animals should have rights because even disabled people do, Socarras turned that around and said disabled people have rights because they are human. "Personhood is about being human," Socarras says.

He also mentioned some responses that could be less effective:

- Scientific. Debating scientific findings on species-specific cognition, communication and self-awareness accepts the premises of animal rights activists – that animals, indeed, are very much like humans in scientific terms. He notes that the tobacco industry made a huge mistake in courts by debating scientifically how addictive smoking is, instead of pointing out that society places responsibility on the person making the decision to smoke.

- Economics. This has been a basis for successful litigation and regulatory and legislative efforts by NABR under the AWA but additional arguments are needed. The fundamental question about what is a person is not likely to be resolved in economic terms.

- First Amendment. This argument says that research is its own justification and that the right to scientific inquiry is a right of free speech. But the right to scientific pursuits does not directly resolve the issue whether the research subjects are persons.

- Human Needs. Human beings have the right to biomedical advances. But people at risk of illness in the future might not have standing to sue for medical progress today. Researchers need to find new ways of articulating that they speak for people in need.

In summary, Socarras says that in this new phase, rights for animals as persons before the law could be pursued in some US courts. Activists are educating receptive judges before the first case is brought and top legal talent is in agreement with animal activists' message. "A purely defensive response is not legally advisable," he says, suggesting that a more proactive approach may be required. ■

Society To Visit New Orleans in November

New Orleans will host Neuroscience 2003, the 33rd annual meeting of the Society for Neuroscience. From November 8 to 12, scientists from around the world will present and discuss the latest developments in neuroscience research.

Although the meeting continues to be the world's largest forum devoted to the exchange of new information on the brain and nervous system, some major changes will be instituted in 2003. For example, this year will be the first time that the meeting adopts a Saturday to Wednesday schedule. The Program Committee and SfN Council endorsed the change in an effort to allow attendees to participate more fully in the meeting. In the past, many attendees departed the meeting before the Thursday sessions.

Short Courses and the Neurobiology of Disease Workshop will be held on Friday, November 7. In previous years, these events were held on Saturday, and slide and poster sessions, special lectures and symposia were held Sunday to Thursday. Slide and poster sessions, special lectures and symposia will begin Saturday, November 8 at 1:00 pm and conclude Wednesday, November 12 at 5:00 pm. The Public Lecture will remain scheduled on Saturday evening at 8:00 pm and will be given by Nora Volkow, newly named director of the National Institute on Drug Abuse. Additional information pertaining to the Neuroscience 2003 schedule of events is available on the SfN Web site.

A new addition to the program in 2003 will be a special lecture on neuroethics. The first speaker in the series, funded by the Dana Alliance for Brain Initiatives, will be Donald Kennedy, a neurobiologist, president emeritus of Stanford University and editor of *Science* magazine. The rationale for the series is to stimulate thought and discussion on issues becoming increasingly relevant to neuroscience. These include questions about the implications of what we learn about the brain for defining behavior, medical ethics and social policy. This emerging set of issues comprises a field of neuroethics in which scientists and ethicist are beginning to reflect on the work of neuroscience in areas such as moral vision, decision-making, conduct and policies.

Because of its size, navigation of the meeting sometimes presents challenges. In 2003, the Society will continue to make it easier to get around the meeting by placing themed sessions near each other whenever possible, thereby reducing distance and time spent getting to and from sessions.

As with Neuroscience 2002, the program for the New Orleans meeting will be printed in seven books. The first book will contain an overview of the meeting, hotel and travel information, general information and maps of the convention center and co-headquarter hotels. The next five books will contain a daily program–at–a–glance and the session listings for each day. The final book will contain the complete author index. As with the Neuroscience 2002 program, all SfN members will receive a meeting CD–ROM Itinerary Planner.

Plans are under way for enhancing the career development resources available for attendees at Neuroscience 2003. The career development services arranged with FASEB will be improved and more professional development workshops will be offered.

As the number of members of the Society has increased during the past year, the number of abstracts submitted also is expected to remain high. In 2002, 13,532 abstracts were submitted.

Abstracts can be submitted electronically or on paper. Abstract submission opened on April 19 and the receipt deadline for electronic submission is Monday, May 19, at 5:00 pm, your local time; the fee is $50. The receipt deadline for paper submission is Monday, May 5; the paper submission fee is $70. The receipt deadline for replacement abstracts is Wednesday, May 28. The deadline for withdrawing abstracts is Monday, June 2.

Please visit www.sfn.org/am2003 for more information about Neuroscience 2003. See you in New Orleans! ■

Dates and Deadlines

Abstracts

Submissions for Abstracts – paper deadline .....May 5
electronic deadline by 5:00 pm (submitter's local time) .....May 19
Receipt of Replacement Abstracts .....May 28
Withdrawal of Abstracts.....June 2

Other

Nominations deadline for chapter graduate student travel awards, postdoctoral fellow Travel Awards and minority travel fellowships.....June 2
Exhibit applications receipt deadline.....June 16

Registration Fees

	ADVANCE Opens at noon on July 21 for members and noon on July 28 for nonmembers. Closed October 1.	ON-SITE ONLINE Opens October 8.	ON-SITE Opens November 2.
Member	$205	$240	$250
Student Member	$65	$75	$80
Nonmember	$365	$400	$410
Student Nonmember	$80	$90	$100
Guest	$20	$25	$30
CME Accreditation	$40	$40	$40

Message from the President

Toward a Neurobiology of Mental Disorders: Scientific and Societal Implications

The neurobiology of mental disorders is at a crossroads. And the neuroscience community can play a pivotal role in the next few years to transform this fascinating field scientifically and to communicate this transformation to other biomedical specialties and to the public.

Studying mental illness from a neurobiological perspective is fraught with challenges. Although many neuroscientists enter the field to understand how the brain sustains complex functions like perception, emotion and cognition, they rapidly come to the conclusion that we lack the conceptual means to frame many of these questions especially if they come close to the idea of "consciousness." For example, how does one capture the concept of a "mood" scientifically and search for its molecular and neural underpinnings?

However, without having solved such philosophical questions, neuroscience has done remarkably well in terms of defining many key features of complex behaviors and brain disorders and beginning to understand their underlying neural mechanisms. Animal models, even if they do not fully mimic human behavior, can capture critical elements of higher order processes. As discussed by National Institute of Mental Health Director Thomas Insel in this issue, sometimes we overestimate the degree of complexity underlying a given behavior. But even for truly complex functions, advances in scientific tools now available have begun to fuel exciting progress.

More importantly, studying the neurobiology of mental illness is not a luxury that neuroscientists can engage in after they have handled more accessible problems. The need is urgent. I remember vividly a statement from a bipolar patient who said: "I am at the end of my rope. I have tried everything. I am counting on you."

THE BURDEN OF MENTAL DISORDERS

"The burdens of mental illnesses . . . have been seriously underestimated by traditional approaches that take account only of deaths and not disability," notes *The Global Burden of Disease*, a report conducted by the World Bank, World Health Organization and Harvard University which was released in 1996. "While psychiatric conditions are responsible for little more than one percent of deaths, they account for almost 11 percent of disease burden worldwide."

The study developed a single measure to allow comparison of the burden of disease across many different conditions by including both death and disability. With this measure, major depression was found to be the leading cause of disability worldwide among persons age five and older.

In the United States, an estimated 22 percent of the population ages 18 and older, roughly 44 million people, suffer from a diagnosable mental disorder in a given year. In developed countries, four of the ten leading causes of disability are mental disorders – major depression, bipolar disorder, schizophrenia and obsessive-compulsive disorder. The annual economic toll in the United States of mental illness is conservatively estimated at $79 billion for lost productivity and $99 billion for care, treatment and rehabilitation. If we were to add the cost of addictive disorders, the number would be staggering indeed.

Huda Akil,
SfN President

But what cannot be seen with any statistic is the debilitating effect that mental illness has on an individual's self-perception. It strikes at the heart of self-concept, is seen as shameful and, along with continuing social stigma, causes two-thirds of those with mental illnesses to avoid seeking treatment. Improved scientific knowledge can help alleviate both the social stigma and the actual medical problems.

THE SCIENTIFIC PATH AHEAD

Severe psychiatric diseases, including mood disorders and schizophrenia, are complex genetic disorders in that they appear to be due to the interplay of multiple vulnerability genes with factors including developmental events and psychosocial environmental stressors. Moreover, it is likely that the genes contributing to these illnesses are heterogeneous and vary across families who express the illness. Thus, while it has long been evident that mental disorders have a significant genetic basis, it has been difficult to pinpoint the responsible genes. The hope is that novel genetic approaches (e.g., SNP and haplotype mapping) might begin to reveal the genetic bases of these disorders. But even if vulnerability genes are identified, the distance between genes and behavior is too vast to allow a direct causal linkage between genes and disease, and it will be necessary to understand the intervening neural events.

The term "neural phenotype" can be used to indicate the neural correlates of a disease state, which is likely the outcome of interplay between genetic endowment and developmental and environmental events. In living humans, neural phenotype can be deduced from a pattern of neural activity detected with neuroimaging tools. Alternatively, in postmortem tissue, it can be described by the pattern of gene and protein expression in the brain that represents the hallmark of the disease. The May issue of the Society's publication *Brain Briefings* discusses how microarray technology might play a role in revealing the neural phenotype associated with particular brain disorders.

The glimpses of neural phenotypes obtained from human studies represent only the starting place for understanding the processes associated with mental disorders. Whether one starts with a genetic variation, a profile of gene expression, a pattern

of brain activity from brain imaging or a combination of these elements, one needs to put these observations in a stringent neurobiological context, and this can only be accomplished via basic research.

Molecular and system neuroscience will define the function of the implicated genes, their expression in neural circuits, their impact on neuronal activity and the effect of their modulation on specific behavior. Tools ranging from tissue culture to transgenic animals will be required to understand the implications of the observations and generate novel hypotheses that can be tested in both animals and humans. This then, requires a true partnership between clinicians and basic scientists, and among psychiatrists, geneticists, neurobiologists, psychologists, pharmacologist and others who can bring their expertise to bear on these exciting but challenging questions.*

Ultimately, the goal is to understand these illnesses sufficiently well to devise better treatments. Even more challenging is the notion that some of these disorders can be prevented. Twin studies show that vulnerability genes do not automatically lead to brain disorders. Clinical evidence suggests that the process of mental illness is itself very damaging, leading to neurodegeneration and deterioration. Preventing the first episode might spell the difference between a normal and a devastated life. Can improved neurobiological understanding help in promoting prevention?

MENTAL HEALTH ADVOCACY

Advocating for mental health research and treatment research on the neurobiology of mental illness will allow us to relate sophisticated neural markers to genetic endowment and to the manifestations of a given mental illness. This can lead to a molecularly and genetically based classification of mental disorders that will have implications for specific classes of treatments. It will also be helpful in "medicalizing" mental disorders and removing the prejudice toward them, not only by the general public, but sometimes even by members of the medical profession.

In *The Surgeon General's Report on Mental Health* issued in 1999, David Satcher stated ". . .The neuroscience of mental health – a term that encompasses studies extending from molecular events to psychological, behavioral, and societal phenomena – has emerged as one of the most exciting areas of scientific inquiry and human inquiry. . . . Indeed, one of the foremost contributions of contemporary mental health research is the extent to which it has mended the destructive split between 'mental' and 'physical' health." While we have indeed come a long way, there is a great deal to be accomplished in this arena.

One tangible area where this destructive split remains is in health insurance. SfN members currently have the opportunity to support legislation providing health insurance coverage for mental health equal to that of traditional physical diseases. This can go a long way towards increasing public understanding of mental disorders as illnesses, not just bad behavior. In late February, I wrote to members of Congress asking them to support the Paul Wellstone Mental Health Parity Act which applies to employers with 50 or more workers and prohibits imposing higher out-of pocket-expenses on patients seeking mental health care than if they sought treatment for physical ailments. Passage of this bill would be a major step toward removing social stigmas and encouraging patients to seek treatment.

> *"Studying the neurobiology of mental illness is not a luxury that neuroscientists can engage in after they have handled more accessible problems."*
>
> – Huda Akil, SfN President

A clear opportunity for enhancing public understanding resides in the Society's educational efforts. I have written about our educational mission in the previous *Neuroscience Quarterly*. I would underscore here that young people are particularly interested in the workings of their minds, particularly concerned about their feelings of anxiety, fear, stress and depression and have few tools to handle them. Giving them a conceptual framework to deal with such issues that is both correct and nonjudgmental will go a long way not only toward educating them, but also helping them.

Finally, social policy is laced with ethical issues that neuroscientists are just beginning to discuss. The implications of neurobiology in medical ethics and social policy are evolving into a new field called neuroethics, and a new lecture on neuroethics, funded by the Dana Alliance for Brain Initiatives, will debut at Neuroscience 2003. Mental illness will need to figure prominently in our neuroethics discussion. Because prescribed drugs could permanently alter an individual's neural circuits and possibly impact on personality, who decides the threshold for using drugs, the appropriateness of the drug to be used and the timing in an individual's life? How should the legal system and society evaluate unethical or criminal behavior as we evolve our concepts of neural and genetic bases of behavior? As we discover genes that predict behavioral traits, how do we use the information wisely and humanely, helping without overreaching our ability to predict?

The challenges confronting us are enormous, both from the scientific and societal standpoints. Many of the questions will not be answered for a long time to come, if ever. But what we can be sure of is that it is far better for humanity to confront the devastating problems of mental illness armed with knowledge, knowledge that we as neuroscientists can provide.

* NOTE: Some of these research areas will be addressed by the speakers participating in the Neuroscience 2003 presidential symposium and presidential lectures. Please check www.sfn.org/lectures for details. For a perspective on several exciting areas of research, see the Q&A with NIMH Director Thomas Insel, page 6. ■

COMMENTS

An Interview with Thomas Insel, Director of the National Institute of Mental Health


Thomas Insel

NQ: **In what new directions will NIMH go and what do you think will have the greatest impact for the public and neuroscientists?**

Insel: First of all, let me say how excited I am to be the new director of the National Institute of Mental Health. We have a key mission to understand mental and behavioral disorders and are in the midst of one of the most productive periods of discovery ever. Understanding diseases of the mind such as anxiety, depression, schizophrenia, autism, etc., is at last beginning to happen largely due to the successes of the field of neuroscience and the Human Genome Project. Over the last five years, we have initiated many projects that will come to fruition during the next several years.

I will be focusing on completing the molecular biology and circuitry of the brain that generates thought and behavior and how abnormalities create mental and behavioral disorders. Thus, the brain basis of emotion, cognition, attention, social behavior and motivation will be driving themes in the neurosciences. We have just completed a strategic plan for mood disorders and will be rolling out initiatives. This rapidly developing research is beginning to provide key insights into the causes of mental illness that have long eluded us.

A word of caution, however. Budget projections indicate that the period of rapid growth is ending for NIH. Preventing "whiplash" will call for careful planning and a focus on mission-oriented science.

NQ: **What are the greatest opportunities for neuroscience research in the study of normal behavior and mental disorders?**

Insel: The major areas are those where we can translate the findings from basic research into the clinical arena, so we can have an impact on people with mental disorders. We need to have the genes, we need to have the circuits and we need to have reasonably good animal models of the disorders. In the area of fear, of emotional learning, we're beginning to get a handle on the genes, the circuits and the models.

In particular, recent studies on the neurobiology of extinction suggest this is a rich area. Most of us have the ability to recover from a traumatic event, but those who don't develop what we call post-traumatic stress disorder (PTSD). The interesting thing about PTSD is that we can model it very well in certain situations with other species. We've learned from these animal models that there is a circuit in PTSD that involves the amygdala and the prefrontal cortex. We've identified pieces of that circuit and we're beginning to learn that there are specific genes that may be quite important for that process. This is an example in which we may be able to make the transition from the basic science lab to the clinic fairly quickly.

In other areas we have part of the story but not the whole thing. For example, in depression and in schizophrenia we're getting some interesting candidate genes, but we still don't have the circuits worked out and we don't have the validity in our animal models.

NQ: **What do you consider to be the major challenges in mental health research over the next decade?**

Insel: We're looking at tremendous advances in molecular, cellular and systems neuroscience. But the challenge is trying to translate our basic research findings to clinical applications. We also have to ensure that the public understands the importance of basic science. Often, the general public assumes that new drugs or new treatments develop almost from whole cloth without realizing that there's often a decade or more of basic science that feeds into new discoveries that have clinical significance. It's important for us and a challenge for us to make sure the public understands the importance of investing in basic science as a pathway to improving therapeutics.

NQ: **What are the keys to uncovering the secrets of complex behaviors?**

Insel: That assumes we know what complex behaviors are. Are we smart enough to know what's complex and what's not complex? I'm reminded of the work of Richard Scheller when he was interested in egg-laying in Aplysia (a shell-less marine snail). He discovered about 20 years ago that what seemed to be an ostensibly complex behavior appeared to be coordinated by a single gene.

Everything we think of as behavior is going to have environmental and genetic components but in this case, the genetic components were surprisingly coherent. My own lab had a similar insight when looking at social memory, which one might think is the most complex form of memory; yet we found that knocking out a single gene basically eradicates social memory without having any effect on any other form of memory. So, the things we think are complex may turn out to have a relatively well-conserved or simple genetic basis. Conversely, I suspect that behaviors that seem simple, like the startle response, may turn out to be remarkably complicated at a genetic level.

NQ: **Some of your research has linked neurochemicals with complex social behavior in voles. What do you see as the broader implications of this kind of research and how will that affect NIMH efforts?**

Insel: My personal interest for many years has been in the realm of what we call social neuroscience. To me it's intriguing because some aspects of social behavior appear to have been carefully sculpted by the evolution of neural systems. If you're thinking about olfactory communication in rodents, audiovocal communication in birds or face recognition in primates, these kinds of behaviors seem to have a very curious and carefully selected neural basis. Deficits in social behavior are integral to several mental disorders, such as schizophrenia and autism. I

am hopeful that comparative studies in social neuroscience may yield insights into the pathophysiology of these mental disorders, although we have a long way to go in bridging basic and clinical studies.

NQ: **Where do you see the most progress being made in the near future in terms of mental health research?**

Insel: I think there are technical developments that are promising and important. One I find really fascinating is the developing science of genomics. We have the mouse genome now in hand and this is incredibly important. It will allow us to get a handle on how variation in sequence leads to variation in function, providing links between genotype and phenotype. Genomics also will have its limits. Understanding epigenetic mechanisms – that is, changes in transcription not related to sequence variation – may prove even more important for mental disorders.

The other technical development that's exciting involves the revolution in imaging and the opportunities to do high field strength imaging in humans and small animals. This could contribute greatly to our understanding of the physiological meaning of some of the imaging signals we've been seeing. Imaging now yields not only an assay of regional blood flow and metabolic activity, but also ***in vivo*** neurochemistry, connectivity, and ultimately development and plasticity.

NQ: **For which disorders do you feel scientists are closer to developing successful treatments?**

Insel: We already have some pretty effective treatments. For most of the major mental disorders – schizophrenia, depression, anxiety disorders – we have fairly effective treatments, although they are not cures. The frustrating thing is that even though we know how to treat many of these disorders, there are still many, many people with these illnesses who are not getting treatment. There's a gap between what we know how to do and what actually happens in the real world. So, one of the challenges for NIMH and for society in general is how do we make sure those treatments are actually being delivered. Part of it – a very important part – involves reducing the stigma of mental disease. It's a long-term problem and I'm hopeful we can make a dent in it.

If you look at the disorders for which we don't have biomedical treatments, the most obvious one is autism. It's of considerable public interest right now, and there's recent evidence that it's more prevalent than previously thought. We have some powerful psychosocial treatments such as behavior modeling but we don't have a medication that is effective for the core symptoms of autism.

We also have a problem with treating refractory depression. This continues to be a serious challenge. Depression represents the second greatest burden of illness for global health outcomes in the 15-to-44 year age bracket. Although most people respond quite nicely to treatments for serious depression, the treatments take as much as six to eight weeks to have an effect. Also, about 30 percent of patients with depression don't respond to the first or second medication given. So, a significant number of patients with depression need a better treatment. We have not developed a new class of antidepressants in the past 20 years.

We've made great progress in the last decade with the development of atypical antipsychotics for treating schizophrenia, but many of these drugs have adverse effects. The greatest source of functional deficit in schizophrenia is from the cognitive problems that come with the disorder and yet all of our treatments really focus on other parts of the syndrome. Thus, there is a tremendous opportunity to develop agents that target the cognitive deficits in the hope that we can facilitate recovery in people with schizophrenia.

"There's a gap between what we know how to do and what actually happens in the real world. So, one of the challenges for NIMH and for society in general is how do we make sure those treatments are actually being delivered."

– Thomas Insel

NQ: **What effect will deciphering the human genome have on understanding behavioral science and mental disorders?**

Insel: Sidney Brenner mentioned an analogy a few months ago. He said that having the human genome sequenced is like having the white pages of the phone book; it's really helpful if you know who you're looking for, but if you don't know who you're looking for (which is the case we're in), you need the yellow pages. So I think for us the challenge is going to be in developing the yellow pages. Once we have genes categorized into functional families we'll have a much better sense of how the human genome operates. That's about 25 years worth of work but that I think it is going to be the real challenge for us. But then, in the last five years there has been clear progress – real progress – in identifying vulnerability genes for schizophrenia.

NQ: **How important are early experience, maternal care, and genetics on the development of depression and other disorders that occur later in life?**

Insel: For the last 10 years or so, NIMH researchers have focused heavily on trying to pull out the genes for these disorders, which have very complex genetics. We all understand that what we've been looking for are vulnerability genes. So, unlike with Mendelian inheritance where you're looking at a single gene that has a very large effect, here we're looking at many genes, each of which has a very weak effect. In some combinatorial way they contribute to a vulnerability to develop the syndrome. What that means to me is that in these complex disorders, the environment is going to have a very major role. This doesn't necessarily mean maternal care – it could be something that's happening very early in development. The challenge now is to understand how environmental factors alter gene expression, sometimes with enduring consequences.

Continued on page 15

Brain Awareness Week 2003

Neuroscience education and public awareness activities worldwide helped promote the eighth annual Brain Awareness Week (BAW) March 10 to 16, 2003. BAW, sponsored by the Society for Neuroscience and the Dana Alliance for Brain Initiatives, featured many events, including the Center for Behavioral Neuroscience's "Brains Rule! Neuroscience Expedition" in Atlanta. A "reverse science fair" where students critiqued scientists' experiments and "SciTrek: Georgia's Technology Adventure," a fair that allowed participants to touch human brains and see their own EEG, were among the highlights.

In Washington, DC, SfN President Huda Akil and Paul Aravich of Eastern Virginia Medical School visited Malcolm X Elementary School to talk to the students about why they became scientists, how the brain works and how drugs affect the brain. A rousing and inspiring speech from Malcolm X principal Vaughn Kimbrough began the day. "The brain is a powerful instrument that you own that can move toward any dream that you want," he told an assembly of first through sixth graders, "You've got to keep your brain clean. No drugs, alcohol or nicotine. The brain will take you where you want to go."

Aravich brought human brain specimens with him and passed them around for each student to hold. "The brain is one of the most marvelous things in the universe. It's also very delicate. What can damage it? Drugs . . . This is an amazing thing between your ears; you've got to take care of it," Aravich said. Students responded enthusiastically to both Avarich and the specimens. Donnell Brooks, 11, said, "He knows a lot about brains! He rocks!" Michelle Thomas, 9, said of the brain, "It was squishy" and Shakera Williams, 9, added, "And slippery!"

Akil described how drugs, cocaine in particular, affect the brain, explaining, "Drugs are hijacking what the brain usually controls for itself." In describing the genetics behind addiction she said, "Not everybody is the same. Some get

Huda Akil with student at Malcolm X Elementary School, Washington, DC.

Right: Proclamation from Mayor Anthony A. Williams

Malcolm X students examine brain specimens.

Students respond to questions.

addicted more easily. Family history is important. If you have an uncle who is addicted, this may mean that you need an extra effort to avoid it."

Students at Malcolm X spent the week prior to the SfN visit learning about the brain and creating poster projects detailing their new knowledge. Shanelle White and Michelle Thomas' fourth grade class did a project on the brain stem. They explained, "The brain stem helps you breathe, think, and [your] heart beat." Kierra Furguson learned from her BAW experience that, "I can become a scientist." Eleven year old Donnell Brooks summed up the week for everyone when he exclaimed, "I had me some fun!"

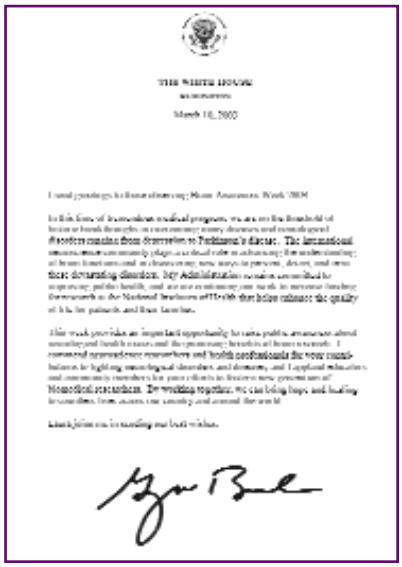
Contestants from all over North America and Canada, fresh from their victory at one of 24 local competitions, competed in the fifth annual International Brain Bee on March 15, 2003 at the University of Maryland in Baltimore. Answering questions on such topics as neuroanatomy, brain imaging, emotions, sensations, consciousness and brain disorders, contestants competed to win $6,000 in scholarship money and a trip for two to the annual meeting of the Society for Neuroscience in New Orleans this November. Saroj Kunnakkat from Lynbrook High School in New York became the 2003 International Brain Bee champion, outlasting Joseph Shivers of Salem High School in Ohio. Following 34 preliminary rounds, they competed in 11 final rounds of challenging questions in which both participants showed their impressive knowledge of the human brain.

In the online survey of SfN members conducted during the summer of 2002, significant support was voiced for expanding general public awareness and education about neuroscience among students and teachers through programs like BAW. This year's events were a step toward achieving that objective. If you are interested in participating in next year's BAW, March 15 to 21, 2004, be sure to visit the BAW Campaign Meeting/Poster Session at the annual meeting in New Orleans this November, or visit www.sfn.org/baw for more information. ■

Paul Aravich showing a student the parts of the brain.

Paul Aravich with class at Malcolm X.

Saroj Kunnakkat, International Brain Bee Winner.



Letter from President George W. Bush observing Brain Awareness Week 2003.

NIH Doubling Completed – Administration Proposes Small Increase in FY2004

After passing 12 continuing resolutions, Congress finally passed the fiscal year 2003 omnibus appropriations bill (H.J. Res. 2) on February 12, 2003. The bill includes $27.2 billion for the National Institutes of Health (NIH), an increase of $3.8 billion from FY2002. Within this amount, the president submitted a request to Congress this past January that would permit the agency to reallocate $136 million of FY2003 funds in order to fund fully the second phase of the John Edward Porter Neuroscience Center. This was great news for NIH. Detracting from the doubling efforts, however, was an across–the–board reduction of .65 percent in virtually all discretionary funding to offset additional funds added through floor amendments.

BUDGET TAPS AND TRANSFERS

Transfers to other agencies within HHS for program evaluation taps will total about $507 million in FY2003. These program taps, a percentage of funding from each institute that is "tapped" and goes to the Agency for Healthcare Research and Quality to evaluate programs at NIH, have long been a part of the NIH funding process.

NIH's budget will be further reduced this year by a $100 million transfer to the International Global Fund to Fight AIDS, Tuberculosis and Malaria. These funds were included in the budget of NIAID. A transfer adding to the NIH budget in the amount of $74 million comes from the Environmental Protection Agency for research at NIH's National Institute of Environmental Health Sciences.

FY 2004 BUDGET PROPOSAL

Tempering the relatively good news of a substantial increase in the NIH budget is the administration's request for FY2004. The president is proposing an increase of two percent ($549 million) for NIH, bringing the total funding in FY2004 to $27.9 billion. While a two percent increase is far below the average increase of 13 percent over the last five years, the administration argues that actual NIH research investment will increase by $1.9 billion, or 7.5 percent when bioterrorism funding is excluded from the FY2003 budget allocation. Nearly half the $3.6 billion increase in FY2003, $1.4 billion, is dedicated to preventing bioterrorism, including biosafety labs, NIH campus improvements, and purchasing anthrax vaccines. These one-time costs will not be funded through NIH in FY2004.

The president's proposed funding increases for nearly all of the individual institutes range from a low of 3.5 percent to a high of 4.4 percent. Two exceptions are a 6.9 percent increase for the National Institute of Diabetes & Digestive & Kidney Disease (NIDDK) and an 8.9 percent increase for the National Institute of Allergy & Infectious Diseases (NIAID). NIDDK would see larger budget increases under the president's plan due largely to designated funding for type 1 diabetes research that was required by a separate congressional authorization, as well as funding for the International Global Fund to Fight AIDS, Tuberculosis and Malaria. NIAID's increase is due largely to proposed increases in funding for biodefense research. Please see the accompanying table for the institutes' percent change from the FY2003 funding and the FY2004 request.

Competitive, peer-reviewed, and investigator-initiated research project grants (RPGs) would represent 55 percent of the total NIH budget under the administration's budget proposal. The budget would increase funding for RPGs by 6.3 percent for a total of $15.2 billion. The president's budget document states that this is 1,211 more grants than the number expected to funded in FY2003 and would allow funding of 39,520 RPGs. NIH estimates that it will fund 10,509 competing RPGs under the president's proposal, an increase of 344 over last year. Nearly all of these will be fully funded in the first year they are awarded. Nearly 27,000 non-competing RPGs would be funded in FY2004, 763 more than last year.

OUTLOOK FOR NIH

The administration and several members of Congress have long had concerns regarding NIH's ability to handle the large infusion of funds created with the doubling. The National Academies Institute of Medicine (IoM) committee was charged by Congress, to use some of the NIH funds to conduct a study of the current structure of NIH and to make recommendations to Congress. The committee's final report is expected in September 2003.

Medical researchers and patient advocacy groups, already worried about the impact of the extended continuing resolutions, are now concerned that an abrupt drop in budget increases could delay progress in developing new medical therapies. Sen. Arlen Specter (R-PA) who chairs the Senate Appropriations Subcommittee on Labor, HHS and Education and ranking member Sen. Tom Harkin (D-IA) led the first effort to double NIH's budget. They have promised to introduce a bill to triple the agency's budget, including the doubling years, by FY2008. Sen. Ted Kennedy (D-MA), the ranking member on the Health, Education, Labor, and Pensions Committee, has said that under the president's budget, the congressional goal to double the rate at which clinical trials are completed will be unattainable.

Though the president's proposed budget is generally used as a template to base spending allocations, it is the Appropriations Committee that has the actual power to allocate funds. Because the Labor-HHS-Education bill that funds NIH is historically very contentious, no legislation was reported out before the end of the fiscal year. That, coupled with the absence of a congressional budget and Republicans controlling both the House and the Senate, allowed the president to wield more power in the appropriations process than is typical.

Donald C. Poppke, acting associate director for budget at the NIH, has said that it is important to look at the overall budget plan taking several years into account. According to Poppke, one year with a minimal increase can be accommodated, but "if it's two percent, two percent, two percent, [for the next three years] that could be troublesome."

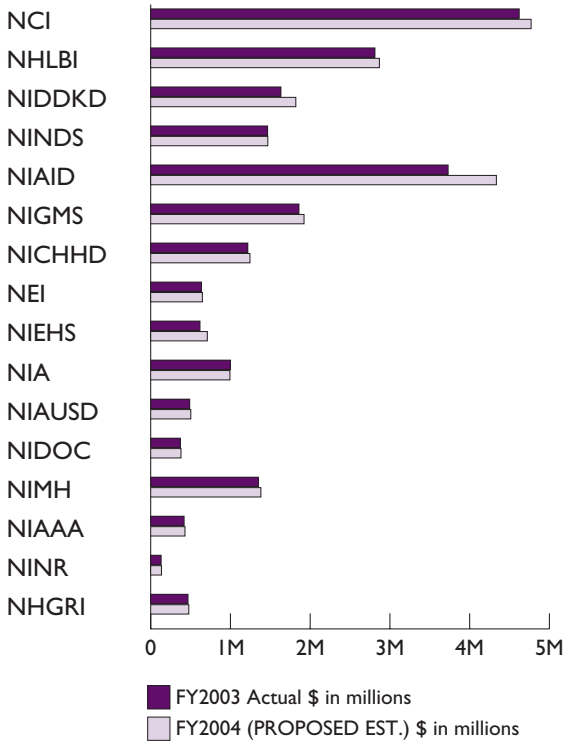
NIH APPROPRIATIONS FOR FY2003 AND FY2004 ESTIMATES

Chart shows FY2003 budget allocations and Bush Administration proposed FY2004 budget, in millions of dollars.

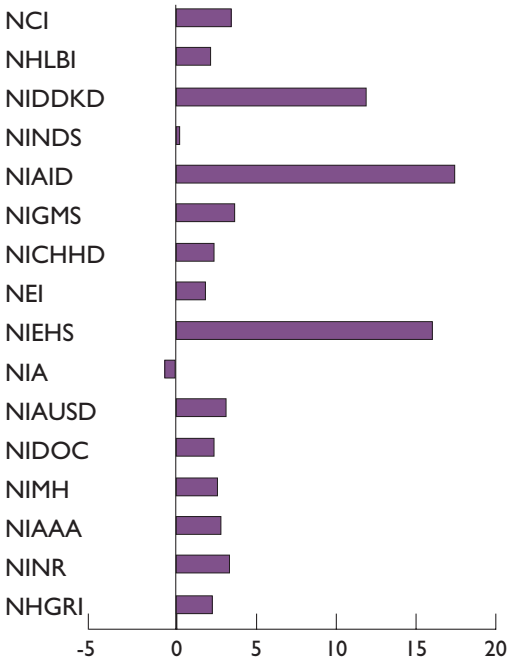
INSTITUTE NAME	FY2003 Actual $ in millions	FY2004 (Proposed Est.) $ in millions	% Change from FY2003 to FY2004
National Cancer Institute	4,622	4,771	3.2%
National Heart, Lung, and Blood Institute	2,812	2,868	2.0%
National Institute of Diabetes and Digestive and Kidney Diseases	1,633	1,820	11.5%
National Institute of Neurological Disorders and Stroke	1,466	1,469	0.2%
National Institute of Allergy and Infectious Diseases*	3,730	4,335	16.2%
National Institute of General Medical Sciences	1,859	1,923	3.4%
National Institute of Child Health and Human Development	1,218	1,245	2.2%
National Eye Institute	637	648	1.7%
National Institute of Environmental Health Sciences	618	710	14.9%
National Institute on Aging	1,000	994	-0.6%
National Institute of Arthritis and Musculoskeletal and Skin Diseases	489	503	2.9%
National Institute on Deafness and Other Communication Disorders	372	380	2.2%
National Institute of Mental Health	1,350	1,382	2.4%
National Institute on Alcohol Abuse and Alcoholism	419	430	2.6%
National Institute of Nursing Research	131	135	3.1%
National Human Genome Research Institute	468	478	2.1%

*$100 million will be made available to the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria. Up to $375 million will be available for enhancing the nation's capability to do research on biological and other agents.

Comparison in millions of dollars, FY2003 & FY2004



Percentage Change from FY2003 to FY2004



NINDS Supports Neural Channelopathy Research

By Meena Hiremath, Randall R. Stewart and Yuan Liu
National Institute of Neurological Disorders and Stroke, NIH

The National Institute of Neurological Disorders and Stroke encourages research on nervous system diseases caused by channelopathies – abnormalities of ion channels, the most basic elements of neuronal electrical function. The proper structure, expression, localization and regulation of channel proteins are essential for their normal activity.

The most commonly identified causes of channelopathies are mutations in genes encoding ion channel proteins that disrupt channel function. Another important cause involves autoimmune attack. In addition, acquired channelopathies may occur during nerve injury or during treatment with therapeutic drugs that block ion channels (such as the cardiac HERG potassium channel) as a side effect.

Channelopathies are the abnormalities of ion channels, the most basic elements of neuronal electrical function.

Channelopathies are broadly studied in heart, kidney and skeletal muscle, but they are seriously understudied in the central nervous system. Recent advances in molecular biology now show that many disorders are associated with ion channel dysfunction, including epilepsy, migraine, ataxia and many rare diseases.

To encourage greater interest in neural channelopathy research, National Institute of Neurological Disorders and Stroke (NINDS) sponsored a workshop in Gaithersburg, MD on November 20 to 21, 2002. Participants included basic channel researchers, molecular and human geneticists, clinical neurologists and representatives from the pharmaceutical industry. They discussed the scientific challenges and technical barriers confronting neural channelopathy research. Among them are the genetics of disease from gene mutations to transcriptional variants; functional identification of channel anomalies by the use of new technologies and bioinformatics; and approaches to targeting and treating channelopathies, from small molecules to gene therapy.

The first session, chaired by Alfred George, Jr. of Vanderbilt University, focused on the genetic complexity of neural channelopathies. This complexity only partially arises from the vast pool of genes expressed in a multitude of different brain areas. Other factors that contribute to gene expression include modifications to newly synthesized ion channel RNA transcripts such as alternative splicing – the generation of different RNA transcripts from the same gene, and RNA editing – the alteration of specific RNA molecules which could result in formation of channels with novel properties. Protein trafficking affects where and when channels are expressed and anomalies in this process can result in channelopathies. As channels and receptors are often dynamically expressed on the surface, the subcellular distribution of the channel is another important factor to consider.

The second session, chaired by Henry Lester of Caltech, outlined new approaches and technologies that are ready to be applied in channelopathy research. Comparative genomics is leading to the identification of new mammalian ion channels. An example is the identification of channels in mammals by associating them to channels of similar ancestry in the nematode, *C. elegans*. One can also identify novel channels by searching for conserved structures of a gene in a sequence database, and then use micro- and macroarrays to determine relative expression levels of channel subunits. Proteomic approaches are becoming a popular means to identify the entire protein repertoire in a particular cell or tissue. An example of this approach is the use of mass spectrometry to analyze proteins and peptides. Such approaches can also be used to determine the phosphorylation states of proteins, (i.e., which amino acids of the protein have been modified by adding phosphate groups) and to analyze protein-protein interactions. Another newly available technology that can expedite the analysis of channel function is planar patch-clamp recording for high-throughput electrophysiology, which allows one to record channel activity from hundreds of cells simultaneously. Conditional protein expression technology (knockouts and/or knockins) can be used to overcome death during embryonic development, to control where and when proteins are expressed in otherwise normal animals, or both.

The final session, chaired by Jeffrey Noebels of Baylor College of Medicine, addressed novel imaging approaches, including directed and random insertions of fluorescent proteins, screening proteins in affected tissues and fluorescence resonance energy transfer assays. This session also focused on the development of new therapeutic strategies for central nervous system channelopathy, including the search to identify compounds that alter channel function, such as use-dependent or small molecule modulators. It is also possible to use transgenic techniques to express modified ion channels to improve neural function. Targeted gene transfer using viral vectors is yet another way to modify channels in neural tissue.

Workshop attendees made several recommendations to NINDS to facilitate neural channelopathy research. These included providing increased infrastructure and technical staff support; assisting with the development and validation of disease-relevant animal models; encouraging collaborations among basic researchers, clinicians and industry; supporting multidisciplinary approaches; and assisting with the determination of single nucleotide polymorphisms in ion channel sequences in control and patient populations.

The most commonly identified causes of channelopathies are mutations in genes encoding ion channel proteins that disrupt channel function. Acquired channelopathies may occur during nerve injury or during treatment with therapeutic drugs that block ion channels as a side effect.

Although NINDS will consider these recommendations, the best progress is often made through investigator- and community-initiated efforts. Since the estimated cost of getting new drugs to market is about $800 million per drug for large pharmaceutical companies, therapies for small and medium markets, which include the diseases caused by altered channels, are often not pursued. In some instances, smaller biotech companies are able to develop and market drugs for a small patient pool. To foster the development of treatments for channelopathies, NINDS encourages collaborations between basic scientists and clinicians so that disease mechanism and treatment can be matched to the patient.

FOR MORE INFORMATION:

Multidisciplinary epilepsy grants:
http://grants.nih.gov/grants/guide/pa-files/PAR-01-111.html.

Translational research programs:
http://grants.nih.gov/grants/guide/pa-files/PAR-02-139.html and http://grants.nih.gov/grants/guide/pa-files/PAR-02-138.html.

Pre-clinical therapy development:
http://grants.nih.gov/grants/guide/pa-files/PAR-02-140.html.

Center core grant program:
http://grants.nih.gov/grants/guide/pa-files/PAR-02-059.html.

On this workshop and other NINDS activities:
http://www.ninds.nih.gov/news_and_events/proceedings.htm.

SfN's First Annual Progress Report

For the first time in its 32 years of existence, the Society for Neuroscience has produced an annual progress report. So much happened during 2002 that a report on significant activities and their implications for the Society's future seemed necessary.

The Society's 2002 annual progress report, titled *Pathways to the Future*, includes a message from SfN President Huda Akil and sections on the Society's mission, membership survey, bylaws changes, new strategic plan, Neuroscience 2002, *The Journal of Neuroscience* and the year in review, which describes many of the activities organized by SfN committees and a section on finance.

The report is included in the mailing of the spring issue of *Neuroscience Quarterly* and is available on the Society's Web site at www.sfn.org.

The annual progress report will provide a regular opportunity to bring SfN members and others who care about neuroscience up to date on important Society activities. It will also explain SfN's mission, its work and its plans for the future to the public, government agencies, advocacy groups, funding organizations and other strategic partners.

The annual report takes a careful look back at a year in which we learned much about our members and their needs. It also looks at the development of the Society's first strategic plan that is helping to mark the pathways to a future where new advances in understanding the nervous system and its functions can be more effectively shared with colleagues and disseminated to the public.

HIGHLIGHTS OF THE REPORT INCLUDE:

- Developing a Strategic Plan. During the summer and fall of 2002, the SfN Council developed the organization's first-ever comprehensive strategic plan. The plan's strategic initiatives for 2003-04 are structured around four elements: scientific research, professional development, public education and science advocacy. Major initiatives of each section are described in the report.

- Conducting a Membership Survey. Nearly 20 percent of the membership responded to the survey last June. Among its many major findings were that the annual meeting was praised for its great breadth and depth across the field of neuroscience. The survey results reinforced the importance the membership gives to the range of neuroscience themes represented at the meeting and the need for the event to become more manageable for attendees. Society members clearly communicated their interest in the area of professional development and career support for scientists from SfN.

- Revising the Society's bylaws. The bylaws were changed to deal only with the major elements SfN's governance. Any details that might change with time – such as the creation of a new committee, administrative changes in membership procedures, the timing of providing election information – were delegated to separate resolutions.

- 2002 Annual Meeting in Orlando. The report reviews attendance, major lectures and symposia, exhibits, professional development and public education workshops, the animal panel, social issues roundtable, public advocacy event, awards, program changes and press coverage.

- *The Journal of Neuroscience*. The annual report reviews how *The Journal* was used by subscribers and others worldwide, institutional subscription numbers, the shift to online access, increase in manuscript submissions, new features and redesign of both the online and print editions.

- Year in Review. Many Society activities that continue throughout the year are described in the report. These include the increase in membership, SfN chapter events, Brain Awareness Week, the International Brain Bee, the Capitol Hill reception, professional development programs, the Nobel Prize in Medicine or Physiology being awarded to SfN member H. Robert Horvitz, programs supporting the responsible use of animals in research and the Society's many science advocacy initiatives such as legislative alerts and letters to Congress.

- Financial Highlights. The report reviews how the Society has been relatively successful in weathering the overall uncertainty affecting much of the not-for-profit sector and the rest of the global economy. The Society remains financially strong, with a surplus of revenues over expenditures in 2002. Attention has been given to strengthening internal financial controls and systems. The Society has continued to make necessary changes and improvements to ensure that it follows current best practices for nonprofit financial management. Included in the report are an opinion letter and the audited financial statements of the Society's auditors PricewaterhouseCoopers for the year ended December 31, 2002. ■

Insel, continued from page 7...

I think this whole field of epigenetics is just emerging as important in neuroscience and in the study of mental disorders. It has to do with how environmental factors even in the early stages of development (in utero) alter the pattern of gene expression and ultimately can have heritable effects on the genome. There's a great deal to learn in this area.

NQ: **In addition to imaging technologies, what technologies hold the most hope for overcoming mental disorders?**

Insel: I think the opportunity to do studies in simple organisms still will be helpful, especially the idea of looking at identified neurons using GFP (green fluorescent protein) constructs. Perhaps even more important will be our ability to look at how parts of neurons communicate and how they change in response to experience. This gives us the chance to look at how neurons change in real time – an extraordinary advance that will help us to better understand how the brain works and how it develops. It's still imaging, but imaging at a subcellular level and being able to look at how dendrites change, how spines form and recede in response to environmental input is an extraordinary advance.

In many areas we have made the shift to plurality. We're able to record from multiple regions simultaneously, which offers us a much better systems look at brain activity. With cDNA microarrays, we can look at 10,000 mRNAs at a time and that will give us a much more educated understanding of the biochemical basis of neural function. The emerging field of proteomics, the integration of knowledge that encompasses the analysis of complete complements of proteins, also holds great promise. This includes not only the identification and quantification of proteins, but also determining their localizations, modifications, interactions, activities and functions. Given that most of our research has focused on less than one percent of the genome (about 300 genes and their products), it's a safe bet that the important factors for mental disorders will come from the genes and proteins that have yet to be discovered.

NQ: **How do you propose that NIMH partner with organizations like the Society for Neuroscience to urge continued funding for neuroscience research and other science advocacy efforts?**

Insel: Obviously the NIMH can't advocate for itself. The best we can do is work with the Society for Neuroscience and other professional organizations to support the best science and to educate the public about the need for research into both basic science and clinical therapeutics.

Prior to becoming NIMH director, Insel was director of the Yerkes Regional Primate Research Center, where he built one of the nation's leading HIV vaccine research programs, and professor of psychiatry at Emory University School of Medicine. At Emory he also directed the Center for Behavioral Neuroscience. ■

SfN Election Process Goes Electronic

The polls are now open for the 2003 SfN Election. All Regular and Emeritus members are encouraged to cast your votes for President-Elect and Treasurer-Elect.

President-Elect candidates:
Moses V. Chao, PhD
Anne B. Young, MD, PhD

Treasurer-Elect candidates:
William T. Greenough, PhD
Nicholas C. Spitzer, PhD

As a result of the approved Bylaws revision, the election will be held electronically. To cast your vote, go to the following Web site: https://www.gosbs.com/sfn2003.

Please be on the look-out for an e-mail from Survey & Ballot Systems, Inc. (SBS), the online election company handling the election. The e-mail will contain the Web site address as well as pertinent login information.

SBS will be handling the entire election process. If you have any problems or questions, please be sure to contact them at sfn@gosbs.com or at 800-766-4561.

NEUROSCIENCE QUARTERLY
SPRING 2003

Published quarterly by the Society for Neuroscience

Circulation: 32,000

SOCIETY FOR NEUROSCIENCE
11 Dupont Circle, NW
Suite 500
Washington, DC 20036
info@sfn.org

www.sfn.org

SOCIETY FOR NEUROSCIENCE
11 Dupont Circle, NW
Suite 500
Washington, DC 20036

Nonprofit Org.
US Postage
PAID
Washington, DC
Permit No. 4929

See you in

New Orleans!

Neuroscience 2003

November 8–12, 2003

www.sfn.org