Written Statement
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Subcommittee on Labor, Health and Human Services, Education & Related Agencies
Appropriations Committee, United States Senate
In support of FY2014 Appropriations for the National Institutes of Health
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Mr. Chairman and Members of the Subcommittee, my name is Larry Swanson, Ph.D. I am the Milo Don and Lucille Appleman Professor of Biological Sciences at University of Southern California. Over the past 30 years my work has focused on the structure and organization of neural structures involved in motivated and emotional behaviors, as well as the development and wiring diagram of the nervous system more generally. This statement is in support of increased funding for the National Institutes of Health (NIH) for FY2014.

On behalf of the nearly 42,000 members of the Society for Neuroscience (SfN), thank you for your past support of neuroscience research at the NIH. SfN's mission is to advance the understanding of the brain and the nervous system; provide professional development activities, information and educational resources; promote public information and general education; and inform legislators and other policymakers.

This is an exciting time to be a part of the neuroscience field. Advances in understanding brain development, imaging, genomics, circuit function, computational neuroscience, neural engineering, and many other disciplines are leading to discoveries that were impossible even a few years ago. These will no doubt help us better understand and treat traumatic brain injury, Alzheimer's disease, Parkinson's disease, Down syndrome, schizophrenia, epilepsy, and post-traumatic stress disorder to name just a few. All told, there are more than 1,000 debilitating neurological and psychiatric diseases that strike over 100 million Americans each year, costing an estimated $750 billion a year.

SfN is appreciative that President Obama recognizes brain science as one of the great scientific challenges of our time. The recently announced Brain Research through Application of Innovative Neurotechnologies (BRAIN) Initiative would enable NIH and other federal agencies to develop initial tools and conduct further planning that will help accelerate fundamental discoveries and improve the health and quality of life for millions of Americans.

The field of neuroscience is poised to make revolutionary advances thanks to decades of global investment and path-breaking research. However, realizing this potential means today's critical seed funds must be backed by sustained, robust investment in the scientific enterprise in the coming decade. SfN is encouraged by the President's request for a modest increase to the budget of NIH. However, flat funding over the last decade has led to the loss of approximately 20 percent of NIH's purchasing power due to inflation, thus hampering the pursuit of the knowledge needed to uncover the mysteries behind biological function, causes of disease, and potential therapies.

Now is the time to take advantage of scientific momentum, to pave the way for improved human health, to advance scientific discovery and innovation, and to promote America's near-term and long-range economic strength. That requires robust investments in NIH that reverse the tide of stagnant and shrinking funding. These investments contribute to the economic growth of local communities in every state as part of the approximately 85 percent of the NIH budget that goes to funding extramural research. In 2012 alone, NIH supported more than 402,000 jobs and $57.8 billion in economic output nationwide. Moreover, adequate funding will help preserve and expand America's role as a preeminent leader in biomedical research, supporting public and private institutions and fostering activity in the pharmaceutical, biotechnology, and medical device industries.

Seizing this moment can only happen if labs are able to pursue promising leads and innovative ideas can move forward. A constricted fiscal environment—compounded by sequestration—will stand in the way of that progress. It's impossible to say what breakthroughs will go undiscovered, but there is no doubt that this fiscal environment will result in delayed discoveries, with potentially huge opportunity costs for human health.

Last year, the Society stood with others in the research community in requesting at least $32 billion for NIH. Today, the need is no less as the funding situation is even more precarious, and the Society urges Congress to reverse the current course and find ways to invest more in biomedical research. We urge Congress to act before sequestration takes full effect, further eroding the short and long-term capacity for discovery. 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.

Brain Research and Discoveries

NIH-funded basic (also known as fundamental) research continues to be essential for discoveries that will inspire scientific pursuit and medical progress for generations to come. Past NIH supported projects have helped neuroscientists make tremendous strides in diagnosing and treating neurological and psychiatric disorders. Given the long-term path of basic science and industry's need for shorter-term return on investment, private industry depends on federally-funded research to create a strong foundation for applied research. More than ever, it is important to support and fund research at levels from the most basic to translational.

The following are just three of the many basic research success stories in neuroscience emerging now thanks to strong historic investment in NIH and other research agencies:

A New Model for Complex Brain Disease

A new development from basic science shows tremendous potential for improving understanding of complex diseases such as Alzheimer's, which affects 5.4 million Americans and costs the United States $200 billion in direct costs annually.

Traditionally, human disease is modeled by identifying and studying single gene mutations that run in families. Brain cells from mice genetically engineered to express this mutated gene can be studied to help illuminate the complex interactions that produce the disease.

Unfortunately for the ease of understanding these diseases, single gene mutations are not the only way to develop most diseases. With Alzheimer's disease, most cases are likely caused by mutations in many different genes. Thus, current models of Alzheimer's likely paint an incomplete picture of the disease.

New developments in stem cell technology are changing this picture. Stem cells are special cells that have the potential to become any other type of cell in the body. Due to advances in genetic engineering, scientists can now trick almost *any* cell into becoming a stem cell. This technique can be used to turn *skin* cells from patients with idiopathic Alzheimer's disease into *brain* cells. These cells are ostensibly identical to the cells in that person's brain, complete with that person's unique genetic risk profile. Research with these cells could potentially help identify subgroups of patients who will respond differently to treatment in clinical trials.

For now, it is not clear whether the brain cells made from this technique are completely identical to the 70-year-old neurons in the brain of a patient with Alzheimer's disease. In addition, these cells are currently prohibitively difficult to create, making them unlikely to replace embryonic stem cells in other applications in the near future. Continued research funding will allow scientists to begin addressing these and other outstanding questions. This research exemplifies the powerful potential to apply basic research well beyond its original intent.

The "Connectome"

Current knowledge about the intricate patterns connecting brain cells (the "connectome") is extremely limited. Yet identifying these patterns and understanding the fundamental wiring diagram or architectural principles of brain circuitry is essential to understanding how the brain functions when healthy and how it fails to function when injured or diseased. Recent research suggests that some brain disorders, like autism and schizophrenia, may result from errors in the development of neural circuits. This research suggests a new category of brain disorders called "disconnection" syndromes.

Advanced technologies, along with faster and more data-efficient computers, now make it possible to trace the connections between individual neurons in animal models providing us with greater insight into brain dysfunction in mental health disorders and neurological disease. Scientists have already used these technologies to examine disease-related circuitry in rodent studies of Parkinson's disease. Their findings helped explain how a new treatment called deep brain stimulation works in people, and are being explored for treatments of other diseases.

Genetics of Schizophrenia

Antipsychotic drugs and improved therapeutic techniques represent great advances in the treatment of schizophrenia, but they do not help everyone. Even when successful, they typically mitigate only psychotic effects, leaving many severely disabled due to other symptoms.

One promising line of research deals with the genetics of schizophrenia. In recent years, neuroscientists have found numerous mutations linked to schizophrenia. However, no single mutation seems to directly lead to schizophrenia, making a genetic test for the condition unlikely for now. Rather, multiple, rare mutations seem to combine to make someone susceptible. These genes seem to affect neural development and neural plasticity—the ability of the brain to reshape its connections as needed.

One of these genes is the Disrupted-In-Schizophrenia-1 (DISC1) gene. DISC1 helps maintain signaling levels of a key chemical in the brain called glutamate. Mice with a mutant form of DISC1 have reduced glutamate signaling and behavioral abnormalities. There is evidence that this deficit is the result of alterations during development which nonetheless have lasting effects later in life.

Knowing the mechanisms by which individual genes may raise or lower the risk of developing certain diseases is an important first step in identifying the pathways involved in those diseases. Future research is needed to probe the complex interactions of multiple genes within a system. Once pathways are identified, they can provide direction for development of new treatments.

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. 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—has been built over generations. Without sustained investment, we will 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 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.