

VA Research Currents

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

Dr. Watson, I presume?

Super-smart computer of ‘Jeopardy!’ fame now being pumped full of medical information

Met Watson—the first computer to go to medical school.

Watson is the IBM supercomputer, named after the company’s first president, that beat two human contestants on the TV game show “Jeopardy!” back in February. Now, VA and academic researchers are going to test the computer’s ability to analyze medical information and help doctors provide good care.

Actually, Watson is not a piece of hardware but an application—what IBM calls a “deep question and answer” program. It runs on more than 90 servers and performs some 80 trillion operations per second.

For the game show, Watson was fed some 200 million pages on topics ranging from history and science to art and pop culture. The content came from Wikipedia and other encyclopedias, newspapers, books, film scripts, and other sources. When asked a question, Watson recognizes “natural language”—plain



Photo courtesy of University of Maryland

Digital doc—Radiologist and informatics expert Dr. Eliot Siegel, with VA and the University of Maryland, is leading an effort to explore how IBM’s powerful Watson computer program can improve health care.

English—and uses Google-like technology to fetch possible answers. Then, it uses thousands of algorithms programmed in by IBM engineers to rank the answers and give the best one.

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Photo by Harold Joel/Getty Images

Open minds

Meeting convened by VA R&D seeks to expand study of complementary, alternative therapies for PTSD

Those who helped reshape VA health care more than a decade ago were fond of saying: “It’s not your grandfather’s VA.”

Anyone looking for proof of the ongoing transformation could find it at a May 17 meeting convened by VA’s Office of Research and Development. The topic was therapies such as meditation, massage, and yoga to help Veterans with posttraumatic stress disorder.

The goal of the 30 or so attendees—including experts from VA, the

Department of Defense, the National Institutes of Health, and academia—was to explore the existing evidence on complementary and alternative medicine (CAM) for PTSD and forge a future research agenda.

According to survey results presented at the meeting, 9 in 10 VA facilities now offer some form of CAM, either in-house or through referrals to outside contractors. The most common form is meditation.

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CAM (from page 1)

Kicking off the meeting, VA Deputy Secretary W. Scott Gould said: “We’ve done a lot of work in many areas of PTSD research that has produced effective treatments, but we are not done preventing, relieving, or curing PTSD in all Veteran patients. And that is why we need to keep our curious minds open and receptive to new ideas. In addition to the outstanding medical care we already provide, we are learning to extend that care to include many CAM treatments.”

At the same time, Gould stressed the importance of focusing the research effort. He said meditation, because it is already offered widely in VA and seems to be a logical approach to helping Veterans cope with PTSD, was a good target for rigorous study.

The discussion at the meeting was lively from the outset. Gould, in response to a question about meditation as opposed to movement-based therapies such as tai chi or yoga, referenced his experience as a tae kwon do practitioner and instructor in the Navy. He acknowledged the meditative aspects of such disciplines, underscoring



Stretching the limits—Yoga, now offered at some 44 VA sites nationwide, is among the non-conventional modalities that may play a role in PTSD care. Here, Veterans with back pain take part in a class at the San Diego VA.

the sometimes blurry definitions of the modalities the researchers would be discussing.

Scant evidence from randomized trials

VA investigators and others have done numerous CAM studies to date. But robust evidence specifically on CAM for PTSD is hard to come by. A VA team tasked with doing a literature review for the meeting culled through hundreds of references and reviewed dozens of studies in-depth, but they turned up only little more than a handful of randomized clinical trials—the most rigorous and respected type of study. Overall, the therapy with the strongest evidence base was acupuncture, followed by relaxation techniques and meditation.

But some attendees at the meeting—including several medical acupuncturists—suggested it might make sense to look beyond randomized clinical trials for evidence to steer future research. One idea

was to take a harder look at the biological mechanisms of CAM treatments.

Looking to biomarkers for evidence of effectiveness

Along those lines, Jack Killen Jr., MD, deputy director of the National Center for Complementary and Alternative Medicine, stressed the need to further explore the efficacy of various treatments before launching into large randomized trials. One approach, he said, would be “looking into what we know about the basic science of therapies such as meditation and acupuncture. Are there unique contributions of these treatments to the pathology of PTSD?”

To better understand the effects of various CAM treatments on brain and nervous-system biology, some attendees suggested measuring heart rate variability, or proteins in the blood or cerebrospinal fluid that serve as biomarkers. Another approach would involve brain-scan technologies such as functional magnetic resonance imaging, magneto-encephalography, or positron emission tomography. All of these methods are increasingly used in VA and academia to study a range of mental health issues, especially PTSD and traumatic brain injury.

“How about pre- and post-brain scans?” asked Capt. Anita Hickey, MD, of the Naval Medical Center in San Diego, who in 2000 became the first Navy physician to become certified in medical acupuncture.

David Atkins, MD, MPH, director of VA’s Quality Enhancement Research Initiative (QUERI) program, suggested expanding the evidence review to look at CAM successes in areas related to PTSD. “Maybe there’s something well-established in an area close to PTSD—such as

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depression—that we can apply. What are we already doing in these areas that’s working, and could we evaluate it for aspects of PTSD?”

CAM as adjunctive, rather than primary, therapy

A theme running through the day was that in VA and most mainstream medical settings, CAM is used mostly as an adjunctive treatment. Citing meditation as an example, psychologist Paula Schnurr, PhD, deputy executive director of VA’s National Center for PTSD, said: “There’s a very big increase in the use of meditation and other CAM techniques. But people are generally using it as adjunctive therapy. They don’t see it as standalone therapy.”



Good karma—Some 30 experts attended a recent VA Research meeting on complementary and alternative medicine for PTSD. At left, Dr. Sat Bir Singh Khalsa chats with Capt. Anita Hickey during a break.

Several of those at the meeting suggested capitalizing on existing trends by focusing research on CAM’s adjunctive role. As Schnurr put it, “Can we use CAM to make existing treatments more effective or more efficient, or to boost retention in treatment?”

Schnurr led a seminal VA clinical trial including 284 women, published in the *Journal of the American Medical Association* in 2007, that helped establish prolonged exposure therapy as a key treatment for PTSD. Among other innovative PTSD work, her group is now developing a “mindfulness meditation” app for smartphones.

Antonette Zeiss, PhD, VA’s acting deputy chief of mental health services, underscored the importance of adjunctive therapies for PTSD. “Let’s not forget that ‘adjunct’ is a huge and important category. It can be an entry point for other treatments, or it can be used to help sustain gains that have been made through other treatments.” She added that her office, concurrent with ORD’s efforts, is looking to fund demonstration projects of meditation for PTSD, leveraging sites that already have existing programs and expertise.

Jill Bormann, PhD, RN, who has pioneered the use in VA of a meditative technique known as mantram (sacred word) repetition, suggested that this type of approach could help prepare patients for participation in psychotherapy. For example, it could help with the distress they might experience in exposure therapy, in which patients gradually re-experience the emotions surrounding their traumas in safe, controlled settings. Bormann admitted that the spiritual nature of her work and certain other CAM approaches “raises flags” among some in the medical community. At the same

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WATSON *(from page 1)*

Now, instead of digesting data on everything from movie stars to motorcycles, Watson is focused on one thing: medicine. A study based at the University of Maryland (UM) is enrolling Watson in medical school, figuratively speaking. Medical journals and textbooks will be its staple diet. Informal information, such as health blogs, may also be part of the mix.

The effort also involves a team at the Baltimore VA Medical Center. The plan is to eventually link Watson with patients' electronic medical records, in a secure way, to supplement the information available to the program for medical decision-making.

The idea is not to replace doctors and their human skill and discretion, but to give them a quick and super-powerful information tool.

"I see Watson's capabilities not as a replacement for physicians, but as an adjunct and tool to organize, highlight and prioritize information to make a physician more efficient and effective, and improve patient safety," says Eliot Siegel, MD, chief of imaging at the VA Maryland Health Care System and a professor of diagnostic radiology and nuclear medicine at UM. He is leading the project for VA and the UM School of Medicine.

Siegel adds that the system can ingest information from a single medical record or multiple ones, at one facility or many. Merging Watson's super analytical ability with VA's richly detailed electronic medical record system could spell a huge leap forward in clinical decision-making.

Taking advantage of voice-recognition technology—and cloud computing to connect to Watson's servers—doctors could conceivably talk into a hand-held device and get real-time advice from Watson to help manage patients.

Siegel says he believes Watson could result in a "renaissance in the application of artificial intelligence" in medicine. ➔

CAM *(from page 3)*

time, she asserted that such approaches could be powerful for Veterans, and that many welcome a spiritual underpinning for their healing journey.

Other practitioners and researchers in the room said CAM techniques might be studied for their role in treating "sub-clinical" PTSD. Less intense symptoms might benefit from the gentler treatments associated with CAM.

Another idea was to explore CAM for problems outside of core PTSD symptoms—such as pain or sleeplessness—that might be getting in the way of patients' ability to engage in standard psychotherapy. "This is a clinically messy population," asserted Frances Stewart, MD, a psychiatrist at the National Naval Medical Center in Bethesda. "They don't walk through the door with just PTSD. Sometimes you can't address the core PTSD symptoms till you've dealt with some of the other issues." She said, also, that CAM could be a gateway for some patients into more conventional forms of treatment.

Caution: Don't lump together CAM therapies

Much of the day's discussion focused on meditation, which is being taught by an increasing number of VA psychologists and other clinicians to their patients. Earlier this year, VA issued a call for research proposals specifically on meditation to treat PTSD, and proposals are now under review. The agency hopes to support up to three clinical trials, lasting up to two years.

Considering the broader range of CAM therapies, and even within the arena of meditation itself, Killen of NCCAM stressed the need to distinguish one modality from another, and to carefully weigh the unique pros and cons of each. He said doing otherwise would be akin to studying "surgery" in general, and not any particular type of operation.

Schnurr concurred. By way of example, she said that while 80 VA sites may be providing "mindfulness" meditation, even that sub-category of meditation could include dozens of variations on the theme. "We need standardization," she emphasized. "That should be a priority." ➔

Complementary and alternative medicine in VA

According to a 2011 survey by VA's Health Care Analysis and Information Group, the use of complementary and alternative medicine has grown substantially in VA over the past decade. About 9 in 10 VA facilities now directly provide CAM therapies or refer patients to outside licensed practitioners.

Meditation is the CAM modality most commonly offered by VA in-house—at 101 sites. Next in popularity is stress management/relaxation therapy, offered at 93 VA sites, followed by guided imagery, progressive muscle relaxation, biofeedback, animal-assisted therapy, music therapy, acupuncture, yoga, and hypnosis or hypnotherapy. (Note: Chiropractic is part of standard care in VA and is not considered CAM. Also, while many Veterans use herbal or nutritional supplements on their own or through non-VA providers, federal regulations prohibit VA from prescribing products that are not approved as treatments by the Food and Drug Administration.)

CAM is used in VA most commonly to help Veterans manage stress or promote general wellness, and to treat anxiety, PTSD, depression, back pain, wellness, headache, arthritis, fibromyalgia, and substance abuse.

Caring for the medic

Having graduated at the top of the Army combat medic course at Fort Sam Houston in 1989, Paula Chapman, PhD, knows firsthand the risks and challenges of this honored military profession. Today, she is putting that insight to use as a researcher.

“I suffered some of my own military trauma and basically had to work my way through it,” admits Chapman candidly. “I had to battle the demons and come out the other end of the tunnel. So that’s why I study what I study.”

An investigator at the Tampa VA Medical Center, Chapman is part of a Defense-funded study called Combat Medic Mettle. The three-year study, now in the data-analysis phase, includes some 800 Army combat medics. More than half served in Iraq or Afghanistan.

The researchers hope to pinpoint the factors that create emotional resilience and enable medics to thrive amid harsh conditions. They also want to learn what combat experiences cause the most stress. The next step will be building training programs that incorporate the findings.

The data collected so far confirm the grim challenges faced by medics during deployment:

- 67 percent saw dead bodies or human remains
- 56 percent saw dead or seriously injured Americans
- 53 percent saw sick or injured women or children they were unable to help

Medic mettle—Army Sgt. Jesse Rosenfield, a flight medic with Task Force Thunder Brigade, tends to an injured soldier aboard a Blackhawk helicopter in Kandahar province, Afghanistan, in April 2011.



As part of her research on Army combat medics and resilience, VA’s Dr. Paula Chapman is studying physiological indicators of stress such as heart activity and galvanic skin response.

- 26 percent reported shooting or directing fire at the enemy, and about 6 percent said they were directly responsible for the death of an enemy combatant.

Medics are expected not only to care for their comrades—and for allied troops and civilians—but to function as warriors. In fact, they may need to render care for the same enemy fighter they shot at moments earlier.

“The combat medic attached to a foot patrol has to also act as a soldier,” says Chapman. “They may be gunning down an enemy combatant at one point, and then have to go provide aid to him.”

“Compassion fatigue” is another concern. By nature, says Chapman, medics want to help other people. When they can’t do so, this causes stress. This is the same problem that was documented among many doctors and nurses who served in Vietnam.

“The caretaker begins to be traumatized and fatigued because of the sheer volume of what they have to do and some of what they’re seeing,” says Chapman. “Remember, medics go into this job because they want to help people. When they see ill or injured persons—especially women and children—and can’t help them because the area’s not secure, that’s likely to have an effect on them.”

Chapman also points out that combat medics often see more action than other soldiers. “They may go out with one squad one night and another squad the next.”

The fact that medics know the foot soldiers they are caring for—unlike doctors or nurses at field hospitals—adds yet another

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Photo by April Peters



Sleep monitoring at home works just as well

—A study involving nearly 300 Veterans found that patients whose sleep apnea was diagnosed at home fared just as well as those who came into a sleep lab for the evaluation. The most common type of sleep apnea occurs when soft tissue at the back of the throat blocks the airway, causing loud snoring and frequent pauses in breathing throughout the night. The potentially dangerous condition is usually treated with a continuous positive airway pressure (CPAP) device. The portable machine has a mask that fits over the nose—or nose and mouth—and emits a steady stream of air to keep the airway open. In the VA study, adherence to CPAP therapy and patient outcomes were similar between those who were evaluated and managed at home and those who visited a sleep lab. The researchers say the findings underscore the value of portable monitoring and home-based management for sleep apnea patients, especially those who have difficulty traveling to sleep clinics. (*American Journal of Respiratory and Critical Care Medicine*, May 1, 2011)

Pre-surgery informed consent: Is less more?

—A study at the Minneapolis VA Medical Center found that knee-replacement patients who received only a simple handout about the procedure prior to surgery were just as likely to retain the information as those who received more extensive education. In the study of 151 patients, led by Terence Gioe, MD, one group received a handout about the risks and benefits of the procedure when they were asked to fill out the standard computer-based consent form. A second group also saw a video on the topic. A third group received the handout, watched the video, and met with a nurse for an educational session. Contrary to what the researchers expected, patients in all three groups scored equally well on multiple-choice tests about their procedure. The tests were given on the day of informed consent, the morning of the surgery, and six weeks later. What *did* seem to make a difference was how satisfied patients were with the informed consent process. Those in any of the three groups who reported more satisfaction with the informed consent process, tended to score better on the

Joint decision—Dr. Terence Gioe of the Minneapolis VA discusses the risks and benefits of knee replacement surgery with patient Tom Moore. See story below on informed consent.

multiple-choice tests. In an interview with *Reuters Health*, Gioe said, “We may be able to do more with simple handouts that patients can review and refer back to after the initial consultation.” (*Arthritis Care and Research*, online April 11, 2011)



Study finds sharp drop in heart bypass rates

—Between 2001 and 2008, the number of cardiac bypass surgeries performed annually in the U.S. dropped by about a third, says a study by a team with the University of Pennsylvania and VA’s Center for Health Equity Research and Promotion. The use of an alternative technique to treat blocked arteries—balloon angioplasty and stenting—remained about the same. The authors say the drop in cardiac bypass operations occurred steadily over the eight-year period, suggesting the downward trend wasn’t due to any single factor, such as the publication of a major clinical trial or the advent of other treatment options. Despite the steady rate of angioplasty and stenting overall, the study found fluctuations in the use of drug-eluting versus bare metal stents. (*Journal of the American Medical Association*, May 4, 2011)



Photo by Lester Kefauver/Getty Images

Tobacco byproduct halts memory loss in lab study

In a study led by a team with the Bay Pines VA Healthcare System and the University of South Florida (USF), cotinine, a compound derived from tobacco, reduced brain plaques and prevented memory loss in a mouse model of Alzheimer's disease. The findings appear in the May 2011 issue of the *Journal of Alzheimer's Disease*.

"It looks like cotinine acts on several aspects of Alzheimer's pathology in the mouse model," says lead author Valentina Echeverria, PhD. "That, combined with the drug's good safety profile in humans, makes it a very attractive potential therapy for Alzheimer's disease."

Though largely refuted in recent research, past epidemiological studies suggested that smoking might somehow curb Alzheimer's disease. Some animal studies on nicotine even found brain-protective properties for the compound. But nicotine's harmful effects make it a poor drug candidate.

The VA-USF team decided to look at cotinine, the major byproduct of nicotine metabolism. Cotinine is nontoxic and lasts longer than nicotine. And its safety has already been shown in human trials looking at its potential to ease tobacco withdrawal.

The researchers gave cotinine daily for five months to young adult mice genetically altered to develop memory problems as they aged. At the end of the five-month study, the Alzheimer's mice treated with cotinine performed better on memory and thinking tasks than untreated Alzheimer's mice. Also, the brains of Alzheimer's mice treated with cotinine showed a 26-percent reduction in amyloid plaques, a hallmark of the disease. Furthermore, cotinine raised production of a protein that promotes the



Photo from Science Photo Library

survival of neurons and enhances attention and memory.

Given that the mice that benefited from cotinine had been in the very early stages of disease, the researchers believe the compound could be useful as a treatment for

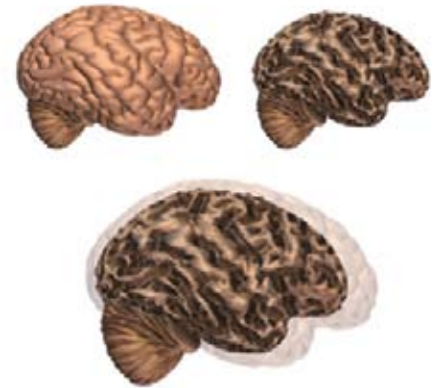


Illustration courtesy of Alzheimer's Association

Smoking and Alzheimer's—

Researchers once thought smoking was protective against Alzheimer's, but that theory has been largely refuted. In any case, a lab study at the Bay Pines VA Medical Center shows that a compound derived from nicotine may help against the disease.

mild cognitive impairment, an Alzheimer's precursor.

The VA-USF team is also studying the potential of cotinine to treat fear-induced anxiety and to help blunt traumatic memories in mouse models of PTSD. ➔



Photo by Shane Suzuki

VIP visit—For more on the recent visit of Sen. Patty Murray (D-Wash.) to VA's Center of Excellence for Limb Loss Prevention and Prosthetic Engineering in Seattle, visit www.research.va.gov.

Inside: IBM's 'Watson' super-computer prepares for a role in medicine

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layer of stress. “Not only do they have to help them, but they know these people,” notes Chapman. “They serve side by side with them, and they may have seen how the injuries occurred. So it goes beyond compassion fatigue—there’s a little more to it with a combat medic.”

Based on the data they have so far, Chapman and her military colleagues point out that depression symptoms appear to be more common than posttraumatic stress symptoms among medics three months post-deployment. But the researchers are continuing to track study participants to see which symptoms subside over time and which get worse.

Chapman’s team is now launching a related study in conjunction with the Army Medical Department Center and School. The effort will focus on traumas that combat medics may have experienced prior to training, as well as baseline risk and protective factors that could reduce or promote resilience. The goal is to learn which risk factors can be ameliorated, and which protective factors enhanced, through combat-medic training.

Chapman and colleagues plan to include experimental tasks to see how



Focus on medics—An Army flight medic (front right) helps Marines carry a wounded Afghan man to a waiting medevac helicopter. VA and Army researchers are studying the factors that help build combat medics’ resilience to stress and trauma.

trainees respond to emotional stress. The researchers will measure the heart’s electrical activity through electrocardiograms. They will also look at other known indicators of stress: respiration, eye movement, muscle response, and galvanic skin response—changes in the skin’s ability to conduct electricity. Emotions such as fear, anger and startle can activate sweat glands, and the extra moisture increases conductivity.

Chapman plans to also help conduct a trial involving Navy corpsmen, who care for Marines on the battlefield. Yet another study in the works will zero in on the issue of loss—how medics are affected when they “lose” soldiers, versus being able to save their lives. She hopes findings from all the research will guide the way to improved training to better prepare medics for their role, which is succinctly defined in their creed: “These things we do so that others may live.” —