

Study finds neuropsychological effects from Iraq deployment

Troops who served in Iraq showed mild deficits in some tasks of learning, memory and attention, compared to non-deployed troops, but scored better on a test of reaction time, according to research by a team from VA, the U.S. Army, and other institutions. The study—the first to include pre- and post-deployment neuropsychological assessments for American troops—appears in the Aug. 2 issue of the *Journal of the American Medical Association*.

According to lead author Jennifer Vasterling, PhD, the effects seen in the study may be temporary—the remnants of an adaptive stress response common to those in or near combat, or any life-threatening situation.

“The pattern of neuropsychological findings revealed in this study is remarkably similar to what might happen, at least transiently, as part of a biological stress response, sometimes known as the ‘flight or fight’ response,” said Vasterling, of the Southeast Louisiana Veterans Health Care System and Tulane University School of Medicine.

The deployed troops also reported more tension and confusion. While their neuropsychological changes persisted even after the researchers adjusted for symptoms of posttraumatic stress disorder and depression—as well as for head injury—it remains unclear

whether the changes may be early signs of PTSD. The post-deployment assessments were done only two or three months after the troops had returned stateside, so it could be the neuropsychological changes they experienced will fade over time, said Vasterling. PTSD is often seen as the outgrowth of a normal adaptive response that continues even after the traumatic situation is over.

“People have a certain biological, psychological adaptation to combat that’s very appropriate,” said Vasterling. “But when it’s perpetuated years after the life-threatening situation, it isn’t so

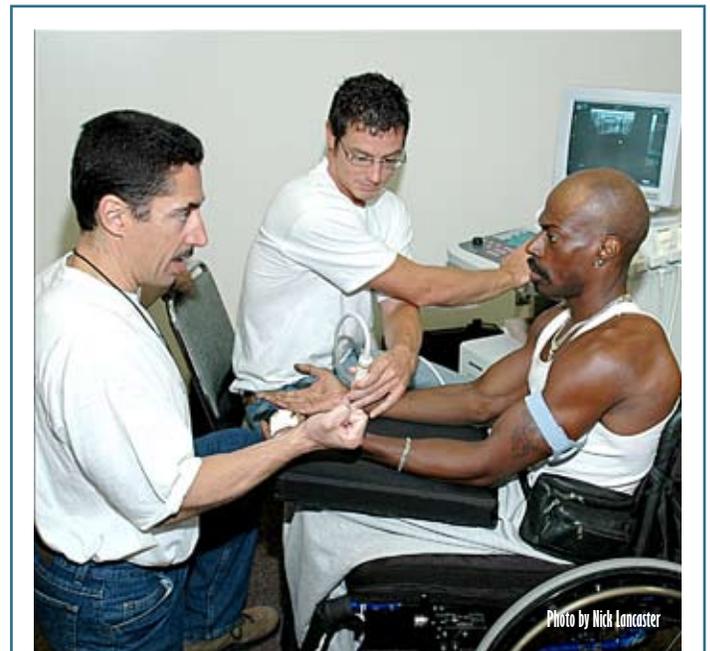
see **IRAQ** on pg. 5

Conference on human subject protection

A two-day VA conference titled “Local Accountability for Human Research Protection in VA facilities” will take place Sept. 6–7 in Baltimore; Sept. 13–14 in San Francisco; and Nov. 29–30 in St. Louis. The event is presented by the Center on Advice and Compliance Help (COACH), an arm of VA’s Program for Research Integrity Development and Education (PRIDE).

According to PRIDE director Lynn Cates, MD, the event “will focus on the concept that a facility’s human research protection program has many important responsibilities in addition to having an IRB [Institutional Review Board] of record.”

see **CONFERENCE** on pg. 3



Veterans participate in research at Wheelchair Games

Brad Impink (center), a fellow at VA’s Human Engineering Laboratories and the University of Pittsburgh, administers an ultrasound to the wrist of Johnny Lee Williams, a wheelchair athlete participating in last month’s National Veterans Wheelchair Games in Anchorage, Alaska. Instructing Williams is Col. Raul Marin of Walter Reed Army Medical Center. On the veteran’s arm is a sensor that measures energy expenditure, duration of physical activity, and other parameters. As part of a study on the role of manual wheelchair propulsion in arm pain and tissue degeneration, the researchers took ultrasounds of participants’ wrists and shoulders before and after they propelled their wheelchairs at a constant rate for 10 minutes.

In pilot trial, paralyzed man operates cursor through brain waves

Researchers with Brown University, VA and other sites reported in the July 13 issue of *Nature* on new technology that allowed a 25-year-old quadriplegic to operate a computer cursor and perform other tasks simply through his thoughts.

The system, called “BrainGate,” uses a tiny sensor implanted in the primary motor cortex, the area of the brain that controls movement. The sensor’s hair-thin electrodes pick up brain signals and send them to an external decoder that translates them into commands for electronic or robotic devices.

Still in the early phases of human testing, the technology has been spearheaded by John Donoghue, PhD, a Brown neuroscientist who became affiliated with VA when the agency established its Providence-based Center for Restorative and Regenerative Medicine in 2004. Donoghue is also chief scientific officer at Cyberkinetics Neurotechnology Systems, a company formed by Brown scientists in 2001 to bring the BrainGate system to market.

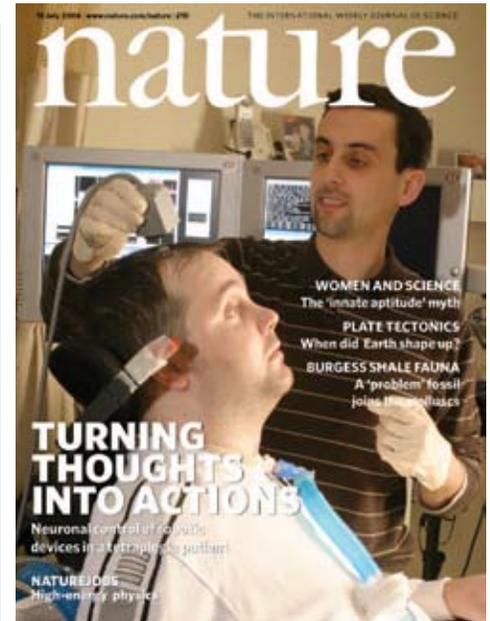
The *Nature* article details the pilot-trial experience of a 25-year-old man whose spinal cord was severed when he was stabbed in the neck in 2001. BrainGate enabled the man to operate a cursor solely through his thoughts, and thereby perform tasks such as opening email, drawing a circle—albeit

somewhat roughly—on a screen, and adjusting the volume on a television set, even while carrying on a conversation. The man was also able to open and close a prosthetic hand and use a robotic arm.

According to the researchers, the trial produced three main findings, some of which replicate earlier findings from primate studies:

- Electrical movement signals persist in the primary motor cortex even years after a spinal cord injury.
- These signals can be recorded, routed outside the brain, and decoded into command signals.
- Paralyzed humans can successfully operate external devices using these command signals.

“What’s truly exciting is [that] the cortical activity of a person with spinal cord injury, controlling a device by intending to move his own hand, is similar to the brain activity seen during preclinical trials of monkeys actually using their hands,” said lead author Leigh Hochberg, MD, PhD. “Whether it is real or attempted movement, neurons seem to respond with similar firing patterns.” Hochberg is with VA, Brown, Massachusetts General Hospital, Brigham and Women’s Hospital, and Harvard Medical School.



The cover of the July 13 issue of *Nature*, featuring work by investigators at Brown University and the Providence VA.

The trial participant kept the implant nine months, apparently with no ill effects. “The brain accepted it very well,” said Donoghue. “It’s removable and replaceable.” The authors note, however, that the signals from the implant did decline after nearly seven months of use.

More research is needed, said Donoghue, to develop a wireless system with a sensor that can stay in the brain many years, and to refine the software that decodes users’ brain signals. The ultimate goal, he said, is to “reconnect brain to limb.”

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Call for abstracts for HSR&D national meeting

VA’s Health Services Research and Development Service (HSR&D) will hold its next national meeting Feb. 21–23, 2007, in Washington, D.C. The theme will be “Managing Recovery and Health through the Continuum of Care.”

Investigators who conduct health-services research focused on veterans are invited

to submit abstracts in one of the following subject areas: access; clinical and system improvements; cost-effectiveness; function; healthy communities; quality; satisfaction; or statistical methods. Detailed instructions for electronic submission of abstracts will be available next month on the HSR&D website: www.hsr.d.research.gov.

Alternative kidney test reveals hidden health risks

Elevated blood levels of the protein cystatin C accurately predict higher risks of chronic kidney disease, cardiovascular disease, and death among elderly people with no known kidney problems—risks that the standard creatinine kidney function test misses entirely, according to a study led by a researcher at the San Francisco VA Medical Center.

“For the clinician who treats older people or others at risk for kidney disease, this is an important message that a normal creatinine should not reassure you that your patient has normal kidney function,” said lead author Michael Shlipak, MD, chief of general internal medicine at the San Francisco VA and associate professor of medicine, epidemiology, and biostatistics at the University of California, San Francisco. “It shows that cystatin is a very promising new tool that complements creatinine in the ongoing effort to detect early kidney disease and prevent its complications.”

The study appears in the August issue of the *Annals of Internal Medicine*.

Shlipak and his colleagues tested blood samples from 4,663 community-dwelling elders who participated in the Cardiovascular Health Study, a national longitudinal study of people aged 65 and older sponsored by the National Institutes of Health.

The researchers measured each participant’s creatinine—an end-product of muscle metabolism that is filtered through the kidneys and has been a standard marker of kidney health for “probably 100 years,” according to Shlipak—and cystatin C, a blood protein also filtered through the kidneys.

They then matched test results with health outcomes up to nine years later.

Among participants with no diagnosed chronic kidney disease, those with high cystatin C had significantly greater risks for poor health outcomes than those with low cystatin C. Individuals in the high-cystatin group were 50 percent more likely to die, nearly twice as likely to die of cardiovascular problems, and 30 percent more likely to die of non-cardiovascular problems.

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CONFERENCE (from pg. 1)

Among the topics to be covered at the training is VA’s upcoming centralized IRB, which the Office of Research and Development expects will be especially helpful to investigators on multi-site studies, and to smaller research programs that do not have their own local IRB. Cates said 54 percent of VA facilities that conduct human research do not have their own IRB—they typically use the IRB of their academic affiliate, or another VA—and many of these sites will be using the Central IRB when it is available.

“We’ll be giving a high-level view of the Central IRB,” said Cates. “It’s not operational yet, and it will be a while before it is. It is just one of many topics at this meeting, but the whole conference is designed to provide a strong foundation for the VA Central IRB.”

The conference will offer an overview of the responsibilities of medical centers, IRBs, R&D committees, and investigators, and feature discussion of many timely and related topics. Among them are cybersecurity and privacy; research impropriety; reporting of adverse events; knowledge of local research context; database research; Memoranda of Understanding; conflicts of interest; and international research.

Cates said that while a wealth of information will be provided at the conference, one of the main goals for her and COACH director Marisue Cody, PhD, is to ensure that participants realize there is ongoing support available for them when they go back to their facilities.

Said Cates, “We plan to be sure they know they can contact us for help.”

For more information on PRIDE, go to the program’s page on the VA research website: www.research.va.gov/programs/pride.

Message from the CRADO

‘A new era of increased accountability...’

By Joel Kupersmith, MD, chief research and development officer

A recent letter to VA field staff from the Office of the Under Secretary for Health discussed VHA’s standards and record of achievement concerning the careful handling and protection of sensitive information related to veteran patients and beneficiaries.

I want to emphasize that clinical investigators and all those involved with research need to hold to these same high standards. According to the Principal Deputy Under Secretary for Health, we have entered into a new era of increased accountability and responsibility. This requires all of us to closely review our policies and practices—and in some cases, change the way we work—to ensure that sensitive information entrusted to us is protected. It is crucial that everyone follow the guidance that this office has provided (available at www.research.va.gov/resources/policies/cybersecurity.cfm) and that you will receive from your facility. Together, we must ensure that the protection of sensitive information remains an utmost priority in all that we do. ■

Recent publications and presentations by VA investigators

Below is a sampling of recent publications and presentations by VA investigators, based on notifications received by R&D Communications (see reporting requirements at www.research.va.gov/resources/policies/pub_notice.cfm.) Every attempt is made to present a cross section of investigators, topics and medical centers. Only VA-affiliated authors are listed here, due to space constraints.

“The Association of Alcohol Consumption and Incident Heart Failure: The Cardiovascular Health Study.” Chris L. Bryson, MD, MS. **Seattle**. *Journal of the American College of Cardiology*, July 2006.

“Barriers to Obesity Management: A Pilot Study of Primary Care Clinicians.” Terry L. Wahls, MD. **Iowa City**. *BMC Family Practice*, June 6, 2006.

“The Cancer and Leukemia Group B Cancer in the Elderly Committee: Addressing a Major Cancer Need.” Harvey Jay Cohen, MD. **Durham**. *Clinical Cancer Research*, June 2006.

“Detecting Depression in Culturally Diverse Populations: Validity of Short Forms of the Geriatric Depression Scale.” Shawkat Dhanani, MD, MPH. **West Los Angeles**. UCLA Center on Aging Research annual conference, June 20, 2006.

“Differential Infection of Mononuclear Phagocytes by *Francisella tularensis*: Role of the Macrophage Mannose Receptor.” Lee-Ann H Allen, PhD. **Iowa City**. *Journal of Leukocyte Biology*, June 2006.

“The E-Cadherin -160 C/A Polymorphism and Prostate Cancer Risk in White and Black American Men.” Z. Laura Tabatabai, MD; Yuichiro Tanaka, PhD; Rajvir Dahiya, PhD. **San Francisco**. *The Journal of Urology*, Aug. 2006.

“Effect of Cell Culture Conditions on the Anticytomegalovirus Activity of Maribavir.” Sunwen Chou, MD. **Portland**. *Antimicrobial Agents and Chemotherapy*, July 2006.

“End-of-Treatment Outcomes in Cognitive-Behavioral Treatment and 12-Step Substance Use Treatment Programs: Do They Differ and Do They Predict 1-Year Outcomes?” John W. Finney, PhD; Rudolf H. Moos, PhD. **Palo Alto**. *Journal of Substance Abuse Treatment*, July 2006.

“Fibric Acid Derivatives in Cardiovascular Disease Prevention: Results From the Large Clinical Trials.” Hanna E. Bloomfield, MD, MPH. **Minneapolis**. *Current Opinion Lipidology*, August 2006.

“Heart Failure, Chronic Diuretic Use, and Increase in Mortality and Hospitalization: An Observational Study Using Propensity Score Methods.” Ali Ahmed, MD; Louis J. Dell’Italia, MD; Robert C. Bourge, MD; Richard M. Allman, MD. **Birmingham**. *European Heart Journal*, June 2006.

“Impact of Human Immunodeficiency Virus Infection on the Prevalence and Severity of Steatosis in Patients with Chronic Hepatitis C Virus Infection.” Edmund J. Bini, MD. **New York**. *Journal of Hepatology*, June 2006.

“Likelihood of Home Death Associated with Local Rates of Home Birth: Influence of Local Area Healthcare Preferences on Site of Death.” Maria J. Silveira, MD, MA, MPH; Laurel A. Copeland, PhD, MPH. **Ann Arbor, San Antonio**. *American Journal of Public Health*, July 2006.

“Oral Conditions and Quality of Life.” Nancy R. Kressin, PhD; Lewis E. Kazis, ScD; Donald R. Miller, ScD. **Bedford**. *Ambulatory Care Management*, April-June, 2006.

“Personal and Treatment Factors Associated with Foot Self-Care Among Veterans with Diabetes.” Mark V. Johnston, PhD; Leonard Pogach, MD; Mangala Rajan, MA. **East Orange**. *Journal of Rehabilitation Research and Development*, March/April 2006.

“The Prevalence and Outcomes of In-Hospital Acute Myocardial Infarction in the Department of Veterans Affairs Health System.” Charles Maynard, PhD; Elliott Lowy, PhD; John Rumsfeld, MD, PhD; Ann E. Sales, RN, PhD; Haili Sun, PhD; Branko Kopjar, MD, PhD; Barbara Fleming, MD; Robert L. Jesse, MD, PhD; Roxane Rusch, RN, MPA; Stephan D. Fihn, MD, MPH. **Seattle, Denver, Washington, DC, Richmond**. *Archives of Internal Medicine*, July 2006.

“A Proteomic Screen Identified Stress-Induced Chaperone Proteins as Targets of Akt Phosphorylation in Mesangial Cells.” Jon B. Klein, MD, PhD; Kenneth R. McLeish, MD. **Louisville**. *Journal of Proteome Research*, July 2006.

“Rural-Urban Disparities in Health-Related Quality of Life within Disease Categories of Veterans.” William B. Weeks, MD, MBA; Amy E. Wallace, MD; Lewis E. Kazis, ScD. **White River Junction, Bedford**. *The Journal of Rural Health*, Summer 2006.

“Subtle Neurologic Compromise as a Vulnerability Factor for Combat-Related Posttraumatic Stress Disorder.” Tamara V. Gurvits, MD, PhD; Linda J. Metzger, PhD; Natasha B. Lasko, PhD; Mark W. Gilbertson, PhD; Scott P. Orr, PhD; Anna M. Charbonneau, BA. **Manchester**. *Archives of General Psychiatry*, May 2006.

“Synthetic Carotenoid Derivatives Prevent Photosensitized Killing of Retinal Pigment Epithelial Cells More Effectively Than Lutein.” Jeffrey R. Kanofsky, MD, PhD. **Hines**. *Experimental Eye Research*, May 2006. ■

IRAQ (from pg. 1)

adaptive anymore, and can be disruptive. We're still in that window when it's awfully close to that life-threatening situation, and we just might be seeing the biological remnants of that right now. The question is, where does it go from here?"

The study included 961 male and female active-duty Army soldiers, 654 of whom were deployed to Iraq between April 2003 and June 2005. The researchers administered a battery of neuropsychological tests to each deploying soldier before and after his or her service in Iraq. Non-deploying troops were given the same tests around the same times.

Compared to their non-deployed peers, deployed troops showed subtle compromises on tasks of sustained attention, verbal learning and visual-spatial memory, and reported more tension and confusion. In contrast, they seemed to have an edge in a neuropsychological test of reaction time, in which they had to click a computer mouse as soon as they spotted a snowflake on the screen.



Lead author Jennifer Vasterling, PhD (right), with study collaborator Susan Proctor, DSc (left), and U.S. Army Maj. Pamela Solet-Lindsay, who helped coordinate assessments at Fort Lewis, WA.

Participants in the study will be assessed again at one year post-deployment, said Vasterling. She said her group will consider two questions: "One would be testing whether these effects are transient, for the group as a whole. The second is whether there'll be a

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The rich history of VA research

Laying the groundwork for affiliation with medical schools

The following is an excerpt from "VA Research, 1925 – 1980," a history compiled by Dr. Marguerite Hays, who directed VA's Medical Research Service from 1974 – 1979 and the overall VA research program from 1979 – 1981. The complete text is expected to be available in print or on CD by early next year.

From 1946 to 1953, the effects of World War II on medicine in general and the VA in particular were notable. The war's impact on literally millions of people, and the concerted response of the world medical community to unprecedented new challenges, brought sweeping changes to the health care landscape. In America, huge numbers of returning veterans already had pushed the VA to its limits and beyond. The era would mark the transformation of the entire VA system, including the rebirth of a near-dormant medical research program.

From the prewar, hospital-based research efforts—scattered randomly at sites where local interest and initiative provided the impetus—emerged a modest, new intramural VA research program. As it gradually took form, initial efforts were made to establish an infrastructure from which coordinated initiatives could be directed. These formative years were marked by limited funding, demands upon hospital space for clinical needs, and creating a new culture among practitioners striving to establish research as a formal part of the VA mission.

A key figure in the overall conversion of the agency was Gen. Omar N. Bradley, who had been appointed by President Truman in 1945 as Administrator of Veterans Affairs. Bradley's enormous public persona had been earned largely on the battlefield. He was viewed, especially among the rank-and-file, as a soldier's soldier—someone who, despite his four stars, understood the basic

needs of his troops. Given the enormous task at hand, Bradley's great credibility would be indispensable in earning the political support needed to push through legislation that would enable the VA to measure up to public expectations.

Bradley immediately named Paul Hawley, M.D., to head the VA's Medical Department. Dr. Hawley had been Chief Surgeon of the European Theater of Operations, adding another dimension of direct familiarity with the medical needs of wounded and returning service personnel. Bradley and Hawley recruited more high-profile leadership with the naming of Paul Magnuson, M.D., as Assistant Chief Medical Director for Research and Education. A dynamic academic surgeon from Chicago, Dr. Magnuson was widely known among the leaders of the nation's medical schools, and became instrumental in associating VA medicine with these institutions.

KIDNEY (from pg. 3)

Their risk of heart failure was 40 percent higher; heart attack, 30 percent higher, and stroke, 20 percent higher. Finally, they were more than three times more likely to develop chronic kidney disease. “In contrast,” the researchers report, “creatinine concentrations had associations with each outcome that were much weaker and significant only for the outcome of cardiovascular death.”

Shlipak: “This tells us that the creatinine test, while broadly useful as a measure of kidney health, is insensitive. If creatinine is high, that’s probably an indication of kidney disease. But if it’s low, you don’t know. You would need to do a cystatin test if there’s any other indication of kidney disease or if the patient is in a group that’s at risk.”

He added, “This is also telling us that kidney function declines much more with age than we realized before.” Shlipak termed this syndrome pre-clinical kidney disease, or pre-CKD.

“We have the tools to slow kidney disease,” he noted, citing blood pressure control, sugar control for diabetes, and medications such as ACE inhibitors. “With a heightened awareness of pre-CKD, we can be more aggressive in taking steps to prevent it.”

The next steps for researchers, said Shlipak, should include longitudinal studies that determine whether a screening test for cystatin C can improve clinical care and health outcomes for large patient populations. “We also want to map out the physiologic consequences of early mild kidney dysfunction, now that we can measure it.”

Among Shlipak’s coauthors was Linda F. Fried, MD, MPH, of the VA Pittsburgh Healthcare System. The work was supported by the National Institutes of Health, the American Federation for Aging Research, VA., and the Robert Wood Johnson Foundation. ■

PECASE awards to VA researchers in Philadelphia, Atlanta

VA researchers David J. Casarett, MD, MA, and Jennifer L. Gooch, PhD, along with 54 scientists from eight other federal agencies, received Presidential Early Career Awards for Scientists and Engineers at the White House on July 26.

The annual awards, established in 1996 and administered by the Office of Science and Technology Policy, recognize early-career scientists and engineers “whose work shows exceptional promise for leadership at the frontiers of scientific knowledge during the 21st century.” VA will provide \$125,000 in research support over five years to each of its awardees.

Casarett, of VA’s Center for Health Equity Research and Promotion in Philadelphia and the University of Pennsylvania, is a physician and health-services researcher specializing in hospice and palliative care. Much of his work has focused on end-of-life decision-making, particularly with regard to hospice enrollment.

Gooch, of the Atlanta VAMC and Emory University, studies the action of the enzyme calcineurin in the kidney. Cyclosporin and other drugs that inhibit calcineurin suppress the immune system, and are often vital in ensuring the success of organ transplants. These drugs, however, can be toxic to the kidneys and result in hypertension and renal failure. Gooch is working to better understand the role of calcineurin in these drug-related effects, as well as in diabetic nephropathy.



PECASE awardees Jennifer Gooch, PhD, and David Casarett, MD, MA, met in July with chief research and development officer Joel Kupersmith, MD (left), at VA research headquarters.

Career milestones

Kent A. Kirchner, MD, chief of staff at the G.V. Montgomery VA Medical Center in Jackson, Miss., received the 2006 Founder’s Medal from the Southern Society for Clinical Investigation. A nephrologist and internal medicine specialist, Kirchner oversees the center’s research program, which currently includes about 70 studies. His own research focuses on diabetes, hypertension and geriatric physical fitness. Among the trials for which he is a principal investigator are two National Heart, Lung and Blood Institute studies: ALLHAT, on hypertension treatment; and ACCORD, which investigates links between cardiovascular mortality and diabetes.

Peter M. Monti, PhD, of the Providence VAMC and Brown University, received the 2006 Distinguished Researcher Award from the Research Society on Alcoholism.

Jennifer Moye, PhD, director of the Geriatric Mental Health Center at the VA Boston Healthcare System, received the Professional Service Award from the American Psychological Association for her contributions as a clinical and research psychologist, including her leadership in developing guidelines for attorneys and psychologists to assess cognitive capacity in the elderly.

Hill happenings

House, Senate bills include \$412 million for research

Editor's note: In August, December and April, VA Research Currents will update readers on congressional action affecting funding for VA research.

On May 19, the House of Representatives passed H.R. 5385, the Military Quality of Life and Veterans Affairs and Related Agencies appropriations bill for the fiscal year ending Sept. 30, 2007.

The bill, which allocates funds for military quality of life functions of the Department of Defense; military construction; VA; and related agencies, provides \$412 million in direct appropriations for VA's medical and prosthetic research program. This is \$13 million above the President's budget request for fiscal year 2007 and the same level of funding as for fiscal year 2006.

On July 20, the Senate Appropriations Committee approved its Military Construction and Veterans Affairs fiscal year 2007 spending bill, which also provides

\$412 million for VA's medical and prosthetic research program.

In addition, the bill stipulates that not less than \$15 million be used for Gulf War Illness research. Action by the full Senate is delayed until after the August recess.

After the Senate passes its bill, the next step is the formation of a Conference Committee, consisting of members from both the House and Senate, to reconcile differences in the two bills. After the differences are resolved, the Conference Committee will issue a Conference Report that is sent to the House and Senate for final passage before being sent to the President for signature.

To view the appropriations bills and track them through the next steps, visit: <http://thomas.loc.gov/home/approp>.

IRAQ (from pg. 5)

subgroup in which this pattern of findings is maintained, and in which cases it could be a prodrome for other sorts of problems."

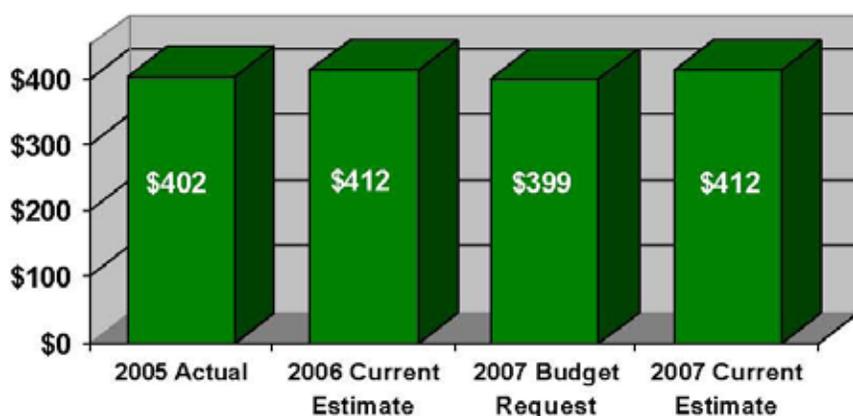
While cognitive impairment is significant among the health problems that have plagued many Gulf War veterans, researchers are unclear on whether the deficits resulted from deployment, partly because of the lack of baseline data. Vasterling and colleagues point out that because of their study's design—the fact that soldiers were assessed before their deployment, and then again relatively soon upon their return to the U.S.—it is unlikely that pre-existing dysfunction, or factors unrelated to deployment, contributed to their neuropsychological changes.

"With research efforts on 1991 Gulf War veterans' health, it was very difficult to be able to account for baseline, pre-deployment factors that may have contributed to post-deployment health concerns," said Susan Proctor, DSc, co-author of the new study and a consultant at the VA Boston Health Care System. An environmental health researcher, she is also with the Boston University School of Public Health and the U.S. Army Research Institute of Environmental Medicine.

Vasterling added that the new findings underscore the importance of interventions such as the Army's Battlemind Training Program, which helps troops transition out of a war-zone mindset. She and Proctor also stressed the importance of looking more closely at brain function in military personnel and veterans—ideally, before and after any war-zone deployment.

Collaborating with Vasterling and Proctor were Paul Amoroso, MDA, MPH, of the Madigan Army Medical Center at Fort Lewis; Robert Kane, PhD, VA Maryland Healthcare System and University of Maryland School of Medicine; Timothy Heeren, PhD, Boston University School of Public Health; and Roberta F. White, PhD, VA Boston and Boston University. The work was funded by the Army and VA.

**VA Medical and Prosthetic Research
Direct Appropriations**
(dollars in millions)



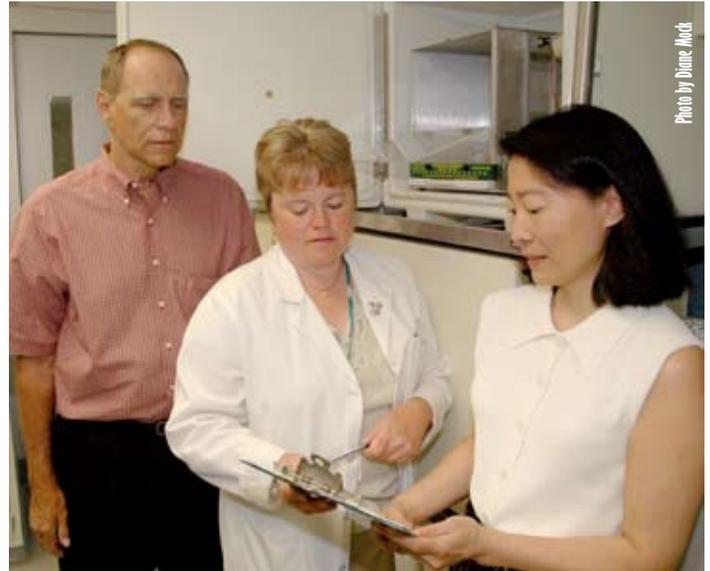
VA lab ranks high in journal's list of top Alzheimer's advances

For its July 2006 special feature on Alzheimer's disease, the journal *Nature Medicine* asked 34 leading scientists to name the most important findings in the field since 2003. Of 18 papers cited in the results, 3 are from the lab of Karen Ashe, MD, PhD, at the Geriatric Research, Education and Clinical Center (GRECC) of the Minneapolis VA, and the University of Minnesota.

Of the papers chosen as most important in the poll, almost all were related to the processing or pathogenesis of beta amyloid, a sticky protein that clumps together and forms plaques in the brain of those with Alzheimer's disease.

Cited by 29 percent of the experts polled and tied for the number-one spot was a paper published in *Nature* in March 2006 in which Ashe and colleagues reported on a newly identified beta-amyloid derivative that appears to disrupt memory, independent of the loss of neurons or the build-up of plaques in the brain. The researchers isolated the compound—called A-beta *56 (A-beta star 56)—from the brains of aging mice that had just begun to show mild memory loss, and injected it into the brains of young rats. Rats treated with the compound were unable to remember the location of a certain object, unlike rats that had not received A-beta *56. The newly identified compound, which has also been found in human brains, could become the target of early-detection tests or drugs that would block its action.

The other papers by Ashe's team were "Tau suppression in a neurodegenerative mouse model improves memory function,"



Karen Ashe, MD, PhD (right), of the Minneapolis VA was senior author on 3 of 18 papers cited in a *Nature Medicine* list of top Alzheimer's advances in the past three years. She is seen here with her VA collaborators on one of the papers: James P. Cleary, PhD, and certified veterinary technician Jacki J. Hofmeister.

published in *Science* on July 15, 2005; and "Natural oligomers of the amyloid-beta protein specifically disrupt cognitive function," which appeared in *Nature Neuroscience* in January 2005. First author on that paper was James P. Cleary, PhD, also with VA's Minneapolis GRECC.

The complete *Nature Medicine* list can be viewed at the journal's website: www.nature.com/nm/index.html. ■

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