Mild neurologic deficits appear to increase PTSD risk

A study of identical male twins, led by a team at the VA Medical Center in Manchester, NH, found that Vietnam combat veterans with posttraumatic stress disorder (PTSD) and their non-combat-exposed twins had subtle neurologic deficits that veterans without PTSD and their twins did not have, suggesting that the deficits are not the result of trauma, but instead may predispose people to PTSD. The study appeared in the May 2006 Archives of General Psychiatry.

Previous studies have found that certain brain structures, such as the hippocampus, which plays a key role in memory, are smaller in people with PTSD. Some researchers have proposed that this diminished volume results from the trauma or the subsequent PTSD, while others see it as a pre-existing condition that may increase the risk of PTSD upon exposure to trauma.

Lead author Tamara V. Gurvits, MD, PhD, and colleagues studied 49 male Vietnam veterans and their non-combat-exposed identical twins. Among the combat veterans, 25 had PTSD and 24 had never had PTSD. All participants underwent a detailed neurological evaluation that included tests to uncover mild deficits in behavior, coordination and learning.

Veterans with PTSD showed more deficits than veterans without PTSD. Likewise, the twins of the PTSD veterans also had more deficits than the twins.

Thinking outside the ‘black box’:

Researchers’ proposed drug labels provide clearer facts for consumers

They’ve brought their message to officials at the Food and Drug Administration, medical colleagues in VA and academia, and—through articles in the Washington Post and other newspapers—tens of thousands of consumers.

Steven Woloshin, MD, MS, and Lisa Schwartz, MD, MS, of Dartmouth Medical College and the VA Outcomes Group in White River Junction, Vt., say Americans need clearer, more balanced information to make good healthcare choices. They’ve studied and written about various facets of the issue, but the focus of their current efforts is an innovative “drug facts box” they’ve designed and would eventually like to see included with all medications. Similar in concept to the Nutrition Facts box found on food products, it would explain the risks and benefits of drugs in plain English, and help patients and doctors alike make better assessments.

“The drug box is designed for both patients and doctors,” said Woloshin. “We hope it would promote doctor-patient communication by making information about new medications more accessible. It’s hard for doctors to find this kind of information at the time of the visit.”

The team’s efforts gained new momentum recently with a $394,000 award from the Attorney General Consumer and Prescriber Education Grant Program. The nationwide program will distribute $21 million in education grants over the next few years as part of a settlement resolving allegations of illegal marketing against drug-maker Warner-Lambert.

Woloshin and Schwartz have tested their drug box in a variety of settings, and are gearing up to do a survey with
a randomly chosen national sample of 500 consumers. Participants will be mailed either a standard drug package or the experimental label for the same drug, and fill out a questionnaire showing how much they understand about the drug’s benefits and side effects.

A study published by the pair and colleague H. Gilbert Welch, MD, in *Health Affairs* in April 2004 found that when consumers read either a standard drug ad or one incorporating the researchers’ “benefit box”—an earlier version of the box explaining benefits, but not risks—they rated the information in the box as “very important” or “important,” and almost all found the data easy to understand. And significantly, perceptions of drug effectiveness were much lower with ads that incorporated the benefit box.

Schwartz suggests that if the benefits of the now-recalled drug Vioxx had been communicated in a similar way, physicians may have been less eager to prescribe it. “Because of the marketing campaign, many people thought it worked better for pain relief than other non-steroidal medications—but that was never true,” she says.

Standard drug ads and package inserts—and even the “black box” warnings required on many drugs with potentially serious side effects—fail to provide balanced information, say the Vermont researchers.

Drug ads don’t quantify benefits

“What you see in the ads is almost exclusively about drug harms—there’s almost never any quantification of drug benefits,” explains Woloshin.

Adds Schwartz: “There are no specific requirements for how drug benefit data are to be presented in the label, and in fact there is little consistency. Almost uniformly, the part of the label excerpted for drug ads doesn’t contain benefit data. So it’s not easy to find out, quantitatively, how a drug works.”

Their pilot box features a table summarizing the outcomes for clinical-trial participants who took a drug and those who didn’t. For example, a mock-up for the sleeping pill Lunesta outlines the results of a study with 788 healthy adults: Those given the drug fell asleep, on average, in 32 minutes, compared to 45 minutes for those given a “sugar pill,” or placebo. Lunesta users slept an average of 6 hours and 22 minutes, compared to 5 hours and 45 minutes for the placebo group. The table also lists side effects in everyday terms—dizziness, drowsiness, dry mouth, nausea—and tells what percentage of people in each group was affected.

Woloshin and Schwartz base the information in their boxes on findings from the largest clinical trials reported in FDA approval documents.

“The data in the [standard] labels is sometimes from studies that are not published, or it’s not easily matched to published studies,” says Schwartz. “We’re always surprised by how hard it is to get the information. It’s fairly work-intensive.”

**Reaching out to and through the press**

Woloshin and Schwartz do an occasional series for the *Washington Post* called “Healthy Skepticism,” in which they show how medical research is often misreported to the public. They’ve received good feedback from doctors, consumers and especially reporters.

“We’ve gotten a lot of really complimentary notes from health journalists who think this is a good way not only to tell a story, but teach some of the background skills needed to understand health reporting,” says Woloshin. The Vermont husband-and-wife team also teach seminars for journalists who want to do a better job of reporting on health research. They are regular faculty for the annual “Medicine in the Media” event sponsored by the National Institutes of Health (http://medmedia.nih.gov).

The researchers say even reporters and editors sometimes question whether readers will be able to digest too many numbers and statistical concepts, even if they’re presented in easy terms. But Woloshin and Schwartz assert the importance of helping consumers adjust to this way of thinking about medicine. “We believe the more people start seeing those numbers, the more they’ll be able to make sense of them,” says Schwartz. “It will require education, but we think seeing this type of information on the benefits and harms of treatment will help people make better medical decisions.”

---

**VA Research Currents**

*is published monthly for the Office of Research and Development of the Dept. of Veterans Affairs by VA R&D Communications 103 S. Gay St., Rm. 517 Baltimore, MD 21202 (410) 962-1800, ext. 223 research.publications@va.gov*
Secondhand smoke linked to glucose intolerance

Amid studies in recent years suggesting that smoking is an independent risk factor for diabetes, VA researchers have shown that even exposure to secondhand smoke may raise the risk of glucose intolerance, a diabetes precursor.

A team led by Thomas K. Houston, MD, and Catarina I. Kiefe, MD, PhD, of VA’s Birmingham-based Deep South Center on Effectiveness Research and the University of Alabama examined data on 4,572 men and women included in the ongoing Coronary Artery Risk Development in Young Adults (CARDIA) study, started in the 1980s. Using baseline data, the researchers classified participants as current smokers; former smokers; never-smokers with exposure to passive smoke; and never-smokers with no passive exposure.

Not surprisingly, smokers showed the highest risk for glucose intolerance, with nearly 22 percent of them developing the condition during 15 years of follow-up. Never-smokers with no passive exposure had the lowest risk, 11.5 percent.

But 17 percent of non-smokers with exposure to secondhand smoke also developed the condition—higher even than the 14-percent risk rate among smokers who had kicked the habit.

“This is one more piece of evidence supporting the risk of secondhand smoke, and one more reason we should encourage our patients to quit smoking,” Houston told Science Daily, a science-news website.

HAND

Committee chairman Sen. Larry Craig (R-Idaho), the lawmaker was able to use the hand to hold a glass of water.

Weir explained how users know how much force to exert when grasping an object: “The hand has no pressure feedback, and if it were ‘pushed’ it could crush a glass. But it must be pushed to do so. Usually, the user controls a myoelectric hand by using vision to see how the fingers are ‘deforming’ around an object. In addition, the motors change pitch as they work harder, and users get used to that.”

Weir’s lab has teamed with a commercial manufacturer to produce several pre-commercial prototypes for clinical testing.

“We give users instructions to take it home and let us know when it breaks—we expect it to break once users do things with it we never predicted, so we want to find that out and iteratively make the mechanism tougher and able to withstand the rigors of everyday use.”

While the partial hand prosthesis only opens and closes, Weir’s team and collaborators at other institutions are developing a more sophisticated prosthesis they hope will move and function almost like a natural hand. The idea is to use implantable sensors to receive input from all 18 forearm muscles involved in controlling the human hand, and develop fuzzy logic to translate those signals into mechanical movements that match the user’s intent. Biomechanics expert Wendy Murray, PhD, at the Palo Alto VA is helping to map out those functions.

The April 27 hearing, convened by the U.S. Senate Committee on Veterans’ Affairs, also featured testimony from VA Under Secretary for Health Dr. Jonathan Perlin, accompanied by Dr. Joel Kupersmith, chief research and development officer; Drs. Fred Wright and Dennis Stevens, associate chiefs of staff for research at the VA Connecticut Healthcare System and the Boise (Ida.) VA Medical Center, respectively; Dr. John Feussner, chairman of the department of medicine at Medical University of South Carolina and former chief research and development officer for V A, who testified from the perspective of an academic affiliate; and Dr. John I. Kennedy Jr., MD, associate chief of staff for acute and specialty care at the Birmingham VAMC, testifying on behalf of the Alliance for Academic Internal Medicine. Full text of their comments is available at http://veterans.senate.gov.
PTSD (cont. from pg. 1) of the non-PTSD veterans. The differences between the groups remained significant even after the researchers adjusted for factors such as age, alcoholism, and exposure to traumatic events other than combat.

According to the authors, “The results clearly support the conclusion that subtle neurologic dysfunction in PTSD does not reflect brain damage acquired along with the PTSD but instead represents a familial vulnerability factor, which likely antedates the traumatic exposure.”

VA authors collaborating with Gurvitz on the study were Linda J. Metzger, PhD; Natasha B. Lasko, PhD; Mark W. Gilbertson, PhD; Scott P. Orr, PhD; and Anna M. Charbonneau.

Quality Enhancement and Research Initiative. He served as acting chief research and development officer for VA from July 2004 to May 2005.

Kevin Volpp, MD, PhD, received the society’s Outstanding Junior Investigator of the Year award. Volpp, an HSR&D Career Development awardee, is affiliated with the Philadelphia VA Medical Center and the University of Pennsylvania, and conducts research at HSR&D’s Center for Health Equity Research and Promotion.

‘Art’ from VA labs sought

Inspired by the front covers of journals such as Science and Nature, this newsletter is seeking to highlight images from the biomedical labs of VA investigators. Original color images of molecules, cells, organisms, tissue or any other research-related subjects that are aesthetically interesting will be considered for publication. JPEGs can be sent to Mitch Mirkin at mitch.mirkin@va.gov, accompanied by a one-paragraph explanation of what the image shows.