

RESEARCH NEWS FROM THE U.S. DEPARTMENT OF VETERANS AFFAIRS • FEBRUARY 2008

Evaluating VA's homelessness programs

Last year marked the 20th anniversary of VA's special programs for homeless veterans. For as many years, psychiatrist and researcher Robert Rosenheck, MD, has been leading efforts to evaluate these programs, which now comprise the nation's—and probably the world's—largest integrated network of homeless treatment and assistance services.

As director of VA's Northeast Program Evaluation Center, based at the West Haven, Conn., VA Medical Center, Rosenheck and his team apply stringent research methodology to investigate a range of health issues and VA programming, with a heavy focus on mental health, including PTSD and substance abuse. These issues often intertwine with homelessness, and Rosenheck has authored or coauthored more than 90 research articles dealing with homeless veterans since he began his VA career.

Research Currents interviewed Rosenheck about issues affecting homeless veterans and about his research in this area.

see **HOMELESS** on pg. 6



Photo by Mitch Martin

This "tent village" outside a Baltimore church was photographed on a 19-degree January morning.



Photo by Jerry Delio

Thermometer helps ward off diabetic foot ulcers

In a VA study including 225 veterans with diabetes, patients who used a special thermometer to check their feet every day for "hot spots" were three times less likely to develop foot ulcers—an insidious complication of the disease that often leads to serious wounds requiring amputation. The study, published in the Dec. 2007 *American Journal of Medicine*, was led by David G. Armstrong, DPM, PhD, a podiatry researcher with VA and director of the Center for Lower Extremity Ambulatory Research at Rosalind Franklin University of Medicine and Science in Chicago.

Dr. David Armstrong led a study showing that the use of an infrared thermometer to detect "hot spots" on the feet could help prevent diabetic ulcers.

Patients used a digital, infrared thermometer to measure the temperature at six different points on each foot, looking for "hot spots" caused by inflammation surrounding damaged tissue. "A wound really will heat up before it breaks down," Armstrong told the Associated Press.

A hike in temperature of more than four degrees between the same spot on the right and left foot triggered the study volunteers to contact their nurse and stay off their feet until temperatures were back to normal. Easing the pressure on feet before cracks develop in the skin promotes healing.

see **DIABETES** on pg. 5

Lithium gives brain boost to rats; may show promise for Alzheimer's

In lab tests at the Cleveland VA, rats that ate a diet spiked with lithium showed gains in three different tests of learning and memory, compared with rats that ate regular chow. The results, published in the Dec. 2007 issue of *Neuroscience*, provide key evidence in a hot debate among experts as to whether lithium—a well-established treatment for bipolar disorder—may also benefit those with Alzheimer's disease or other dementias.

How lithium affects the brain

Based on cell-culture and animal tests, scientists already have evidence that lithium promotes healthy neurons and boosts the levels of certain beneficial brain chemicals. Lithium has also been found to stop the telltale brain signs of Alzheimer's disease—plaques of a sticky protein called amyloid and twisted fibers, or tangles, of tau protein. This preclinical research “clearly indicates that lithium is likely to work for Alzheimer's disease,” says Seong Shim, MD, PhD, senior author on the new study.

But little past research has directly tested the effects of lithium on cognitive function, even in animals. According to Shim and co-authors Christine Nocjar, PhD, and Michael Hammonds, PhD, their report describes the “first [well-controlled study] showing that chronic treatment of therapeutic doses



Dr. Seong Shim's animal studies suggest that lithium, long used to treat mood disorders, may also help the brain in other ways.

of lithium enhances learning.” Nocjar and Shim are with VA and Case Western Reserve University, and Hammonds is with VA and Cleveland State University.

The study included three different tasks commonly used to assess learning in rodents. In one, for example, the animals had to learn and remember which holes among many empty ones contained food. In another, the researchers grouped the rats in different chambers and then placed them alone in other chambers. The scientists then tracked how much time the rats spent in the chambers where they had been with other rats—a measure of their ability to recall and seek out those locations where they had enjoyed social contact.

In all three tests, rats eating lithium chow outperformed rats on regular chow. “Importantly,” notes Shim, “this enhancement was shown under clinically effective and safe serum levels of lithium at the time of testing.”

Whether the results can eventually be translated into a therapy to prevent or treat brain decline in aging adults, or, more specifically, to treat Alzheimer's, remains to be seen. Lithium is not technically a drug but a mineral, similar to salt. While it has been used widely for decades as an effective treatment for bipolar disorder—also known as manic depression—and other mood disorders, it has a very narrow therapeutic range. This means the effective dose is very close to a toxic dose, and doctors have to prescribe the drug carefully and regularly monitor patient's blood levels of the drug. Too high a dose could cause tremors, slurred speech, confusion, nausea and other serious side effects. According to Shim, though, the side effects of lithium are well-known and manageable. “Many elderly people take lithium as a long-term therapy for treating mood disorders,” he points out.

Mineral may offer unique benefits

Shim stresses that lithium may offer unique advantages as a therapy for dementia, citing the results of the past decade of research in his lab and others. “Lithium not only blocks the formation of plaques and tangles, as other experimental drugs can do, but it also has diverse neurotrophic and neuroprotective actions” that support memory and learning, says Shim. A prime example is that lithium appears to strengthen the formation and activity of synapses—the spaces between neurons where brain signals are transmitted by chemical messengers.

Shim says it is not clear whether lithium's two distinct properties—the ability to prevent Alzheimer's plaques and tangles, and the ability to nurture and strengthen brain cells—share the same underlying mechanism. In any event, he is eager to see the mineral tested in clinical trials specifically focused on Alzheimer's disease treatment and prevention. ■

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New 'CRADA' policy will foster collaborations

VA has issued a directive mandating the use of Cooperative Research and Development Agreements (CRADAs) for industry-sponsored research at all VA medical centers. The measure, to take effect March 26, is expected to facilitate and expand collaborations between VA researchers and companies in the pharmaceutical and biomedical arena.

CRADAs are used by all federal agencies that do research in partnership with non-federal entities, and VA has used them in the past. But VA's model form was recently updated and is now ready to be used on a much wider scale than before.

Among other benefits, the standardized contracts will create consistency throughout the VA system, making it easier for VA investigators at multiple sites to participate in clinical trials including hundreds or even thousands of veterans. Until now, agreements for clinical trials involving VA and industry have typically been based on contracts provided by the companies and were not uniform across the VA system. Use of the new CRADAs is expected to streamline negotiations with sponsors and make it simpler to launch and conduct trials of promising new drugs and medical devices.

"This new directive will make it easier for VA and private sector leaders in the health care industry to combine resources in research projects that serve to benefit veterans," said Joel Kupersmith, MD, VA's chief research and development officer. "These projects will enhance the quality of care for our nation's veterans and advance medical science in ways that benefit the entire nation."

Information on a Feb. 20 conference on the use of CRADAs in VA can be found at www.navref.org/cradaconference. ■

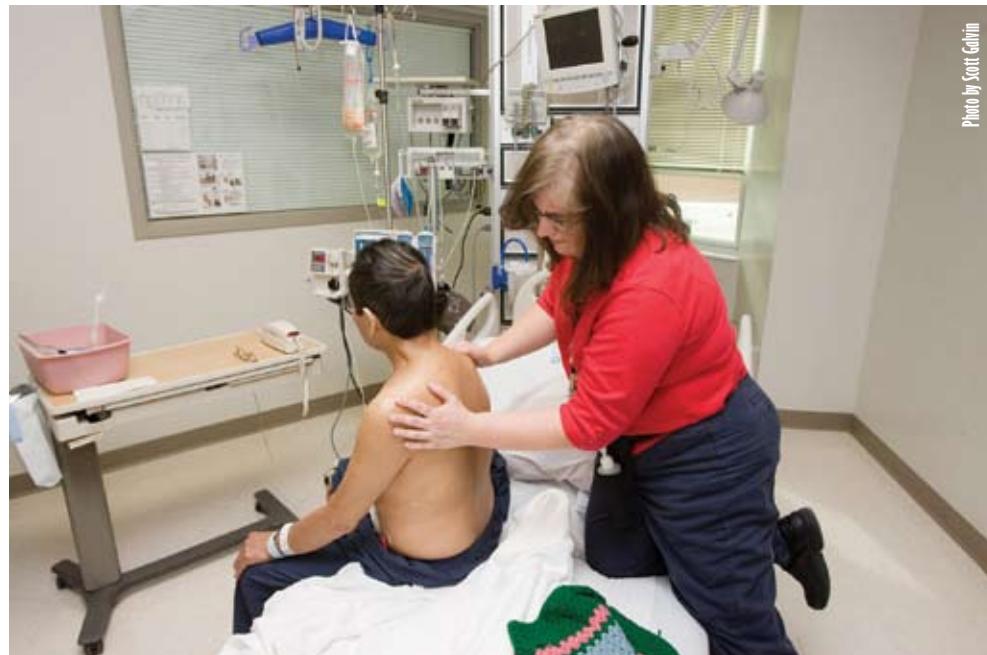


Photo by Scott Galvin

Massage therapist and lead study author Allison Mitchinson, MPH, tends to a patient at the Ann Arbor VA.

Massage shown to help surgery patients recover

In the largest and most rigorous trial of its kind to date, veterans who received a therapeutic back massage after undergoing major chest or abdominal surgery, in addition to routine post-operative care, reported less pain and anxiety than those receiving only routine care, or those also given personalized attention from a massage therapist but no massage. The results appeared in the Dec. 2007 *Archives of Surgery*.

According to senior author Daniel Hinshaw, MD, a surgeon at the Ann Arbor VA Medical Center and researcher with that site's Geriatric Research Education and Clinical Center, patients in past decades commonly received massages from nurses to ease post-operative pain, but the practice has faded. "Now we have ... evidence for massage," he told *Time* magazine. "We can see a real effect."

The study involved 605 men, most in their 60s, at the VA medical centers in Ann Arbor and Indianapolis. The patients were divided into three groups: usual care, which included pain drugs; usual care plus a 20-minute visit from a massage therapist that included talking but no massage; or usual care plus a 20-minute therapeutic back rub, for up to five days after the surgery.

All the patients improved over the few days following their operations, but the reductions in pain and anxiety were most pronounced in the massage group, especially on the first day after surgery. Anecdotally, said Hinshaw, some patients reported that massage gave them as much pain relief as a morphine drip. There were no differences among the groups, however, in the rates of decrease in long-term anxiety, length of hospital stay, opiate use, or complications.

Hinshaw and lead author Allison Mitchinson, MPH, a certified massage therapist, say massage may work by creating a competing sensation to block pain, or stimulating the

New method may ease use of ‘nanocomposites’ in medicine, industry

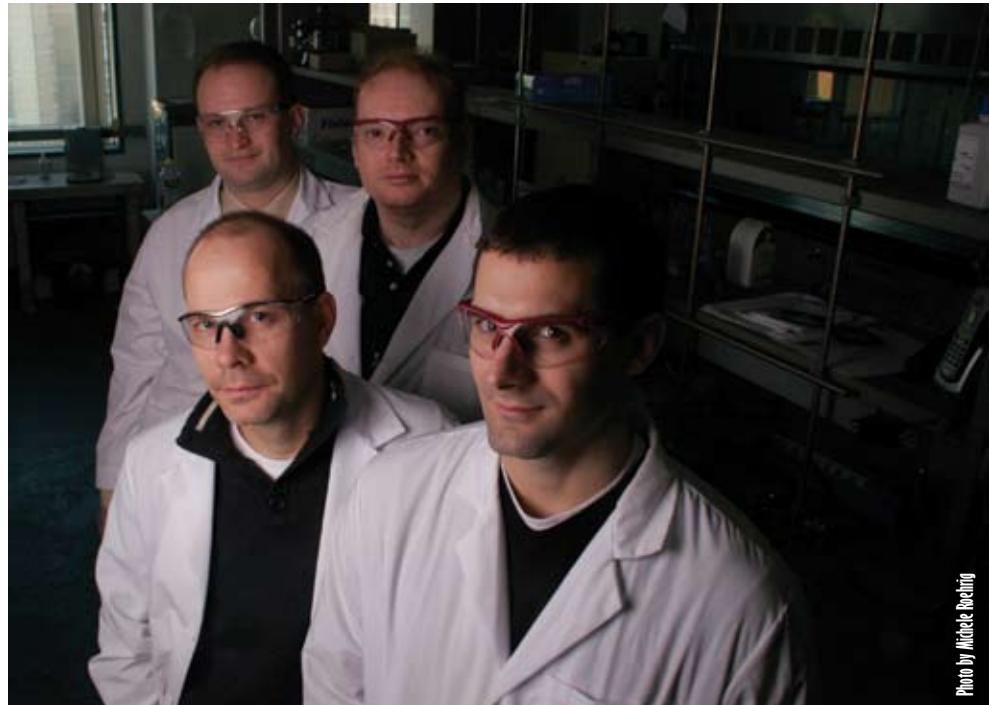
A team led by scientists at Case Western Reserve University (CWRU) and VA’s Cleveland-based Advanced Platform Technology (APT) Center has devised a new way to create nanocomposites that may broaden the use of these space-age hybrid materials in medicine, rehabilitation technology and countless industries. The work was featured in the December 2007 issue of *Nature Nanotechnology*.

Nanotechnology scientists use powerful microscopes to manipulate molecules so tiny that 10,000 could fit across a human hair. To make nanocomposites, scientists incorporate particles of a reinforcing substance—such as carbon nanotubes or cellulose nanofibers—into a plastic to enhance its properties. The resulting composite material may be stronger, for example, or more heat-resistant than the original plastic.

Other nanocomposites, mainly still in the research phase, would incorporate a molecular “switch” that would enable minuscule devices to work inside the human body to treat wounds or deliver medicine. Other applications might be in prosthetics, where ultra-small componentry would allow engineers to simulate natural functions of muscles and limbs.

Twist on standard approach

The challenge in making nanocomposites, though, is getting the filler—called nanoparticles—to disperse evenly in the matrix material, usually a plastic of some kind. What tends to happen is that “the filler particles don’t disperse—they stick to each other and form globs of filler in the matrix,” says CWRU polymer scientist Christoph Weder, PhD, senior author on the paper. This “aversion to dispersion” prevents the resulting hybrid material from gaining the unique benefits of the mixture.



Drs. Jeff Capadona, Christoph Weder, Dustin Tyler and Stuart Rowan led a team at VA and Case Western Reserve University that developed a novel nanotechnology technique that could prove valuable for medical, rehabilitative and industrial uses.

The new method devised by the CWRU-VA team is a twist on the conventional approach. Instead of injecting the filler into the polymer, Weder and colleagues have learned how to first get the filler particles to lock into place within an acetone-based gel, which is then filled with polymer. A crude analogy would be pouring concrete (the polymer) into a trench reinforced by a grid of ribbed steel bars, or rebar (the filler particles). “We’re first building the nano-network, and then filling it with a polymer,” says Weder.

Lead author Jeffrey Capadona, PhD, a bioengineer with VA’s APT Center and CWRU, says the new method can be used with a variety of different polymers and fillers, making it broadly applicable. “We wanted to show that the nature of these nanofibers is not really that critical,” said Capadona. “So whoever has problems creating a nanocomposite with nanofibers and whichever polymer may be interested in this technique.”

For filler, the CWRU-VA researchers mainly used “cellulose whiskers” that are readily obtainable from renewable plant sources like wood or cotton. Another source for their nanofibers: small sea invertebrates called tunicates, a few inches long, which cling to docks in certain areas of the country. After being harvested by the scientists—the team goes on annual field trips to the Rhode Island shore—the organisms undergo a series of chemical and mechanical processing steps in the lab, including a spin in a kitchen blender. Their skins yield strong, stiff, string-like fibers that are a few millimeters long and tens of nanometers wide—just the right dimensions for nanocomposites.

The researchers say that their adaptable, innovative method allows them to successfully mix filler and matrix materials that wouldn’t otherwise blend together well, and may pave the way for a new generation of nanocomposites in the future. ■

Photo by Michele Roehrig

Central Texas VA team to study brain injuries

Researchers at the Austin VA and the University of Texas will be using a powerful MRI scanner to study brain injuries in troops returning from operations Enduring Freedom and Iraqi Freedom, and testing whether a computer-based brain-training program leads to improvements in cognitive symptoms.

The Brain Imaging and Recovery Laboratory of the Central Texas Veterans Health Care System, recently funded with \$4.2 million from VA, will take advantage of a 3-Tesla MRI scanner housed at the University of Texas.

According to its director, Robert Van Boven, MD, DDS, the program will be the first to conduct research combining the three types of brain scans the machine can perform: Functional magnetic resonance imaging (fMRI) shows brain function in real time by tracking blood flow to active regions; magnetic resonance spectroscopy (MRS) detects abnormalities by measuring brain chemicals; and diffusion tensor imaging (DTI) uncovers microscopic flaws in the connections between neurons by tracing the movement of water molecules in the brain.

"We hope we can better characterize and improve sensitivity to detect so-called 'invisible brain injury,'" said Van Boven. According to the Centers for Disease Control and Prevention, some 20,000 U.S. troops may already have suffered traumatic brain injuries (TBI), usually as the result of blasts. Many of these injuries are too subtle to detect with standard methods, says Van Boven.

The program will also be evaluating innovative cognitive-training software in collaboration with its developer, Michael Merzenich, PhD, of the University of

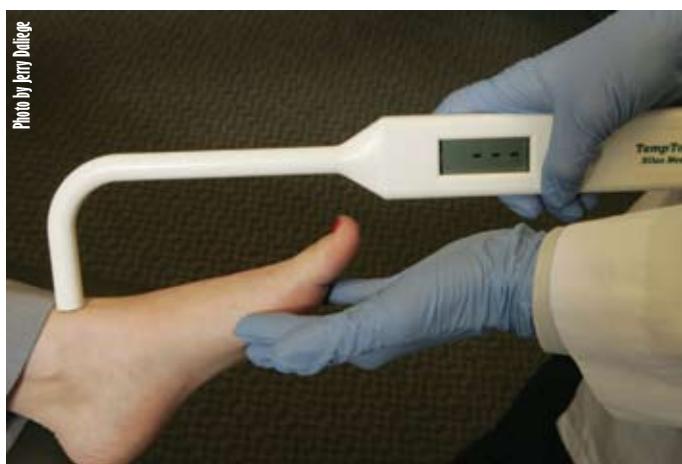


Photo by Jerry Delidge

Diabetes patients checking their feet regularly with a thermometer like the one seen here were three times less likely to develop foot ulcers.

DIABETES (from pg. 1)

People with diabetes are at risk for foot ulcers because the disease damages nerves in the feet, causing a loss of feeling. Irritations such as blisters from shoes or minor cuts can go unnoticed and eventually become infected, feeding off the extra sugar in the blood. Diabetes also leads to poor blood circulation, which can hamper healing. In severe infections, gangrene can set in, sometimes necessitating amputation. Meticulous home care and regular check-ups by a podiatrist can help, but according to Armstrong, "A way for patients to self-monitor early warning signs of an ulcer could dramatically reduce further complications."

More than a quarter of VA patients have diabetes, and some 15 percent of these veterans will develop a foot ulcer during their lifetime. At least three-quarters of nontraumatic amputations in VA involve patients with diabetes.

Based on Armstrong's latest results and those from an earlier, smaller study, the maker of the thermometer, Xilas Medical, has received funding from the National Institutes of Health to develop a version similar to a bathroom scale. Patients would step on the computerized scale and it would alert them to trouble spots requiring attention, and even signal their doctor. ■

Stroke-rehab innovator to hold endowed professorship

Leslie Gonzalez-Rothi, PhD, a VA and University of Florida researcher known for her innovative studies on rehabilitation for stroke and other brain injuries, has been named the Bob Paul Family Professor of Neurology at the University of Florida College of Medicine. "Endowed professorships are among the highest honors the College can bestow on a member of its faculty, and are reserved for a scholar of national and international acclaim," noted Bruce Kone, MD, the school's dean.

Gonzalez-Rothi is the program director of the Brain Rehabilitation Research Center (BRRC) and an investigator at the Geriatric Research, Education and Clinical Center at the Gainesville VA Medical Center. Over the past 25 years, her research has focused on understanding the workings of the brain in language and other tasks, and exploring new therapies to treat disorders in these areas. Her BRRC colleagues include biomedical engineers, neurologists, speech therapists and psychologists.

HOMELESS (from pg. 1)

RC: *Are veterans at higher risk for homelessness?*

RR: There is a relationship between military service and homelessness, but it's largely explained by other factors. There's not an independent relationship. Vietnam veterans, for example, are not more likely to be homeless than other men their age.

RC: *Does exposure to combat, and subsequent PTSD, put people at higher risk for homelessness?*

RR: Combat-related PTSD is not more common among homeless people. PTSD in general, however, is probably more common in this population. People who have been involved in street life have often had violent experiences, and many people who are homeless were abused as children. But when we looked at whether there was an unusually high rate of military PTSD among the homeless, we did not see a correlation.

A study we published back in 1991 found that the proportion of homeless veterans who had served in Vietnam and been exposed to combat fire was the same as among non-homeless veterans. Based on this and other studies, there does not appear to be a causal relation between homelessness and military service, Vietnam service in particular, or exposure to combat.

RC: *So what are the root causes of homelessness among veterans and other Americans?*

RR: Homelessness is clearly a function of two things: low incomes and high rents. Incomes among low-wage workers have been declining since the mid-1970s. Public support benefits have also been declining, so poor people have less money. At the same time, housing costs have gone up, and the availability of low-income housing has been declining. This is what creates homelessness.



Homelessness, reflected in this downtown Baltimore street scene, is "clearly a function of two things: low incomes and high rents," says VA researcher Robert Rosenheck, MD, who has studied issues relating to homeless veterans for two decades.

RC: *What about issues like substance abuse and mental-health problems?*

RR: The people who end up on the street are those who are most vulnerable—those with alcohol and drug problems, mental illness, social isolation. If you look at the gap between the number of people in the U.S. with low income and the availability of housing they could afford—it's something like nine million units—we come up short. So it's like a game of musical chairs. Someone's going to end up on the street.

RC: *Which mental-health problems in particular are most common among homeless veterans?*

RR: The most common broad mental-health diagnosis is alcohol abuse. Affective disorder is also quite common. Schizophrenia got a lot of attention early on, but it's not that common in this population.

see **HOMELESS** on next page

Veterans and homelessness

- About a third of homeless adults in the U.S. are veterans.
- Some 195,000 veterans are homeless on any given night.
- About 45 percent of homeless veterans are affected by mental illness, and slightly more than 70 percent suffer from alcohol or drug abuse.

VA's programming for homeless veterans has expanded considerably since it was first introduced in 1987. Today, VA, often in partnership with community-based providers, offers medical, psychiatric and substance-abuse treatment; domiciliaries, drop-in centers and comprehensive homeless centers; and supported housing, employment assistance and compensated work therapy. For a full description go to www.va.gov/homeless.

HOMELESS (from previous page)

RC: Are homeless veterans—or homeless people in general—at higher risk for suicide?

RR: No, but homeless people are at greater risk for mortality, largely due to medical problems.

RC: VA has a comprehensive, diverse array of homeless programs (see box). To what extent has their effectiveness been validated?

RR: VA's programs have been more studied than any others in the country. We've done evaluations of all the components, and our programs have been compared to non-VA programs. From a theoretical standpoint, the research that has not been done, and that no one will ever do, is comparing specialized homeless services with no services. That would be unethical. The question comes up, though: Are these programs better than if we did nothing? We think they are, but no one could ever do an experimental study of neglect versus an intervention.

RC: What have you found regarding the HUD-VASH program, which involves joint Supported Housing between VA and the Dept. of Housing and Urban Development?

RR: We did a cost-effectiveness study of HUD-VASH, which is a state-of-the-art intervention for the homeless. We assigned homeless veterans with psychiatric or substance-abuse disorders to one of three groups. The first received HUD-VASH services—Section 8 vouchers and intensive case management. The second received case-management only, and the third received only standard VA care.

We found that those in the HUD-VASH program were housed 16 percent more days than those in group two and 25 percent more than those in group three. People in HUD-VASH were homeless for shorter periods of time, they got out of homelessness more quickly, they had better housing and better social support, and they had reduced alcoholism.

RC: There's a trend among providers of homeless services toward "Housing First." How does that compare with HUD-VASH?

RR: Housing First says you go straight from the street into your apartment. Our model is somewhat more flexible, in that some people will be given treatment beforehand, such as detox or substance abuse treatment. It's usually very time-limited, and then they go into the apartment. There's a transitional step for those who need it. In our study of HUD-VASH, about half the clients had some residential treatment before they went into an apartment.

RC: What other VA homelessness programs has your research shown to be effective?

RR: We did a study of Supported Employment specifically for homeless veterans and showed it to be significantly more effective than usual employment services in getting people employment. We also did a study of a specialized program for homeless female veterans and looked, in particular, at a psychotherapy called "Seeking Safety." It proved to be effective in reducing symptoms and improving well-being. It's now being implemented more widely. Another example of a program we found to be effective was the Critical Time Intervention, which offers short-term intensive case management to help people transition into community housing. We showed that the intervention was effective, and are now doing a demonstration of a larger version that includes peer support.

RC: It sounds like VA has implemented some effective programs to get homeless people into housing. But do these programs work over the long term?

RR: Some people say that once you get people out of homelessness, they fall right back into it. But we've done studies of three to five years and found that once we get people housed, they tend to be stable and stay housed. ■

Brochure, video for prospective research participants

The Center on Advice and Compliance Help, part of VA's Program for Research Integrity Development and Education, has available free educational materials for veterans considering participating in research studies in VA. The materials, available in English and Spanish, are general in nature and do not replace the specific information given to veterans who choose to enroll in a particular study.

The brochure pictured below provides veterans with a balanced view of VA research and summarizes their rights should they decide to enroll in a study. Also available are an eight-minute video and a poster, intended for display in VA medical centers.

To download, view or request these materials go to www.research.va.gov/pride/resources.

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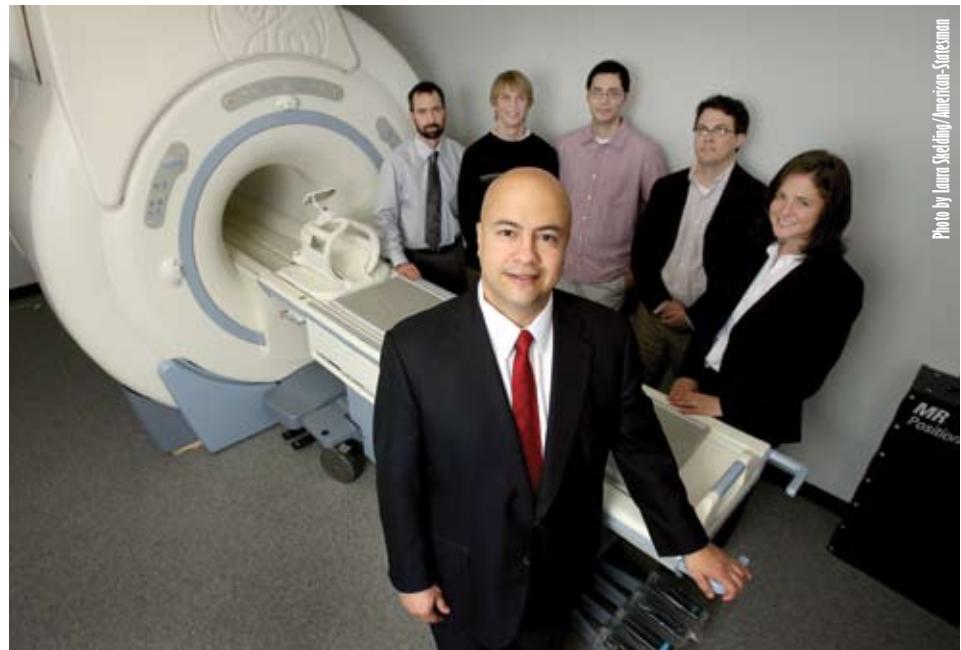
MASSAGE (from pg. 3)

release of endorphins, the body's natural "feel good" chemicals. Massage's therapeutic benefits also include increased blood flow and skin temperature, and, according to many experts, enhanced lymphatic circulation and connective-tissue healing. In any case, Hinshaw told *Time*, "Patients crave contact. They want some kind of comforting presence."

Mitchinson says only a few VA hospitals currently offer massage, but she is hopeful that the latest evidence from her study and others will lead to wider implementation. "The acceptance of massage within the medical community and the general public has really grown in the last few years. There's definitely a growing recognition of its place in healthcare." ■

HSR&D national meeting

"Implementation across the Nation: From Bedside and Clinic to Community and Home" is the theme for the 2008 national meeting of VA's Health Services Research and Development Service, being held Feb. 13 – 15 in Baltimore. For more information go to www.hsrn.research.va.gov.



Dr. Robert Van Boven, director of VA's new Brain Imaging and Recovery Laboratory, is seen here with team members (left to right) Dr. Greg Harrington, Justin Henderson, Mohamad Fakhreddine, Dr. Chris Hamilton and Claire Miller

BRAIN (from pg. 5)

California, San Francisco. In a study of the software, conducted at the San Francisco VA and other sites, older adults who used the program improved their age-correlated memory scores by about 10 years. The findings appeared in the *Proceedings of the National Academy of Sciences* in 2006.

Van Boven and colleagues will test the software over 18 weeks in a home-based recovery program with 120 veterans with mild or moderate brain injury, to see if it improves their memory and executive function. The research participants will also undergo the three types of brain scans mentioned above. The findings, says Van Boven, may advance evidence-based cognitive rehabilitation for TBI. ■