

VA Research Currents

RESEARCH NEWS FROM THE U.S. DEPT. OF VETERANS AFFAIRS



Photo by Emerson Kanders



Photo by Robert Farrell

High-tech artificial arm at VA headquarters—

Top: Fred Downs Jr., former chief of prosthetics and sensory aids for VA, wears the DEKA prosthetic arm as he shares a light moment with Col. Geoffrey Ling of the Defense Advanced Research Projects Agency. Below: Downs shows the arm to children of VA employees who were spending the day at VA headquarters for Take Your Child to Work Day. Read more in the Research Week summary at www.research.va.gov.

Brain-computer milestone

Study volunteers with paralysis use thoughts to operate robotic arms

VA researchers and colleagues reported in the May 16 online edition of *Nature* that two study volunteers with tetraplegia—paralysis of all four limbs and the torso—were able to grasp objects with robotic arms that they controlled with their own thoughts. They used an investigational system called BrainGate, which harnesses brain signals to command external devices.

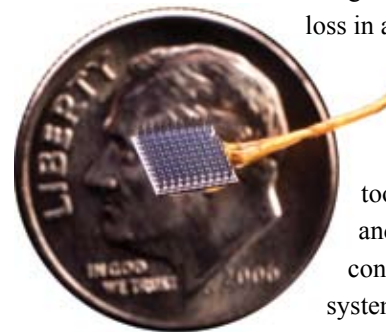
One of the participants, a 58-year-old woman, was able to pick up a bottle of coffee and bring it to her lips to drink. This was the first time she was able to serve herself since she became paralyzed nearly 15 years ago.

The research team included scientists from the Providence VA Medical Center, Brown University, Massachusetts General Hospital, Harvard Medical School, and German Aerospace Center.

The woman and a 66-year-old man, who is a Veteran, took part in the research. They had each been paralyzed by a brainstem stroke years earlier that robbed them of control of their arms and legs.

The research involved two different robotic arms. One, the DLR arm, was developed by the DLR Institute of Robotics and Mechatronics as an assistive device. The other, the DEKA arm, was developed as a prosthetic arm by DEKA Research and Development, through funding from the Defense Advanced Research Project Agency. VA and DARPA have worked with

DEKA engineers and Veterans with limb loss in a separate study designed to optimize the arm's design and function.



Above: The brain implant used in the study.

Early work on BrainGate took place at Brown University, and VA has helped fund its continuing development. The system uses a tiny brain implant

Vietnam-era twin study yields genetic brain map

How do genes affect brain formation and function? Scientists may now be able to learn more thanks to a new “brain atlas” developed by VA researchers and colleagues.

The research, described in the March 30 issue of *Science*, involves twins who served in the military during the Vietnam era.

More than 406 twins took part, in San Diego or Boston, as part of the larger Vietnam Era Twin Study of Aging. The Veterans underwent MRI scans of their brains. Because of the twins’ genetic similarity, the researchers were able to deduce what role genes play in forming the brain.

The study zeroed in on the cortex, the outer layer of the brain. Dense in “gray matter,” this region is where higher-level thinking takes place.

“What we’ve done is create the first brain atlas based only on genetic data,” says VA and University of California, San Diego, psychologist William Kremen, PhD, the study’s lead investigator.

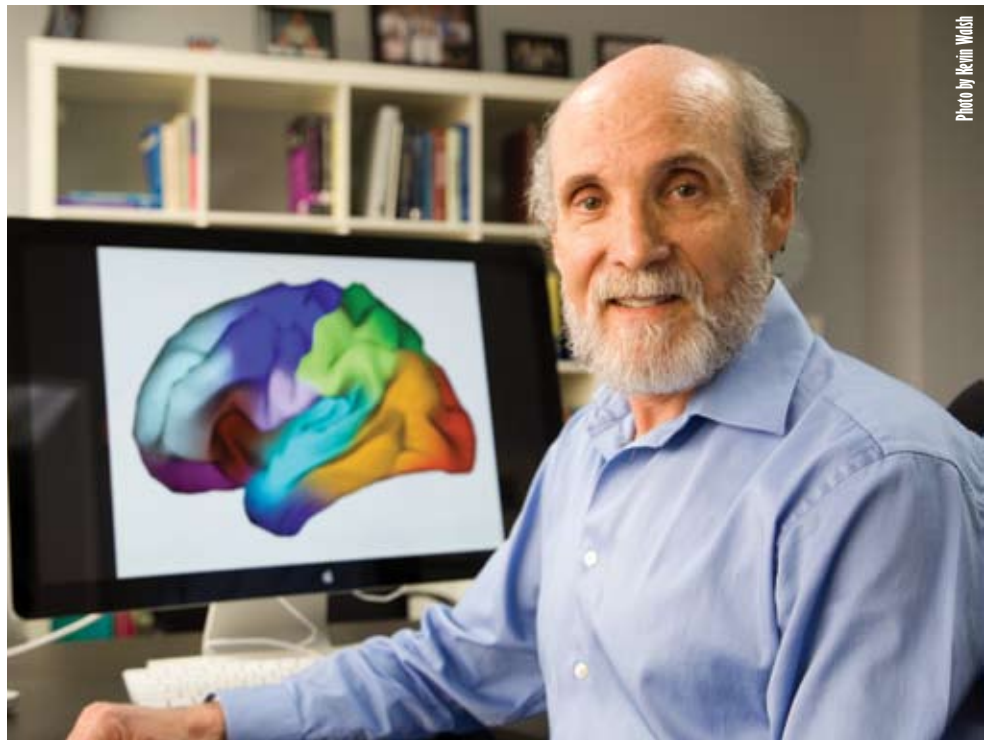


Photo by Kevin Walsh

Map quest—Dr. William Kremen led a team that came up with a new “map” of the brain, showing regions that appear to be influenced by the same sets of genes.

Traditional brain maps divide the brain into regions based on structure and function. As early as 1909, German scientist Korbinian Brodmann studied the different cells and tissues in animal and human brains and identified more than 50 distinct areas. Through decades of experimentation, scientists have learned more about each area’s role. Still absent from the picture, though, is knowledge of what role genes play.

The new study did not pinpoint the role of specific genes. However, it did yield a map of the brain divided into clusters, each of which appears to be affected by a distinct set of “genetic influences,” says Kremen.

Using a mathematical model, the researchers determined that 12 such clusters was the optimal breakdown. Each area is marked by a different color on their new brain atlas. Explains Kremen, “You could

look at the atlas and say, for instance, that a lot of the same genetic influences are at play in the blue region, and those are different than the genetic influences in the yellow area.”

How will the new atlas be used? One potential application, says Kremen, is genomics research. Neuroscientists are conducting many “genome-wide association studies” in which they collect DNA from study volunteers and try to piece together which gene variants are tied to certain conditions, such as posttraumatic stress, alcohol addiction, or Alzheimer’s disease.

Using the genetic atlas, says Kremen, “Researchers may be more likely to pinpoint the genetic influences that underlie the various structures in the brain.”

Read an expanded version of this feature online at www.research.va.gov/currents.

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Fitness or ideal weight: Which holds the key to long life?

There are lots of intricate data to support the point, but the research findings of Peter Kokkinos, PhD, can be summed up in two words: “Inactivity kills.”

According to Kokkinos, “This comes through over and over again in the studies, no matter what type of population we’re assessing.” For more than two decades, the VA investigator has explored the link between fitness and longevity. In his world, fitness—or aerobic capacity—is measured by people’s endurance on a treadmill.

The research confirms that being able to exercise more is a good thing: It can add years to your life. No surprise there. But dig deeper, and there is news that may come as a mild surprise to many.

According to numerous studies, being unfit is more deadly than being overweight, or even obese. If you can walk up two flights of stairs without stopping, for instance, even if you’re carrying 20 or even 40 extra pounds on your frame, you’re likely to outlive a lean couch potato who can barely manage one flight of stairs without getting winded. We’re talking statistically, of course—after researchers have adjusted for variables such as age, smoking, and medical history.

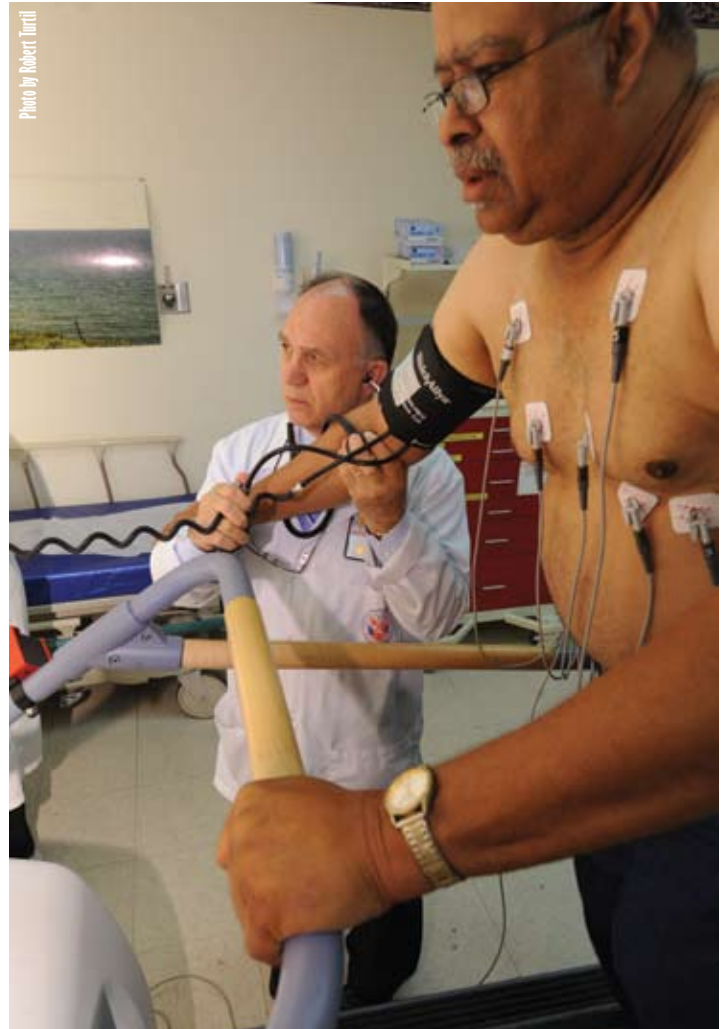
That’s what health experts glean from epidemiologic data on hundreds of thousands of people, says Kokkinos. He and his collaborators, both within VA and at other institutions across the U.S. and abroad, including his native Greece, have contributed heavily to the literature in this field.

Kokkinos, who heads a cardiac exercise lab at the Washington, DC, VA Medical Center and is a professor of medicine at Georgetown and George Washington universities, says the bottom line is that fitness is a powerful driver of longevity that trumps the ill effects of any other risk factor, such as diabetes, hypertension, and excess weight.

So if your genes keep you forever in an uphill battle against flab, all is not lost. Get on a treadmill. Ride a bike. Whatever it is that moves you, get moving. According to Kokkinos, it doesn’t take much to nudge yourself into a healthier fitness bracket that will lower your mortality risk.

“A brisk walk on a daily basis can do it,” he says. “The goal is to accumulate between 150 and 200 minutes per week of moderate exercise. That’s all you need.”

A trim 62-year-old, Kokkinos himself pursues a moderate exercise regimen. “I jog and brisk walk. At my age, I don’t need to



Stress manager—Dr. Peter Kokkinos oversees a cardiac stress test for Albert McMillan, 63, at the Washington, DC, VA Medical Center. Patients walk or run on the machine as the speed and elevation increase, until they feel fatigued. Researchers use the results to calculate fitness levels.

do a whole lot. I also add some resistance training—that’s also important, to maintain muscle strength and bone density.” He shuns extreme measures. “I go by the saying, ‘Everything in moderation.’ It worked thousands of years ago, and it works today.”


The researcher and his colleagues at the Washington, DC, VA Medical Center are applying the lessons they’ve learned on behalf of Veterans. The group has developed a program they call Lifestyle Intervention for Veterans—known by its catchy acronym LIVE. Says Kokkinos, “It’s designed to empower the participants to develop and pursue a healthy lifestyle.”

see **FIT** on next page




Fostering fitness—

Fitness researcher Dr. Peter Kokkinos meets with Veteran Albert McMillan at the Washington, DC, VA Medical Center. McMillan was preparing for a cardiac stress test. Kokkinos and other researchers have tracked the results of such tests, and correlated them with information in other VA databases, to learn more about the link between fitness and lifespan.

Read an expanded version of this feature at www.research.va.gov/currents. 

FIT (from previous page)

The program covers exercise, nutrition, and stress management. At the outset, Veterans get their fitness level tested. “In most cases, it’s below the average for their age group,” says Kokkinos. For the next 10 to 12 weeks, participants come to the hospital to exercise two days a week and work out at home the other days. “The message I give them is that diabetes is their enemy. I tell them, ‘It’s a relentless enemy. You must fight back. Proper exercise, diet, and stress management are your weapons. Fight back!’”

Kokkinos says both he and the participants have been pleasantly surprised by the results. “In just 10 weeks, they turn things around. Their fitness level increases by about 15 to 30 percent. They lose weight, lower their blood pressure, and improve their blood sugar levels. They have more energy, sleep better, and feel better about themselves. Overall, their quality of life improves.” 

Low fitness deadlier than excess weight

Between 1986 and 2010, more than 20,000 Veterans underwent cardiac stress tests—walking on a treadmill, with electrodes taped to their chest—at the VA medical centers in Washington, DC, and Palo Alto, Calif. Some were undergoing routine physicals. Others were being checked for exercise-induced ischemia—blockages in blood flow to the heart, made worse by physical exertion.

The results of the stress tests, along with other data in the Veterans’ electronic health records, have been a gold mine for Peter Kokkinos, PhD, and other VA researchers interested in learning about the link between exercise capacity and longevity. They have authored a string of publications, dating back to the late 1980s, that have helped answer numerous questions. Among them: Does being fit extend life even for those with diabetes, hypertension, or obesity? Is low fitness truly a more critical risk factor than any other?

The answer to both questions is “yes,” according to many studies. One example is a study by Kokkinos’ group that appeared in *Diabetes Care* in May 2012. In the report, the group described what they call the “BMI [body mass index]-mortality paradox.” Looking at more than 4,000 white and African American men with diabetes, the team found that the greater the exercise capacity, the lower the mortality risk, regardless of other risk factors, including obesity. There was also a twist: Among all the Veterans in general and African Americans in particular, mortality risk dropped as the Veterans got heavier. Compared against leaner Veterans with equal exercise capacity, fatter Veterans lived longer, on average. Similar patterns have been seen past studies. Researchers have yet to understand this puzzle. (See online sidebar on the “obesity paradox” at www.research.va.gov/currents.)

Preventing colon cancer deaths: New VA study aims to find out which method works best

Veterans at 42 VA medical centers will take part in a major new study to find out which screening method works best to curb mortality from colorectal cancer.

Colorectal cancer is the third most common cancer in the U.S. It is also the second leading cause of cancer deaths, behind lung cancer. VA diagnoses some 4,000 new cases of the disease each year in Veterans.

The ambitious study will be the largest VA Cooperative Studies Program effort to date, aside from the ongoing Million Veteran Program. The trial will enroll up to 50,000 Veterans over the next two to three years and follow them for a decade to track deaths, cases of colon cancer, and other outcomes.

Researchers will compare two screening methods. One is colonoscopy, considered the “gold standard” for early detection of the disease. In the procedure, doctors insert a long, thin, flexible tube to view the entire colon, and any precancerous growths—known as polyps—can be snipped out right on the spot. But the procedure is invasive and costly, and occasionally causes




Putting screening tests to the test—Study coordinator Elaine Nevins explains a colorectal cancer screening procedure to Navy Veteran Alex Pryor at the Seattle VA Medical Center.

complications, such as a tear in the intestines.

The other method is fecal occult blood testing (FOBT), a simple test in which a small plastic device is used to sample feces, which is then checked in the lab for signs of

hidden blood. The study will use a relatively new form known as fecal immunochemical testing (FIT). The test has its pluses, but the extent of its effectiveness in reducing mortality is unclear.

Most screening guidelines—including VA’s—recommend either FOBT every year or colonoscopy every 10 years, and it is those two approaches the new study will compare. A third option some patients choose is sigmoidoscopy (which examines just part of the colon) every five years, along with FOBT every three years.

VA Research Currents spoke with the leaders of the study, known as CONFIRM (for Colonoscopy versus Fecal Immunochemical Testing in Reducing Mortality from Colorectal Cancer) about what they hope to learn. Read the interview at www.research.va.gov/currents. 



Dr. Jason Dornitz, seen here, and Dr. Douglas Robertson are co-leading a major new VA study comparing two methods of screening for colorectal cancer.

Read an expanded version of this feature at www.research.va.gov/currents.

Hospital privacy curtains are haven for germs—

Hospital privacy curtains are rapidly contaminated with potentially harmful germs, according to a study at the University of Iowa and VA’s Center for Comprehensive Access and Delivery Research and Evaluation. Over three weeks, the team analyzed repeated swabs from curtains in 30 rooms and found frequent contamination—generally within a week after curtains were replaced. The germs included methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant *enterococcus* (VRE), both of which are major problems for U.S. hospitals. Increased hand-washing is among the recommendations offered by the researchers, but a number of other solutions are also being explored, such as antimicrobial curtains. VA and other health care systems have beefed up infection-control measures in recent years, with impressive results—such as those reported by VA researchers in April 2011 in the *New England Journal of Medicine*. But studies continue to reveal new trouble spots in hospitals, and researchers are still seeking better ways to curb germ spread. (*American Journal of Infection Control*, online March 29, 2012)



Eye tremor may predict Parkinson’s—

Using sophisticated eye-tracking tests, researchers at the Richmond VA Medical Center and Virginia Commonwealth University found that patients with Parkinson’s disease, even those with a recent diagnosis, displayed an “ocular tremor” that was not found in non-Parkinson’s patients. The study included 112 patients with Parkinson’s, 18 of whom had not yet begun any treatment, along with 60 “control” patients without the disease. All the Parkinson’s patients, whether on medication or not, showed an inability to maintain a stable fixed gaze when shown a target on a computer screen. Of the healthy participants, only two had the same problem—and one of them went on to develop Parkinson’s symptoms within two years. Study co-author Mark Baron, MD, a neurologist at VA’s Richmond-based Parkinson’s Disease Research, Education, and Clinical Center, told *Medscape Medical News* that the test “could provide clinicians with a simple means to accurately diagnose Parkinson’s disease, with accuracy well exceeding that of [other] clinical assessments.” (*Archives of Neurology*, online April 9, 2012)



High fiber intake linked to healthier gums—

A new analysis of data from the VA Dental Longitudinal Study shows that eating more fiber—especially certain fruits, vegetables, and grains—slows the progression of periodontal disease in older men.



Photo by Jeff Bowen

Fiber in diet is denture deterrent—Eating fiber-rich fruits and vegetables may help avoid the need for dentures or dental implants by preventing the loss of teeth and the bone supporting the teeth, suggests a VA study of older men.

The researchers, from the VA Boston Healthcare System and other sites, found that men who reported eating greater quantities of high-fiber foods—those with more than 2.5 grams of dietary fiber per serving—had less gum disease. Each additional serving in the daily diet cut the risk of lost teeth by about a third, and the risk of bone loss by about a quarter. The high-fiber foods that seemed to have the most benefit were apples, bananas, prunes, oranges, blueberries, broccoli, Brussels sprouts, sweet potatoes, spinach, peanuts, oatmeal, and other grains. (*Journal of the American Geriatrics Society*, April 2012)



For knee replacements, hospital ranking may not be crucial—

Some key outcomes were similar for patients who had total knee arthroplasty whether or not they had the surgery at a hospital ranked as among the best for orthopedics by *U.S. News and World Report*. The study was conducted by investigators at the University of Iowa’s Carver College of Medicine and VA’s Center for Comprehensive Access and Delivery Research and Evaluation. Using Medicare data, they compared outcomes for nearly 65,000 patients, looking at post-surgery complications, length of stay in the hospital, and hospital readmission. The study found no significant differences in these areas. The researchers didn’t examine outcomes such as patient satisfaction, long-term functional improvement, and pain relief. Lead author Peter Cram says the take-home message of the study is that “there are good hospitals across the country, and limiting yourself to the top-ranked hospitals is not always necessary.” *U.S. News and World Report*

rankings are used widely by hospitals to market their services and by patients to choose where to receive care. Past studies have suggested that hospitals ranked high by the magazine do perform better, but most of these studies have looked only at heart care. (*Mayo Clinic Proceedings*, April 2012)



MEG scans to detect brain injury

injury—A new study by VA, the Department of Defense, and the University of California, San Diego, has yielded further evidence that a type of brain scan called magnetoencephalography (MEG) may be a useful tool for diagnosing traumatic brain injury (TBI). Many mild TBIs go undetected in conventional CT or MRI scans. MEG, on the other hand, seems able to pick up the subtle abnormalities in brain waves caused by these injuries. MEG works by capturing the magnetic impulses put out by brain cells. In the study, MEG detected mild TBI in 87 percent of cases and moderate TBI in 100 percent of cases. The study included 45 Veteran, military, and civilian patients with mild TBIs—about half from blasts. Also included were 10 patients with moderate TBI, all from non-blast causes, such as automobile accidents, sports injuries, or falls. Study leader Mingxiong Huang, PhD, says the new MEG techniques his team developed use automated processes that are highly accurate and objective, with little reliance on the subjective judgment or assessment of radiologists performing the scan and interpreting the results. The team is also conducting work that combines MEG with another type of imaging, a form of MRI known as diffusion tensor imaging. The two together may have an even stronger ability to accurately detect mild TBIs. (*Neuroimage*, online April 20, 2012) —



Photo by April Tibbs



Photo by Kevin Walsh

Top: Dr. Terence Gioe of the Minneapolis VA discusses the risks and benefits of knee replacement surgery with patient Tom Moore. **Bottom:** Drs. Roland Lee (foreground) and Mingxiong Huang are using MEG and other newer types of brain imaging to detect traumatic brain injuries that might be missed by conventional CT or MRI scans. See related stories, left.

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BRAIN *(from page 1)*

about the size of a baby aspirin, with nearly 100 electrodes. It is placed just under the skull on the brain’s motor cortex, which helps control movement.

The electrodes, or sensors, are close enough to individual brain cells to pick up their impulses. A wire bundle runs from the electrodes and outside the body to a computer that translates the signals into commands for devices.

In past studies, BrainGate volunteers achieved point-and-click control of a cursor on a computer screen, and basic control of a simple robotic device. The new findings are the first demonstration and peer-reviewed report of people with tetraplegia using brain signals to control a robotic arm in three-dimensional space—as opposed to a two-dimensional computer screen.

The volunteers used the robot arms to reach for and grasp foam targets that were placed in front of them, held by flexible supports. The woman also used the DLR robot to pick up a bottle of cinnamon latte, bring it to her mouth, drink through a straw, and return the bottle to the table.

BrainGate pioneer John Donoghue, PhD, MS, recalled a moment in the



Neuroscience milestone—A 58-year-old Massachusetts woman who suffered a paralyzing brainstem stroke 15 years ago while working in her garden was able to serve herself coffee using the BrainGate system and a robotic arm.

research that can be seen in a video of the experiments that was made available to the media: “If you just watch her reaction after she picks up the cup [and drinks], that smile captures everything.”

“Her smile at the moment is something I, and our research team, will never forget,” added his colleague, lead author Leigh Hochberg, MD, PhD.

Significantly, even after a decade and a half, the motor cortex part of the brain that was “disconnected” from its original target by a stroke was still able to direct the complex movement of a robotic limb. The brain cells, in essence, had “remembered” how to send the right signals.

To read more and access links to a video showing the BrainGate system in action, visit www.research.va.gov/currents. 