Written Statement
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Subcommittee on Commerce, Justice, Science, and Related Agencies
In support of FY 2016 Appropriations for the NSF

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 NSF 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 NSF and of neuroscience research. Thank you also for your support and investment in the NSF portion of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. As one crucial part of the federal investment in neuroscience, NSF-funded BRAIN programs fuel future discoveries across many areas of neuroscience and other research disciplines as well.

The Society stands with others in the research community in requesting at least $7.7 billion for NSF 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. In recent years, funding has failed to keep pace with inflation and more importantly with the remarkable scientific opportunities made possible by new ideas and new technologies. For example, NSF's proportional share of the mandatory spending caps would result in 14,000 fewer grants awarded by 2021. Investigations that hold the potential for life-altering breakthroughs are at risk. 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 NSF-funded basic science to fundamentally new approaches to the advancement of health and well-being for all Americans. We cannot continue to limit an agency that funds 25% of basic science research at colleges and universities in this country and helped produce 212 Nobel Prize recipients since 1952.

Cross-Disciplinary Neuroscience

NSF-funded basic research is essential for discoveries that will inspire scientific and medical progress for generations. The work supported by NSF has led to the development of new technologies that have revolutionized neuroscience research. The following examples are just a few of the many basic research success stories in the science of the brain emerging thanks to interdisciplinary research funded by a strong historic investment in NSF and other research agencies.

Brain at Rest

Brain imaging and cognitive neuroscience have helped identify neural circuits that are active when we are engaged in a specific task, such as thinking about words or speaking them. Observing the brain's response to reminders of a person's past experience have helped map the excessive excitability of "fear circuits" in the brains of those suffering posttraumatic stress disorder. However, little attention was paid brain activity when subjects were seemingly at rest, allowing their minds to wander. Marcus Raichle, an NSF grantee, who was just awarded the prestigious Kavli prize, notes that like everyone else, he had ignored this "resting state" before asking subjects in a brain scanner to begin a specific task. However, he began to notice that when his subjects began their task, some areas of the brain increased their activity as expected, but surprisingly some areas of the brain showed a significant decrease in activity. Ultimately Raichle and others recognized that when apparently at rest, the brain has very specific patterns of activity that has come to be known as the "default mode network". This serendipitous discovery has important implications not only for understanding how our brains normally work, but appears to shed light on several important diseases. It has been observed that the earliest patterns of damage in Alzheimer's disease seem to map onto the default mode network. Similarly the brains of patients with schizophrenia seem to have difficulty switching out of the default mode into "task" mode when engaging in ordinary tasks of thinking and acting. This discovery is beginning to yield clues to what goes wrong in the brain in these and other neurologic and psychiatric disorders.

Targeted Gene Editing

Even bacteria get infected by viruses, and have thus evolved an immune system. While studying the fundamental question of how bacteria protect themselves from the viruses that infect them, scientists discovered CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats). Using the CRISPR system, some species of bacteria are able to cut up the genomes of invading viruses, and to do so with such specificity that they do not harm their own genomes. CRISPR has been turned into a breakthrough research tool using NSF-funds. Indeed CRISPR, in a few short years, has become the most widely used tool for editing the genomes of experimental organisms, thus creating animal models of disease with an efficiency not previously imagined. CRISPR acts as a pair of "guided scissors," taking advantage of normal cellular machinery to make precise changes to the genetic code. Without NSF funding, CRISPR might not have become the critical tool that it is today.

Animal models of disease are a crucial part of science, including neuroscience. Investigating complex functions of the living nervous system is impossible in humans, so neuroscientists must turn to animal models. The ability to insert human genetic variants associated with disease in animal models, most commonly mice, helps advance understanding of how genetic risk factors affect the cells and networks of the brain and ultimately behavior. CRISPR has markedly sped up

the process of making such genetic modifications and has permitted precise targeting of specific genomic regions.

This new technology may help scientists understand the biological origins of complex brain disorders, providing new targets for therapeutic intervention. In addition to its almost unlimited potential in basic and applied research, CRISPR may eventually facilitate gene therapy in humans by enabling doctors to directly correct faulty genes in the cells of bodily tissues such as muscle, liver, and bone marrow. Proof-of-principle studies have already been successful in correcting disease-causing mutations mouse models of muscular dystrophy and a fatal liver disease, and are under way with often lethal blood diseases.

High Resolution Microscopy

An NSF-supported discovery was honored with the 2014 Nobel Prize in Chemistry. W. E. Moerner's work on increasing the resolution of optical microscopes has been funded by NSF for several decades, starting as a graduate student. Moerner, along with Eric Betzig of the Howard Hughes Medical Institute, and Stefan W. Hell of the Max Planck Institute for Biophysical Chemistry in Germany, "bypassed a presumed scientific limitation stipulating that an optical microscope can never yield a resolution better than 0.2 micrometers." The techniques they developed allow scientists the ability to view brain structures in ever-increasing detail.

Instead of averaging over the whole brain, or even over a small brain area, scientists are now able to investigate single molecules and cells on the order of one nanometer (thinner than a strand of human DNA). The ability to view the brain at the nanoscale is making it possible for scientists to see how molecules create synapses between nerve cells in the brain and track the aggregation of proteins involved in Parkinson's disease, Alzheimer's disease, and Huntington's disease within individual cells. The discoveries that led to this Nobel Prize-winning work are important because—unlike other methods that produce a nanoscale resolution—light-based microscopes are non-invasive, allowing these measurements to be taken of living specimens. Scientists can now visualize how cells interact with each other, how proteins fold around the cell, the effect of drugs on individual cells, and much more. The questions that can be answered with this technology will greatly expand our understanding of the complex biological processes happening inside every cell and has the potential to revolutionize our understanding of the brain.

Neuroscience: An Investment in Our Future

While appreciating the consistent investment made in NSF, greater investment is essential if we are to unlock the full potential of major research advances in genomics, brain development, brain circuitry and imaging, computational neuroscience, neural engineering, and many other disciplines. 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.

All told, debilitating neurological and psychiatric diseases strike over 100 million Americans each year, costing an estimated $760 billion annually. Otherwise beneficial increases in life span 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. Through NSF's $144 million contribution to its Understanding the Brain project (including $72 million targeted for the BRAIN Initiative), we are continually increasing our knowledge about the inner workings of the brain, including non-invasive methods for imaging the human brain and understanding the potential link between

human and computer cognition.

Resources provided to NSF support the nation's best and brightest researchers at the forefront of promising discoveries, graduate students at the start of their careers, and the development of advanced scientific tools and infrastructure that will be broadly available to the research community. These researchers are addressing some of the vexing issues facing the field of neuroscience, such as allowing those who are paralyzed to move through world using their thoughts via brain-machine interfaces and learning more about brain function by observing real-time communication between living neurons in jellyfish. NSF is uniquely positioned to address these hurdles because of its emphasis on integrative and interdisciplinary research and its long history of funding research that leads to the development of life-changing neurotechnologies.

In addition to life-altering discoveries, NSF research supports quality jobs and increases economic activity. In FY 2013, NSF supported research through 10,829 awards, directly involving approximately 299,000 senior researchers, post - doctoral associates, teachers and students. Ninety percent of the NSF budget goes right back to fund extramural research in every state. Many of my colleagues can point to their first NSF grant as their launching pad for a career in science.

Without a 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.

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 steeped in modern technology. The current funding environment is taking a toll on the energy and resilience of these young people. America’s scientific enterprise — and its global leadership — was built over generations. NSF alone has awarded over 46,500 Graduate Research Fellowships since 1952. Many young scientists receive their first grants from NSF on their way to having careers as independently-funded investigators. Without sustained investment, we could quickly lose that leadership. 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 NSF 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.