National Institute of Neurological Disorders and Stroke

Strategic Priorities and Principles

June 2010

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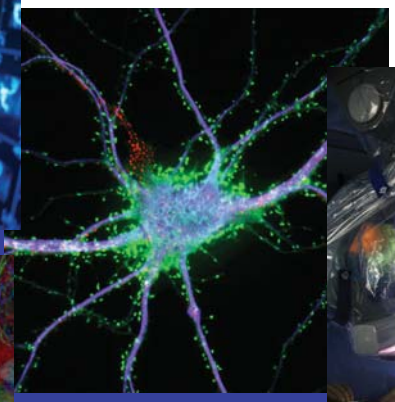
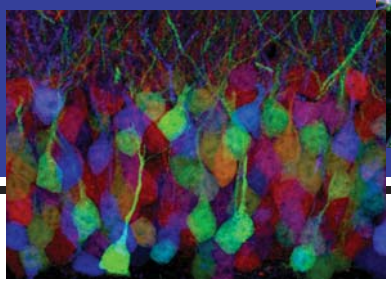
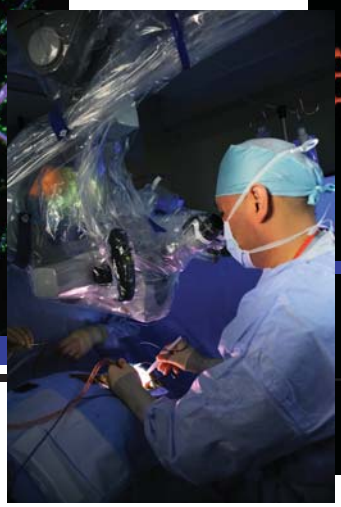
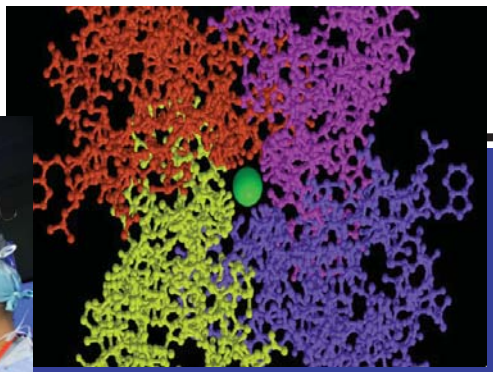








Director's Message and Introduction

NINDS Director Story Landis, Ph.D.

In the decade since the NINDS released its "Neuroscience in the New Millennium" strategic plan, there has been substantial progress toward our mission—to reduce the burden of neurological diseases through research. Brain imaging and discoveries in genetics have revolutionized how many neurological conditions are diagnosed. Surgical interventions, such as deep brain stimulation, have proven remarkably effective for many people with essential tremor and Parkinson's disease and are showing promise for several other disorders. New drugs are available for multiple sclerosis, epilepsy, chronic pain, and other diseases, and advances in prevention have contributed to a continuing decline in age-adjusted death rates from stroke. Innovative brain-computer interfaces and prosthetic devices offer exciting opportunities to restore neurological and motor functions lost after injury or disease. Furthermore, insights into the development of the nervous system, brain plasticity, molecular alterations that cause disease, and the role of non-neuronal cells in the brain are transforming how we think about the brain and approaches to treating maladies.

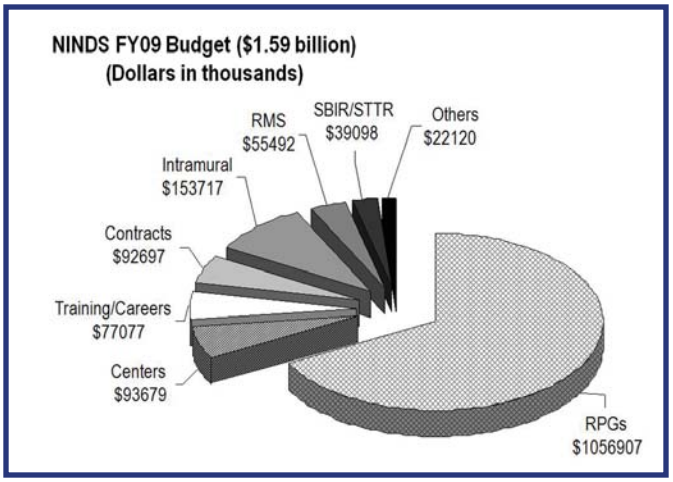
Over the next decade, our challenge will be to translate the discoveries about the brain into improvements in health and to push the frontiers of basic research yet further. To develop strategies to meet this challenge, the NINDS completed a planning effort that began with a "blue sky" look toward a future vision for neuroscience research and neurology. Planning then focused on practical strategies for improving NINDS effectiveness across basic, translational, and clinical research and the spectrum of neurological diseases within the NINDS mission. Toward that end, the NINDS assembled expert advisory panels who were provided extensive access to information about NINDS programs and charged with recommending specific actions for NINDS to take. Because the panels recognized that science can advance rapidly and in unexpected ways, they emphasized how the NINDS should set priorities in order to facilitate and help direct new discoveries, rather than recommending specific research topics the Institute should support. However, the panels also highlighted key scientific opportunities for progress that would yield benefits across many neurological disorders. The Institute also consulted the National Advisory Neurological Disorders and Stroke (NANDS) Council during the planning process and sought input from the research and patient advocacy communities and the broader public. NINDS gratefully acknowledges the contributions of all of these sources as we now present our new strategic plan, which will guide the Institute over the next five to ten years.

Although the NINDS strategic planning process preceded the current administration, many planning recommendations are remarkably consistent with the priorities of the new administration and the NIH Director. The emphasis of the planning panels' guidance and of the planning process itself on data driven program evaluation and management action, for example, is aligned with administration priorities for science management. Other recommendations correspond directly with NIH-wide goals on translational research and on reinvigorating the research community. NINDS has already begun to implement recommendations that can and should be addressed quickly. We are also attending to issues that the panels advised the Institute to explore in more detail through further data analysis, expert meetings, and other avenues. We will provide periodic updates on our implementation of this strategic plan in the coming years.

About NINDS

The National Institute of Neurological Disorders and Stroke (NINDS) is one of 27 Institutes and Centers that comprise the National Institutes of Health (NIH), within the Department of Health and Human Services (DHHS). The mission of the NINDS is to reduce the burden of neurological disorders through research. Hundreds of disorders, both common and rare, affect the nervous system. Together, these diseases afflict people of all ages, cause an enormous burden in lost life, disability, and suffering, and cost billions of dollars each year in medical expenses and reduced productivity.

In FY 2009, Congress appropriated $1.59 billion to the NINDS. The NINDS Division of Extramural Research supports neuroscience research at academic institutions, medical centers, research institutes, and small businesses throughout the U.S. The NINDS awards research grants to individual laboratories and teams, provides research resources for the neuroscience community, supports scientific workshops, funds training and career development, and delivers health



information to the public. Approximately 9% of the budget is allocated to the NINDS Intramural Research Program on the NIH campus in Bethesda, Maryland.

NINDS Goals

To accomplish its mission, the NINDS must address two fundamental goals:

- *Understand how the normal brain and nervous system develop and work, and what goes wrong in disease and injury, and*
- *Translate basic and clinical discoveries into better ways to prevent, treat, and promote recovery from neurological disorders.*

NINDS and the Future

The "Blue Sky" look at the future explored how new tools, technologies, and conceptual approaches can be brought to bear on advancing the NINDS mission in the future. More important than the specifics was the recognition of general themes that will change the context in which NINDS will operate. Challenges and opportunities from within and beyond science will affect how the NINDS carries out its mission. Blue sky discussions cannot predict the future, but do alert NINDS to be open to new opportunities, whether they arise from scientific breakthroughs or societal change.

Perhaps the most predictable change ahead is that many neurological disorders will become more frequent as the U.S. population ages, increasing the urgency of the NINDS mission. Changes in national health care delivery will have consequences for research. Electronic medical records and new payment structures, for example, could enhance clinical research participation or, alternatively, present new obstacles. The need for better information about the comparative effectiveness of therapies will increase as more interventions become available. Studies of gene, environment, and lifestyle contributions to common diseases are essential to the development of an evidence-based focus on preventing neurological disease and sustaining optimal brain function throughout life.

In addition to the NINDS, other government agencies, the pharmaceutical industry, the biotechnology sector, and non-governmental organizations all contribute to research that addresses neurological disorders. As the scope and capabilities of other research organizations change, the NINDS should adapt, fostering appropriate and productive relationships with all of these organizations to catalyze progress. Likewise, as the NIH itself changes and science reveals new intersections of interest among its parts, the NINDS should coordinate and cooperate within the NIH while attending to the Institute's unique mission.

Increased access to information has raised the public's expectations for transparency and accountability from the NINDS. New information and communications technologies may also enhance sharing and collaboration among scientists, physicians, and the disease community. However, finding and integrating what is reliable and useful within the torrent of information challenges both researchers and the public. How the NINDS gathers information for its own uses and the Institute's role in helping researchers and the public navigate the information stream are both likely to change in the future.

Recent scientific advances give an inkling of transformative changes that lie ahead. Advances in stem cell biology and brain plasticity open new prospects for repairing the brain and expediting therapy development. The discovery of gene and protein defects responsible for hundreds of disorders is leading to understanding of disease mechanisms, better research tools, and rational targets for drug development. Scientists are moving from the "parts list" to understanding of how the systems work and what goes wrong. Recent experiments in animals, for example, give surprising encouragement that at least some developmental neurological disorders may be reversible. Similarly, researchers are using new tools to map the brain cell circuits that determine how we learn, think, remember, and react to our environment. The decreased costs of gene sequencing, improvements in brain imaging, emerging technologies for telemedicine and remote monitoring, and surrogate markers that reduce the time and cost for therapy development are among the other game changing developments that seem just down the road.

In fifteen years...

What will the neuroscience research landscape look like?

What challenges and opportunities can we expect?

Scientific opportunities will always exceed the resources available to pursue them. NINDS responsibility to be a good steward of the public resources is heightened in economically trying times. As the NINDS sets priorities, the Institute must recognize that future progress depends on engaging a diverse and talented scientific workforce. To recruit and sustain the next generation of researchers, the NINDS must ensure that research is not just intellectually rewarding and socially useful, but also a viable career.

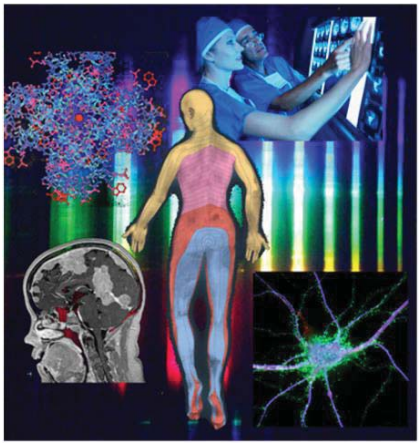
Key Principles

Against this backdrop, the planning process (see *Appendix*) identified the following overarching principles for the NINDS:

- Invest across the full spectrum of basic, translational, and clinical research
- Promote basic, translational, and clinical research according to their distinct needs
- Establish a data-driven process to identify unmet scientific opportunities and public health needs within and across neurological diseases
- Support research resources and technical advances that catalyze new discoveries
- Communicate and collaborate with the public and with others involved in biomedical research
- Train a robust and diverse neuroscience research workforce
- Adopt a culture of evaluation and continuous improvement across all NINDS programs

Invest across the full spectrum of basic, translational, and clinical research

The NINDS mission requires a balance of basic, translational, and clinical research. Physicians and scientists in academia and industry agree that basic research is essential for long-term progress against neurological diseases. Basic research seeks to understand how the nervous system develops and works and what goes wrong in disease. The private sector supports little basic neuroscience research because the return on investment in any specific line of research is unpredictable, even results that constitute major scientific advances may not yield marketable intellectual property, and the time between a basic finding and a practical application can be decades long. As a result, the NIH supports most basic medical research in the U.S. Although each NIH Institute and Center has a well-defined mission with respect to disease, several NIH components support complementary programs of basic neuroscience research that advance the missions of all. The NINDS has the largest neuroscience research budget of any NIH Institute or Center and so plays a crucial role in sustaining basic neuroscience research.



The NINDS, with the largest neuroscience research budget of any NIH Institute or Center, invests across the full spectrum of basic, translational, and clinical research.

Similar to the essential NINDS role in basic research, the Institute has a responsibility to support translational and clinical research that the private sector will not undertake. Translational research brings new therapeutic and diagnostic strategies through preclinical testing in cells and animals to readiness for clinical testing in people. Clinical research includes clinical trials to test the safety and effectiveness of new therapies, epidemiological investigations, and studies of disease and the normal nervous system in people. Rare diseases with small markets, bold therapeutic strategies that carry a high risk of failure or require long time horizons, new uses for existing drugs, epidemiological studies of risk factors, studies of disease mechanisms in people, and comparison of the effectiveness of available prevention strategies and treatments are among the many translational and clinical opportunities that the NINDS, rather than industry, is most likely to move forward.

Finally, even when clinical trials demonstrate that new interventions are effective, the findings may not be put into practice as they should. For example, more than a decade ago an NINDS funded clinical trial demonstrated that the clot busting drug tPA can improve the outcome from stroke when properly administered, leading to the first Food and Drug Administration (FDA) approved emergency therapy for stroke. However, tPA is used for only a small percentage of stroke patients who might benefit. As suggested by the disease and the clinical advisory planning panels, the NINDS has begun to explore opportunities for research on understanding and addressing barriers to the dissemination and implementation of research findings about disease prevention and treatment. A scientific workshop in the fall of 2009 brought together experts in implementation research and comparative effectiveness research from academia, the private sector, other government agencies, and NIH Institutes to inform the NINDS about opportunities that fall within the Institute's mission.

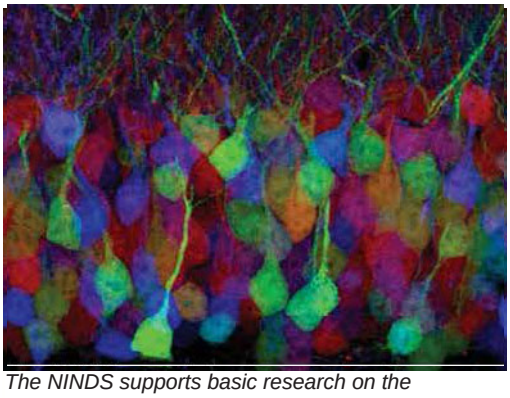
NINDS must recognize that a natural tension arises from the need to support the full spectrum of basic, translational, and clinical research with finite resources. As the NINDS undertakes initiatives and programs to meet changing opportunities, the Institute must monitor the distribution of basic, translational, and clinical research and maintain a balance that maximizes the Institute's impact on public health. In response to recommendations from the planning process, the NINDS has established an internal working group to track the Institute's investments across the spectrum of research and to explore the potential impact of new policies and initiatives on portfolio balance.

Promote basic, translational, and clinical research according to their distinct needs

Basic, translational, and clinical research pose different challenges and require different management and support strategies.

Basic research

For reasons noted above, the NIH has a key role in supporting basic research to understand how the nervous system develops and operates, and what goes wrong in disease. Of all areas of research, basic research most benefits from the unfettered freedom of the research community to respond to scientific opportunity. Thus, investigator-initiated, peer-reviewed research is the foundation of the NINDS basic research program.



The NINDS supports basic research on the nervous system, such as the work pictured here: a visualization of the mouse brainstem developed through "Brainbow," a genetic technique which labels individual neurons in different colors. (Credit: J. Livet and J.W. Lichtman, Harvard University.)

NINDS basic research is approximately equally divided between research on the normal development and working of the nervous system and research related to disease mechanisms. The cluster organization of the NINDS extramural program reflects the range of NINDS research. The program clusters focus on: ion channels, synapses, and neural circuits, which are the fundamental elements of the nervous system; the control of the environment of nerve cells by supporting cells; neurodegeneration, including the shared mechanisms of nerve cell death that contribute to many diseases; the role of genes in the normal and diseased nervous system; nervous system repair and plasticity, including stem cells, regeneration, and neural prostheses; and systems and cognitive neuroscience, which includes sensation, perception, movement, learning, memory, attention, thinking, and emotion. Maintaining this breadth of basic research on both the normal and disease nervous system is essential to the Institute's mission.

Translational Research

The NINDS has long pursued translational research opportunities that are not likely to be targeted by others. For more than 30 years, the Anticonvulsant Screening Program http://www.ninds.nih.gov/research/asp/index.htm has successfully catalyzed the development of epilepsy drugs, the Neural Interfaces Program https://www.ninds.nih.gov/Current-Research/Focus-Tools-Topics/Bioengineering/Neural-Interfaces has pioneered devices to restore lost nervous system functions, and investigator-initiated grant projects have led directly to industry development of Food and Drug Administration (FDA)-approved therapies.

In 2003, the NINDS established a broad program to better exploit the rapidly emerging translational research opportunities across all neurological disorders. This Cooperative Program in Translational Research supports academic and small business investigator-initiated preclinical therapy development. The program uses milestone-driven funding and peer review expertise and criteria tailored to therapy development, rather than to discovery research. The Institute has also piloted innovative approaches to therapy development targeted to particular diseases.
The Spinal Muscular Atrophy (SMA) Project, for example, developed and is implementing a drug development plan via a "virtual pharma" strategy that engages the resources needed via contracts and collaborations.

Translational programs require a different management strategy than basic research. Unlike basic research, in which the endpoint is unpredictable and the process is exploratory, translational research is product-driven, with prescribed steps. These steps include meeting standards set by the FDA and may involve industry partners. As for basic research, peer review is essential to ensure scientific quality, but review criteria must recognize the different requirements of preclinical therapy development. In supporting translational research, the NINDS must allow translational investigators the flexibility to pursue novel ideas, while ensuring that projects stay on track to develop a testable therapy. The nature of translational research is that, despite the best efforts, the probability of success is low and many projects fail. Milestone-based funding allows the NINDS to invest in translational research projects with the understanding that the institute will terminate projects early if they are no longer making headway, and shift funding to more promising opportunities.

The Neurotherapeutics Grand Challenge, a collaboration led by NINDS together with 15 other NIH Institutes and Centers, supports the development of new small molecule drugs that will transform the treatment of nervous system diseases.

In accord with recommendations of the planning process, the NINDS created a new Office of Translational Research to take a more active and better coordinated approach to managing translational research. The Institute has recruited an Associate Director for Translational Research with extensive drug development experience to lead this office and to serve as a liaison among the academic research community, industry, the FDA, and clinicians. To assist researchers who are new to translational research, the NINDS should provide guidance about the therapy development process through

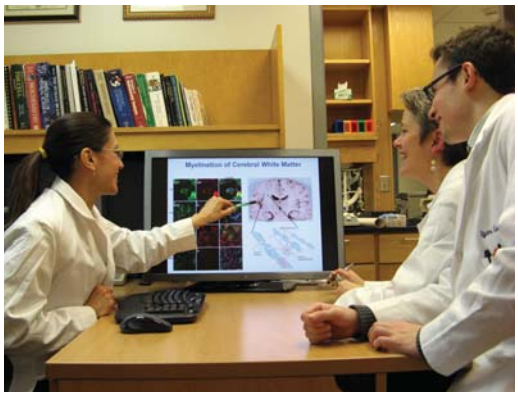
outreach and educational activities. In determining whether to establish new translational programs, the NINDS will institute a transparent, systematic process to identify the most suitable diseases and approach.

In keeping with planning panel advice, the NINDS is exploring new ways to engage small businesses in developing and commercializing diagnostics and therapeutics, which will include better use of the Congressionally mandated Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs https://www.ninds.nih.gov/Funding/Small-Business-Grants. In June 2009, the institute convened an expert panel to advise on how to make better use of the SBIR and STTR programs. Based on that advice, the Institute is moving the management of these programs to the Office of Translational Research and taking steps to speed review and funding, enhance outreach, better track outcomes of the investment, and otherwise improve administration of these programs.

Among its activities in 2011, the Office of Translational research is leading the Neurotherapeutics Grand Challenge http://neuroscienceblueprint.nih.gov/bpdrugs/index.htm in collaboration with 15 other NIH Institutes and Centers that work together through the NIH Blueprint for Neuroscience. The goal of this ambitious program is to support the development of new small molecule drugs that will transform the treatment of neurological, psychiatric, or other nervous system diseases or conditions.

Clinical Research

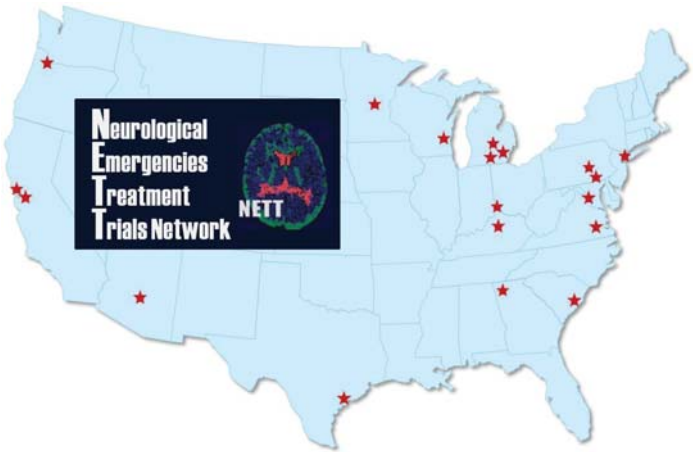
The NINDS supports an extensive program of investigator-initiated clinical research, including more than 1000 grants that involve human subjects. The majority of NINDS-funded clinical studies are observational, including brain imaging investigations and large epidemiological studies that assess risk factors for stroke and other diseases, with special attention to health disparities. In 2007, the NINDS also supported more than 150 clinical trials, of which 28 were large multi-center trials designed to test the safety and efficacy of an intervention. The impact of major NINDS clinical trials on the public health has been substantial. According to one published, peer-reviewed estimate, the payback of this program alone far exceeds the investment in all NINDS research [The Lancet 367:1319-27, 2006 http://www.ncbi.nlm.nih.gov/pubmed/16631910].



The NINDS supports an extensive program of investigator-initiated clinical research, including more than 1000 grants that involve human subjects. (Credit: Tara DeSilva.)

Among specific clinical programs, the Institute has developed clinical trials networks, including the Neurological Emergency Treatment Trials Network (NETT) https://www.nett.umich.edu/, which focuses on neurological emergencies; the NIH Exploratory Trials in Parkinson's Disease (NET-PD) https://parkinsontrial.ninds.nih.gov/index.htm, which expedites testing of drugs to slow the course of Parkinson's disease; and the Specialized Programs of Translational Research in Acute Stroke (SPOTRIAS) which is developing new approaches to early diagnosis and treatment of acute stroke patients. The NINDS also supports early stage clinical trials and undertakes efforts to improve clinical trials through the development of quality of life outcomes measures, common data elements, and other activities.

The management of clinical research, especially large clinical trials, presents unique challenges. The problems inherent in recruitment and retention of a representative population of study participants, as well as regulatory issues, can incur delays that add to the already large expense. The NINDS established an Office of Clinical Research and recruited an Associate Director for Clinical Research who will identify and implement strategies to reduce these barriers and ensure that the NINDS is investing in clinical research with the greatest potential to reduce the burden of neurological disease and improve public health. The Associate Director will work with the NIH to address issues in clinical research and its regulation that go beyond the NINDS. In accord with recommendations of the planning panel, the Office of Clinical Research is already taking steps to foster trials with high impact on disease and institute priority, and to support their successful completion. These include streamlining the clinical trials application process, promoting innovation in clinical trials methodology, identifying means to improve patient recruitment and retention, enhancing efficiency in trial implementation, supporting training opportunities for new clinical researchers, fostering communication and partnerships among stakeholders (including patients,



A map of sites participating in the Neurological Emergencies Treatment Trials Network (NETT), one of several NINDS-supported clinical research programs.

researchers and industry), and providing clinical research resources, including common data elements that will enable comparison and sharing of clinical data across studies.

Connections across Basic, Translational, and Clinical Research

Although basic, translational, and clinical research flourish under different conditions, they cannot succeed in isolation from each other. Translational research builds upon basic and clinical research advances that reveal disease mechanisms and potential targets for therapeutic agents. Design of a preclinical therapy development project requires from its inception consideration of how the final product will be tested and used in the clinic. The interaction goes both ways -- throughout the history of neuroscience insights from translational and clinical research have been a major driver of basic research. NINDS program directors, who often manage research across the spectrum of research relevant to a particular disease, and the NINDS Associate Directors for extramural basic research, translational research, and clinical research, will work closely to strengthen connections among the NINDS basic, translational, and clinical research programs.

Establish a data-driven process to identify key scientific opportunities and public health needs across and within neurological diseases

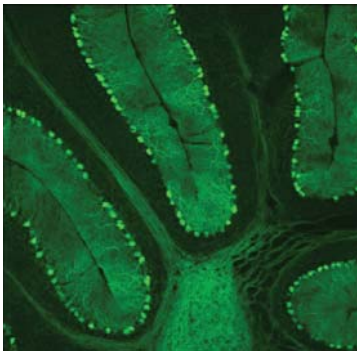
The NINDS will continue to emphasize investigator-initiated, peer-reviewed research. However, a portfolio shaped by this process alone does not ensure optimal investment across diseases with respect to scientific opportunity and public health burden. The NINDS can promote research in areas that do not receive sufficient attention through a range of activities. These actions include issuing grant and contract solicitations, convening scientific workshops, creating research resources, bringing the community together to establish goals through disease-specific planning, and allocating staff resources to work with the scientific community to increase investigator initiated research. Because NINDS resources are limited and competition for funding is intense, the Institute needs a more systematic and transparent process to determine when to take action for a particular disease or research area and what actions to take.

Systematic priority-setting requires better analysis tools and methods. New ways to dynamically classify and cluster neurological diseases according to current biological understanding, for example, could aid the identification of shared mechanisms across diseases, and in turn, yield new opportunities for collaborative research. The NINDS is continuing to explore tools to analyze the distribution of NIH research projects across areas of neuroscience, some of which were used to gather data for the planning process. The NINDS is also supporting the development of computer models that estimate the potential public health impact of proposed clinical trials, which is one of the issues to consider in selecting clinical trials for funding.

As one approach towards improved systematic assessment of opportunity, the NINDS will pilot test a "disease landscape" process. Disease landscapes systematically collect and analyze data on the public health impact, unmet scientific opportunities, and ongoing research and timelines at the NIH and elsewhere for a given disease or group of related disorders. To assess readiness for translational research, for example, the NINDS will consider whether a tractable biological target has been clearly associated with a disease, whether laboratory tests and starting materials are available for therapy development, and whether there is a feasible trajectory toward clinical testing. Considerations for investment in clinical trials will include whether there are potential interventions that can achieve an effect within the timeframe of the disease, whether measures of disease progression are available, and whether sufficient patient recruitment is feasible. The disease landscape process, or other systematic approaches, can inform the Institute's priority setting by identifying unmet opportunities both within each disease and for issues that cut across diseases.

Support research resources and technical advances that catalyze new discoveries

Improvements in technology often drive advances in neuroscience. Modest investments to provide research resources or to overcome technical challenges can spur progress by enhancing the capabilities of individual researchers. The NINDS has supported development of and access to a wide range of resources and tools for the neuroscience research community, often in cooperation with the other NIH Institutes and Centers of the NIH Blueprint for Neuroscience http://neuroscienceblueprint.nih.gov/. These resources include the NINDS Human Genetics DNA and Cell Line Repository http://ccr.coriell.org/Sections/Collections/NINDS/?SsId=10, the Gene Expression Nervous System Atlas (GENSAT) http://www.gensat.org/index.html, the NeuroMab monoclonal antibody facility http://neuromab.ucdavis.edu/, animal testing facilities for preclinical therapeutics development, mutant mouse repositories, clinical data repositories, a pediatric brain imaging atlas, brain banks, informatics resources, and a toolkit for behavioral assessment, among many others.



The NINDS-supported Gene Expression Nervous System Atlas (GENSAT) project provides the scientific community with tools to catalog, map and electrophysiologically record from individual cells in the mammalian brain. Above: Pcp2-EGFP expression in the Purkinje neurons of the adult mouse cerebellum.

The NINDS recognizes the need to respond to changes in science and in the needs of the research community when considering future investments in new tools and resources. The NINDS will seek input from the research community to determine which resources would have the greatest potential impact and are not easily accessible through the private sector. In response to planning recommendations, the NINDS has already begun to reassess ongoing programs and shift its support away from resources that are no longer needed.

Although the emphasis of NINDS strategic planning is on how to manage research, rather than what research to fund, the strategic planning process highlighted several scientific areas for investment that could have an important impact on a wide spectrum of neurological disorders. Effective strategies to deliver therapeutics across the blood-brain barrier, for example, could open up many new opportunities for treating neurological diseases. The blood-brain barrier protects the brain from harmful substances in circulation, but prevents access to potentially therapeutic agents for many brain and spinal cord disorders. Medicinal chemistry services would allow academic researchers to optimize promising small molecule therapeutics so that they are more likely to succeed in clinical testing. Animal models that recapitulate key features of human disease could provide new insights into disease mechanisms and enable better testing of potential new therapeutics. Biomarkers can expedite drug development and clinical trials by providing measurable indicators. Biomarkers could provide, for example, monitors of disease progression or of whether a candidate therapeutic is hitting its expected target. Support for collaboration through disease-focused research consortia, shared databases, and research material repositories can enable scientists to answer questions that may not be possible through individual laboratory efforts.

Communicate and collaborate with the public and with others involved in biomedical research

Maintaining open and productive relationships with the general public and with public, private, and non-profit organizations involved in biomedical research is crucial to advancing the NINDS mission. Non-governmental organizations are playing an increasingly important role in research, often in cooperation with small biotechnology companies. The NINDS will improve its communication with the public about Institute investments and their outcomes. The NINDS will continue to seek input from the public on its priorities and policies through the NANDS Council, Requests for Information, and public meetings.

The NINDS will also continue to engage the scientific community to ensure that the NINDS is responsive to their needs and challenges. To assist its grantees in developing medical interventions and research tools for clinical use, the NINDS will reach out to regulatory agencies, such as the FDA, and to professional societies. The NINDS will explore appropriate ways to engage the biotechnology and pharmaceutical industries and the investment community to ensure a smooth hand-off of products from the academic setting into the marketplace.

NINDS collaborates with private and non-profit organizations on projects such as the grassroots community education program Know Stroke in the Community*; shown here are Stroke Champions at a training session in Boston.*

To make the most of its resources, the NINDS must also collaborate with other NIH Institutes and Centers to address shared interests and challenges. Each NINDS Institute and Center has a unique mission. However, as science reveals underlying causes of disease and strategies for treatment, those missions often intersect. It is therefore essential that the parts of the NIH collaborate, not compete, whenever common scientific opportunities emerge. Two recent examples illustrate the possibilities. In keeping with strategic planning panel recommendations on disease consortia, the NINDS is co-sponsoring with the NIH Office of Rare Disease Research 9 of the 18 new NIH Rare Diseases Clinical Research Network (RDCRN) disease consortia announced October 2009, and administering the network's coordinating center. And, in line with recommendations of the clinical panel, the NINDS is cooperating with three other NIH Institutes in the SPRINT (Systolic Blood Pressure Intervention Trial) clinical trial http://clinicaltrials.gov/ct2/show/NCT01206062. The NINDS and the National Institute on Aging (NIA) are supporting an additional component of this major clinical trial, which is supported by the National Heart Lung and Blood Institute (NHLBI) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The added study focuses on the impact of aggressively lowering systolic blood pressure on reducing cognitive impairment, an important early indication of dementia.

NIH Institutes and Centers interact constantly, through formal working groups and informal contacts among scientific staff. Most NINDS initiatives involve multiple parts of the NIH. Among the structures that facilitate interaction, the **NIH Blueprint for Neuroscience Research** is a framework for cooperation that brings together sixteen Institutes and Centers. Blueprint initiatives create tools, resources, and training opportunities for the neuroscience research

community and more recently are taking on Grand Challenges that cross the missions of multiple Institutes. The Blueprint also fosters discussions and interaction across the NIH, contributing to a culture of cooperation. Similarly, the **NIH Common Fund** supports research to address challenges that cut across the entire NIH, many of which are directly relevant to the NINDS mission. The NINDS will continue to take leadership roles in Blueprint and Roadmap initiatives and seek out opportunities to leverage resources beyond its boundaries to advance its mission.

Train a robust and diverse neuroscience research workforce

A talented, diverse, and well-trained workforce is essential to the future of research, both in academia and the private sector. The NINDS supports individual and institutional training and career development awards and also supports trainees via research project grants to their mentors. The Institute has taken bold steps in recent years to enhance support for early-career investigators and physician scientists in the current competitive funding environment.

NINDS supports individual and institutional training and career development awards and also supports trainees via research project grants to their mentors.

These include new mechanisms of support and policy changes. Because the strategic planning process could not devote the attention to training and career development that is warranted by their importance, the NINDS will take up this topic more thoroughly as a follow up to the strategic planning process.

Adopt a culture of evaluation and continuous improvement across all NINDS programs

In addition to using a more rational process to establish new programs, the NINDS must monitor the effectiveness of all programs, and renew, change, or terminate programs based on rigorous assessments. Even a program with a sustained record of success may outlive its usefulness as science and technology change.

To guide this monitoring process, the NINDS will develop an evaluation plan for each new program before it begins. Each plan will provide a clear statement of the initiative's purpose and goals, a schedule for providing early, interim, and long-term assessment to the Institute leadership and the NANDS Council, and a statement of the outcome indicators and benchmarks for each assessment. The specific indicators will be appropriate for each program and the stage of assessment. The NINDS must be mindful of the difficulties of evaluating science, but the Institute must, to the extent possible, devise indicators that are both objective and reflect the essential goals of each program.

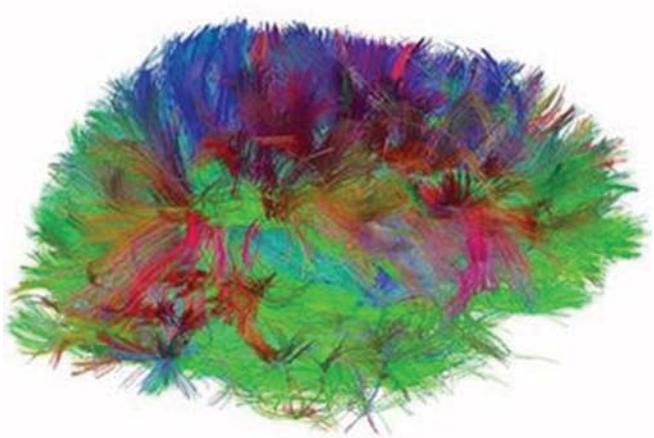
Next Steps

The four planning panels could not give sufficient attention to all key issues that confront the NINDS. The Institute will continue to examine other topics in the future, with a similar emphasis on data driven analysis and broad input. Planning focused on health disparities and diverse workforce development and on global health are now underway. The importance of training and career development was noted above. The NINDS Intramural Research Program is also slated to undergo an evaluation by a Blue Ribbon Panel, following a formal assessment process that NIH has established for Institute intramural programs.

In implementing this strategic plan, the NINDS will draw upon the detailed discussions and recommendations of the **four planning panels**, on Requests for Information and other inputs from the public and scientific community to the strategic planning process, and on subsequent information-gathering and meetings that follow up issues raised in the course of planning activities. The Institute will implement some recommendations quickly – indeed the Institute has already acted on several suggestions from the panels. One important lesson from the planning analyses, however, is that the NINDS must explicitly protect funding for investigator-initiated research—the Institute should not merely allocate to investigator-initiated research what is left over after more specific priorities are addressed. To maintain robust investigator-initiated research and sustain the scientific workforce with finite resources, the NINDS will address other issues arising from planning as is prudent, given available resources, over the next 5 to 10 years. The Institute will develop annual goals to address other recommendations and will report on progress each year.

Appendix: Strategic Planning Process

In 1999, the NINDS strategic plan **"Neuroscience in the New Millennium"** set broad scientific goals for neuroscience research across the breadth of the NINDS mission, recognizing that basic understanding about the nervous system and disease was the foundation for progress against neurological disorders. Since the Millennium plan, the NINDS has developed disease-specific plans for stroke, epilepsy, brain tumor, Parkinson's disease and various genetic diseases, and the Institute has participated in NIH-wide planning for autism, diabetes, obesity, and other disorders. Complementing these plans, the NINDS has supported more than 100 **scientific workshops** since 2000. Workshops bring the scientific community together to assess current understanding and set research priorities for diseases, cross-cutting research themes, emerging technologies, and clinical issues. In all, the Institute has issued more than 125 solicitations to address recommendations from plans and workshops, including major new programs for translational research, research resources, and other continuing needs.



Diffusion spectrum imaging (DSI) produced this brain map in which nerve bundles appear as thread-like structures. Scientists are pursuing new technologies to visualize and understand the brain through the Human Connectome Project, an initiative of the NIH Blueprint for Neuroscience Research. Such projects illustrate the way in which the NINDS strategic planning process looks ahead to identify major opportunities in neuroscience and explore the landscape of science and society in which the NINDS will act. (Image Source: Van J. Wedeen, M.D., MGH/Harvard U.)

Building on this foundation, in 2007 the NINDS launched a new strategic planning process. The Institute first took a **"blue sky"** look at the future to identify major opportunities in neuroscience and explore the landscape of science and society in which the NINDS will act. The NINDS sought public input on a series of broad blue sky questions through a Request for Information (RFI)and held workshops with basic and clinical neuroscientists from academia and industry, representatives from public groups, and NIH professional staff.

In 2008, the NINDS began a rigorous process to develop pragmatic recommendations to improve the Institute's effectiveness. With the guidance of a steering committee that included members from the National Advisory Neurological Disorders and Stroke (NANDS) Council, the NINDS formed four external advisory panels, each paired with an internal NINDS staff working group. The four planning modules focused on basic, clinical, translational, and disease research activities, respectively. The Institute recruited panel members from academia, industry, and the public, among them basic scientists from diverse areas of neuroscience and neurologists and neurosurgeons who treat adults and children. Because of the importance of the NINDS mission, an extraordinarily talented group of experts dedicated extensive time and effort to the planning process. The NINDS Director asked each group to assess current NINDS activities, to identify which programs are working well and not, and to recommend how the Institute can more effectively pursue its mission. To support that charge, the NINDS provided an unprecedented depth of information about current programs. The NINDS also solicited input from patient voluntary groups through another Request for Information, after shaping the questions for the RFI together with representatives of patient groups at the Institute's regular meeting with voluntary organizations. The external panels analyzed information, requested and received additional data, and deliberated through face-to-face meetings, interaction with NINDS staff, phone conferences, and email exchanges. Each panel reported its findings and recommendations to the NANDS Council in February 2009 and the panels' full reports are archivedat: https://www.ninds.nih.gov/About-NINDS/Strategic-Plans-Evaluations/Strategic-Plans/NINDS-Strategic-Plan-and-Priorities#Strat%20plan%20modules. Based on the panel recommendations and other input received during the planning process, NINDS developed an integrated strategic plan that was posted online for public comment and then finalized in June 2010.

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