

VA Research Currents

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

Studies boost Alzheimer's home safety Research offers guidance for family caregivers

The Camerons live in a tidy two-bedroom rancher just across from the Merrimack River, outside of Boston. A former gunner's mate in the Navy and library custodian, Donald, 74, was always good with his hands. These days, though, his wife, Ann, has to keep power tools away from him. She also has to make sure he doesn't wander off onto the busy two-way street outside their home. Donald has Alzheimer's disease, and his memory is declining with time.

"It's become more difficult, especially in the past year," says Ann.

She and other family caregivers have been taking part in studies at the Bedford

(Mass.) VA Medical Center aimed at boosting home safety for those with Alzheimer's.

The first goal of the research was learning what types of changes are practical and effective for families. The National Institute on Aging, Alzheimer's Association and other organizations have put out home-safety tips for years. But not all the tips are equally doable for caregivers.

"Many of the recommendations that were available were not research-based," says lead investigator Kathy Horvath, PhD, RN. "They were often overwhelming to people, and they didn't know where to

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Home safety makeover—

Dr. Scott Trudeau of VA and Boston University helped Ann and Donald Cameron improve the safety in their home. Donald, a Navy veteran, received a diagnosis of Alzheimer's disease three years ago. For a slideshow explaining some of the changes the Camerons made, visit www.research.va.gov.



RNA revelation

Scientists hope discovery will lead to new therapies to fight cancer

In 2006 and 2007, two of the world's leading science journals—*Science* and *Nature*—featured news reports on an intriguing discovery in the lab of Rajvir Dahiya, PhD, with VA and the University of California, San Francisco.

The discovery had to do with RNA—the lesser-known chemical cousin of DNA. For decades, scientists had seen RNA as little more than a molecular middleman charged with helping to translate DNA's genetic instructions into

Leading lab—The VA-University of California, San Francisco, group whose findings on RNA made news in the biomedical world was led by urology researcher Dr. Rajvir Dahiya (right) and included (from left) Dr. Long-Cheng Li, Dr. Emily Noonan, Dr. Robert Place, and Deepa Pookot.

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begin. Some recommendations were just lacking in the detail that people need.”

As an example, she cites the suggestion to highlight the edges of steps with white or colored duct tape, to provide contrast. People with Alzheimer’s have trouble with perception and are more likely to trip and fall. “As one family member asked us,” says Horvath, “does the tape have to go on all the stairs? Does it have to go across the entire stair? Just in the middle? These are the kinds of details people have questions about.”

Horvath and colleague Scott Trudeau, PhD, OTR/L, an occupational therapist, set out in their first study to test which interventions worked best. One factor they explored was cost: Caregivers were unlikely to make changes that were too pricey. The average cost of home-safety products installed in families’ homes in the study was \$79. This included items such as grab bars for the shower, nightlights, stove-knob covers, and child-safety locks for cabinets.

Families also were unlikely to make changes that took too much time, required technical help, caused an inconvenience, or altered the look of the home.



Dr. Scott Trudeau, an occupational therapist and researcher at the Bedford (Mass.) VA and Boston University, helps Ann Cameron apply duct tape to the edge of a brick landing in the home she shares with her husband, Donald (background), who has Alzheimer’s disease. The tape creates visual contrast, making the step easier to see and helping to prevent trips and falls.

Says Horvath, “Something might sound like a great idea from the professional’s viewpoint, but if people aren’t going to do it, what have you accomplished?”

Their study resulted in a 25-page, illustrated, simple-language guide. The booklet was tested for “health literacy” to make sure people could easily understand the instructions.

It’s now being tested with 160 families. Among the questions the researchers are looking at: Will caregivers who receive the toolkit (the booklet plus a shopping bag full of low-cost safety items) be more likely to make changes than those who receive only a standard checklist of recommendations? Will they experience less strain? Will their loved ones with Alzheimer’s engage in fewer unsafe behaviors?

The researchers point out that no approach is foolproof. “There’s no such thing as a completely safe home,” says

Trudeau, who has worked with people with dementia for 15 years. “What we can do is make the home environment safer, for both the caregiver and the person with Alzheimer’s.”

Nothing, he says, can replace the need for close supervision of someone with memory and judgment problems, “but the modifications we recommend can lessen the intensity of the vigilance required on the part of caregivers.”

Horvath and Trudeau’s research is conducted through VA’s New England Geriatric Research, Education and Clinical Center; and the Alzheimer’s Disease Center at Boston University. Funding is provided by VA and the National Institute on Aging. To view photos and more details about the home-safety changes they recommend for family caregivers of those with Alzheimer’s disease, visit www.research.va.gov.

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Wandering woes

Many of the home-safety changes that benefit people with Alzheimer's and their family caregivers are good things to do for any older person—for example, removing throw rugs from bedrooms or hallways, or installing grab bars in the shower. Other changes are specific for those with memory loss: placing car keys or cleaning supplies out of sight, for instance, or replacing stove knobs with special safety covers.

"Wandering" is one behavior specific to Alzheimer's and other forms of dementia that concerns many family caregivers. The following are among the wandering-prevention tips in *Keeping the Person with Memory Loss Safe at Home*, a booklet being tested as part of a study at the Bedford VA Medical Center and Boston University:

- Send for an ID bracelet from the Alzheimer's Association "Safe Return" program (1-888-572-8566).
- Give the name and a recent picture of your family member to the police in case he or she wanders away and gets lost.
- Use a motion sensor to warn you when the person wanders to an exit door or to a "risky" room, such as the kitchen, and install slide-bolt locks at the top or bottom of exit doors.

For more examples of dementia-specific home-safety tips, see the slideshow at www.research.va.gov.

Attaching a slide-bolt lock.



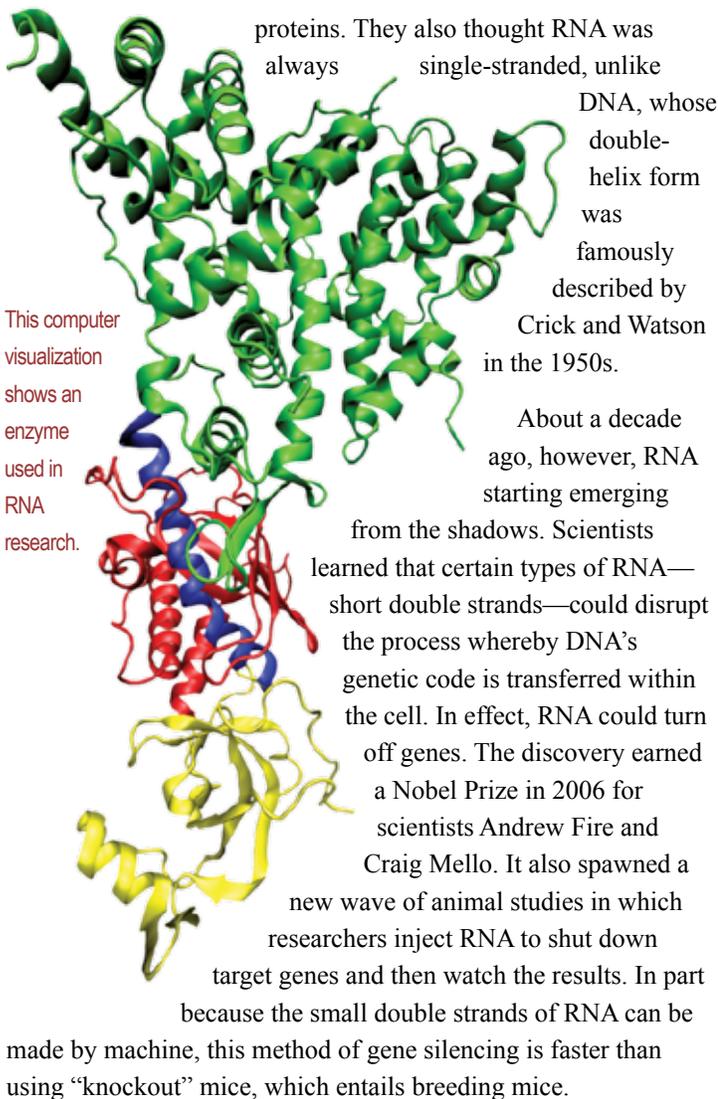
Top: For shaving, Trudeau and Horvath recommend a cordless rechargeable electric razor. Bottom: Replacing stove knobs with special safety covers. For more details, view the slideshow at www.research.va.gov.

New screening tool for dementia

A new screening tool developed by a team with VA and the University of California, San Francisco, may help doctors predict older people's risk of developing Alzheimer's disease. Research on the tool was published in the May 13 online issue of *Neurology*.

Several of the items on the 15-point scale are well-known risk factors for Alzheimer's disease, such as older age, low scores on tests of thinking skills, and the presence of a gene linked to the disease. Others are surprising: for example, lower body weight, no alcohol drinking, past bypass surgery, and slowness with physical tasks such as buttoning a shirt. To develop the index, the researchers examined 3,375 older people with no evidence of dementia and followed them over six years. During that time, 480 of the people, or 14 percent, developed dementia. The researchers then determined which factors best predicted who would develop dementia and created the point index. —

RNA (from page 1)



Then, along came Dahiya and colleagues with another twist in the RNA story: They discovered that short double strands of RNA, whose ability to interfere with gene expression was revealed by Fire and Mello, can not only turn off genes but also turn them on. This process has come to be dubbed RNAa—“a” for “activation.” Researchers were now faced with yet another shift in the gene-expression model they had relied on for years.

Dahiya says scientists are coming around to accepting RNAa as a valid phenomenon—especially now that other labs have produced findings similar to those first published by his group in the *Proceedings of the National Academy of Sciences* in 2006.

“This is the beginning of a new paradigm. I’m sure that over time people will be more inclined toward this concept,” says

Dahiya, who heads the Urology Research Center at the San Francisco VA and UCSF. Crucial players in his team’s groundbreaking RNAa studies were Robert Place, PhD, a postdoctoral fellow studying prostate cancer in Dahiya’s lab; and Long-Cheng Li, PhD, who was a postdoctoral fellow with Dahiya for nine years and is now on the faculty at UCSF.

Demonstrating the existence of RNAa was a milestone in itself. But now Dahiya’s group has moved onto the next step: exploring how the phenomenon can be applied therapeutically. In one lab experiment, published last year in *Molecular Cancer Therapeutics*, they used synthetic bits of double-stranded RNA to activate a tumor-thwarting gene called p21 in human bladder-cancer cells. “About 75 to 80 percent of the cancer cells showed inhibition,” says Dahiya.

More recently, they achieved similar results with kidney cancer cells. Those findings appear in the July 15, 2009, *International Journal of Cancer*.

A more natural way to treat cancer

Taking advantage of naturally occurring “tumor suppressor genes” has been one of the holy grails of cancer research for two decades. Scientists have tried different ways of introducing them into the body. But so far, no method has proved safe and reliable. Piggybacking the genes onto supposedly harmless carrier viruses that can infiltrate cells is one approach that’s been widely tried. But some clinical trials using this method have been halted because of infections and other serious side effects.

RNAa, like its converse, RNA interference, is promising because it occurs naturally in the body as a way of regulating gene expression. Dahiya and others hope injecting RNA into the body will prove less problematic than injecting tumor suppressor genes.

His team is now taking cell lines from human bladder, prostate and kidney cancer, transplanting them into mice to grow tumors in those organs, and then injecting small double-stranded RNA directly into the tumors.

“Our target is to go straight into the tumor, not systemically,” says Dahiya. In theory, the RNA will activate the appropriate tumor suppressor gene, which will in turn kill the cancer cells. Dahiya hopes he can collaborate with others at VA and UCSF to launch a clinical trial within the next three to four years, most likely focused on prostate cancer.

“If all turns out well,” says Dahiya, “we can eventually start trials in patients, injecting the RNA straight into the prostate.” ➔

VA study probes care for American Indians, Native Alaskans

Researchers with VA have published a series of articles on how the agency is working with the Indian Health Service (IHS) to serve American Indians and Alaska Natives who are eligible to receive care in both government health systems.

Part of the research involved the first-ever linking and merging of administrative records from the two health systems. That analysis appeared in the June issue of *Medical Care* and the March-April issue of *Women's Health Issues*. The researchers also interviewed healthcare providers and veterans to better understand dual use, reporting those findings in the June issue of the *Journal of General Internal Medicine*.

Among the key findings:

- American Indians and Alaska Natives who use VA are demographically similar to other VA users. For example, most served in wartime, especially the Vietnam era, and 93 percent are male. They also have similar medical conditions, such as PTSD, hypertension and diabetes, but are more likely to be receiving “complex care.”

- Dual users are more likely to receive primary care from IHS and diagnostic and mental health care from VA.

- The majority of women dual users are non-veterans who receive VA care through care-sharing or other agreements between the two agencies.

- From the perspective of VA and IHS clinicians, the key barriers to improving outcomes and access for American Indian and Alaska Native veterans include the distance between VA and IHS facilities; inadequate information-sharing



Dr. Mary Neill sees an American Indian veteran of World War II at a VA clinic in southern Oregon.

Dual users tend to receive primary care from IHS and diagnostic and mental-health care from VA.

and coordination of clinical care; a lack of information about local VA or IHS resources for the veterans; and difficulties with VA enrollment and eligibility determination.

Lead researcher Josea Kramer, PhD, with the Geriatric Research, Education and Clinical Center at the VA Greater Los Angeles Healthcare System, said providers with VA and IHS are eager to boost collaboration between the agencies. “I was impressed by the goodwill and strong desire by clinicians in both VA and IHS to work together to better coordinate care for their mutual patients,” she said.

Her group outlined several recommendations in their reports, based on feedback from VA and IHS staff. One idea is establishing a shared electronic health record between the agencies. Kramer said such a project is already in the works but faces several regulatory and technical challenges.

Other recommendations: issuing direct referrals between VA and IHS facilities; designating staff to coordinate between the two agencies; delivering VA care in tribal communities through a model similar to VA’s Community-Based Outpatient Clinics; and expanding education about eligibility and availability of services and about the needs of American Indian and Alaska Native veterans.

The study team also convened a panel of leaders from both agencies to prioritize the recommendations. The results of that effort are yet to be published. —

‘Image rehearsal’ may ease PTSD nightmares—A noninvasive treatment called “image rehearsal therapy” resulted in fewer nightmares and some improvement in PTSD symptoms for 15 veterans taking part in a small clinical trial at the Portland VA Medical Center. The therapy has patients think about changing the scenario of a recent nightmare. They then write down the more peaceful version and mentally rehearse it in a relaxed state. The study volunteers, who attended six group sessions to practice the technique, reported fewer nightmares after six months, but no effects were seen on sleep quality, depression, or the impact of the nightmares that did occur. (*Journal of Traumatic Stress*, online May 14)



Among older veterans, women less likely to get immunized—A team with VA’s Los Angeles-based Center for the Study of Health Care Provider Behavior studied the records of more than 48,000 VA patients aged 65 and older and found that

men were more likely than women to receive immunizations against influenza and pneumonia. For influenza, 73 percent of men versus 69 percent of women were vaccinated. For pneumonia, the rates were 87 versus 83 percent. The researchers concluded that although overall immunization rates are higher in VA than in community settings, older female veterans may benefit from educational outreach in this area. (*Journal of the American Geriatrics Society*, online June 8)



Depression common in kidney disease—Doctors know depression is common among patients with end-stage renal failure who are on dialysis. But is it equally common in those with milder forms of kidney disease? The answer is yes, according to a study by a team at the Dallas VA and University of Texas Southwestern Medical Center. They conducted clinical interviews with 272 patients with varying stages of chronic kidney disease

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CAREER MILESTONES



Pascal Malassigné, of VA and the Milwaukee Institute of Art and Design, was named Outstanding Educator in Industrial Design in the Midwest by the Industrial Designers Society of America. Malassigné has designed a number of innovative rehabilitation products for the spinal-cord-injured veteran population, such as folding, motorized prone carts for

those who can’t use wheelchairs because of pressure ulcers or other medical reasons.



Sunil Ahuja, MD, a physician-researcher at the South Texas Veterans Health Care System, won a Distinguished Clinical Scientist Award from the Doris Duke Charitable Foundation. The award, \$1.5 million to be used over five to seven years, will be used to investigate genes that influence patients’ susceptibility to

HIV infection and AIDS. The results could help in the design and evaluation of HIV vaccines. Past research by Ahuja and colleagues has already identified two genes that play a major role in AIDS.

Veena Shankaran, MD, with VA’s Center for the Management of Complex Chronic Care in Hines, Ill., earned the Young Investigator Award for 2009 from the American Society of Clinical Oncology Cancer Foundation. The award, which includes a \$50,000 grant, was presented for her research titled “The Out-of-Pocket Costs and Burden for Medicare-Eligible Cancer Patients and their Caregivers.”



Ken Heilman, MD, an investigator with VA’s Brain Rehabilitation Research Center and director of the University of Florida’s Cognitive and Memory Disorder Clinics, received the 2009 President’s Award from the Association of VA Speech-Language Pathologists. Heilman was cited, among other accomplishments, for boosting cooperation among disciplines to better understand communication disorders resulting from brain injury, stroke and progressive neurological diseases.

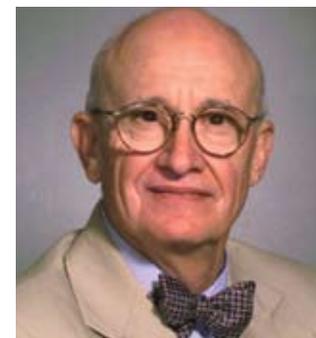




Photo by Mitch Mirkin



Photo by Nick Lancaster



Photo by Kevin Walsh

Veterans on the MOVE!—

A team of VA researchers and clinicians reports in the July 2009 issue of *Preventing Chronic Disease* on the design and rollout of VA's MOVE! program, designed to help veterans lose excess weight, keep it off, and improve their overall health through exercise, sensible eating and other lifestyle changes. According to the article, the health-promotion program is now in place at nearly all VA medical centers and as of June 2008, more than 100,000 patients had taken part in at least one visit. The article also describes an evaluation of the program that is now under way, looking at factors such as numbers of veterans involved; average percent change in body weight and body mass index at six months, one year and beyond; and staff time spent coordinating the program. Seen in the photos: walking the track at the Baltimore VA Medical Center; swimming at a veterans' sports competition; and a yoga class at the San Diego VA. For more information on MOVE! visit www.move.va.gov.

and found that one in five was depressed, regardless of kidney-disease stage. Factors linked with depression were diabetes, another mental illness, and a history of drug or alcohol abuse. (*American Journal of Kidney Disease*, online June 2)



Transplanted neurons reduce spinal cord pain in rats—

A team at the Miami VA Medical Center transplanted human nerve cells that secrete two natural body chemicals—GABA and glycine—into rats with induced spinal cord injury. When the cells—about a million of them—were transplanted within two weeks after the rats' injury, the animals' pain symptoms, such as hypersensitivity to touch and heat and severe tingling in their hindlimbs, completely and permanently disappeared. If the transplant took place *after* two weeks, the symptoms only partially reversed. According to the authors, "These data suggest not only that these cells are safe and efficacious, but also that they could be an effective clinical tool for treating SCI-associated neuropathic pain." (*Journal of Rehabilitation Research and Development*, 46(1))

HIV therapy linked to low bone density—An international team including researchers at the Washington, DC, VA Medical Center found that continuous antiretroviral therapy—a more aggressive form of treatment for those infected with HIV—decreases bone mineral density more than intermittent treatment. The study followed 214 volunteers at clinics in the U.S., Australia and Spain for an average of more than two years. The effects on bone density were not linked to any one drug in particular. Decreased bone density has been observed for a number of years in patients with HIV, but researchers are still working to better understand whether the decline is due to the virus itself, drug treatment or other factors. (*AIDS*, online June 15)



Parsing press releases—A study by the Vermont-based VA Outcomes Group found that "press releases from academic medical centers often promote research that has uncertain relevance to human health and do not provide key facts or acknowledge important limitations." The study was funded by the National Cancer Institute. (*Annals of Internal Medicine*, May 5, 2009) —

Effort launched to stem mental-health stigma

A multimedia program aimed at combating the stigma surrounding PTSD and other mental-health issues was launched in June by the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE).

The “Real Warriors” campaign bolsters existing mental-health programs in VA and the Department of Defense and features a website (www.realwarriors.net) where service members or veterans can access information and resources 24/7 and chat online with psychological health coaches. They may also call the program’s outreach center at 866-966-1020.

“One of our key efforts is related to outreach and advocacy and promoting resilience,” said VA’s Sonja Batten, PhD, deputy director of the DCoE. “The tag line of the campaign is ‘Real Warriors, Real Battles, Real Strength.’ The idea is that it takes the courage of a warrior to ask for help.”

Among its other activities, the DCoE conducts research in collaboration with VA and other partner organizations.

HIGHLIGHTS



Royal shake—Wearing an advanced prosthetic arm now being tested at VA medical centers, Gulf War veteran and VA prosthetics intern Paul Yarbrough shakes hands with Britain’s Prince Harry, who recently visited the VA New York Harbor Healthcare System. Yarbrough used the arm, featured on the cover of last month’s *VA Research Currents*, to operate a power drill and perform other tasks. The arm was developed by DEKA Integrated Solutions with funding from the Defense Advanced Research Projects Agency. Its design will be optimized through the three-year VA study.

The arm, part of DARPA’s “Revolutionizing Prosthetics” initiative, has six pre-programmed grasps for the hand segment, and additional grips can be programmed in. This enables users to pick up, handle and use a wide range of everyday objects, from keys to power tools. Another aspect of the arm’s versatility is that it can be used with a variety of control systems. One example: A shoe insert with pressure sensors that works like a joystick.