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VA Research Currents

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

Yoga study finds mix of health benefits

Drill sergeants and yoga instructors may seem like polar opposites. But a group of veterans at the VA San Diego Healthcare System is now dutifully "following orders" from their yoga teachers—and feeling less pain as a result.

According to a pilot study appearing in the November *Journal of Alternative and Complementary Medicine,* veterans with chronic low-back pain who took part in at least eight weekly yoga classes reported a significant reduction in pain. They also reported improvements in mood, energy and quality of life. The more classes they attended, the greater the gains.

The data were based on survey feedback from 33 men and women, average age 55, who had back pain for at least six months before starting yoga.

"The decreased pain, decreased depression, and increased energy and quality of life are all very important findings," said lead author Erik G. Groessl, PhD, a psychologist and health-services researcher with VA and the University of California, San Diego. "Pain is their main complaint, but depression is also important in this population."

VA physician Sunita Baxi, MD, who studied yoga therapy extensively in India, started the classes at the San Diego VA in 2003. Weekly classes have been ongoing

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Boot camp wasn't like this—Veterans (from left) "Big D" Donaldson, Jay Shufeldt and Art Harrison take part in a yoga class with instructor Dawn Landon at the San Diego VA.

Photo by Kevin Welsh

VA screenings yield data on military sexual trauma

A VA study found that about 15 percent of female veterans of the wars in Iraq and Afghanistan who use VA health care experienced sexual assault or harassment during their military service. The rate among men was much lower—less than 1 percent.

The study was presented Oct. 28 at the American Public Health Association annual meeting. The researchers examined screening data on more than 125,000 veterans of operations Enduring Freedom and Iraqi Freedom who were seen at any VA facility between September 2001 and October 2007.

"Rates obtained from VA screening cannot be used to estimate the actual rate of military sexual trauma experiences for all those serving in the military," noted coauthor Rachel Kimerling, PhD, of the

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Gene therapy for chronic pain gets first test in people

Scientists with VA and the University of Michigan are launching a phase 1 clinical trial for the treatment of cancer-related pain, using a new way of delivering a pain-relieving gene to the nervous system.

The team will use a gene transfer vector—a carrier molecule used to ferry genes into cells—created from herpes simplex virus (HSV), the virus that causes cold sores. The vector will carry the gene for enkephalin, one of the body's own natural pain relievers.

"In preclinical studies, we have found that HSV-mediated transfer of enkephalin can reduce chronic pain," says David Fink, MD, a staff neurologist at the Ann Arbor VA and chair of the department of neurology at University of Michigan Medical School. Fink developed the vector with collaborators over two decades, in part with VA funding.

Fink and colleagues will recruit 12 patients with intractable pain from cancer to examine whether the vector can be used safely to deliver its cargo to sensory nerves.

The trial represents two firsts, says Fink: It is the first human trial of gene therapy for pain, and the first study to test a nonreplicating HSV-based vector to deliver a therapeutic gene to humans. Fink says the technique may hold promise for treating other types of chronic pain, including pain from nerve damage, which often occurs in diabetes.

Collaborating across disciplines—Neurologist David Fink (left), with VA and the University of Michigan, meets with UM oncologists Frank Worden and Susan Urba to discuss a study the group is leading on gene therapy for chronic pain in cancer patients.

The HSV vector, genetically altered so it cannot reproduce, has a distinct plus, Fink says: "Because HSV naturally travels to nerve cells from the skin, the HSV-based vector can be injected in the skin to target pain pathways in the nervous system."

Chronic pain is a difficult clinical problem, explains Fink, partly because the molecular targets of conventional pain drugs tend to be widely distributed in the nervous system. As a result, "off target" side effects of the drugs often preclude their use at fully effective doses.

"This provides the rationale for using gene transfer to treat pain," Fink says. "We use the vector to deliver and express a chemical that breaks down very quickly in the body. The targeted delivery allows us to selectively interrupt the transmission of pain-related signals and thus reduce the perception of pain.

The therapy being tested may provide pain relief that is difficult to achieve through opiate drugs.

"We hope that this selective targeting will result in pain-relieving effects that cannot be achieved by systemic administration of opiate drugs," says Fink. "This trial is the first step in bringing the therapy into clinical use."

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Editor: Mitch Mirkin

A leg up on back pain—A VA study has confirmed that yoga can relieve low-back pain and provide other health benefits.

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ever since, attracting a mix of veterans—including many recent returnees from Iraq and Afghanistan.

A study at the Tampa VA found that about 45 percent of returning veterans enrolling at the facility had pain of some kind. Of those veterans, some 40 percent had low back pain.

Yoga classes take place in at least a handful of other VA centers across the nation. The Minneapolis VA, for example, offers yoga—as well as the gentle Chinese martial art tai chi—to recovering polytrauma patients. The Dallas VA offers a class as part of its women's wellness program. Outside VA, Walter Reed Army Medical Center has also been using yoga, mainly to treat PTSD in combat troops.

Past research has found a wide range of health benefits for yoga, including reduced back pain. But these studies have typically included mostly women. And they have not focused on people with multiple health problems. Baxi and Groessl's VA study included mostly men and analyzed a variety of outcomes covering physical and mental health. The researchers hope their results will help broaden yoga's appeal within VA, especially as a therapy for veterans with chronic pain.

"People are realizing the danger of long-term use of narcotic pain medications and want something with no side effects," says Groessl.

The group now plans a larger, longer trial of yoga that will measure outcomes such as pain, disability, function, depression, anxiety, energy, and overall quality of life.

Yoga facts

- Yoga originally developed as part of ancient Indian medicine and philosophy.
- In the U.S. today, it is practiced by an estimated 16 million people.

Leading the charge toward evidence-based medicine

Think of them as the Sherlock Holmes of VA research.

Since 2007, two groups of VA investigators—one in California, the other in Oregon—have been tackling tough and timely research questions of particular importance to VA policymakers. The researchers are part of the Evidence Synthesis Program (ESP) funded by VA Health Services Research and Development.

Like detectives, ESP investigators comb through evidence—in this case, published research findings. They look for clues others may have missed. They rigorously evaluate, analyze and synthesize data. They uncover previously unrecognized patterns and reveal new insights. Their goal is to provide the best possible information to guide medical care. The end product is a comprehensive, incisive report that gets disseminated widely within VA, primarily to top health care planners and managers. The reports also get published in the general medical literature for clinicians worldwide to learn from.

Preponderance of evidence—The Portland-based ESP group of Dr. Mark Helfand (second from left) includes Dr. Devan Kansagara, Dr. Steven Dobscha and Michele Freeman.

Reports available online

So far, seven ESP reports have been completed. Veterans and the general public can see them at www.hsrd.research.va.gov/publications/esp. The topics are diverse, but all are strongly relevant to veteran care: pain in polytrauma patients; high blood sugar or pain in hospital patients; racial and ethnic disparities in care; and others.

Joseph Francis, MD, MPH, deputy director of VA's Office of Quality and Performance, says his and other offices within the Veterans Health Administration rely on ESP for guidance.

"As we reshape our policy initiatives to be more evidence-based, one cannot overstate the importance of a thorough, unbiased assessment of the medical literature," says Francis. "Many of the key questions facing VHA—how to address suicide risk, manage polytrauma, or reduce health disparities—require a balanced approach to identify, evaluate and summarize relevant scientific studies so that appropriate treatment guidelines or policies can be formulated. ESP has contributed to all of these, and its importance is growing."

According to David Atkins, MD, MPH, associate director for Health Services Research and Development, ESP has helped improve care in VA and beyond. A report on osteoporosis in men not only led to new screening procedures in VA but helped change the clinical guidelines of the American College of Physicians. Another on drug therapy for a common prostate condition led to changes in which medications are available to VA patients. And a report on women's health was "incorporated into the national agenda for reforming the delivery of care to women veterans," says Atkins.

Francis notes that "ESP is a wonderful means for researchers to interface with the VA health care system and see their efforts have a direct impact on care."

Program builds on existing infrastructure

Mark Helfand, MD, MPH, MS, leads the ESP team based at the Portland VA Medical Center. His counterpart at the VA Greater Los Angeles Healthcare System is Paul Shekelle, MD, PhD. Both VA physician-researchers also lead Evidence-based Practice Centers funded by the federal government's Agency for Healthcare Research and Quality (AHRQ). Those

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ESP *(from previous page)*

centers, 14 in all nationwide, do work similar to what ESP does, but on a broader scale—the focus is not health care for veterans but for Americans in general. Rather than duplicate what AHRQ has done with its evidence centers, VA "buys time" from these centers—in effect, building on staff and expertise already in place. The collaboration is a prime example of federal agencies leveraging their resources.

"VA is taking advantage of the infrastructure that AHRQ built—that's what makes this program possible," says Helfand. "If we had to have all the trained librarians and research associates and other resources required to do this work, there would be a much larger cost to VA for the same product."

Helfand also points out another way in which taxpayer dollars are well-spent through ESP.

"If VA is asking us, what's out there that really works that we should be doing in VA, we don't have to review the primary literature ourselves. We can start by using other researchers' systematic reviews and evidence reports. We evaluate their quality, their thoroughness, their relevance to the questions that VA has asked. Then we can supplement by updating the evidence with the most current information and further evaluating how it all applies to VA settings and populations."

Helfand emphasizes that ESP reports go broader and deeper than other types of literature reviews.

"There's a lot of terminology out there. Most people think of a systematic review as a narrowly defined review of randomized clinical trials. That's something we're rarely asked to do. We're usually asked to look at a much wider scope of evidence."

As an example, he cites his team's recent report on pain in polytrauma patients. "We went so far beyond that narrow notion of the systematic review," says Helfand. "We looked, for instance, at case reports—single examples of something that may have helped in what can be a frustrating or desperate situation. Not to say that something definitely works, or is effective, but to help guide VA's future research and orient it toward promising innovations."

That aspect of ESP—its ability to pinpoint critical issues requiring further study—makes it especially valuable to the overall VA research program.

"We're very proud of the work they're doing," says Seth Eisen, MD, MSc, director of Health Services Research and Development. In addition to informing VA policymakers, says Eisen, the ESP reports "help identify the next issues that need to be addressed through research."

Women at higher risk—According to the Department of Defense, women service members were the victims in 1,916 out of 2,085 unrestricted reports of sexual assault in the military in 2007.

TRAUMA *(from page 1)*

Palo Alto branch of VA's National Center for PTSD, "but our results do help guide mental health treatment for veterans in our health care system." Kimerling is also with VA's Center for Health Care Evaluation.

Both men and women who said they were sexually assaulted or repeatedly harassed in the military—termed military sexual trauma (MST) by VA—were more likely to have a diagnosis of a mental health condition than those who did not report MST. Women with MST had a 59 percent higher risk for mental health problems, while the risk among men with MST was 40 percent higher. The most common conditions linked to MST were depression, PTSD, anxiety, adjustment disorders and substance abuse disorders.

"These data highlight the importance of VA's universal screening policy and early intervention among veterans who have experienced sexual trauma, to prevent long-term consequences," said lead author Joanne Pavao, MPH, of the National Center for PTSD.

Under VA policy, all male and female veterans are screened for MST. Free treatment for MST-related conditions is provided at all VA health care facilities.

A related VA study published in June in the journal *Psychiatric Services* found that VA's MST screening program has boosted rates of mental health treatment. The study examined the rates of VA mental health care use in the three-month period following screening for 573,640 veterans screened in 2005. The rates of positive screens were 19.5 percent for women and 1.2 percent for men.

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Self-monitoring of anti-clot drug has some pluses

The results of a VA clinical trial involving nearly 3,000 veterans at 28 VA medical centers, presented Nov. 12 at the scientific meeting of the American Heart Association, may help doctors decide on the best way to manage patients taking the drug warfarin to prevent harmful blood clots.

Traditionally, doctors monitor patients on warfarin, sold as Coumadin, over several visits. They test how fast the blood clots and adjust the dose accordingly: Too low a dose won't prevent clots, and blood flow to the heart, brain or other areas of the body could be blocked. Too high a dose could lead to internal bleeding.

Nowadays, patients have the option of tracking their own response at home using handy blood analyzers known as INR monitors. INR stands for international normalized ratio—a measure of how fast the blood clots. Patients do a finger-stick, apply a drop of blood to a test strip, and feed the strip into the device. The procedure is not unlike that used by people with diabetes to check their blood sugar. Warfarin patients can then convey the results to their doctor or nurse without having to come into the clinic.

The VA study aimed to test how well patient self-monitoring works. Most importantly, would it help prevent negative outcomes such as strokes or bleeding incidents?

The answer, according to the five-year study, is no. While the outcomes overall were better than those found in most non-VA studies, there was no significant difference between patient self-testing and a more conventional approach—"high quality" management by a health care team—in terms of strokes, major bleeding incidents, or death.

"The data show that any extra benefit of patient self-testing would be modest at best," said study co-leader David Matchar, MD, an internist with the Durham VA and Duke University School of Medicine.

More on the Home INR Study

- Included 2,922 patients from 28 VA medical centers.
- 98 percent of patients were male, average age 67.
- Study began in 2003 and ended in 2008.
- Funded by VA's Cooperative Studies Program.

No place like home—Study participant John Stoffel, 82, of Wisconsin, said he found the INR monitor easy to use and liked not having to travel to a clinic to get his clotting rate checked.

Self-testing, however, did boost patients' satisfaction with warfarin therapy and increase the amount of time they were in the appropriate dose range.

Study co-leader Alan Jacobson, MD, a cardiologist and researcher with VA and Loma Linda University School of Medicine, suggested that one take-home message of the study is that "patients who are being systematically monitored—no matter by what means—are likely to have good outcomes." He said self-monitoring may be a good option for many patients, especially for those who live in rural areas or who otherwise have difficulty getting to a clinic.

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According to the website of the Department of Defense Sexual Assault Prevention and Response Office, "[DoD] does not tolerate sexual assault and has implemented a comprehensive policy that reinforces a culture of prevention, response and accountability that ensures the safety, dignity and well-being of all members of the Armed Forces." For 2007, there were 2,688 total reports of sexual assault involving service members, both deployed and non-deployed. Dr. Kaye Whitley, director of the DoD office, told *USA Today,* "There is concern about the number of sexual assaults, and we're working very hard to prevent them."

The study by Kimerling, Pavao and their team was funded by VA Health Services Research and Development.

Drinking green tea may stop skin cancer—A lab study led by Santosh Katiyar, PhD, of VA and the University of Alabama at Birmingham strengthens earlier evidence that drinking green tea may inhibit skin cancer. Previous research by the group established the benefits of topically administering to mice the main anti-cancer component in green tea, a robust antioxidant known as EGCG. In the new research, Katiyar and colleagues added a mix of green tea's beneficial compounds—known as polyphenols—to the drinking water of mice exposed to ultraviolet radiation. The tea-based mixture promoted DNA repair, thwarted inflammation and stopped the formation of tumors in the mice. (*Journal of Investigative Dermatology,* online Nov. 20, 2008)

Obesity and prostate cancer risk—A team at the Durham VA and Duke University Medical Center challenged past study findings suggesting that obesity is associated with a lower risk for prostate cancer risk. They analyzed 441 prostate biopsies and found, after adjusting for certain clinical characteristics, that obesity was actually associated with a 98-percent higher risk. (*Urology,* Nov. 2008)

Kidney impairment linked to bone loss—A team at VA's Minneapolis-based Center for Chronic Disease Outcomes Research found that older men with reduced kidney function were at higher risk for hip bone loss. The study included 404 men who were followed, on average, more than four years. Previous studies on the link between kidney function and bone loss had yielded mixed findings. The authors of the new study say "health care providers should consider renal function when evaluating older men for risk factors for bone loss and osteoporosis." (*Osteoporosis International,* Nov. 2008)

Drink your green tea—Santosh Katiyar, PhD, of VA and the University of Alabama at Birmingham has shown that the "polyphenols" in green tea inhibit the formation of skin tumors in mice exposed to ultraviolet light. *(See item at left.)*

Drug found ineffective for heart failure—An international study led by the chief of cardiology at the San Francisco VA Medical Center, Barry Massie, MD, found that the drug irbesartan was no more effective than placebo in treating a common form of heart failure. Irbesartan itself is used mainly for hypertension and not heart failure, but it is considered representative of the class of medications known as angiotensin receptor blockers, or ARBs, which are widely used for heart failure. The more than 4,000 patients in the study had a form of the condition known as preserved ejection fraction heart failure. According to Massie, "We really don't understand the nature of heart failure with preserved ejection fraction. It's likely not a single disease or syndrome, and, so far, it has been difficult to come up with a therapy that makes a difference. This study at least tells us that ARBs are probably not the answer." (*New England Journal of Medicine,* online Nov. 11, 2008)

Privacy curtains in hospitals could spread germs—The curtains between hospital beds can harbor drug-resistant bacteria and may be playing a role in the spread of the germs, suggests a study at the Cleveland VA Medical Center. A team led by Curtis Donskey, MD, director of infection control at the hospital, found that 42 percent of curtains were contaminated with vancomycin-resistant enterococci; 22 percent with methicillin-resistant Staphylococcus aureus; and 4 percent with Clostridium difficile. Moreover, it appeared the germs were easily transferred when study personnel wearing gloves touched the curtains and then pressed their hands into "hand imprint cultures." Donskey noted that his VA hospital, like many others, washes privacy curtains every four months or whenever they are visibly soiled. (*Infection Control and Hospital Epidemiology,* Nov. 2008)

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CAREER MILESTONES

Psychologist cited for Iraq role

Veterans Affairs research scientist Keith Humphreys, PhD, will receive the 2009 American Psychological Association award for Distinguished Contributions to Psychology in the Public Interest for his work in building mental health service systems for VA and Iraq.

Humphreys directs VA's Program Evaluation and Resource Center in Palo Alto and is a professor at Stanford University. He was in Washington, D.C., in 2004 helping to develop VA's national Strategic Plan for Mental Health when he was asked to volunteer on a task force set up by the Substance Abuse and Mental Health Services Administration. The mission: rebuild the Iraqi Ministry of Health's shattered mental health care system.

"It was a daunting prospect, but also an exciting one," said Humphreys. "As soon as I met Dr. Sabah Sadik, Iraq's national mental health adviser, I was hooked. It wasn't just the level of need he described, but it was also his courage and that of his colleagues that inspired me to join up."

Humphreys has since conducted mental health trainings and policy consultations with Iraqi medical professionals in Turkey, Jordan, Egypt and Iraq, where he expects to return this spring. Meanwhile, he also helped guide a major increase in VA's national network of mental health services, strengthening the agency's position as one of the world's largest and most recognized authorities on mental health services.


Dr. Keith Humphreys

"We are proud to see Dr. Humphreys recognized for his service, and honored that he continues a long legacy of VA researchers and physicians standing at the forefront and establishing modern medicine," said VA Secretary Dr. James B. Peake.

Humphreys said the award serves to recognize his "wonderful colleagues in VA and in Iraq. They are a credit to their profession and a lifetime source of inspiration and friendship to me."

Neural-regeneration researchers garner awards

Two researchers at VA's Center of Excellence on Restorative Function in Spinal Cord Injury and Multiple Sclerosis, based at the West Haven (Conn.) VA Medical Center and affiliated with Yale University, recently received awards for their work.

Robert J. Brown, MD, a postdoctoral fellow at the center, received the James J. Peters Spinal Cord Injury Scholarship Award from United Spinal Association to supplement his VA funding. Brown's research involves treating spinal cord tumors or injuries in rats by administering precursor cells that foster neuron growth.

Jeffery D. Kocsis, PhD, who codirects the West Haven center, received the da Vinci Lifetime Achievement Award from the Michigan Chapter of the National Multiple Sclerosis Society. Kocsis has been a pioneer in studying the use of cell transplants to restore and preserve function in the injured central nervous system. The research may eventually lead to new treatments for both spinal cord injury and multiple sclerosis.