Written Statement

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Subcommittee on Labor, Health and Human Services, Education and Related Agencies
Appropriations Committee
In Support of FY22 Appropriations for the National Institutes of Health

Chair DeLauro, Ranking Member Cole, and members of the Subcommittee, on behalf of the Society for Neuroscience (SfN), we are honoured to present this testimony in support of robust appropriations for biomedical research at the National Institutes of Health (NIH). SfN urges you to provide at least $46.1 billion, a $3.2 billion increase over FY21, in funding for existing institutes and centers at NIH for FY22, including $496 million from the NIH Innovation Account for 21st Century Cures programs and $560 million for the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. Dr. Moses Chao and I, as Chair of the Government and Public Affairs Committee and President of SfN respectively, understand the critical importance of federal funding for neuroscience research in the United States. I currently serve as a researcher and as a Professor in the Department of Psychology at Cambridge University and Dr. Chao is a professor of Cell Biology, Physiology and Neuroscience, and Psychiatry at the New York University School of Medicine. Our research serves as two examples of the wide variety of neuroscience research advancing our collective understanding of the brain.

My own research focuses on the neural and psychological basis of drug addiction and is dedicated to understanding the maladaptive engagement of the learning, memory, and motivational mechanisms underlying compulsive drug use. Drug abuse and addiction have devastating consequences at the individual, family, and society levels. My research group made significant advances in showing structural and neurochemical changes in the brain associated with behavioral impulsivity confer a major risk on vulnerability to develop cocaine addiction. We have also demonstrated the neural circuit basis of transition from recreational to compulsive use of opioids, stimulants, and alcohol, revealing commonalities as well as differences in the neural basis of addiction to these drugs. This understanding has opened the door to development of novel pharmacological and psychological treatments for addiction that may promote and maintain abstinence from drug use.

Dr. Chao's research efforts focus on growth factors (also called neurotrophins) in the brain. These proteins are crucial for everything from neuron differentiation, growth, and survival during development to learning and memory in children and adults. Deficits in neurotrophins are involved in neurodegenerative disorders such as Alzheimer's, Parkinson's and Huntington's diseases, and Amyotrophic Lateral Sclerosis (ALS), as well as limiting recovery after stroke or brain injury.

Dr. Chao and I cover different areas of neuroscience research, though we have come together to convey the need for further and ongoing investment in neuroscience research. SfN believes strongly in the research continuum: basic science leads to clinical innovations, which leads to translational uses impacting the public's health. Basic science is the foundation upon which all health advances are built. To cure diseases, we need to understand them through fundamental discovery-based research. However, basic research depends on reliable, sustained funding from the federal government. SfN is grateful to Congress for its investments in biomedical research and increases for NIH over the last six years. Growing the NIH budget over $12 billion in that period is exactly the kind of sustained effort that is needed, and your continued support will pay dividends for years to come.

The Importance of the Research Continuum

NIH funding for basic research is critical for facilitating groundbreaking discoveries and for training researchers at the bench. For the United States to remain a leader in biomedical research,

Congress must continue to support basic research that fuels discoveries as well as the economy. The deeper our grasp of basic science, the more successful those focused on clinical and translational research will be. We use a wide range of experimental and animal models not used elsewhere in the research pipeline. These opportunities create discoveries – sometimes unexpected discoveries – expanding knowledge of biological processes, often at the molecular level. This level of discovery reveals new targets for research to treat all kinds of brain disorders affecting millions of people in the United States and beyond.

NIH basic research funding is also a key economic driver of science in the United States through funding universities and research organizations across the country. Federal investments in scientific research fuel the nation's pharmaceutical, biotechnology and medical device industries. The private sector utilizes basic scientific discoveries funded through NIH to improve health and foster a sustainable trajectory for American's Research and Development (R&D) enterprise. Basic science generates the knowledge needed to uncover the mysteries behind human diseases, which leads to private sector development of new treatments and therapeutics. This important first step is not ordinarily funded by industry given the long-term path of basic science and the pressures for shorter-term return on investments by industry. Congressional investment in basic science is irreplaceable on the pathway for development of drugs, devices, and other treatments for brain-related diseases and disorders.

For example, in 2019, NIH launched – at Congress's direction – the cross-institute Helping to End Addiction Long-term (HEAL) Initiative to respond to the ongoing opioid public health crisis. Through this program, NIH supports the development of new medications to treat all aspects of the opioid addiction cycle and invests in preclinical and translational research in pain management. This work is vital to the translation of exciting new discoveries in the treatment of addiction. In our lab, we have shown a novel opioid receptor antagonist greatly decreases opioid, cocaine, and alcohol use in animal models, as well as showing its efficacy and safety in experimental studies in humans. We have further revealed reducing the impact of maladaptive drug memories can promote abstinence from drug use, as well as be effective in treatment of anxiety disorders and post-traumatic stress disorder (PTSD). The NIH, especially NIDA and NIAAA, supports the great majority of the global research on addiction and its treatment; this is a shining example of how governmental funding for research in the US leads the world and inspires related and collaborative research internationally on this major brain disorder.

Another example of NIH's success in funding neuroscience is the BRAIN Initiative. While only one part of the research landscape in neuroscience, the BRAIN Initiative has been critical in promoting future discoveries across neuroscience and related scientific disciplines. By including funding in 21st Century Cures, Congress helped maintain the momentum of this endeavor. Note, however, using those funds to supplant regular appropriations would be counterproductive. There is no substitute for robust, sustained, and predictable funding for NIH. SfN appreciates Congress' ongoing investment in the BRAIN Initiative and urges its full funding in FY22. Some recent exciting advancements in NIH funded neuroscience research include the following:

Personalized medicine for treating depression

Major depressive disorder (often referred to as "depression") is one of the most common mental disorders in the United States, affecting more than 17 million adults each year in the United States alone. While there have been great strides in pharmacological treatments for depression, a patient's response to any given antidepressant will vary widely based on their particular brain chemistry. A group of researchers funded by NIH recently used a machine learning algorithm to analyze patients' brain waves and predict their response to sertraline, a popular antidepressant. These data were taken from an NIMH funded study that used electroencephalography (EEG) to measure the brain's response to taking either a placebo or sertraline. Using an algorithm specially designed to analyze EEG data, the researchers were able to predict whether patients would respond to sertraline treatment based on brain waves measured

before treatment. This work is a critical step towards quickly determining the most effective treatment for patients based on their personal brain chemistry and illness.

Understanding how COVID affects the brain

In addition to its well-documented effects on the respiratory system, it has become clear that SARS-CoV-2, the virus responsible for COVID-19, has a profound effect on the brain, with neurological symptoms from dizziness and mental fogginess to encephalitis and stroke appearing in COVID-19 patients. SARS-CoV-2 has been found in the cerebrospinal fluid (CSF) of some of these patients, indicating the virus was able to cross into the brain. To understand how the virus could enter the brain, researchers with NIH COVID-19 research funding used stem cells created from human skin cells to make clusters of brain cells called organoids. These organoids were made of cells found in different areas of the brain, and the researchers found that SARS-CoV-2 had a high infection rate for cells from a specialized region called the choroid plexus. The choroid plexus is the region of the brain that creates the CSF cushioning the brain and spinal cord; it is known as a site of infection for other viruses. This finding provides a lead on the location through which SARS-CoV-2 may be entering the brain and a potential target for developing treatments of the neurological effects of COVID-19.

COVID-19 is a Challenge and Opportunity for Neuroscience Research

Unfortunately, the COVID-19 pandemic slowed progress in neuroscience research, with social distancing requirements hampering ongoing research related to the brain. Investment in neuroscience research, including on the neurological aspects of the SARS-CoV-2 virus and the COVID-19 pandemic itself is needed but cannot be allowed to eclipse or replace regular funding for neuroscience research. We urge you to identify ways to ensure current necessary funding increases to address the COVID-19 emergency do not slow progress on other important and innovative research, including the groundbreaking research in neuroscience and mental health. SfN is grateful Congress requested NIH seek to understand the psychosocial and behavioral health consequences of COVID-19. SfN encourages the Subcommittee to fund basic research on the biology of COVID-19 impacts on brain function as well as impacts on the nervous system in preclinical models and, by extension, on humans. In doing so, SfN encourages Congress and the NIH to prioritize intentional collaboration and coordination to effectively allocate scarce resources so researchers may investigate all facets of infectious and non-infectious disease.

Ongoing research already demonstrates the need for scientists to examine the neurological impacts of COVID-19. While mortality due to SARS-CoV-2 may be primarily due to its effects on the lungs, it is now apparent the virus damages many other organs, including the central nervous system. We need to understand how these direct and indirect effects on other organ systems are producing chronic diseases and long-term disability, making people more susceptible to other chronic disorders covered by the different NIH Institutes. A recent study (Lancet article, Taquet et al 2020) shows an increased risk of psychiatric conditions after COVID-19 diagnosis. Symptoms, such as anxiety, depression, post-traumatic stress disorder, and insomnia were reported. These data, though incomplete, suggest brain impairment occurs as a result of COVID-19 infection. Furthermore, it was found people with two copies of the risk gene for Alzheimer's disease were more likely to have severe COVID-19 (Kuo et al J. Gerontology 2020). These findings, coupled with incidents of memory loss, brain fog and hallucinations reported in the *New York Times* (3/23/21) demand increased resources to study the impact of this virus on the peripheral and central nervous systems, as well as the immune and inflammatory systems. The COVID-19 public health emergency provides an important example of the critical need for collaborative research and coordinating data and resources across institutes. A balanced and collaborative research effort across institutes will likely be the path toward solving these multiple issues.

Congress & NIH Must Support Access to Models Necessary for Neuroscience Discovery

Adequate NIH funding is necessary to advancing our understanding of the brain; however, full realization of this funding's promise requires appropriate access to research models, including non-human primate and other animal models. Animal research is highly regulated to ensure the ethical and responsible care and treatment of the animals. SfN and its members take their legal and ethical obligations related to this research very seriously. While SfN recognizes the goal of the reduction, refinement, and eventual replacement of nonhuman primate models in biomedical research, much more research and time is needed before such a goal is attainable. Premature replacement of non-human primate and other animal models may delay or prevent the discovery of treatments and cures—not only for neurological diseases like Alzheimer's disease, addiction, and traumatic brain injury, but also for communicable diseases and countless other conditions. There are currently no viable alternatives available for studying biomedical systems that advance our understanding of the brain and nervous system; or when seeking treatments for diseases and disorders like depression, addiction, Parkinson's Disease, and emotional responses. This research is critically important and has the opportunity to benefit countless people around the world. SfN urges Congress to work with the NIH to ensure this important research can continue.

Funding in Regular Order

SfN joins the biomedical research community supporting an increase in NIH funding to at least $46.1 billion for existing NIH institutes and centers, a $3.2 billion increase over FY21. This increase is consistent with those provided by this committee for the past few years and provides certainty to the field of science, allowing for the exploitation of more scientific opportunity, more training of the next generation of scientists, more economic growth and more improvements in the public's health. Equally as important as providing a reliable increase in funding for biomedical research is ensuring funding is approved before the end of the fiscal year. Your success in 2018 in completing appropriations prior to the start of the fiscal year was a tremendous benefit to research. Continuing Resolutions have significant consequences on research, including restricting NIH's ability to fund grants. For some of our members, this means waiting for a final decision to be made on funding before knowing if their perfectly scored grant will be realized, or operating a lab with 90 percent of the awarded funding until appropriations are final. All of the positive benefits research provides in this country may be negatively impacted by these real time considerations. SfN strongly supports the appropriation of NIH funding in a timely manner which avoids delays in approving new research grants or causes reductions in funding for already approved research funding. Meeting the example Congress set in 2018 would be another substantial benefit to science.

SfN thanks the subcommittee for your strong and continued support of biomedical research and looks forward to working with you to ensure the United States remains the global leader in neuroscience research and discovery. Collaboration among Congress, the NIH, and the scientific research community has created great benefits for not only the United States but also for people around the globe suffering from brain-related diseases and disorders. On behalf of the Society for Neuroscience, we urge you to continue this strong support of biomedical research.