Written Statement
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Subcommittee on Labor, Health, and Human Services, Education, and Related Agencies
Appropriations Committee
In support of FY 2015 Appropriations for the NIH

Mr. Chairman and members of the Subcommittee, my name is Carol Ann Mason, Ph.D. I am a professor of pathology and cell biology, neuroscience, and ophthalmic science at Columbia University. I study the development of visual pathways in mammalian brains, with a focus on how neurons in the eye are encoded to project to the correct side of the brain, setting up the circuit for binocular vision. This statement is in support of increased funding for NIH for fiscal year 2015.

I am pleased to submit this testimony in my capacity as president of the Society for Neuroscience (SfN). On behalf of the nearly 40,000 members of SfN, thank you for your past support of neuroscience research at NIH. SfN's mission is to advance the understanding of the brain and nervous system; provide professional development activities, information and educational resources; promote public information and general education; and inform legislators and other policymakers.

The Society stands with others in the research community in requesting at least $32 billion for NIH for FY 2015. Sequestration is taking an enormous toll on biomedical research, coming on top of recent years when funding has failed to keep pace with the cost of research – let alone the scientific opportunities that are available. SfN urges Congress to reverse the current course and find ways to invest more in biomedical research. Let's work to put biomedical research on a trajectory of sustained growth that recognizes its promise and opportunity as a tool for economic growth and, more importantly, for advancing the health of Americans.

Neuroscience: An Investment in Our Future

Even in the face of the difficult funding situation, the last several years have been a tremendously exciting and productive time for neuroscience discoveries. Major research advances on brain development, imaging, genomics, circuits, computational neuroscience, neural engineering, and many other disciplines are leading to new tools, new knowledge, and greater understanding that were unimaginable even a few years ago. Sustained investment to fuel and speed these discoveries is essential to American health and economic well-being for many reasons.

First, major investment in basic and translational neuroscience is not only fueling an enduring and vital scientific endeavor; it is the essential foundation for understanding and treating diseases that strike nearly 1 billion people worldwide. All told, there are more than 1,000 debilitating neurological and psychiatric diseases that strike over 100 million Americans each year, producing inestimable hardship for millions of America families and costing the U.S., in a conservative estimate, at least $760 billion a year, with expenses in the trillions looming for conditions such as Alzheimer's disease. Advances made possible by publicly-funded basic research will help better understand and treat traumatic brain injury, Alzheimer's, Parkinson's disease, Down syndrome, schizophrenia, epilepsy, and post-traumatic stress disorder, to name just a few. With so much promising research, now, more than ever, it is time to fan the flames of research in order to ensure lifesaving breakthroughs continue.

Additionally, NIH funding is an investment in America's current economic strength.

Funding for research supports quality jobs and increases economic activity. NIH supports approximately 400,000 jobs and $58 billion in economic output nationwide. Eighty-five percent of the NIH budget fund extramural research in communities located in every state.

Finally, without robust, sustained investment, America's status as the preeminent leader in biomedical research is at risk. Other countries are investing heavily in biomedical research to take advantage of new possibilities. Even with the growing philanthropic support, private sector cannot be expected to close the gap. The lag time between discovery and profitability means that the pharmaceutical, biotechnology, and medical device industries need federally-funded basic (also known as fundamental) research to develop products and treatments. The foundation that basic research provides is at risk if federally-funded research declines.

The BRAIN Initiative

SfN appreciates that both Congress and the administration recognize brain science as one of the great scientific challenges of our time. The Brain Research through Application of Innovative Neurotechnologies (BRAIN) Initiative – announced by the President last April - will enable NIH and other federal agencies to develop tools and plans that will help accelerate fundamental discoveries and improve the health and quality of life for millions of Americans. An eminent group of neuroscientists with diverse research interests is helping to formulate a scientifically-driven direction for the initiative, and SfN thanks public leaders for their interest and early support for a truly transformative scientific grand challenge that would need major financial emphasis in future years.

The overarching goal of the BRAIN Initiative is to map the circuits of the brain and the activity within those circuits to understand our unique cognitive and behavioral capabilities. The Initiative has a strong focus on developing technologies which has the potential to benefit all of neuroscience and even non-neuroscience research. BRAIN, like other major brain-related initiatives around the world, demonstrates the global interest in tackling the mysteries of the brain. But BRAIN – as with all the neuroscience research that takes place with federal support – can only be successful if it is part of a broad neuroscience commitment across Congress and the Administration. Such an investment will also help ensure the U.S. remains a global leader, as other nations and regions are now rapidly ramping up their investments in neuroscience research.

Cross-Disciplinary Neuroscience and the Promise of Brain Circuits

NIH-funded basic research continues to be essential for discoveries that will inspire scientific and medical progress for generations. Past NIH-supported projects have helped neuroscientists make tremendous strides in diagnosing and treating neurological and psychiatric disorders.

A prime example of the importance of funding research at levels from the most basic to translational is the current focus on understanding brain circuits. Circuits in the brain underlie every thought, emotion, and action we take. Current knowledge about the intricate patterns connecting brain cells is extremely limited. Identifying these patterns is essential to understand healthy brain function and dysfunction in injury or disease. Research suggests that some brain disorders, like autism and schizophrenia, may result from errors in neural circuit development.

Elucidating brain circuit structure and function is an enormously challenging endeavor; the brain consists of billions of cells, and each cell contacts thousands of others. These cells communicate with precisely-timed signals, which then activate a multitude of biochemical pathways that influence every process in the cell. However, scientists are beginning to map the functions of brain circuits with previously unheard-of specificity using cutting-edge technologies, and learning how these circuits produce behaviors.

The following examples are just a few of the many basic research success stories in the science of brain circuitry emerging now thanks to interdisciplinary research funded by a strong historic investment in NIH and other research agencies.

Optogenetics

Optogenetics is a technique which uses light to activate specific populations of neurons with millisecond precision. It is difficult to overstate how revolutionary optogenetics is for neuroscience research. With optogenetics, flashes of light are used to activate neurons that have been genetically modified to contain a light-sensing protein. This precise control over specific populations of neurons at specific times was impossible until a confluence of basic research in marine biology, genetic engineering, cellular biology, and fiber optic technology facilitated its development; together these developments created an approach that enables the proteins to be used as "on switches" for cells. Introduced a decade ago, optogenetics is now used by hundreds of labs; it is one of the many neurotechnologies that today is transforming the field's ability to understand brain function, and is being used to study brain circuits in both normal function and disease, including Parkinson's disease, as described below. The development of this technology also perfectly demonstrates the often serendipitous nature of scientific discovery and the need to fund both research on all levels, from basic to translational to clinical.

Understanding the Development of Vision

My own area of research is the development of the circuits underlying vision. For binocular vision to function, the brain must receive information from both eyes. Nerve fibers from each retina grow to the 'optic chiasm,' at the midline of the bottom of the brain. Here, nerve fibers from each eye cross to the other side of the brain. Other axons, however, are repelled at the midline and project to the same side of the brain. These connections underlie binocular vision which enables animals, including humans, to calculate how far objects lie in the distance. One area of my research focuses on this question and the molecular mechanisms that prompt some growing nerve fibers to "stop in their tracks" and reroute to the same side. These two groups of cells in the eye, each taking different routes, are endowed with distinct genes that direct their time of birth and their growth to the regions where they make their synaptic connections. Understanding their genetic "signatures" and growth helps us to learn how to encourage stem cells to be integrated into the diseased eye and injured nerve fibers to regrow in the correct circuits. We also investigate how the retinal pigment epithelium (RPE) surrounding the eye, directs retinal development. Perturbations in the RPE occur in albinism and in juvenile forms of macular degeneration, the latter leading to blindness, and our gene identification efforts are important for gene therapy at early stages of the disease. Moreover, understanding how tracts are laid down is essential for unraveling the basis of defects in fiber pathways and synapse formation in neurodevelopmental disorders such as autism. This research is made possible with support primarily from NIH, especially the National Eye Institute and with a team of innovative and collaborative scientists and trainees in my lab and in our community, and provides a foundation for future discovery and new understanding about diseases of the eye and other neurodevelopmental conditions.

Deep Brain Stimulation

Deep brain stimulation (DBS) is a tool that emerged as a result of advances in health research. DBS involves a surgical procedure in which a neurostimulator device—similar to a heart pacemaker—is implanted to deliver electrical stimulation to targeted areas in the brain. While both DBS and optogenetics have emerged as instrumental methods to influence circuits, DBS has also been developed into a revolutionary therapy for the treatment of neurological disease. The electrical pulses delivered through the electrodes can transiently disrupt abnormal activity that occurs in localized circuits of diseased brains, such as in Parkinson's patients.

DBS has created a new way to approach the treatment of Parkinson's disease. Many patients experience pronounced relief from symptoms that include tremor, stiffness, slowed movement, and walking problems. Moreover, DBS can allow patients to reduce the dosage of their medication, providing relief from debilitating motor side-effects. Additionally, advances in materials science to create more flexible electrodes and in imaging research to produce higher resolution images of the brain will improve the precision and outcome of this intervention.

At this time, how and why DBS works is unknown. Insight into its mechanism of action came from optogenetic studies in rodents of the brain circuits that control movement. By systematically manipulating precise areas of the circuit affected by this disease, scientists were able to implicate the connection between two areas of the brain as the most effective target for DBS. These studies will also inform the design of other interventions in Parkinson's, and establish a model for study of basic brain circuitry to inform DBS treatment.

DBS has also had success in treating both intractable depression and epilepsy, and has the potential to improve therapies for a whole host of brain diseases and disorders—as long as the correct target is identified. Because stimulating adjacent regions in the brain can have vastly different effects, researchers are attempting to better understand the complex brain circuits that control our normal functions (e.g., movement, emotion) and how they can go wrong (e.g., addiction). They also are tweaking the physical devices used, as well as the frequency and strength of the electrical pulses delivered. As we understand more about language of the brain through the research made possible by NIH funding, new applications of DBS will be possible.

The Future of American Science

As the subcommittee considers this year's funding levels, please consider that significant advancements in the biomedical sciences often come from young investigators. As a director of the PhD training program of a leading neuroscience department, I see firsthand that the current funding environment is taking a toll on the energy and resilience of these young people and their career choice. America's scientific enterprise—and its global leadership—has been built over generations. Without sustained, consistent investment, we will quickly lose that leadership. Dramatic swings in funding have stifling and irreversible impacts on progress; a closed laboratory can't simply open again when funding is restored. The culture of entrepreneurship and curiosity-driven research could be hindered for decades.

We live at a time of extraordinary opportunity in neuroscience. A myriad of questions once impossible to consider are now within reach because of new technologies, an ever-expanding knowledge base, and a willingness to embrace many disciplines. To take advantage of the opportunities in neuroscience we need an NIH appropriation that allows for sustained, reliable growth. That, in turn, will lead to improved health for the American public and will help maintain American leadership in science worldwide. Thank you for this opportunity to testify.