STATEMENT OF
JOEL KUPERSMITH, M.D.
CHIEF RESEARCH AND DEVELOPMENT OFFICER
VETERANS HEALTH ADMINISTRATION
DEPARTMENT OF VETERANS AFFAIRS
BEFORE THE
DOMESTIC POLICY SUBCOMMITTEE,
OVERSIGHT AND GOVERNMENT REFORM
U.S. HOUSE OF REPRESENTATIVES

SEPTEMBER 29, 2010

Good morning Chairman Kucinich, Ranking Member Jordan, and Members of the Subcommittee. Thank you for inviting me to address the current state of neuroscience research, including efforts to discover and develop new treatments and diagnostic tools for brain and nervous system disorders. The Department of Veterans Affairs (VA) is committed to providing innovative, evidence-based approaches to clinical treatment that will provide our Veterans with the highest quality of care.

The rich history of more than 85 years of accomplishment by VA researchers has improved Veterans' lives and advanced the practice of medicine throughout the United States. VA has one of the largest medical research programs in the country, which includes close academic affiliations with major universities and medical schools nationwide. This year, nearly 3,400 VA researchers have worked on more than 2,300 studies and have been supported with nearly $1.9 billion in funding from all sources. We appreciate Congress' continued support of our research efforts. Today's dedicated VA researchers are focusing on traumatic brain injury (TBI), post-traumatic stress disorder (PTSD), post-deployment health, women's health and a host of other issues key to ensuring the well-being of our Veterans.

VA benefits from supporting many clinical researchers who are able to translate the latest research findings into improved patient care, and who use their knowledge of patient care to develop further studies. Neuroscience has for many years been a major VA research endeavor. One of the Nobel Prizes awarded to VA investigators was to Dr. Andrew Schally for work on neuropeptides, which are hormone-like substances produced by the brain. His work developed a whole new realm of knowledge concerning the brain's control over body chemistry.

My testimony today will discuss VA's neuroscience research programs, including our work on the DEKA prototype of the next-generation prosthetic arm, and VA's commitment to collaborate with other Federal partners.

VA's Research Programs

VA's Office of Research and Development (ORD) within the Veterans Health Administration has long served as a leader in supporting novel treatment approaches. It supports pre-clinical, clinical and health systems research, and benefits greatly from being embedded in VA's comprehensive health care system with state-of-the art electronic medical records. VA ORD funds investigator-initiated research at levels that encourage VA's best scientists to participate in Veteran-centric research, within ORD's intramural research program. Seventy percent of these VA research scientists are also clinicians who provide care to Veterans. The majority of projects submitted for funding consideration originate with these clinician–scientists who treat Veterans in their clinical activities and who design their research proposals in a manner that reflects the medical issues they encounter while making treatment decisions.

Within our intramural research program, VA supports scientifically meritorious research with the goal of improving the health care of Veterans. A VA scientist first submits an application according to standard requirements for the specific funding mechanism that is scientifically peer-reviewed to evaluate significance, approach, research feasibility, and other factors. If deemed to be highly meritorious, the proposal would be recommended for funding. VA also supports the development and training of new scientists specifically through a career development program that provides salary and research support to investigators just beginning their research careers. Under the provisions of the program, the awardee works closely with scientific expert mentors to conduct research on important topics. Career development awardees, including clinicians and non-clinicians, often make long-term career commitments to VA by moving from career development mentored awards to become independent established VA scientists. Currently VA is funding career development awards in many neuroscientific and psychiatric topics, including Parkinson's disease, TBI, PTSD, stroke, rehabilitation, substance use disorders, sensory loss, and spinal cord injury.

VA promotes research across the range of disorders and diseases affecting Veterans, but I will highlight our neuroscience work in a few areas: PTSD, Substance Abuse, TBI, Spinal Cord Injuries and advanced prosthetics. Collaborations within the field of neuroscience between and among relevant partners are occurring and are crucial to help advance research in these areas. VA investigators are widely supported by Department of Defense (DoD) collaborations and National Institutes of Health (NIH) grants, as well as others, on a variety of research projects.

Post Traumatic Stress Disorder Treatment Research

VA has led efforts to discover new PTSD treatments including a large cooperative clinical research trial focused on Prolonged Exposure Therapy. There is a great need to understand the psychological and biological impact of trauma exposure in the Veteran population to most effectively understand, prevent, and treat PTSD and other adjustment disorders. Current research efforts in this area are looking to advance our understanding of these adjustment disorders. VA is currently supporting over 100 studies focused on PTSD at a cost of more than $27 million, including research focused on women Veterans and across different deployment eras such as Vietnam Veterans and those from operations in Iraq and Afghanistan. Many efforts are also directed to further understand the reactions when a traumatic event or experience such as combat occur, because knowledge of accompanying chemical and physiological changes may lead to better prevention and treatment. Some of this work includes modeling PTSD pre-clinically or tracking physiological reactions in laboratory settings. Overall, VA is spending more than $80 million to support mental health research.

There are a number of challenges VA and others face in treating PTSD. These challenges include an insufficient evidence base for treatment effectiveness and the complications presented by the Veteran population, who may have more severe comorbidity issues. In response, VA is spearheading the national dissemination of two evidence-based psychotherapies that have proven to be the most effective treatments for PTSD—Cognitive Processing Therapy and Prolonged Exposure Therapy. These treatments have also been validated by the Institute of Medicine report on treatment for PTSD that established these were the best treatments for PTSD.

VA research directly affects patient care through guidelines developed jointly with the DoD. VA's National Center for PTSD (NCPTSD) engages in collaborative research and educational projects with DoD, including the current revision of the Joint VA/DoD PTSD Clinical Practice Guideline. All of VA's Clinical Practice Guidelines are created jointly with DoD. Other NCPTSD collaborative projects with DoD include a VA/DoD Mental Health Guideline Tool Kit Development and Guideline Implementation strategy. In this effort, VA's NCPTSD is working with DoD to optimize the use of VA and DoD resources to develop the best mental health clinical practice guideline tool kits and guidelines to facilitate the use of evidence-based mental health care for Servicemembers and Veterans. VA currently has 29 ongoing DoD-funded research grants in this area.

Substance Use Disorder Research

VA has also recently partnered with the NIH to solicit research proposals in the area of comorbid substance use disorders and PTSD in the Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veteran population. This solicitation resulted in funding for new programs, including four supported by VA with a focus on smoking patterns following deployment, readjustment for members of the National Guard, issues unique to women Veterans, and how to improve treatment. A few examples of treatments currently being studied include an inexpensive medication to relieve trauma-related sleep disturbances, a novel drug in an early stage to alleviate PTSD symptoms, complementary and alternative therapies for PTSD, and strategies to engage Veterans in early PTSD treatment.

Traumatic Brain Injury (TBI)

In fiscal year (FY) 2010, VA is providing approximately $19 million for TBI research. In FY 2010, VA started two Centers of Excellence (one in Houston, TX and the other in Boston, MA) and one Research Enhancement Award Program (San Francisco, CA) that are devoted to detecting and treating TBI. VA is very invested in researching mild to severe TBI and the many issues and unknown consequences that accompany this prevalent injury.

VA is at the cutting edge in developing methods for detecting mild TBI (mTBI) through the use of biomarkers, imaging, and eyetracking assessments. Eyetracking studies are being tested for diagnoses of mTBI. Nerve fibers involved in eye movements are susceptible to the injuries that may occur from exposure to blast, and this type of research could be a helpful detection tool in theater.

Researchers are also developing innovative therapeutics for brain repair to improve care. In addition, VA is funding research involving Veterans with TBI and:

- Detecting risks for suicide in this population, which is at greater risk for mental health-related issues and suicide;
- Studying the prevalence of co-morbid balance and hearing impairments related to TBI, because the sensory organs of the ear are extremely vulnerable to blast injury, and the ears contribute to both hearing and balance;
- Studying the efficacy of tele-rehabilitation, because VA realizes that access to care is essential, and VA is leading the way in telemedicine and tele-rehabilitation research and care;
- Understanding and meeting the needs of caregivers of TBI patients, because caregivers of these Veterans experience increased levels of emotional stress, impacting the caregiver's mental and physical health;
- Improving "awakening" in TBI patients with disorders of consciousness, particularly for Veterans with severe TBI that may have long-term disorders of consciousness;
- Studying how the effects of repetitive brain injuries combined with aging, on long-term brain health and whether these injuries can lead to neuro-degenerative diseases; and
- Investigating the links between PTSD and TBI and how these conditions can be differentiated to improve diagnoses.

Some of VA's basic neuroscience research on TBI is directed toward clinical issues that affect our Veterans. The principal role that VA plays in treating Veterans with TBI is to improve their lives and health as much as possible and to support their reintegration to society. VA research is supporting several projects in this area:

- A project to study the development of molecules with neurotrophic properties that can pass the blood-brain barrier to mediate brain repair after TBI.
- A project to study the effects of locomotor training on closed-head TBI-induced disabilities. Currently, there is not a clear understanding of the neurobiology of long-term cognitive, motor, and behavioral disabilities induced by TBI. Rehabilitation can enhance the recovery of these abilities, and this study will investigate the mechanism and impact of therapeutic locomotor training to significantly decrease the magnitude of TBI-induced disabilities.
- A collaborative project with the National Naval Medical Center to investigate a possible causal mechanism of TBI on PTSD using a rat model of mTBI to determine the neurobiological consequences of a blast injury.

Spinal Cord Injuries

VA is investing substantially in Spinal Cord Injury (SCI) research. For example, VA recently started an SCI consortium, led by some of VA's best researchers, to better address the needs of Veterans with these conditions. The Consortium's studies include regeneration genetics, imaging methods on regeneration and plasticity of nerves after injury, and the testing of combination therapies in non-human primate models of SCI.

Combination therapy is a major project being tested by VA researchers who are a part of the Consortium. Combination therapy uses "scaffolding" such as cartilage to plant stem cells to generate and grow spinal cells and repair the injury. This therapy is only in the phase of testing involving non-human primates. Another therapy being developed by VA researchers is Functional Electrical Stimulation (FES). FES applies low-level electrical currents to either generate or suppress activity in the nervous system. FES can stimulate physical or bodily functions to produce and control the movement of otherwise paralyzed limbs for standing and hand-grasping, activate visceral bodily functions such as bladder control or respiration, create perceptions such as skin sensitivity, help stop experiences such as pain or spasm, and facilitate natural recovery and accelerate motor relearning.

VA's FES Consortium and Center of Excellence (CoE) on FES is working in collaboration with the private educational institution of Case Western Reserve University

(CWRU) in Cleveland, Ohio, and the public hospital system of CWRU's Metro Health Medical Center. These researchers, engineers, and clinicians work to develop technological solutions, such as FES, that improve the quality of life of individuals with neurological or muscular skeletal impairments. This is a prime example of public-private collaborations resulting in promising research.

Another example of a collaborative effort is NIH's National Institute on Drug Abuse (NIDA) and VA's partnership on spinal cord injuries (SCI). Many military personnel returning from Iraq and Afghanistan experience pain. Pain is often co-prevalent with PTSD, persistent post-concussive syndrome, and sleep disorders; it interferes with daily functioning and adversely affects quality of life. Inadequate treatment opens the gate to analgesic misuse and substance use disorders. A prominent VA researcher is working on chronic pain conditions and how they relate to the abnormal activity of sodium channels. Sodium channels are an integral part of the nervous system and in transmitting messages. The normal activity of these channels can be disrupted following injury to the nervous system (e.g. spinal cord injury or multiple sclerosis), or to the pain receptors themselves (burns), leading to chronic pain. The researcher and his team are currently examining ways to alter the activity of the sodium channels and to develop novel non-opiate methods to treat chronic pain following injury and disease.

Another recent advance in the field of pain research involving VA indicates that an assessment called brain fMRI (functional magnetic resonance imaging) has the ability to determine functional activity-based measures of pain-related processes, the analgesic effect, and potentially the states of pain. Brain fMRI is non-evasive, uses no radiation and offers high quality results. This collaborative effort with NIDA fosters interactive and innovative partnerships between NIH imagers, investigators and VA pain clinicians. These teams unite the expertise of each Federal agency to achieve the following aims:

1) Detect, characterize and validate "fingerprints of pain" using imaging data in combination with self-report scales and other phenotypes of pain;

2) Harmonize the assessment of the effectiveness of various types of pain management techniques used at VA; and

3) Create a pain registry for comparative effectiveness research and to confront the complex cascade of the many associated conditions that Veterans with chronic pain have.

This approach, which combines the direct observation of bedside care and work in the laboratory, will enable a positive transformation of current advances in the science of pain and pain management into objective evaluation and prediction of drug responses and disease progression, development of novel non-opiate medication and intervention, and better patient care, matched to the needs of the individual. As the research evolves, these labors will help develop innovative concepts for the next stage of evidence-based studies and pave the way for new partnerships that share common interest and resources between the NIDA and VA.

VA Clinical Research of DEKA Arm
(Funded by DARPA with prototypes being produced by DEKA Research and Development Corporation)

The DEKA Arm initiative is an excellent example of the mutually beneficial results that occur when VA and DoD work collaboratively to better serve those who have lost arms in combat. This initiative, coordinated by VA in Providence, Rhode Island, consists of three VA sites and one DoD site, the Center for the Intrepid at Brooke Army Medical Center in San Antonio, TX. Twenty-one male and female research participants have completed the study, including Veterans and Servicemembers.

The Next-Generation Defense Advanced Research Projects Agency (DARPA) Prosthetic Arm System incorporates major technological advances such as flexible socket design and innovative control features, hardware, and software that together enable enhanced functionality that promises to surpass any currently available prosthetic device. Ongoing results of this VA clinical research are contributing to the design efforts leading to the optimization of a revised version of the Next-Generation DARPA Prosthetic Arm System. VA will employ a similar design to conduct usability research on the revised arm system. The expectation is that the results of these efforts will lead to commercialization of a refined, highly usable product. The DEKA Arms are

currently only being tested in research laboratories and are not yet available for Veterans to take home for use.

VA is planning additional follow-on studies in upper extremity prosthetics, particularly take-home trials pending the availability of arms. This is the final step in the research process prior to routine clinical provision of the arms to our Veterans and active duty Servicemembers. If the research is successful and the arms become commercially available, this will allow Veterans to obtain DEKA Arms through VA's Prosthetic and Sensory Aids Service in the VA Amputation System of Care. VA is also looking at the transition of these advanced prosthetics arms to additional applications, such as mounting on wheelchairs for Veterans with high-level spinal cord injuries, enabling the Veteran to control the arms to increase independence in activities of daily living. These innovations would not be possible without the collaboration of DoD and other Federal partners.

Brain Computer Interface

Another exciting development is the brain computer interface, also known as "BrainGate" research. This is an important effort that addresses questions of how Veterans with physical limitations can still engage the physical environment with their minds. For example, Veterans often use a joystick to control a powered wheelchair, but if they lose the use of their hands, brain computer interface research can help identify new methods to improve functionality. The concept behind this technology is that we can record the activity of single cells in the brain and then use computers to "decode" the neural signals into "commands". These commands could potentially be used to control mechanisms such as a computer mouse and its buttons or a wheelchair with a joystick.

Researchers are also looking at this technology for use by Veterans with high level spinal cord injuries or neurodegenerative conditions such as Amytrophic Lateral Sclerosis, where the Veteran can no longer use his or her arms and hands. Research has already demonstrated the feasibility of this technology to allow users to control computers and wheelchairs directly from signals in the brain. VA is just beginning a research study to see if a brain computer interface can control advanced prosthetic

arms. The DEKA arm is currently controlled by sensors mounted on the feet, so it can only be used when sitting or standing and not while walking. The hope is that in the future BrainGate technology will be available for controlling advanced prosthetic arms.

Artificial Retinal Implant

Another successful collaboration between VA and private facilities involves a project receiving support from Harvard Medical School, the Massachusetts Institute of Technology and Cornell University (Nanofabrication Lab) and VA's CoE on Innovative Visual Rehabilitation, which is working on an artificial retinal implant. This project is trying to develop a microelectronic retinal implant to restore functional vision to Veterans with certain forms of blindness, including age-related macular degeneration, which is the leading cause of blindness within the industrialized world and among U.S. Veterans; retinitis pigmentosa, which is the leading cause of inherited blindness in the world; and also retinal damage that accidentally occurs from exposure to range-finders, which are in widespread use by the military.

Recent accomplishments that will lead to development of a device for human implantation include:

- Successful animal implantation of a device which implemented new key features in the ability to wirelessly monitor the status of each electrode and its tissue interface, improving robustness of bi-directional communication to the implant;
- Detailed characterization of the electrochemical properties and charge-injection behavior of the iridium oxide electrodes over time in model body fluids at body temperature;
- New transmitter circuits for data telemetry, which deliver data wirelessly via an inductive link to the retinal prostheses; and
- A new system that may be used to extract visual features from the Veteran's environment that would be suitable for transmission to a retinal implant device.

Federal Collaborations

VA has extensive relationships with our Federal partners, particularly NIH and DoD, to ensure Veterans receive the most from research. VA's research partnership

with NIH is exemplified by the Deep Brain Stimulation (DBS) Study which VA is conducting in collaboration with NIH's National Institute of Neurological Disorders and Stroke. VA is proud to partner with NIH on this ongoing study which is the largest trial of its kind to date. This and other ground-breaking research on Parkinson's disease ensures that we provide the best care possible for Veterans with this common debilitating disease. VA cares for about 40,000 Veterans with Parkinson's disease. DBS is often recommended for people who no longer respond well to medication alone. In DBS, surgeons implant electrodes in the brain and run thin wires under the skin to a pacemaker-like device. Electrical pulses from the battery-operated device jam the brain signals that cause motor symptoms such as stiffness and tremors. Thousands of Americans have seen successful results from DBS, but questions have remained about which of two stimulation site in the brain yields better outcomes. The latest DBS study results, recently published in the New England Journal of Medicine, show that DBS is equally effective at either of two sites in the brain.

Since FY 2007, more than 80 VA researchers have been receiving over $70 million in funding on issues of importance to both DoD and VA. These issues include PTSD, TBI, prosthetics, rehabilitation, psychological health and well-being for military personnel and families, deployment-related injuries and illnesses, and polytrauma. VA and DoD also partner on several Centers of Excellence and serve on interagency committees related to research. VA and DoD share a common vision in studying military personnel from pre-deployment to post-deployment to better understand the population we serve. VA and DoD collaborate through every phase of research program management from planning new and targeted initiatives, collaborating on active research studies, sharing findings, reviewing portfolios and setting priorities. VA also participates actively on DoD Joint Program Committees for PTSD and TBI, and VA and DoD experts serve on scientific peer review panels for each Department.

VA partners with the DoD on the Defense Center of Excellence (DCoE) for Psychological Health and Traumatic Brain Injury. VA has co-located two VA-DoD liaisons and subject matter experts at DCoE, one for psychological health and another for traumatic brain injury. VA and DCoE jointly chair the Substance Abuse and Mental Health Services Administration (SAMHSA)-sponsored Federal Partners Reintegration

Work Group, which works to ensure improved transition of Veterans from active duty into civilian life, reducing stigma associated with mental disorders and other supportive activities.

Conclusion

Thank you again for this opportunity to speak about VA's work to better understand and treat neurologic and psychiatric diseases and injuries, specifically PTSD, substance use disorders and TBI. In our ongoing quest to deliver the latest in treatment, technology, and rehabilitation services to America's Veterans, VA supports robust basic, clinical and systems research efforts to develop an evidence-base for new approaches to health care. VA is proud to spearhead innovative research that improves the lives of Veterans, their families and caregivers, and ultimately many others in the Nation who benefit from VA's research advancements. I am prepared to answer any questions the Subcommittee might have.