



# RESEARCH CURRENTS

Research News from the U.S. Department of Veterans Affairs



Photo by Joe De Sciose

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Photo by Michael Moody

### A drop in testosterone prescriptions, despite upward trend in diagnoses

Testosterone therapy rates are on the rise worldwide, with some reports citing an “epidemic” of testosterone prescribing. VA may be bucking the trend, however, according to research by a team with the University of Washington and VA’s Pacific Northwest region.

The results suggest that despite increases in testing, and in the actual proportion of men with low testosterone levels, the number of VA patients who received testosterone therapy has actually decreased.

Testosterone therapy isn’t necessarily a bad thing. Numerous studies have shown the negative effects of testosterone deficiency, from erectile dysfunction and decreased libido to increased risk of osteoporosis, weight gain, and depression. But while the hazards of low testosterone are well-documented, so too are the risks of therapy. Recent studies have suggested a link between testosterone therapy and heart disease, sleep apnea, and even prostate cancer.

For the study, researchers with VA and the University of Washington identified male Veterans aged 40 - 89 years and examined what proportion were tested, diagnosed, and subsequently treated for low testosterone between 2002 and 2011.

They saw an increase in the total number of

◀ A study in VA’s Pacific Northwest region found that despite increases in testing, and in the actual proportion of men with low testosterone levels, the number of VA patients who received testosterone therapy has actually decreased.

male VA patients within the target age group, from 129,247 in 2002 to 163,572 in 2011. Part of the increase, they say, is due simply to the fact that men are living longer.

The proportion of men in the target group who were tested for low testosterone also increased during the same time frame, from slightly more than 3 percent to nearly 6 percent.

Among those tested, the overall number of men with low testosterone levels increased as well, from 35 percent to more than 47 percent.

Despite that increase, though, the number of men who received testosterone therapy within a given year decreased during the study period, from 31 to 28 percent. That contrasts with results from studies outside VA looking at testosterone therapy trends.

The researchers explain that for one thing, Veterans in VA care are more likely to have comorbidities that directly contribute to lowered testosterone. Also, rather than prescribe testosterone therapy, clinicians may choose to address what they believe is the root cause—being overweight, for example. In many cases, write the researchers, it’s more relevant to try and remedy the underlying cause rather than simply try to raise testosterone levels.

(*Andrology*, March 2015)

### Study adds evidence on link between PTSD, heart disease

In a study of more than 8,000 Veterans living in Hawaii and the Pacific Islands, those with posttraumatic stress disorder had a nearly

50 percent greater risk of developing heart failure over about a seven-year follow-up period, compared with their non-PTSD peers.

The study adds to a growing body of evidence linking PTSD and heart disease. The research to date—including these latest findings—doesn’t show a clear cause-and-effect relationship. But most experts believe PTSD, like other forms of chronic stress or anxiety, can damage the heart over time.



Photo by Spc. Richard Del Vecchio

U.S. Army soldiers receive instruction while waiting for Iraqi detainees to unload from a bus in Baghdad in 2008. Veterans with PTSD are at higher risk of heart failure as they age, according to a new VA study.

“There are many theories as to how exactly PTSD contributes to heart disease,” says Dr. Alyssa Mansfield, one of the study authors. “Overall, the evidence to date seems to point in the direction of a causal relationship.”

The study tracked 8,248 Veterans who had been outpatients in the VA Pacific Islands system. The researchers followed them an average of just over seven years. Those with a PTSD diagnosis were 47 percent more likely to develop heart failure during the follow-up period. The researchers controlled for differences between the groups in health and demographic factors.

Out of the total study group, about 21 percent were diagnosed with PTSD. Of the total 371 cases of

heart failure during the study, 287 occurred among those with PTSD, whereas only 84 cases occurred among the group without PTSD.

Combat service, whether or not it led to a full-blown PTSD diagnosis, was itself a strong predictor of heart failure. Those Veterans with combat experience were about five times more likely to develop heart failure during the study period, compared with those who had not seen combat. Other predictors of heart failure were advanced age, diabetes, high blood pressure, and overweight or obesity.

(*American Journal of Public Health*, April 2015)

### Strong statin-diabetes link seen in large study of Tricare patients

In a database study of nearly 26,000 beneficiaries of Tricare, the military health system, those taking statin drugs to control their cholesterol were 87 percent more likely to develop diabetes.

The study confirms past findings on the link between the widely prescribed drugs and diabetes risk. But it is among the first to show



A pharmacist scans a prescription at the Joint Base McGuire-Dix-Lakehurst pharmacy, serving Tricare customers. VA research based on the records of nearly 26,000 Tricare patients shows a link between statin drugs and increased diabetes risk.

the connection in a relatively healthy group of people. The study included only people who at baseline were free of heart disease, diabetes, and other severe chronic disease.

“In our study, statin use was associated with a significantly higher risk of new-onset diabetes, even in a very healthy population,” says lead author Dr. Ishak Mansi. “The risk of diabetes with statins has been known, but up until now it was thought that this might be due to the fact that people who were prescribed statins had greater medical risks to begin with.”

Mansi is a physician-researcher with the VA North Texas Health System and the University of Texas Southwestern in Dallas.

In the study, statin use was also associated with a “very high risk of diabetes complications,” says Mansi. “This was never shown before.” Among 3,351 pairs of similar patients—part of the overall study group—those patients on statins were 250 percent more likely than their non-statin-using counterparts to develop diabetes with complications.

Statin users were also 14 percent more likely to become overweight or obese after being on the drugs. Mansi points out that other studies have arrived at a similar finding through different research methods. The study also found that the higher the dose of any of the statins, the greater the risk of diabetes, diabetes complications, and obesity.

Mansi stresses that the study doesn’t definitively show that statins cause diabetes, nor does it mean people should stop using the drugs, which are widely prescribed to help people lower their cardiac risk factors.

“No patient should stop taking their statins based on our study, since statin therapy is a cornerstone in treatment of cardiovascular diseases and has been clearly shown to lower mortality and disease progression,” he says. “Rather, this study should alert researchers, [clinical] guideline writers, and policymakers that short-term clinical trials might not fully describe the risks and benefits of long-term

statin use for primary prevention.”

He adds: “I myself am a firm believer that these medications are very valuable for patients when there are clear and strict indications for them. But knowing the risks may motivate a patient to quit smoking, rather than swallow a tablet, or to lose weight and exercise. Ideally, it is better to make those lifestyle changes and avoid taking statins if possible.”

(*Journal of General Internal Medicine*, online April 28, 2015)

### Cognitive behavioral therapy as effective as light therapy for seasonal affective disorder

People with winter seasonal affective disorder, or SAD, could benefit as much from cognitive behavioral therapy as they do from light therapy, the current gold-standard for treatment, according to new research.

The findings could offer patients additional treatment options, and perhaps a better long-term solution, says Dr. Kelly Rohan, a professor at the University of Vermont who completed her residency and post-doctoral fellowship at the G.V. Montgomery VA Medical Center in Jackson, Miss.

“People would like for us to split these treatments out and say one is more effective than the other or that one works better for certain patients, but in terms of the data it is neck and neck. The treatments were not distinguishable in terms of their performance,” says Rohan.

The study randomized 177 adults who were experiencing a current bout of SAD. Eighty-eight were given light therapy. The rest underwent cognitive behavioral therapy. In the end, both groups experienced remission rates of 47 percent.

Previous studies support the effectiveness of light therapy in treating seasonal affective disorder, although the reasons are not entirely clear. Many



An airman uses a “happy light” at Ellsworth Air Force Base in 2014. A clinical trial by VA researchers and colleagues found that light therapy and cognitive behavioral therapy are equally effective for seasonal affective disorder.

researchers suspect the light may replace lost sun exposure due to shorter days and reset the body’s internal clock, or circadian rhythms. For this reason, most clinicians who use light therapy advocate morning treatment.

The CBT used in the study was an adaptation of traditional cognitive therapy. “We had to condense the treatment into a shorter time frame in order to fit the winter season,” says Rohan. “It’s kind of a CBT boot camp.” The participants underwent twelve 1.5-hour sessions, delivered twice per week over six weeks, in groups with a community therapist. Participants focused on behaviors that would help them cope with winter, such as changing negative thoughts related to the weather or season, and were encouraged to engage in pleasurable activities during the winter to counteract avoidance.

Light therapy is effective, says Rohan, but it requires a person to commit to daily therapy every winter. Not all patients may be willing or able to adhere. CBT, on the other hand, is based on the assumption that people learn skills in treatment to fortify themselves against recurrence after treatment ends.

(*American Journal of Psychiatry*, online April 10, 2015)

## Compound in magnolia may combat head and neck cancers

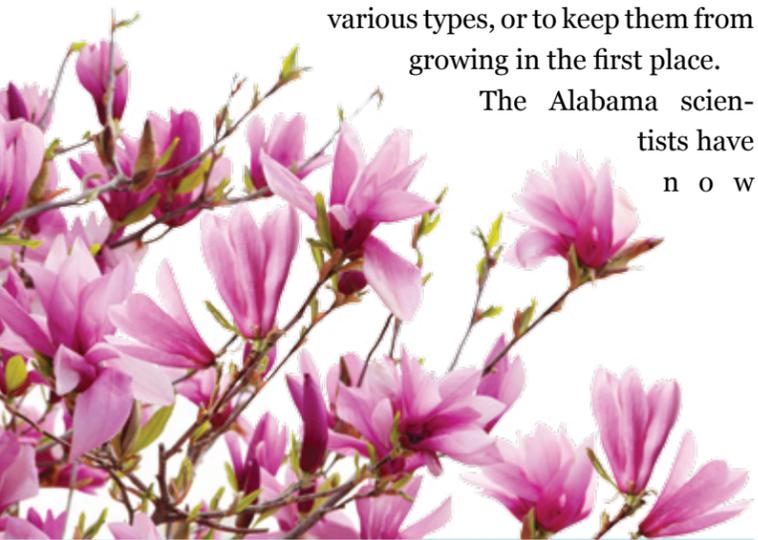
Magnolias are prized for their large, colorful, fragrant flowers. Does the attractive, showy tree also harbor a potent cancer fighter?

Yes, according to a growing number of studies, including one from VA and the University of Alabama at Birmingham.

The study focused on squamous cell head and neck cancers, a scourge among those who use tobacco and alcohol. According to the National Cancer Institute, at least 3 in 4 head and neck cancers are caused by the use of tobacco and alcohol. The cancers have only a 50 percent survival rate, killing some 20,000 Americans each year.

Enter honokiol—chemical formula C<sub>18</sub>H<sub>18</sub>O<sub>2</sub>. As one of the major active compounds in magnolia extract, the phytochemical has been used for centuries in traditional Chinese and Japanese medicine to treat anxiety and other conditions. More recently, scientists have been discovering that the compound, found in magnolia bark, is a wily and versatile adversary of cancer. It seems to exploit many biochemical pathways to shrink tumors of various types, or to keep them from growing in the first place.

The Alabama scientists have now



Honokiol, a compound derived from the bark of the magnolia tree, is proving to be a potent cancer fighter in lab studies. ©iStock/Dole08

shown how it works against head and neck cancers: It blocks a protein called epidermal growth factor receptor, or EGFR. Prior research has found that almost all head and neck cancer cells display an over-abundance of the protein, and it had been suggested in the literature as a potential target.

The VA-UAB team says, based on its lab studies, that honokiol binds more strongly with EGFR than does the drug gefitinib (sold as Iressa), which is commonly used to treat head and neck cancers.

The researchers tested honokiol on cell lines derived from human cancers of the oral cavity, larynx, tongue, and pharynx. In all cases, the botanical shut down the aberrant cells. The team also tested it against tumors implanted into mice, with similar results.

Senior author Dr. Santosh K. Katiyar and his colleagues wrote, “Conclusively, honokiol appears to be an attractive bioactive small molecule phytochemical for the management of head and neck cancer which can be used either alone or in combination with other available therapeutic drugs.”

(*Oncotarget*, online May 19, 2015)

## Pilot study yields promising results on Swedish massage for knee pain

Put down the pill bottle—get a massage instead. Lots of people with arthritis pain would be happy to hear this advice from their doctor. But researchers are still testing the benefits of this therapy with ancient roots—whom it helps, for what conditions.

Now, a team at Duke University and the Durham (N.C.) VA Medical Center has shown in a small pilot study that Swedish massage is an acceptable and feasible treatment for VA health care users with osteoarthritis of the knee. Moreover, the Veterans who took part in the study reported, on average, about a 30 percent improvement in pain, stiffness, and function.

Dr. Adam Perlman of the Duke Integrative



Veterans with osteoarthritis of the knee benefited from Swedish massage in a VA-Duke University pilot study.

Medicine Center, working with VA colleagues, led the trial, involving 25 Veterans. The group was mostly men, whites and African Americans, with an average age of 57, and an average BMI of around 32, which is above the obesity threshold.

Perlman led an earlier clinical trial that found the therapy effective for knee osteoarthritis in a general population. But he wanted to put Swedish massage to the test for VA patients.

For one thing, most VA patients are men, who as a group might be somewhat less receptive than women to the idea of massage. Think about who typically goes to spas.

Second, VA patients are more likely than the general population to have multiple health problems—physical or mental. This could complicate how massage is delivered, or its effects.

As it turns out, the idea of Swedish massage sat well with the Veterans in the study.

Almost all of those who started the study—23 out of 25—completed the eight weekly one-hour massage sessions, given at Duke Integrative Medicine, about a mile from the Durham VA. More than 90 percent of them said they wanted to continue to receive massage

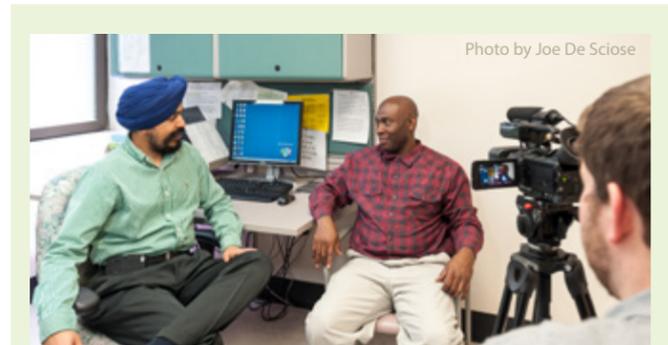
as part of their arthritis treatment plan. Nearly 90 percent said they thought other Veterans would try massage if it were offered in VA.

Dr. Kelli Allen, a VA health services researcher who worked on the study, says recruiting a diverse mix of VA arthritis patients for the study posed no particular challenge.

“We had comparable rates of recruitment, among eligible participants, as those we have seen in clinical trials of other behavioral and lifestyle interventions among Veterans with osteoarthritis. That was an important aspect of feasibility

for us to assess in a pilot study. Our experience suggests there is indeed interest in massage therapy among VA health care users.”

(*Journal of Alternative and Complementary Medicine*, June 2015)



## Here's the story

Journalists and marketers have long used people's personal stories to get their point across. Now, VA health researchers are tapping into the same power.

Read more at [www.research.va.gov/currents/winter2015/winter2015-24.cfm](http://www.research.va.gov/currents/winter2015/winter2015-24.cfm).

## Veterans as tour guides around the VA: New research method gleans insights from patients

Seeing VA medical centers through the eyes of the Veterans who come there for care—that was the goal of recent studies by a VA team. The researchers used guided tours, given by the patients themselves.

Navy Veteran Pernell Baker is a patient at the Washington, DC, VA Medical Center. VA patients like him took part in “guided tour” research at other VA sites to let researchers know their thoughts and feelings about the care they receive.

Photo by Robert Turtil



Seeing VA medical centers through the eyes of the Veterans who come there for care—that was the goal of recent research by a VA team.

The researchers used guided tours, given by the patients themselves. Thirty Veterans took part. Each one individually gave a tour, taking a researcher around the medical center for about 30 to 45 minutes.

“We asked the Veterans to take us through what would be a typical visit for them—what clinics they would go to, where they would go if they needed help finding something, where they would go to wait for things,” says VA investigator Dr. Sara Locatelli. “The participants were in charge. We followed them.”

The approach is new in health care settings.

“I’ve seen this method used in community-based research, looking at things like how navigable a neighborhood is for residents, or whether there is enough green space. But I hadn’t seen it used before in health care systems,” says Locatelli, with the Center of Innovation for Complex Chronic Healthcare, based at the Hines (Ill.) VA Hospital.

Locatelli and colleagues Dr. Sherri LaVela and Stephanie Turcios will present the work at a July 2015 national meeting of VA health services researchers. The team previously published the study, and a related one based on guided tours by VA health care providers and other employees, in the *Patient Experience Journal* and *Health Environment Research and Design Journal*.

### Comments on everything from wall color to waiting time

Locatelli says she came upon the guided-tour method when her group was developing a proposal for VA’s Office of Patient-Centered Care and Cultural Transformation. The group, under LaVela’s direction, was eventually funded to study two VA pilot sites where a suite of changes were underway, aimed at making VA care more patient-centric.

Those changes covered everything from the color of patient on the walls—the goal being to use more soothing, calming hues—to the physical layout of clinics, to the routines that patients would go through on their visits.

The guided tours yielded frank comments from Veterans on all of the above.

“I feel good about going through most areas, especially up and down the corridor and around the [cafeteria],” said one participant. “[In] the Atrium, there’s plenty of light.”

But said another: “Typically the lobby is full of a bunch of people. ... People on top of people. ... It is overwhelming when you come through here because you don’t know where you are going.”

The researchers audio-recorded the tours as they followed along, asking follow-up questions and posing the occasional open-ended query. They later coded and analyzed the Veterans’ remarks, paying close attention to the emerging themes.

Many of the “tour guides” commented on the



“We asked the Veterans to take us through what would be a typical visit for them. ...”

signage around the medical center.

“In terms of getting around, everyone—Veterans and employees alike—had comments on signs in the facility,” says Locatelli. “They often had problems with the signs, especially when they were too small or contained a lot of information, or weren’t up to date. As part of patient-centered care, there has been a lot of reorganization of clinics, but the signs

and see your primary care provider. If they write you a prescription, you first go wait in this line to talk to a pharmacist, right in the primary care clinic. That’s to tell you about interactions, to see if you have any questions—standard pharmacist counseling. After that, you go to a completely different area of the hospital, where the pharmacy is, to pick up the prescription.”

The problem was, says Locatelli, that “some people who didn’t realize that the pharmacist wasn’t in the pharmacy. So they immediately went from the primary care clinic to the pharmacy and sat there for 20 or minutes before asking someone ‘when is my prescription going to be ready?’ And it was only at that point that they learned they had missed a step.”

Even some providers—those writing the prescriptions—weren’t aware of the correct procedure, says Locatelli.

“They were erroneously telling Veterans, ‘OK, I sent the prescription, you can go to the pharmacy to pick it up.’ They didn’t know the Veteran was supposed to first talk to a pharmacist in the primary care clinic.”

Those types of insights, gleaned from the guided tours, could be valuable nuggets for clinic or medical center directors, says Locatelli. They might want to rethink the process, or perhaps ensure that patients—and providers—are better informed.



Photo by Robert Turtil  
Steve Borowsky receives care at the Washington, DC, VA Medical Center. Veterans like him took part in “guided tour” research at other VA sites to share their experiences as VA patients.

haven’t always been up to date. So people could get confused and lost.”

### Tours shed light on confusing pharmacy process

Veterans’ confusion could also stem, in some cases, from changes to the process of care. Locatelli shares an example:

“Veterans and employees alike talked about the complicated processes around receiving prescriptions. At some facilities, what you do is you go in

### Non-researchers may be able to use method

She says qualitative research such as focus groups or the guided-tour method typically involves small samples—in this case, 30 Veterans and 25 employees—and may not be generalizable in the same way that large surveys or database studies might be. However, the research can point to “relationships between variables that you can then further explore in a quantitative way,” says Locatelli. For example, some findings from the guided tours might be useful items for medical centers to include in patient surveys.

For that matter, health care managers may be able to harness the power of guided tours for their own sites, even without the formal expertise of trained researchers.

“For the most part, it’s about listening, keeping on your toes, and being able to ask timely follow-up questions on the fly. There are lots of people who have that skill set,” says Locatelli.

“If I am the director of a primary care clinic,” she adds, “and I want to do these guided tours with some of my patients, I am probably going to be familiar enough with the particular environment and processes to be able to come up with some pretty good follow-up questions. Of course, I would have to

be careful to not ask the questions in a biased way that is going to push people toward answering in a certain way.”

### Tours elicit strong sense of Veteran identity

One especially noteworthy theme that came up in the guided tours was Veteran identity. By and large, says Locatelli, Veteran patients expressed a strong sense of identity with their fellow Veterans—and, by extension, with VA.

“They identified themselves as Veterans—that’s an important part of who they are—and they see their receiving care through VA as an extension of that identity. They said things like, ‘Even though there are problems—the wait times can be long sometimes—this is the best place for me for the issues I have.’ They talked a lot about camaraderie—just sitting in the clinic and knowing they could turn to anyone around them and talk to them, and relate to that person.

“Working in the VA, it wasn’t surprising, because we see those interactions on a daily basis,” says Locatelli. “But it was neat to hear them articulate that.” ★



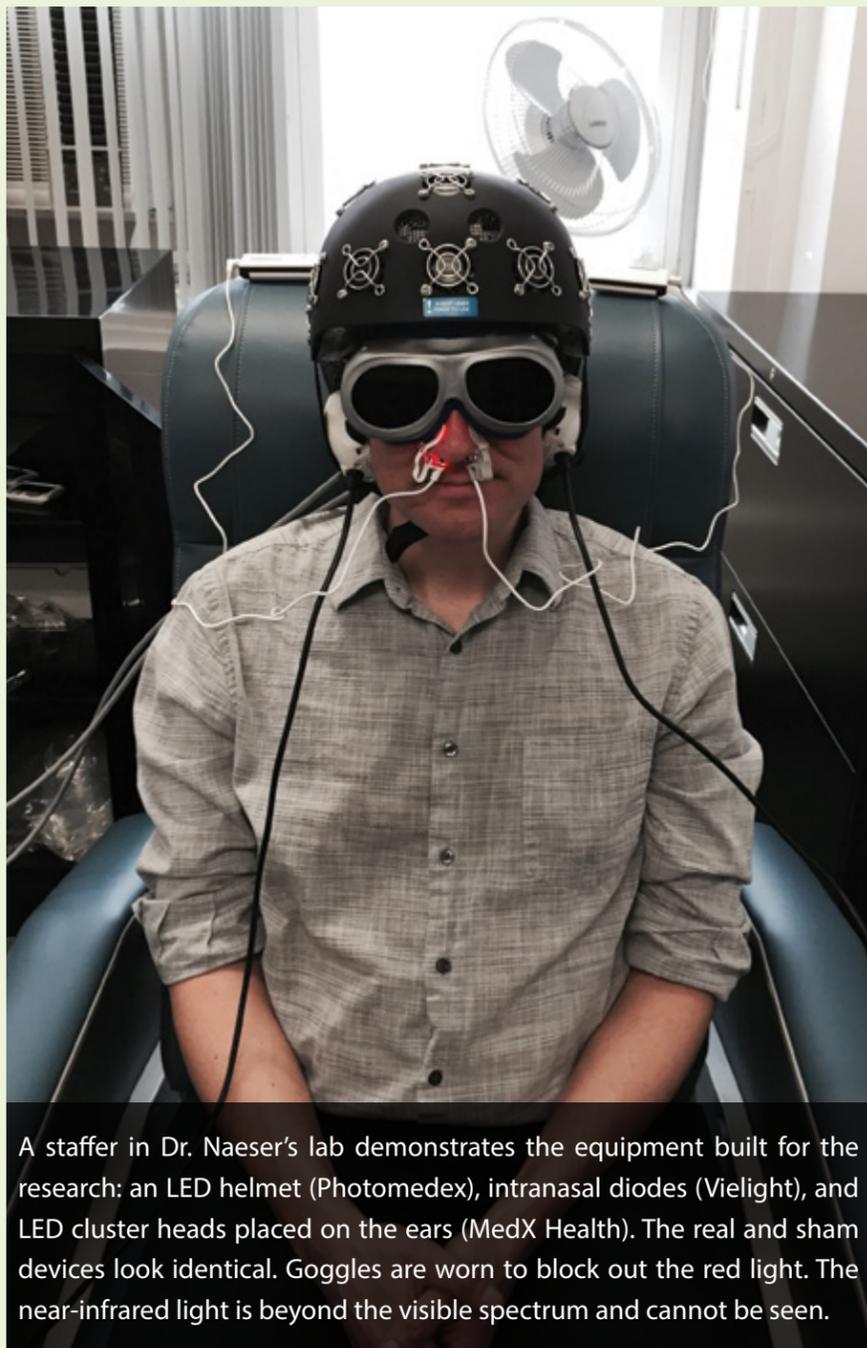
### New studies to use MVP data

VA is funding four new studies that will use genetic and other data from its Million Veteran Program to answer key questions on heart disease, kidney disease, and substance use—high-priority conditions affecting Veterans.

Read more at  
[www.research.va.gov/  
currents/0715-4.cfm](http://www.research.va.gov/currents/0715-4.cfm)

## VA study with 160 Gulf War Veterans will test red, near-infrared light to help brain function

An innovative therapy that applies red and near-infrared light to the brain is now being tested at the Boston VA for Gulf War Illness, TBI, and PTSD.



A staffer in Dr. Naeser's lab demonstrates the equipment built for the research: an LED helmet (Photomedex), intranasal diodes (Vielight), and LED cluster heads placed on the ears (MedX Health). The real and sham devices look identical. Goggles are worn to block out the red light. The near-infrared light is beyond the visible spectrum and cannot be seen.

Following up on promising results from pilot work, researchers at the VA Boston Healthcare System are testing the effects of light therapy on brain function in Veterans with Gulf War Illness.

Veterans in the study wear a helmet lined with light-emitting diodes that apply red and near-infrared light to the scalp. They also have diodes placed in their nostrils, to deliver photons to the deeper parts of the brain.

The light is painless and generates no heat. A treatment takes about 30 minutes.

The therapy, though still considered “investigational” and not covered by most health insurance plans, is already used by some alternative medicine practitioners to treat wounds and pain. The light from the diodes has been shown to boost the output of nitric oxide near where the LEDs are placed, which improves blood flow in that location.

“We are applying a technology that’s been around for a while,” says lead investigator Dr. Margaret Naeser, “but it’s always been used on the body, for wound healing and to treat muscle aches

and pains, and joint problems. We’re starting to use it on the brain.”

Naeser is a research linguist and speech pathologist for the Boston VA, and a research professor of neurology at Boston University School of Medicine (BUSM). She is also a licensed acupuncturist and has conducted past research on laser acupuncture to treat paralysis in stroke, and pain in carpal tunnel syndrome.

### How do the diodes work?

The LED therapy increases blood flow in the brain, as shown on MRI scans. It also appears to have an effect on damaged brain cells, specifically on their mitochondria. These are bean-shaped subunits within the cell that put out energy in the form of a chemical known as ATP. The red and near-infrared light photons penetrate through the skull and into brain cells and spur the mitochondria to produce more ATP. That can mean clearer, sharper thinking, says Naeser.

Naeser says brain damage caused by explosions, or exposure to pesticides or other neurotoxins—such as in the Gulf War—could impair the mitochondria in cells. She believes light therapy can be a valuable adjunct to standard cognitive rehabilitation, which typically involves “exercising” the brain in various ways to take advantage of brain plasticity and forge new neural networks.

“The light-emitting diodes add something beyond what’s currently available with cognitive rehabilitation therapy,” says Naeser. “That’s a very important therapy, but patients can go only so far with it. And in fact, most of the traumatic brain injury and PTSD cases that we’ve helped so far with LEDs on the head have been through cognitive

rehabilitation therapy. These people still showed additional progress after the LED treatments. It’s likely a combination of both methods would produce the best results.”

The LED approach has its skeptics, but Naeser’s group has already published some encouraging results in the peer-reviewed scientific literature.

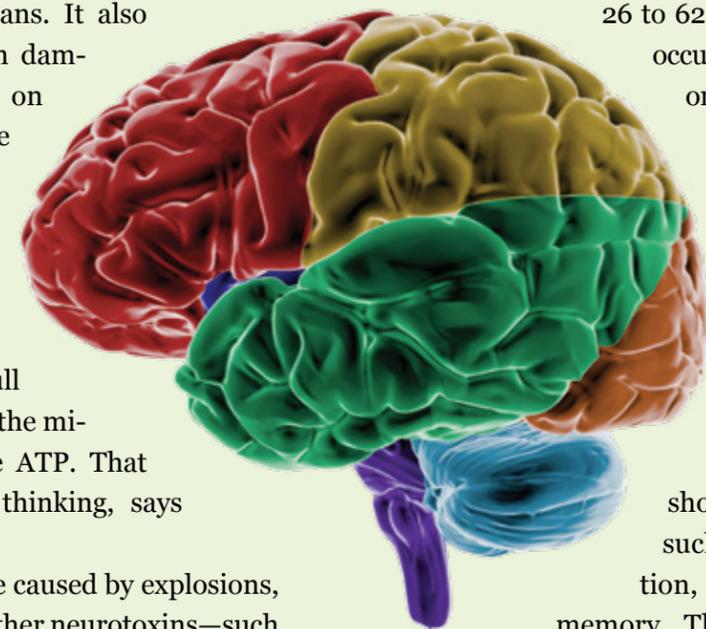
### Results published from 11 TBI patients

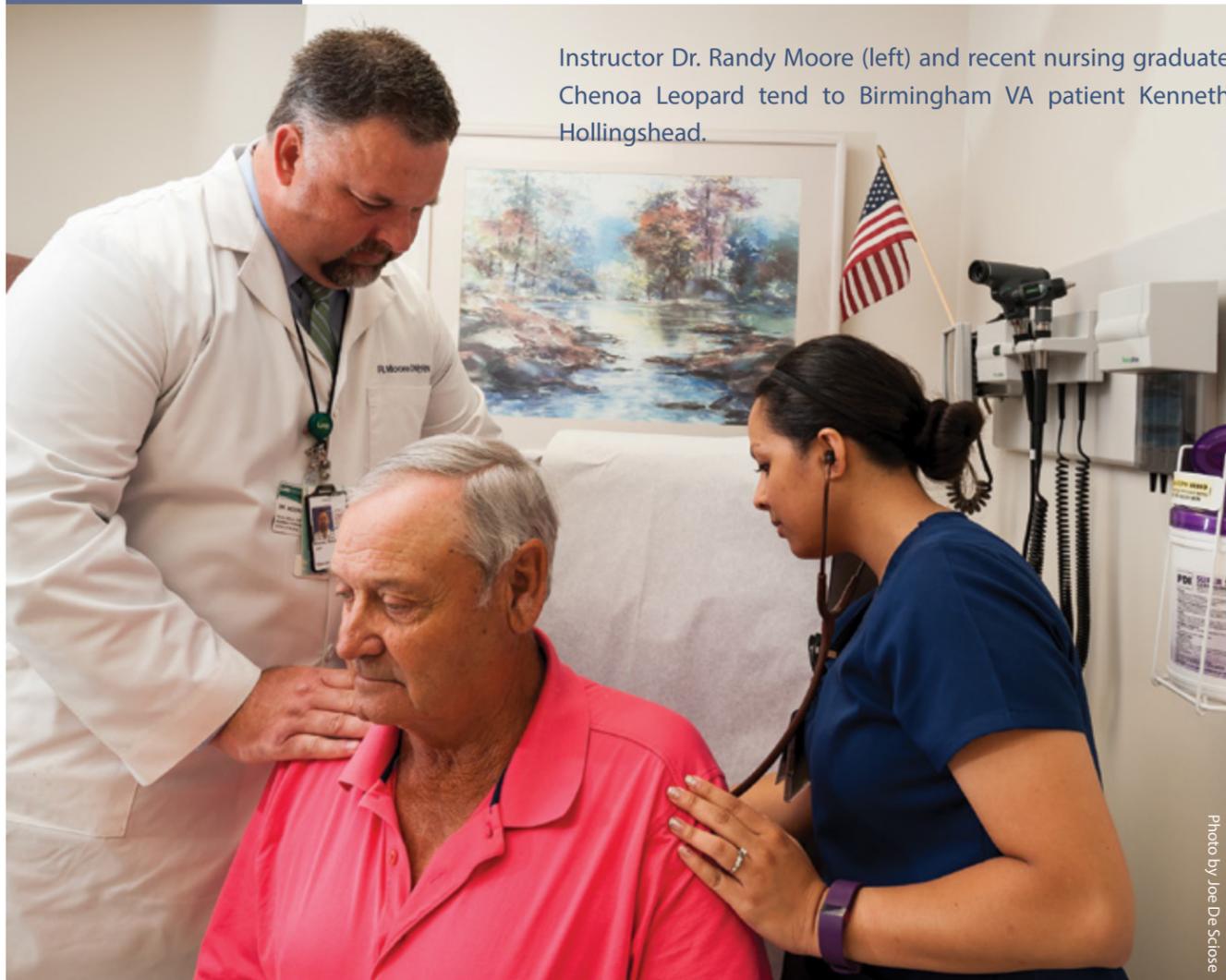
Last June in the *Journal of Neurotrauma*, they reported the outcomes of LED therapy in 11 patients with chronic TBI, ranging in age from 26 to 62. Most of the injuries occurred in car accidents or on the athletic field. One was a battlefield injury, from an improvised explosive device (IED). Neuropsychological testing before the therapy and at several points thereafter showed gains in areas such as executive function, verbal learning, and memory. The study volunteers also reported better sleep and fewer PTSD symptoms.

The study authors concluded that the pilot results warranted a randomized, placebo-controlled trial—the gold standard in medical research.

That’s happening now, thanks to VA support. One trial, already underway, aims to enroll 160 Gulf War Veterans. Half the Veterans will get the real LED therapy for 15 sessions, while the others will get a mock version, using sham lights.

Then the groups will switch, so all the volunteers will end up getting the real therapy, although they won’t know at which point they received it. After





Instructor Dr. Randy Moore (left) and recent nursing graduate Chenoa Leopard tend to Birmingham VA patient Kenneth Hollingshead.

Photo by Joe DeSciose

## Training the next generation of nurses: Studies highlight success of VA's partnership with nursing schools

Innovative partnerships between VA medical centers and their affiliated nursing schools are preparing a new generation of nurses who are well-attuned to Veterans' health issues, whether they end up working in VA or other health systems.

Nobody wants a urinary catheter inserted. But if you need the procedure, you want it done right.

Nursing instructor Dr. Randy Moore says his VA site and others are ahead of the curve in using a new type of swivel clamp that helps secure the catheter. One benefit? Lower infection risk. He is passing along the technique to his students.

"This is something that many nursing students don't get any hands-on practice with. Here, they do. So our students are learning the latest and greatest through their clinical experience at the VA."

Moore, based in Birmingham, Ala., is in the vanguard of nursing education. He is part of a program called VANAP, for VA Nursing Academic Partnerships. Now in its second year, following a multiyear pilot phase, it builds on existing partnerships between VA medical centers and nearby nursing schools. Schools selected to take part—there are now 25 active sites nationwide—get support from VA to beef up their enrollment and develop their Veteran-centered curriculum.

VA's Office of Academic Affiliations provides seed money the first five years to aid in implementation and growth. Afterward, the partnerships support themselves through internal funding from the local VA and its affiliated nursing school.

Either way, students get an

intensive and well-coordinated clinical experience in VA, tightly focused on Veterans' care.

In turn, as shown in studies, VA reaps a range of benefits. They include enhanced recruitment and retention of nurses, and an upsurge in evidence-based nursing practice. The staffing piece is big: Amid a nationwide

"They've been acculturated into VA. They understand the culture and respect the mission."

shortage of nurses, VA has felt the pinch, with 4 in 10 VA nurses eligible to retire within the next couple of years.

### Spillover effects on VA staff nurses

One recent evaluation, published in May 2015 in the journal *BMC Nursing*, looked at the pilot version of VANAP, called the VA Nursing Academy (VANA). The study found positive "spillover" effects from the five-year program on VA staff nurses who worked on clinical units alongside students. For starters, only 20 percent of these nurses perceived the presence of students as making their work more difficult.

Most felt no extra burden—a finding that contrasts with past studies on nurse training at large.

What's more, the more involved the VA staff nurses were with the training, the greater their job satisfaction.

"Greater interaction with the students, more information on the program, and a preceptor

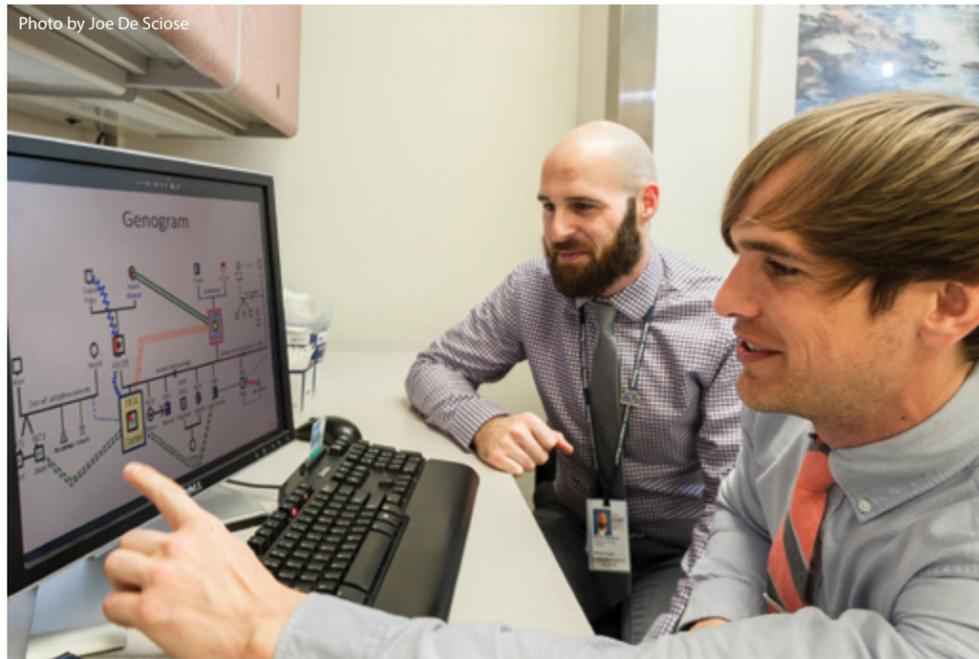
[teacher] role were all ... associated with greater program satisfaction," wrote the study authors, from VA, RAND Corporation, and UCLA. Dr. Aram Dobalian led the evaluation.

Coauthor Dr. Tamar Wyte-Lake, a VA health services researcher in Los Angeles, says some VANA sites had "dedicated education units" where almost every VA nurse became a teacher, in essence, at least part of the time.

"Basically everyone on the unit becomes part of the teaching team," says Wyte-Lake. "It becomes a very intense experience."

Chenoa Leopard just finished her four-year nursing degree and passed her RN licensing exam.

Daniel Wyers (left), a nurse practitioner student at VA and UAB, shows instructor Chance Nicholson an informatics tool he is studying to help incorporate patients' family histories into their electronic health records.



She is now hoping to come on staff at the Birmingham VA, where her husband, a Navy Veteran, receives care. She attests to the rigor and efficiency of the VANAP experience from a student perspective.

### Cohesive clinical experience

“One benefit was that we got to have consistent clinical groups and site locations,” says Leopard. “Since we were already familiar with our clinical group and site each semester, we were able to begin patient care right away.”

According to the research, that type of cohesiveness makes a difference not only for the students, but for the VA nurses who work with them. The effect is further enhanced when the VANAP faculty are themselves part of the VA nursing staff. That doesn't always happen—VANAP faculty are sometimes recruited from outside VA—but it often does.

Wyte-Lake: “In some situations in nursing education, students are just ‘dropped off’ at their unit. And the staff aren't really told what the goals are. They're basically told, have these students shadow you.

“You could see a big difference between that type

of experience and one in which a faculty member is coming in whom you know, whom you're able to engage with, who's telling you, these are the goals, this is what we're talking about this week in school. This is what we're trying to get at. Try to have the students get this type of experience.”

### Impact similar to that of medical school partnerships

Dr. Mary Dougherty, director of nursing education in VA's Office of Academic Affiliations, says the positive effects on VA nurses who work with VANAP students is just one part of a much larger picture.

She says VANA and now VANAP have had an impact similar to that of VA's storied partnership with the nation's medical schools, which began after World War II as a way to help care for the waves of returning Veterans.

“There is empirical evidence,” she says, “that these nursing partnerships produce significant value similar to the medical academic partnership.”

Dougherty, a former Army reservist whose husband served in the Air Force for 40 years,

is passionate about advancing Veterans' care. She lists a string of accomplishments, all in areas critical to VA health care, that she says can be traced to VA's special nursing education programs. “We were able to change the culture and produce concrete results, such as reducing psychiatric inpatient recidivism, reducing length of stay in ICUs, improving the therapy for diabetes.”

Driving those results, she says, is the bond that programs like VANAP create between the academic side of nursing—what is taught in the classroom and practiced in labs—and real-world clinical practice.

“This is what the standard should be,” argues Dougherty. “Having two separate divisions—practice and academia—doesn't work. Practice will shrivel if you don't have scholarship and research. And scholarship and research go off track if they are not grounded in practice.”

### Mutually beneficial relationship

This ideal is playing out in Birmingham, as at other VANAP sites.

Moore, a former Navy nurse who is now co-director of the VANAP undergraduate program at the Birmingham VA and the University of Alabama at Birmingham (UAB) School of Nursing, says he first goes over concepts in the classroom. Then, his students move to the lab, where they might practice on a mannequin or each other. Then, it's on to the clinic.

“I take my students into VA for their clinical rotations. If you think of a PhD doing bench research, and how they get that into practice—my degree as a doctor of nursing practice is to take research and apply that at the bedside. VANAP provides a good avenue to do that, to take the latest evidence-based



practices and make sure they are disseminated at the hospital, both among the students and among the RNs at the bedside.”

Chance Nicholson, a psychiatric nurse practitioner at UAB who teaches graduate students in VANAP, says: “It's a mutually beneficial relationship. The clinical aspect of VA gives us a place to disseminate the research and evidence-based practice that we do as part of our job. The folks at the VA are the ones who are putting it into practice and seeing it work. By our keeping the VA people abreast of the newest information, on top of what they're already doing, we learn from each other.”

The academic spirit infuses VA nursing practice in a variety of ways, says researcher Wyte-Lake. For

Photo by Joe De Sciose

example, units participating in VANAP have started “journal clubs” where nurses get together to talk about recent studies and how they can apply the findings in their work.

Also, VA preceptors, who are not full-fledged faculty but who do hands-on teaching on the VA hospital units, get exposure to the academic side of nursing. Nicholson says the preceptors are invited to share their knowledge in the formal classroom or lab setting.

“We give them an opportunity to teach over here at the school,” he says. “They share some of their evidence-based practices with our students.”

### Programs spurs higher education for nurses

Some VA preceptors, inspired by their taste of higher-level nursing education and perhaps encouraged by personal contacts they make at the university, decide to pursue more advanced degrees, such as a doctor of nursing practice, or a doctor of nursing science.

That’s been one of the findings from the research by Wyte-Lake and colleagues. In a 2014 study published in the *Journal of Professional Nursing*, in which they interviewed more than 200 nurses who took part in VANA at 15 sites, they found a strong link between VANA participation and enrollment in an advanced nursing degree program.

Having more young people graduate as RNs, and having more nurses go on for their master’s or

doctoral degrees, will help solve the nation’s overall nursing crisis. VANA and VANAP have already made a dent in VA’s shortage.

### ‘Everything is Veterans’

Dougherty says by the time VANAP students have completed their four-year degree—and their post-bachelor’s residency in VA—they are well-attuned to the VA environment.

“They’ve been acculturated into VA. They understand the culture and respect the mission.”

She presses the point that while VANAP students do get a strong nursing education, the *raison d’être* of the program is to help VA meet its organizational goals. It is designed mainly to help VA meet the challenges of caring for the nation’s Veterans.

“This is all done within a model that focuses on the major priorities within the organization,” says Dougherty. “For us, that is Veterans. Everything is Veterans.”

As for those graduates of the program who end up working outside VA, they will contribute to Veterans’ care in other ways, leveraging what they learned in VANAP.

Moore: “We know there are some 24 million Veterans in the U.S., and only about 8 million receive some portion of their care inside VA. We want our graduates to be conscious of Veterans’ health issues, wherever they encounter those Veterans.” ★



Photo by Tony F. Barnett

### Can aspirin ward off cancer?

A VA lab study found that a daily dose of aspirin was effective at blocking breast tumor growth. Previous studies have already shown a similar effect on colon, gastrointestinal, prostate, and other cancers.

Read more at [www.research.va.gov/currents/spring2015/spring2015-25.cfm](http://www.research.va.gov/currents/spring2015/spring2015-25.cfm).

## VA study with 160 Gulf War Veterans will test red, near-infrared light to help brain function

*Continued from page 13*

each Veteran’s last real or sham treatment, he or she will undergo tests of brain function.

Naeser points out that “because this is a blinded, controlled study, neither the participant nor the assistant applying the LED helmet and the intranasal diodes is aware whether the LEDs are real or sham. So they both wear goggles that block out the red LED light.” The near-infrared light is invisible to begin with.

### Upcoming trials to focus on TBI, PTSD

Besides the Gulf War study, other trials of the LED therapy are getting underway:

- Later this year, a trial will launch for Veterans age 18 to 55 who have both traumatic brain injury (TBI) and posttraumatic stress disorder—a common combination in recent war Veterans. The VA-funded study will be led by Naeser’s colleague Dr. Jeffrey Knight, a psychologist with VA’s National Center for PTSD and an assistant professor of psychiatry at BUSM.
- Dr. Yelena Bogdanova, a clinical psychologist with VA and assistant professor of psychiatry at BUSM,

will lead a VA-funded trial looking at the impact of LED therapy on sleep and cognition in Veterans with blast TBI.

- Naeser is collaborating on an Army study testing LED therapy, delivered via the helmets and the nose diodes, for active-duty soldiers with blast

TBI. The study, funded by the Army’s Advanced Medical Technology Initiative, will also test the feasibility and effectiveness of using only the nasal LED devices—and not the helmets—as an at-home, self-administered treatment. The study leader is Dr. Carole Palumbo, an investigator with VA and the Army Research Institute of Environmental Medicine, and an associate professor of neurology at BUSM.

Naeser hopes the work will validate LED therapy as a viable treatment for Veterans and others with brain difficulties. She foresees potential not only for war injuries but for conditions such as depression, stroke, dementia, and even autism.

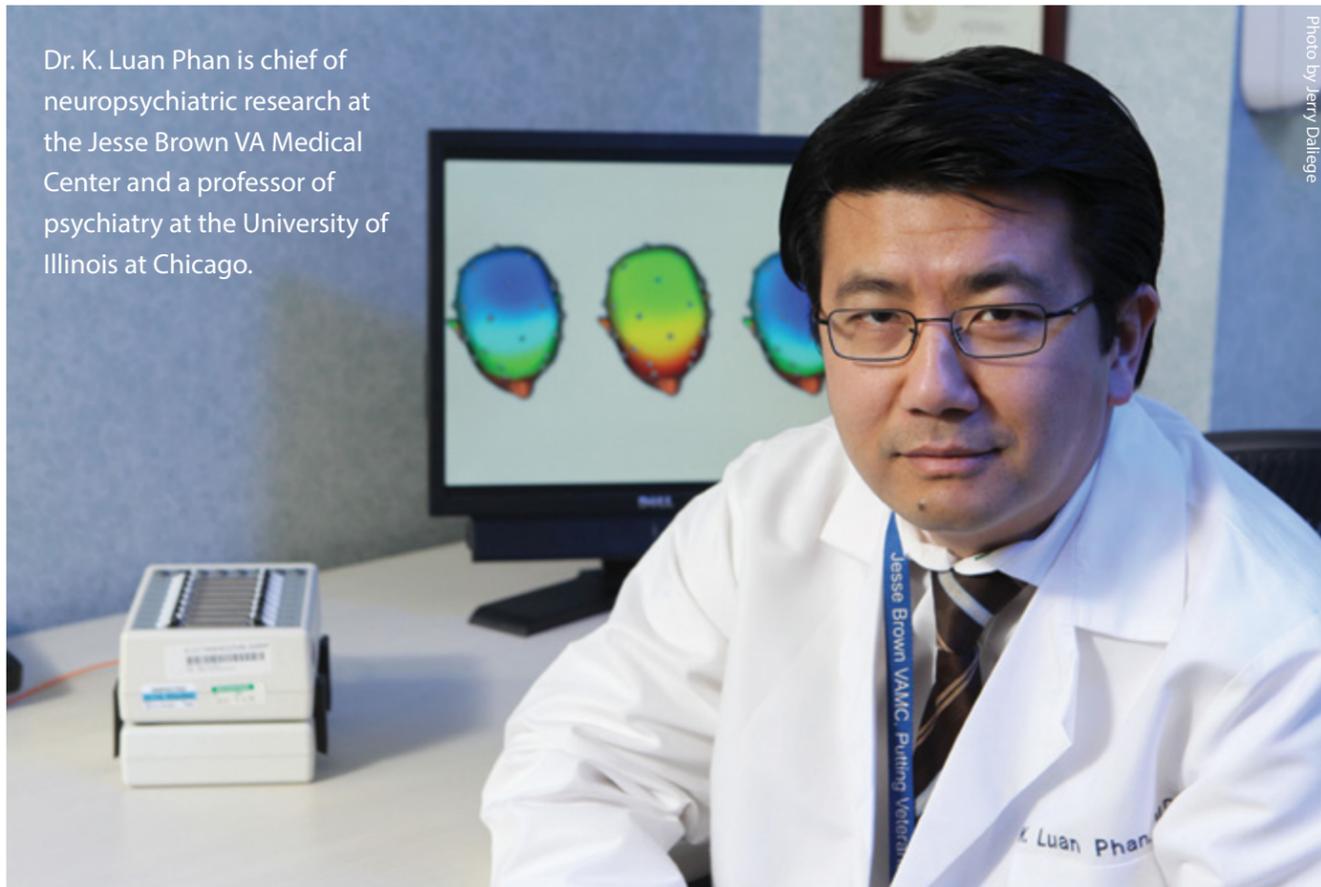
“There are going to be many applications, I think. We’re just in the beginning stages right now.” ★

**“We are applying a technology that’s been around for a while.”**

## In pursuit of precision medicine for PTSD

Brain scans of war Veterans with posttraumatic stress disorder have led researchers to an area of the prefrontal cortex that appears to be a good predictor of response to treatment with SSRIs—the first-line drug treatment for PTSD.

Dr. K. Luan Phan is chief of neuropsychiatric research at the Jesse Brown VA Medical Center and a professor of psychiatry at the University of Illinois at Chicago.



Brain scans of war Veterans with posttraumatic stress disorder have led researchers to an area of the prefrontal cortex that appears to be a good predictor of response to treatment with SSRIs—the first-line drug treatment for PTSD.

The findings, which came out online June 26, 2015, in the journal *Neuropsychopharmacology*, are hopeful news amid a new national push toward

“precision medicine,” in which doctors will tailor drug regimens and other treatments based on patients’ individual gene profiles or other factors. President Obama announced the initiative earlier this year.

So far, though, little of this approach is in use in everyday psychiatry.

“This is the holy grail for brain imaging,” says lead

researcher Dr. K. Luan Phan, chief of neuropsychiatric research at the Jesse Brown VA Medical Center and professor of psychiatry at the University of Illinois at Chicago. “We hope in the future to be able to use scans to help distinguish PTSD from other illnesses, and then to predict how well someone will do with a certain medication, or with talk therapy. What we envision is being able to say to a patient, ‘Given your scan value, you have an X percent chance of getting better on this treatment.’”

The approach, says Phan, will benefit patients and providers alike: “We’ll be saving a lot of resources on the clinical side, and more importantly, we’ll also not be wasting patients’ time sending them for a treatment that is not likely to help them.”

### Study involved 34 Veterans

His latest study included 34 Iraq and Afghanistan Veterans, half of them with PTSD. They all got functional MRI scans, which track blood flow in the brain to show which areas are using the most oxygen—a sign of increased activity.

The researchers saw that among the PTSD group, who were all taking the drug paroxetine (sold as Paxil),

One nuance in the findings was that the brain area that appeared to predict response to SSRIs—the right ventrolateral prefrontal cortex—was not the exact area that appeared to be affected by SSRI treatment. According to the fMRI scans, it was a related area—the left dorsolateral prefrontal cortex, which has similar functions—along with another region called the supplementary motor area, that showed more activation after treatment.

Phan explains: “It would be intuitive that something you’re trying to correct would also be the very same thing that would predict how well you do. But data from our lab and others suggest this isn’t always true. A mechanism of change could be different than a predictor of change. One area could change with treatment, but another area could predict your treatment response.”

In any case, while the results need replication in larger trials, they point to a potential method to target drug therapy for PTSD patients.

“Patients with the least recruitment of prefrontal emotion regulatory brain regions may benefit most from treatment with SSRIs, which appear to augment activity in these regions,” the researchers wrote.



“We hope in the future to be able to use scans to help distinguish PTSD from other illnesses, and then to predict how well someone will do with a certain medication, or with talk therapy.”

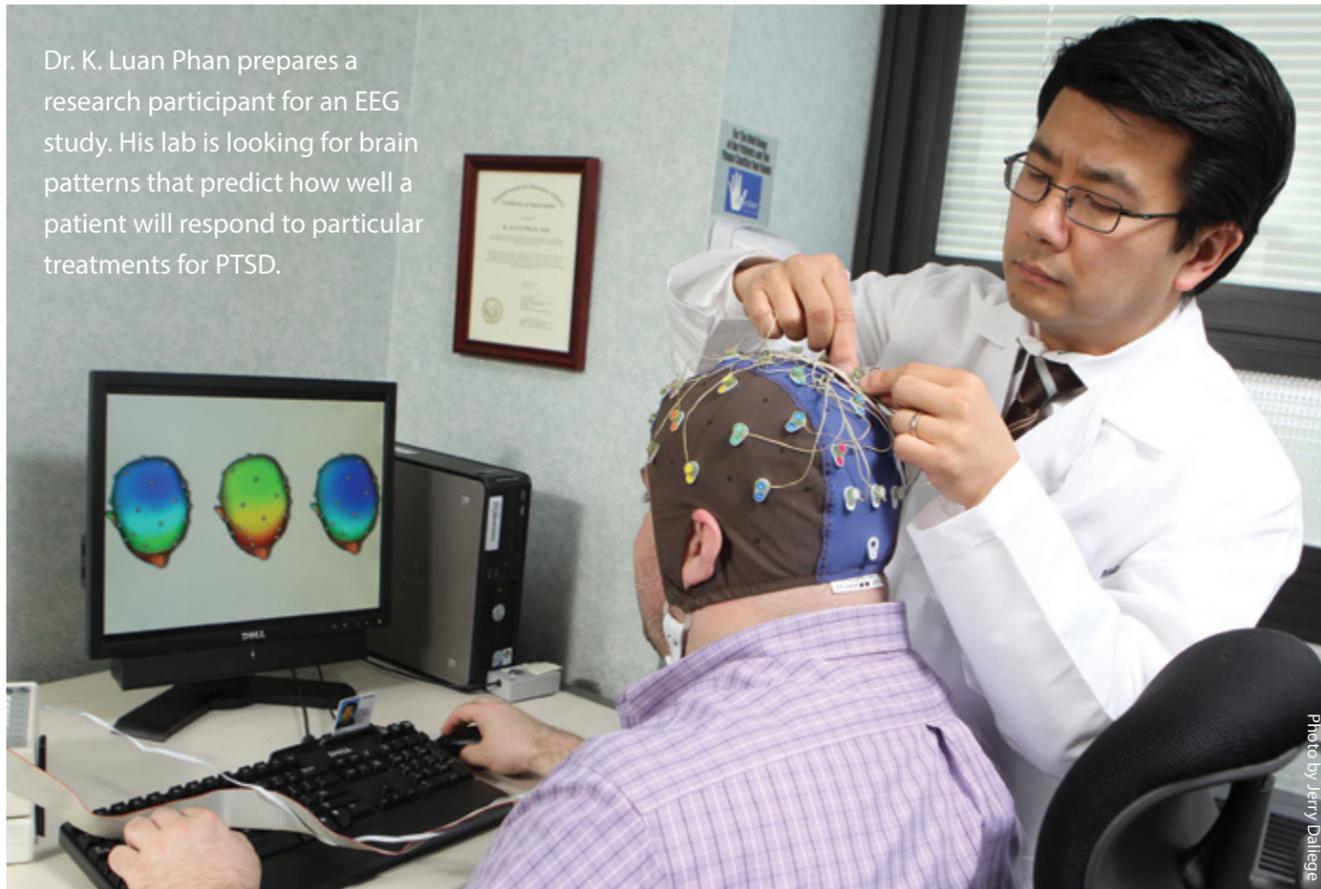
the patients who showed the most improvement from the SSRI were those who showed the least activation, prior to treatment, of a brain area called the right ventrolateral prefrontal cortex, also known as the inferior frontal gyrus. The region is known to help with emotional regulation. It serves as a rational counterbalance to parts of the brain that generate raw emotion. It helps with tasks like impulse control, cognitive flexibility, and executive function. “These are all ingredients of emotional regulation,” says Phan.

The first author was Annmarie MacNamara, a post-doctoral research fellow in Phan’s lab.

### Other SSRIs similar, but may have subtle differences

Paroxetine and sertraline (Zoloft) are both part of the SSRI class of antidepressants. They are currently the only drugs approved by the Food and Drug Administration to treat PTSD. Another SSRI, fluoxetine (Prozac), also has evidence of effectiveness

Dr. K. Luan Phan prepares a research participant for an EEG study. His lab is looking for brain patterns that predict how well a patient will respond to particular treatments for PTSD.



for PTSD, but it's not yet approved for that purpose. Phan says the study was limited to patients using paroxetine, because while all SSRIs work similarly, there may be subtle differences among them, and the researchers wanted to control for this. He noted that some patients may respond well to one SSRI but not another.

His lab is also involved in other efforts to tailor PTSD therapy based on brain patterns. In one VA-funded study, he is using a type of electroencephalography (EEG)—in which Veterans wear an electrode-studded cap on their head—to trace brain patterns that may eventually serve as biomarkers. The research method is much less expensive and more portable than brain imaging—and it carries an added advantage for combat Veterans, notes Phan.

“Functional MRIs typically cost around \$500,

and they are often not tolerated well by our Veterans,” he says. “It can be a very claustrophobic experience. You can feel trapped in the tube, in this dark, tight space. And there are loud random noises that many Veterans have told me remind them of artillery fire.”

Besides being distressing for the Veterans, says Phan, this can all detract from the research: “It’s problematic on two fronts. It makes them move during the scan, which is not great for our science. Also, it may evoke different kinds of emotions that we’re not explicitly looking to test in the scanner. It induces a different emotional state that is hard to control for.”

**Larger VA-Army study comparing PTSD treatments, looking for brain markers**

Phan is also collaborating on a multisite randomized, controlled clinical trial that is

comparing different PTSD treatments. The team is looking at how each affects the brain and whether brain markers can predict response to a particular treatment.

The trial began in 2011 with VA and Army funding and is still ongoing at three VA sites and at Massachusetts General Hospital. It has involved more than 400 Iraq and Afghanistan Veterans with PTSD. Some are being treated with sertraline, and others with a type of psychotherapy called prolonged exposure therapy, which is one of the two main talk therapies used in VA for PTSD. Others in the study are receiving a combination of the two.

Lead investigator Dr. Sheila Rauch, with the Atlanta VA Medical Center and Emory University, says it’s too early in the study to compare how each of the therapies affects the brain—that is, which precise regions get activated or calmed—but some clues may come from past work on depression.

“Based on previous research on depression, we see some changes that are similar between treatments, but we also see distinct patterns,” says Rauch.

She, like Phan, believes the scanning approach may eventually yield reliable biomarkers to guide PTSD treatment, but she says it will likely take several more years.

“Within PTSD, this research is in the early stages,” she says. “We need larger studies that will allow replication and application to a treatment population,” and those generally take at least five years to implement and yield results, she says. “This is a marathon and not a sprint. Expecting an overhaul in the next couple of years is unrealistic, but I do think 10 years from now, PTSD care will be even more advanced and effective than it is today. We are moving in the right direction, but we are not there yet.” ★

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## Did you know?

Dr. Dudley Childress (1934 – 2014) had humble roots in small-town Missouri and went on to become one of the world’s leading prosthetics engineers. It was on his grandparents’ farm that he first took an interest in machinery. He studied electrical engineering at the University of Missouri, where he was also a star quarterback. After a stint in the Army Reserve, Childress joined VA and Northwestern University and helped pioneer myoelectric control, which applies electrical signals from muscles to prosthetic limbs. His lab later developed the “sip and puff” wheelchair and many other technologies. He received VA’s Magnuson Award in 2002 for his achievements on behalf of people with disabilities.



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