NEW INITIATIVES

The National Research Action Plan
VA and the departments of Defense (DoD), Health and Human Services, and Education recently made public a wide-reaching plan to improve access to mental health services for Veterans, service members, and military families.

Once implemented, the plan will be used to improve scientific understanding of PTSD, TBI, various co-occurring conditions, and suicide. Other goals of the plan include providing effective treatments for these diseases, and reducing their occurrence.

Centers of Innovation/new QUERI projects
VA’s Health Services Research and Development Service (HSR&D) funded 19 new Centers of Innovation (COINs), effective Oct. 1, 2013.

The mission of the COIN program is to engage clinical and operations partners within the agency from the outset of VA health services research, and to thereby increase the work’s impact on Veterans’ health.

FROM THE CHIEF R&D OFFICER

Welcome to the first issue of VA Research Quarterly Update (VARQU)! As part of our effort to communicate the accomplishments and ongoing work of VA researchers, we have created this quarterly electronic newsletter specifically with VA leaders and other key stakeholders in mind.

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FROM THE CHIEF R&D OFFICER

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Every issue of VARQU will include information about new initiatives being undertaken by the Office of Research and Development (ORD); synopses of significant articles authored or co-authored by VA researchers that have appeared in prestigious scientific and medical journals; brief summaries of news articles about VA research and our researchers; and mentions of awards and honors our clinician-investigators have received in recent months. We’ll also include a question-and-answer session with one or more of our scientists—sometimes, along with their collaborators from partnering agencies—on a timely issue.

Each of our e-newsletters will be organized around a theme related to improving care for Veterans, and most of the items you’ll read about in that issue will be relevant to that theme. This issue focuses on Caring for the Returning Service Member.

Among the areas of investigation our researchers are vigorously pursuing are finding ways to address Veterans’ mental health issues, including posttraumatic stress disorder (PTSD); continuing research into traumatic brain injury (TBI) and its treatment; developing and testing prosthetic components to optimize health and independence; and helping Veterans with polytrauma (multiple

NEW INITIATIVES

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The National Research Action Plan

“At VA, ensuring that our Veterans receive quality care is our highest priority,” Secretary Eric K. Shinseki said in announcing the completion of the plan. “Investing in innovative research that will lead to treatments for PTSD and TBI is critical to providing the care our Veterans have earned and deserve.”

Among the highlights of the plan is the establishment of two joint DoD/VA research consortia at a combined investment of $107 million. These include the Consortium to Alleviate PTSD, a collaboration led by the University of Texas Health Science Center—San Antonio, and the Chronic Effects of Neurotrauma Consortium, led by Virginia Commonwealth University.

All four federal agencies will continue collaborations with academia. They will also standardize, integrate, and share data as appropriate, build new tools and technologies, and work to maximize the impact of research findings.

Among the specific goals for the next two to four years are exploring genetic risk factors for mental health conditions; identifying changes in brain circuitry that result from PTSD and TBI; confirming biomarkers for PTSD and TBI; and establishing new data-sharing agreements.

Centers of Innovation/new QUERI projects

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COIN researchers will conduct innovative studies in targeted areas that contribute to improvements in VA care, enhance research collaborations within and across medical centers, encourage innovative contributions by independent researchers, and facilitate the implementation of research findings. COINs will also help VA continue to transform itself into a continuous learning health care system.

The 19 COINs are located in Ann Arbor, Mich.; Bedford and Boston, Mass.; Charleston, S.C.; Durham, N.C.; Hines, Ill.; Houston, Texas;
NEW INITIATIVES

At the COIN based in Little Rock, researchers are studying how to best provide mental health care via videoconferencing, among other topics. (Photo by Jeff Bowen)

Indianapolis, Ind.; Iowa City, Iowa; Los Angeles, Calif.; Minneapolis, Minn.; North Florida/South Georgia and Tampa; North Little Rock, Ark.; Palo Alto, Calif.; Pittsburgh and Philadelphia, Pa.; Portland, Ore.; Providence, R.I.; Salt Lake City, Utah; Seattle, Wash.; Denver, Colo.; and West Haven, Conn. (Three of the COINs are partnerships between two different VA medical centers.)

To help further ensure that VA research has the greatest possible impact on VA care, HSR&D announced three funding opportunities relating to partnership-oriented research under the Quality Enhancement Research Initiative (QUERI).

The first of these opportunities is partnered rapid-response projects, which is QUERI’s principal mechanism to study the process of implementing new treatments or care processes. The second is service-directed projects, which focus on improving care by facilitating the adoption of new treatments or care processes in VA. The third is partnered evaluation centers, which are created in conjunction with a VA operational partner and are designed to aid the evaluation and implementation of new national VA initiatives.

The Journal of General Internal Medicine will be publishing a special supplement on VA partnered research in December 2014. A call for abstracts for the publication was sent out in November 2013, with manuscripts due in March 2014.

FROM THE CHIEF R&D OFFICER

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complex, severe injuries) to regain as much function, independence, and quality of life as possible.

I hope you find the information in this issue useful. Please feel free to email me or Mitch Mirkin in VA Research Communications (mitch.mirkin@va.gov) if you have any comments on this issue or suggestions for future issues. Thank you for your interest in VA research.

Timothy O’Leary, MD, PhD
Acting Chief Research & Development Officer

IN THE NEWS

Dr. Maurice Dysken, geriatric psychiatrist at the Minneapolis VA Health Care system, led a VA study testing vitamin E and other treatments for Alzheimer’s disease. (Photo by April Eilers)

A VA cooperative study on Vitamin E for Alzheimer’s disease made headlines worldwide on the last calendar of 2013, with print and broadcast stories produced by United Press International, the Associated Press, and dozens of major print and broadcast news outlets around the globe. The study

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found that vitamin E, known for its antioxidant power, helped slow brain decline among older people with mild to moderate Alzheimer’s disease. The study involved 613 Veterans at 14 VA medical centers and was led by Maurice Dysken, MD, of the Minneapolis VA Health Care System.

VA research instrumental in development of new guidelines for cholesterol-lowering medicines—Research conducted by several VA investigators was instrumental in the development of new guidelines to help providers determine when and whether to prescribe cholesterol-lowering medications for their patients. Among the news outlets covering this story were CNN, The New York Times, and Time magazine. Instead of basing prescriptions on a patient’s low-density lipoprotein (LDL) level—the “bad” cholesterol that can lead to heart attack and stroke—new guidelines suggest that providers calculate their patients’ risk of having a heart attack in the next 10 years based on factors including age, cholesterol levels, blood pressure and blood pressure medication use, diabetes status, and smoking status. Rodney Hayward, MD; Timothy P. Hofer, MD, MSc; and Sandeep Vijan, MD, all of the VA Ann Arbor Center of Excellence for Clinical Management Research, are among the VA researchers who

VA and DoD team up to study trazodone for PTSD

VA, through its Cooperative Studies Program, and the Department of Defense (DoD) are developing a joint multisite trial under an interagency agreement to evaluate the drug trazodone hydrochloride as an adjunct to antidepressants for the treatment of combat-related PTSD in Iraq and Afghanistan Veterans. Study chairs Lieutenant Colonel Gary Wynn, MD, of the U.S. Army, and John Krystal, MD, of the VA Connecticut Healthcare System and Yale Medical School, provided details in an interview.

VARQU: Would you briefly describe the project your team is undertaking?

Krystal: This project is the result of a “think tank” organized from leaders in the PTSD field that tried to identify a high-priority medication that was already approved by the Food and Drug Administration (FDA) for other psychiatric disorders, and that was very commonly prescribed for the treatment of PTSD, but for which no definitive data existed regarding its efficacy for that treatment. This process identified the drug trazodone.

Trazodone is very widely prescribed to reduce sleep disturbance, nightmares, and other symptoms of PTSD, and it is approved for the treatment of depression and widely prescribed for other kinds of sleep impairments. Trazodone, unlike the typical sleep medication, is not an addicting medication, and its track record in clinical experience is suggestive of effectiveness for PTSD. This made it a very attractive medication to study.

We propose to test the effectiveness of trazodone as a treatment for PTSD by comparing it to an inactive medication, or placebo, during 12 weeks of treatment. We’re going to be studying OIF/OEF/OND active-duty military personnel with PTSD as well as Veterans with PTSD.

Wynn: The gap between our clinical experience and hard data on trazodone for PTSD is so enormous that it cries out to be studied in order to be
A CHAT WITH OUR EXPERTS

What’s the current status of the project, and when do you expect it to be completed?

**Wynn:** We have submitted the project to the VA Central Institutional Review Board (IRB) and have had our first discussions. We still have to go through the DoD Central IRB, and hold discussions with the FDA, and then we will get to the point of starting.

Our current projection to start is the summer of 2014, and we have set it up so that the project will be completed within one year. So all the recruitments and study will be done within a 12- to 14- month window—the summer of 2015—with results available to leadership a couple of months afterwards, and then publication, hopefully, in 2016.

Currently, we have 25 VA study sites that are going to come online and one DoD consortium that will be working. A large single DoD site and a diffuse network of VA sites will together provide the research capacity and subjects that will allow us to complete the study within a one-year period of time.

What would you consider a positive result of this study, and how would this positive result benefit service members and Veterans?

**Krystal:** I’d like to see the medication show that it can reduce the symptoms of PTSD, and I’d be thrilled if we could also show there was a beneficial overall impact on the quality of life of these military personnel and Veterans. The way we measure reductions in PTSD symptoms is to use a very well-validated rating scale that was developed by VA’s National Center for PTSD for the assessment of PTSD symptoms. And the way we evaluate overall quality of life is by the use of other rating scales that tell us how meaningful the clinical change was for the lives of military personnel and Veterans.

**Wynn:** No matter whether or not we find that trazodone works for PTSD, the results will still be important. If we get a negative result, we can inform providers that the use of trazodone may not be helping PTSD symptoms. That is still important to know, in the sense that this new knowledge would influence practice. We think it’s going to work, and if it does, that will validate years and decades of clinical experience.

IN THE NEWS

Ann McKee, MD, co-director of the VA Center for the Study of Traumatic Encephalopathy in Bedford, Mass. was cited in an article appearing in newspapers throughout Wisconsin for her work in examining the brains of dozens of former National Football League players, and finding signs of a degenerative brain disease in athletes with a history of concussions. In her studies of athletes, Veterans, and others, she has found a link between multiple blows to the head and chronic traumatic encephalopathy (CTE). CTE is associated with memory loss, confusion, impaired judgment, paranoia, impulse control problems, aggression, and progressive dementia.

Dr. Ann McKee, seen here presenting to medical students, oversees several brain banks for the Bedford (Mass.) VA Medical Center and Boston University. (Photo by Frank Curran)

The West Haven (Conn.) VA Medical Center held an all-day conference on Oct. 30, 2013, to mark the 25th anniversary of the founding of the Center for Neuroscience Continued on page 6
Krystal: I would add that I have led several large studies in the past that have had similar aims: trying to show the effectiveness of understudied and often underutilized medications. The reality is that these studies are not always positive. A negative study, one that has failed to find that the medication was effective, can serve to divert treatment away from an ineffective medication towards other medications that are likely to be more effective for the symptoms. So even a negative result can improve care for military personnel and Veterans.

What are the advantages of working together with another federal agency on a research project, and are there any disadvantages?

Wynn: The advantages for us have been enormous. VA brings decades of experience in running large, multisite clinical trials, and has very seasoned, experienced researchers who have an understanding of the intricacies of these kinds of projects. On the DoD side, we don't have experience at that level. We have some experience, but not the 40-plus years of methodological research that the VA Cooperative Studies Program has. They bring to the table such an amazing skill set.

We bring a variety of assets as well, so there's a lot of collaborativeness that's just great. The challenge is that we're two large federal agencies with our own sets of policies and practices and our own cultures. When you mix into this that we're doing this as a well-regulated FDA trial, we now have three large federal agencies trying to work together.

It has been an interesting and, at times, challenging experience to navigate inter-institutional complexities, but the benefits have far outweighed the problems we've had. We're working out the kinks and laying the groundwork for future studies of this type.

Krystal: I would say that one of the best parts of this project has been my developing friendship and collaboration with LTC Wynn; this project has been both an enjoyable and productive collaboration.

We recognize that PTSD is an area in which we have very limited options, especially in terms of validated medication treatment, and that this is a critical gap in our treatment portfolio, and the kind of study we're talking about could have a direct and significant impact on the treatment of PTSD. So it makes it a very exciting activity to pursue.
Why women in combat may develop PTSD at a greater rate than men—Researchers led by Melissa A. Polusny, PhD, of the Minneapolis VA Health Care System and the University of Minnesota questioned 712 male and 89 female National Guard members both before and after combat tours in Iraq or Afghanistan. They found 22.5 percent of the women, compared to 12.2 percent of the men, met screening criteria for probable PTSD following deployment. This is consistent with previous studies.

The researchers hypothesized that some of this disparity could be traced to pre-deployment events, such as sexual stressors. They didn’t find a direct correlation, but they did find that women who had undergone trauma before being deployed had an increased risk of developing PTSD after exposure to combat, relative to other women in combat. This was not true in men. The researchers also learned that men who relied on their military unit as a source of support but were disappointed by the support they received were more likely to develop PTSD than were women in similar situations. Another key finding was that women who had undergone combat-related stressors, such as being injured in war, were more likely than men to develop PTSD as a result.

Polusny and her colleagues also found evidence suggesting that deployment may be particularly stressful for female military service...
HONORABLE MENTIONS

BrainGate team awarded $1 million prize—A team of VA and Brown University researchers won a $1 million prize for their work in developing a brain-computer interface that could help restore independence for people with severe paralysis. The prize was offered by the Moshe Mirilashvili Memorial fund, and was presented by Israeli President Shimon Peres in Tel Aviv in October 2013. The prize is awarded for a recent breakthrough in the field of brain technology. The investigation-

(From left) Drs. Arto Nurmikko and John Donoghue accept a bronze brain statue, part of the $1 million Moshe Mirilashvili Memorial Fund B.R.A.I.N. Prize, from Israeli President Shimon Peres.

al brain-computer interface that received the award, called BrainGate, uses a small device about the size of an aspirin with an array of 1,000 tiny microelectrodes that is implanted in the brain to pick up brain signals and enable the user to control a robotic arm or other assistive device using only his or her thoughts.

Donoghue, Boninger, elected to IOM membership—Michael L. Boninger, MD, co-director of the Rehabilitation Research and

NOTEWORTHY PUBLICATIONS

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members who must manage their lives and family responsibilities from afar, potentially exposing them to the dual stress associated with both war zone and family-related concerns. The authors caution that the study’s scope included a relatively small subset of mostly Caucasian women. Therefore, the findings are tentative and require replication. (Journal of Psychiatric Research, published online Dec. 2, 2013)

How Boston-area Veterans with PTSD were affected by the Boston Marathon Bombing—Many Veterans living in the Boston area who have been diagnosed with PTSD experienced flashbacks, unwanted memories, and other psychological effects as a result of the bombing that took place near the finish line of the Boston Marathon in April 2013, according to VA’s National Center for PTSD.

Researchers conducted 71 telephone interviews within a week of the bombing. Because they had symptom data from Veterans they had interviewed two months previously, they were able to compare their level of PTSD symptoms with results from the interviews.

Of those interviewed, 38 percent reported that they were emotionally distressed by the bombing and the subsequent lockdown of Boston and other communities. A majority of those participating said the bombing caused them to experience flashbacks and the reemergence of unwanted memories related to their own past trauma.

“This study highlights the fact that tragic local and national events of this type can have a significant impact on the health and well-being of individuals already suffering with PTSD,” said lead investigator Mark Miller, PhD, staff psychologist for the National Center for PTSD’s Behavioral Science Division in Boston. “It is crucial that relevant health care organizations are prepared in the wake of tragedy to care not only for those who are directly impacted, but also for those with preexisting psychological conditions, including our nation’s Veterans.” (Journal of Traumatic Stress, Dec. 2013)

A blood test to predict suicide risk?—A series of ribonucleic acid (RNA) biomarkers in blood may help identify people at risk for committing suicide, according to researchers at the Richard L.
Roudebush VA Medical Center in Indianapolis, Ind., and Indiana University. The biomarkers were found at significantly higher levels in the blood of both bipolar disorder patients with thoughts of suicide as well as in a group of Veterans and other people who had committed suicide. All of the research subjects were men.

Principal investigator Alexander B. Niculescu III, MD, PhD, believes the research offered the first “proof of principle” for a blood test that could provide an early warning of someone who would be at higher risk for an impulsive suicide act. He and his colleagues followed a large group of patients diagnosed with bipolar disorder, completing interviews and taking blood samples every three to six months. They found that the marker SAT1 and a series of other markers provided the strongest biological signal associated with suicidal thoughts.

Then they worked with the local coroner’s office to take blood samples from suicide victims, and found that some of the same markers were significantly elevated. Finally, they analyzed blood test results from two additional groups of patients and found that high blood levels of the biomarkers were correlated with suicide-related hospitalizations as well as hospitalizations that had occurred before

Continued on page 10
Although the study’s design had a number of limitations, such as being limited only to men, Niculescu hopes that biomarkers ultimately can help identify people at risk of suicide. This, along with tools including neuropsychological tests and socio-demographic checklists, can lead to preemptive intervention and counseling—and to saved lives. (Journal of Molecular Psychiatry, Dec. 2013)

Do Veterans like the DEKA arm?—Twenty-two percent of new military amputees have upper limb amputations. To meet their needs, the Department of Defense’s Advanced Research Project Agency (DARPA) worked with DEKA Research and Development Corporation to develop the DEKA arm.

The lightweight arm enables amputees to perform a range of tasks, from picking up a key to using a power drill. It has pre-programmed grip levels in its hand segment, and allows users to raise, twist, and bend their arm almost as they would their natural limb.

The DEKA arm was initially tested and refined in a multiyear, multisite, VA-funded study. In the most recent report from that study, led by Linda Resnik, PT, PhD, of the Providence VA Medical Center, 24 upper-limb amputees were fitted with a second-generation (Gen 2) DEKA arm and 13 were fitted with a third-generation (Gen 3) arm, and were surveyed about their experiences after being trained on its use.

In all, 79 percent of Gen 2 and 85 percent of Gen 3 users indicated that they either wanted to receive, or might want to receive, a DEKA arm. In addition, 95 percent of Gen 2 users and 91 percent of Gen 3 users indicated that they were able to perform new activities they had been unable to perform with their own prosthetic device. (Prosthetics and Orthotics International, published online Nov. 28, 2013)

Editorial asserts need for more pain education among clinicians—When the term “Pain as the Fifth Vital Sign” was initially promoted by the American Pain Society in 1996 to raise awareness of pain treatment among health care professionals, VA quickly incorporated the slogan into its own philosophy of care.

VA developed an extensive toolkit to implement pain assessment and management in all its patients, and the Joint Commission, which
NOTEWORTHY PUBLICATIONS

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Fred Downs Jr., former chief of prosthetics and sensory aids for VA, wears the DEKA prosthetic arm as he shares a “fist bump” with Col. Geoffrey Ling of the Defense Advanced Research Projects Agency during National VA Research Week 2012. (Photo by Emerson Sanders)

accredits health care facilities, recommended in 2000 that pain be assessed in all patients throughout the nation.

In a recent editorial, Natalia E. Morone, MD, and Debra K. Weiner, MD, of the VA Pittsburgh Healthcare System and the University of Pittsburgh argued that the increased focus on assessing and documenting pain has had unintended consequences. They point out that there has been a near doubling of prescriptions of opioid medication in the last two decades, and an increase in prescription opioid-related unintended deaths.

The authors assert that the “fifth vital sign” has proved to be more complex to assess, evaluate, and manage than the American Pain Society, VA, and the Joint Commission originally anticipated. They argue that expanding pain education and training among clinicians is critical to remedy the issues that have emerged. (Clinical Therapeutics, Dec. 2013)

HONORABLE MENTIONS

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robotic and intelligent systems “are likely to transform the quality of life and independence of people for years to come.” Cooper, an Army Veteran who himself uses a wheelchair for mobility, is the founding director of VA Human Engineering Research Laboratories, located at the Pittsburgh VA Medical Center.

OTHER RECENT PUBLICATIONS


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VA Research Currents provides Veterans, the general public, and other stakeholders of VA research with news about research results, new initiatives, major awards, research funding, and other matters of interest. The newsletter is updated frequently on our website and produced in print four times per year. Archived issues dating back to 2004 are available on the website.

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