Written Statement

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Subcommittee on Labor, Health, and Human Services, Education, and Related Agencies
Appropriations Committee
In support of FY 2016 Appropriations for the NIH

Mr. Chairman and members of the Subcommittee, my name is Steven E. Hyman, and I am privileged to offer this testimony in support of increased funding for NIH for fiscal year 2016. I offer this testimony in my capacity as president of the Society for Neuroscience (SfN). I am also director of the Stanley Center for Psychiatric Research at the Broad Institute of MIT and Harvard as well as Harvard University Distinguished Service Professor of Stem Cell and Regenerative Biology. The Stanley Center is focused on using human genetic analysis to discover the neurobiological bases of neuropsychiatric disorders with a view to discovering new treatments.

The mission of SfN is to advance understanding of the brain and nervous system. Drawing on knowledge from the life sciences, physical sciences, and engineering, brain research is among the most promising and productive areas of science today. Given the tremendous human and economic toll of brain disorders worldwide — including autism, depression, schizophrenia, multiple sclerosis, Parkinson's disease, and Alzheimer's disease — it is among those areas of research in which continued progress is most powerfully needed. SfN leads efforts to disseminate and discuss emerging neuroscience discoveries, hosting one of the world's largest annual scientific meetings and publishing two leading scientific journals. SfN works to cultivate the next generation of scientists and physicians by providing professional development and training activities. SfN is also committed to actively educating the public about the brain both in health and in illness, and to engaging policymakers regarding the tremendous progress and potential of brain research. On behalf of the nearly 40,000 members of SfN, I thank you for your past support of the NIH and of neuroscience research. Thank you also for your support and investment in the NIH portion of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. As one crucial part of the federal investment in neuroscience, NIH-funded BRAIN programs will accelerate future discoveries across many areas of neuroscience and throughout the life sciences more broadly.

The Society stands with others in the research community in requesting $33 billion for NIH for FY 2016. This level of support would help mitigate some of the damage done to the scientific enterprise of the United States by sequestration, which has taken an enormous toll on the research enterprise. Following the first year of sequestration cuts in FY2013, approximately 640 fewer competitive research project grants were issued and 750 fewer new patients admitted to the NIH Clinical Center. The last four years, including 2014, have seen the lower success rates for Research Project Grants than in the previous thirteen. In recent years, funding has failed to keep pace with inflation and, more importantly, with the remarkable scientific opportunities that hold the potential for life-altering breakthroughs. It is time to put research on a trajectory of sustained growth that recognizes its promise, its importance as a springboard for economic development, and the centrality of NIH-funded science to new and more effective approaches to the advancement of health and well-being for all Americans.

Cross-Disciplinary Neuroscience
The basic research funded by NIH at universities and hospitals across the nation leads to discoveries that will inspire scientific and medical progress for generations. Such research also serves as a springboard for industry, which cannot take on the long-term investment or risks inherent in basic science. Past NIH-supported projects have helped neuroscientists make tremendous strides that have led to advances in the diagnosis and treatment of neurological and psychiatric disorders.

The following examples are just a few of the many success stories made possible by brain research funded by a strong historic investment in NIH and other research agencies.

New Light on Autism, Schizophrenia, and Alzheimer's disease
Among the risk factors for many common, devastating brain disorders, genetic contributors loom large. Identification of risk genes is critically important, because they can provide clues both to biomarkers and ideas for new therapies.

For more than a decade, it has been relatively straightforward to identify disease genes in the cases where a single gene produces illness, as in the case of familial Alzheimer's disease and some very severe forms of autism. However, such situations are quite rare. Illness in the vast majority of people with Alzheimer's disease, autism, and epilepsy, and virtually all people with schizophrenia, results from the interaction of many small variations in the genetic code together with environmental risk factors. While it has long been recognized that identification of the precise genetic risk factors for these disorders would be extremely valuable in lighting the path to new treatments, such clues seemed out of reach. The human genome project changed that, providing technology and computing tools that would make it possible to identify the small genetic signals that contribute to disease, previously hidden a sea of healthy human DNA sequence variation.

Through its research support and wise policies that encouraged collaboration and sharing of data, NIH has played a central role in moving the genetic analysis of common brain disorders forward. Finding the "signal" in the "noise" required very large patient samples that took years to assemble. During the past year, important progress has been reported in identifying genomic regions involved in common forms of Alzheimer's disease, autism, epilepsy, schizophrenia, and multiple sclerosis. While there remains a challenging path if we are to transform these new understandings into effective new treatments, these important newly reported clues have had a galvanizing effect in universities, hospitals, and in industry. The result is many new ideas and efforts to attack these disorders.

Navigating the World
The most advanced surveillance system is built into the brain. It comes equipped with a system that maps the locations and the order of a lifetime of events. Through new research tools and insights, scientists are coming to understand how the brain permits us to navigate the environment. Recent discoveries show that finding the way in the world is inexorably linked to the brain structures and processes by which memories are stored. While the brain is making mental maps to help a person navigate, it is also overlaying remembered experience onto those maps. The very same cells and circuits that help us navigate is the one that is damaged first in

Alzheimer's disease. One of the first symptoms of Alzheimer's disease is that its victims can no longer find their car, and often can no longer find their way home. Further insight into how the brain builds networks can potentially lead to interventions that spare millions of people from the debilitating effects of memory disorders.

The importance of this work is underscored by the fact that the 2014 Nobel Prize in Physiology or Medicine was awarded to three pioneering neuroscientists who study navigation. Their work on the very basic science of how individual brain cells code the body's position in space has opened the door for important translational research studies. Building on this groundbreaking work, NIH-funded researchers are currently investigating the computations cells perform to determine position in space; the relationship between spatial memory and decision-making; and novel interventions targeted at this system to improve cognitive abilities in a host of disorders that damage memory.

Bypassing Barriers

Studies funded by NIH are helping researchers understand the blood-brain barrier, which helps block harmful substances from entering the brain. Unfortunately, many life-saving drugs are also unable to cross it, and thus cannot reach their target. An estimated 98 percent of potential drug treatments for brain disorders are unable to penetrate the blood-brain barrier. Researchers are developing techniques to open this barrier and allow medicines to enter. These techniques resulted in successful delivery of chemotherapy to patients with brain tumors, anti-clotting drugs to stroke patients, and other important treatments.

Scientists are also developing new strategies for attaching drugs to molecules that naturally cross the barrier. This method has shown success in several animal models by allowing drugs for conditions like Parkinson's disease to enter the brain. Through this research, scientists are creating new ways to open the blood-brain barrier so that life-saving drugs can reach specific targets without also opening the barrier to substances that must be excluded. Researchers are hopeful that new knowledge of the blood-brain barrier function, and new methods for drug delivery to the brain, will one day lead to better treatments for some of the most challenging and intractable disorders.

Neuroscience: An Investment in Our Future

Despite the difficult funding environment, the last several years have been a tremendously exciting and productive time for neuroscience discoveries. Major research advances in genomics, brain development, brain circuitry and imaging, computational neuroscience, neural engineering, and many other disciplines have occurred. Progress in these areas is leading to new tools, new knowledge, and an understanding of the brain that was unimaginable even a few years ago. Consider what could be learned with a more favorable funding posture and how it could be applied to human health.

Sustained investment to stimulate and speed these discoveries is essential to American healthcare and economic well-being. 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 one billion people worldwide. At home, there are more than 1,000 debilitating neurological and psychiatric diseases that strike over 100

million Americans each year. This, in turn, produces severe hardship for millions of families and costs the U.S. economy at least $760 billion a year, with future expenses reaching the trillions looming for several conditions. Otherwise beneficial increases in life span may be may be profoundly undercut by neurodegenerative diseases such as Alzheimer's disease and other dementias. Advances made possible by publicly-funded research will help us maintain, and perhaps someday restore, healthy brain function. With funding from NIH, researchers can continue working towards lifesaving breakthroughs such as developing ways for paralyzed people to regain control of their lives by using thoughts to move a robotic arm or investigating the recently discovered set of ten blood compounds that might be used to identify older adults at risk for developing memory deficits. NIH's funding should reflect the effort needed to achieve these innovations.

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 NIH's budget funds 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 growing philanthropic support, the 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.

Conclusion

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 and robust 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.