

A National Newsletter for Veterans and their Health Care Providers

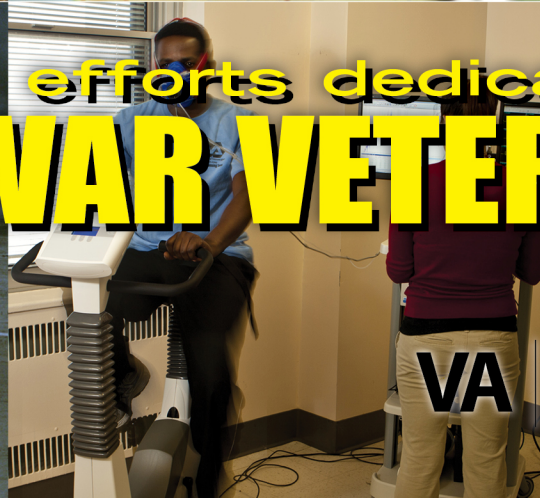
WRIISC Advantage

SPRING/SUMMER 2015



GULF WAR 25TH ANNIVERSARY (1990-2015)

Research efforts dedicated to
GULF WAR VETERANS



VA



U.S. Department of Veterans Affairs
Veterans Health Administration
Office of Public Health

Nearing the 25th Anniversary of the Gulf War, this edition of **WRIISC Advantage** highlights our continued efforts to conduct meaningful research related to Gulf War Veteran health concerns.

Gulf War Research at VA and the WRIISC's Role



MANY GULF WAR VETERANS returned home in 1990 and 1991 with a number of health concerns. *Note: Desert Shield/Desert Storm (1990-1991) Veterans are referred to as Gulf War Veterans (GWVs) in the edition.* Approximately 30% reported chronic symptoms that became known as Gulf War Illness (GWI) or chronic multisymptom illness. These symptoms, such as pain, fatigue, and cognitive problems often occur at the same time. While providing Veterans with clinical care remains at the core of VA's commitment, determining the underlying causes of these symptoms and developing evidence-based treatment practices are just as essential. As part of a VA-wide response plan, the Office of Research and Development provides research funds to scientists at VA Medical Centers to better understand how to treat these symptoms and improve the overall health of GWVs. VA has developed a strategic plan for Gulf War (GW) research (<http://www.research.va.gov/pubs/docs/GWResearch-StrategicPlan.pdf>) which includes developing diagnostic laboratory tests ("biomarkers") and treatments as well as communicating research results. In recent years, VA has increased the number of research

Research related to Gulf War Veterans remains imperative.

studies and has placed particular emphasis on clinical treatment trials. We have learned a lot about the health problems of GWVs, and VA remains committed to conducting the additional research that still needs to be done.

WRIISC researchers and clinicians have worked closely together with the common goal of improving clinical care for GWVs through research and applying it to clinical practice.

Studies completed at the WRIISC focus on all aspects of GWI; from physiological and behavioral studies to neuroimaging studies and how best to deliver health care to GWVs. Findings from these studies provide insight into the health of GWVs, add to the foundation for future research studies, and bring effective treatments closer to reality. Sharing our research results with clinicians and Veterans and their family members is an essential part of offering higher quality care for Veterans. At the WRIISC, enhancing health status and life quality for Veterans is at the forefront of our mission. GWV-related research remains imperative. Read on to find out more about our current research program for GWVs. ↪

"VA's War Related Illness and Injury Study Center (WRIISC) program is a terrific resource for post-deployment Veterans with complex health conditions that have no known cause, medical histories that include many tests and treatments with little improvement in their symptoms, or possible deployment-related environmental exposures."

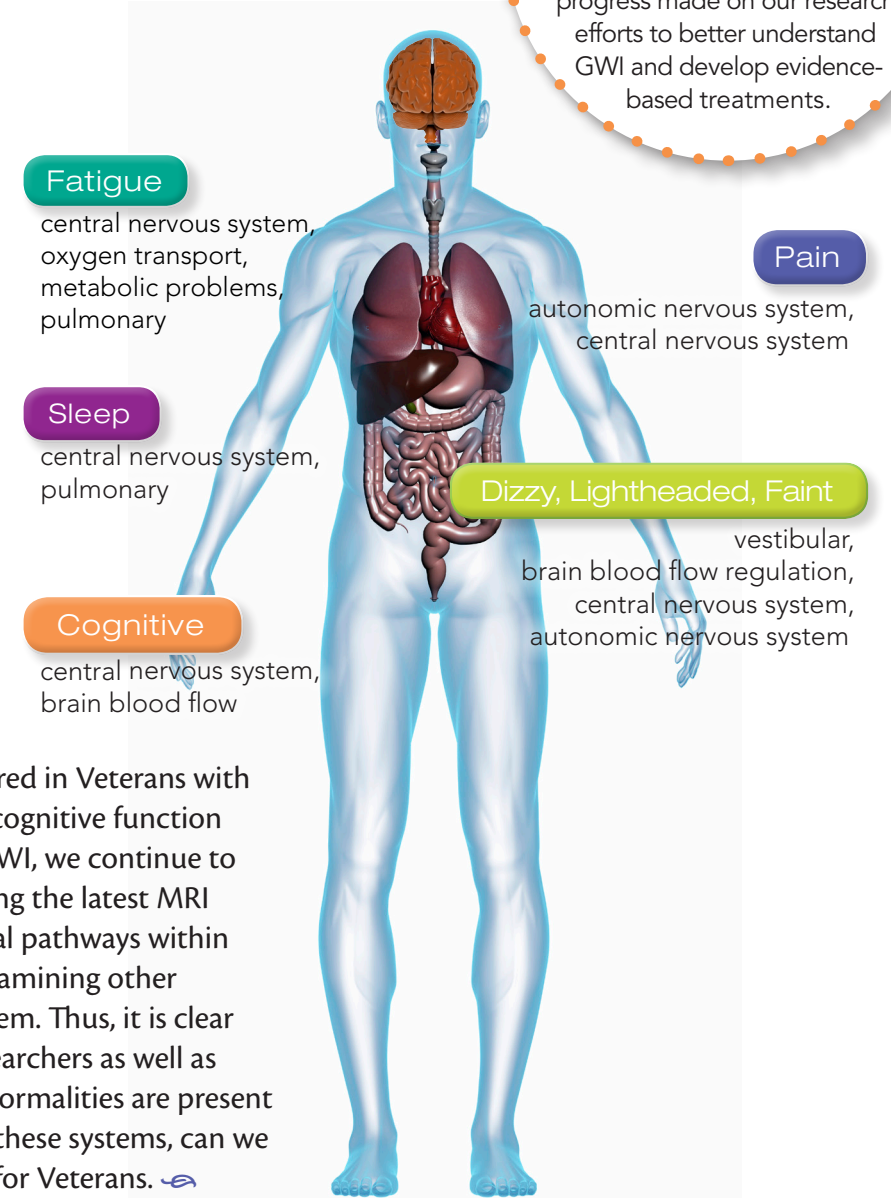
—Carolyn M. Clancy, MD, Interim Under Secretary for Health

Understanding the Pathophysiology of Gulf War Illness

IN A RECENT SURVEY the WRIISC performed on 542 Veterans with GWI, 94% reported fatigue, 92% cognitive problems, 86% pain, 86% sleep problems, and 72% dizziness and lightheadedness or fainting. Despite the high report of symptoms, we still do not understand what role underlying physiological problems play in these symptoms. Recent data has begun to demonstrate that several physiological systems are affected in GWI, which might help to explain some of these symptoms.

For example, the WRIISC and other investigators have started finding that Veterans with GWI are demonstrating impaired mitochondrial function (study description on next page). Examining other systems, it appears that pulmonary function may also be affected, resulting in an inability to deliver oxygen, a critical component of metabolism and another possible cause of fatigue. Scientific examinations of the nervous system by WRIISC researchers and others have found that control of blood vessels and the heart are compromised in GWI, which impacts blood flow and may contribute to fatigue as well as lightheadedness and fainting. Additionally, the WRIISC has found that brain blood flow is impaired in Veterans with GWI. Without proper brain blood flow, cognitive function is also impaired. To better understand GWI, we continue to examine other approaches including using the latest MRI techniques to understand how the neural pathways within the brain are functioning. We are also examining other sensory systems such as the balance system. Thus, it is clear both from data obtained by WRIISC researchers as well as others that underlying physiological abnormalities are present in Veterans with GWI. Only by studying these systems, can we work towards new, effective treatments for Veterans. ↪

On May 7th, the WRIISC gladly participated in the 4th Veterans Service Organization **Gulf War Research Day** sponsored by the Disabled American Veterans (DAV). WRIISC researchers shared progress made on our research efforts to better understand GWI and develop evidence-based treatments.



Research Volunteers Needed!

- ▶ To be a good research study it's often important to include **healthy** volunteers.
- ▶ Participating in research can be beneficial to you and to other Veterans.

Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with Gulf War Illness

GWV INVOLVES SYMPTOMS across multiple organ systems. Therefore, studying only one organ system is inadequate to better understand the complexity of GWI. Symptoms across multiple organ systems in GWI may share a common problem, which is impaired energy production. Mitochondria are parts of cells found in every organ system throughout the body and are responsible for about 90% of the energy necessary for proper cellular function. If the mitochondria become damaged or no longer function as they should— the cells that make up organs could become injured or die.



Yang Chen, MS, a doctoral candidate from Rutgers Biomedical and Health Sciences, Rutgers extracts DNA for analysis.

Principal Investigator Michael Falvo, PhD, of the NJ WRIISC, is currently studying whether mitochondria are damaged and/or not properly functioning in Veterans with GWI. This is a study titled, "Diagnostic Utility of mtDNA Content and Exercise Challenge in Gulf War Illness." Volunteers will be asked to visit the NJ WRIISC for two consecutive days. During these visits, Veterans will be asked to perform maximal exercise testing on a bike and provide blood samples before and after exercise. Exercise is being used as a challenge to the energy production system or mitochondria. In addition, volunteers will complete questionnaires and other tasks to evaluate their fatigue and symptoms. It is hoped that results of this study will lead to the development of future treatments.

Non-Pharmacologic Treatments for Chronic Pain in Veterans with Gulf War Illness

GWVs WITH CHRONIC PAIN and additional symptoms often associated with GWI can participate in a study at the CA WRIISC funded by the Congressionally Directed Medical Research Programs (CDMRP) and awarded to Dr. Peter Bayley, Associate Director of Cognitive Neuroscience, and Louise Mahoney, Director of Clinical Yoga Program. The idea for the study came about as a result of observations of Veterans who participated in the CA WRIISC clinical yoga program. These Veterans reported beneficial effects from simple yoga breathing and postures, without the fatigue that often occurs after other forms of exercise. In fact, many Veterans reported increased energy and improved daily functioning.

While the cause of GWI remains unknown, one theory is related to autonomic nervous system (ANS) dysfunction resulting from experiences or exposures that occurred while in the military. Yoga is known to produce measurable changes in the ANS and has proven useful in treating stress-related disorders. Controlled breathing techniques can be used to stimulate both the sympathetic and parasympathetic nervous system to help restore a healthy balance. If ANS dysfunction is involved in producing symptoms of GWI, bringing balance back to that system can relieve symptoms and promote a greater sense of ease and well-being.

The study will compare the efficacy of yoga with a behavioral intervention which includes standard pain-reducing activities. An additional goal is to provide Veterans in both groups with

life-long skills to help reduce pain and improve their overall health and sense of well-being.

Cognitive Rehabilitation Treatment of Veterans with Gulf War Illness

VETERANS WITH GWI face many challenges that prevent them from doing the things they want to do. Dr. Lisa McAndrew and her team at the NJ WRIISC are trying to help Veterans with GWI who experience cognitive difficulties. They found that GWI doesn't impact how smart Veterans are, but GWI can slow down a Veteran's thinking process, which makes things like concentrating, planning, and managing physical symptoms difficult. This difficulty impacts daily activities, such as grocery shopping or keeping appointments. For example, a Veteran with GWI may have to rest before going out to lunch or plan to have special food there. Plans may also have to be made to accommodate their physical symptoms. For instance, the Veteran may need to plan to go out for lunch early when s/he has more energy. Slowed thinking makes it hard to do this extra planning.

Principal Investigator Dr. McAndrew and her team explore if helping Veterans with GWI and slowed thinking facilitates them in doing the things they want. Their study, "Cognitive Rehabilitation Treatment of Veterans with Gulf War Illness," is looking at both a Cognitive Rehabilitation approach as well as a Health Education approach. This clinical trial will examine whether a Cognitive Rehabilitation Treatment improves daily activities as compared to a Health Education Treatment.

Complementary and Alternative Medicine (CAM) for Sleep, Health Functioning, and Quality of Life in Veterans with Gulf War Illnesses



A Veteran receives auricular (ear) acupuncture treatment at the DC WRIISC facility at the Washington, DC VA Medical Center.

THIS NEW WRIISC STUDY with Principal Investigator Dr. Matthew Reinhard, DC WRIISC Director, will soon be available for GWVs' participation. For this clinical trial, Veterans will be introduced to CAM, such as meditation and acupuncture, with the hope that these treatments will target GW symptoms and improve overall quality of life for participants. Participating Veterans will be randomly assigned to one of two groups. One group will receive GW Health Education classes that promote wellness and prevention through providing information. The second group will attend classes for meditation and auricular (ear) acupuncture. Both of these will be offered for one hour for eight consecutive weeks. Veterans will be followed by the research team for an entire year. Eventually all participants will have access to CAM services. Through meditation and acupuncture practice the clinical study team hopes to improve sleep and quality of life for Veteran participants and provide evidence for these modalities as an effective treatment for the Gulf War Cohort.

VA NATIONAL RESEARCH TO HELP GULF WAR VETERANS

The "Gulf War Era Cohort and Biorepository Pilot Project," led by Principal Investigator Dr. Dawn Provenzale (pictured right) at the Durham VA Medical Center, began recruiting in 2014. The project aims to develop a research database, including survey, clinical, and environmental exposure data, and to collect blood specimens from GWVs across the country. The specimens will be processed and stored at the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), a fully equipped, state-of-the-art biological specimen collection and processing center. This project will provide valuable tools that allow researchers to examine and understand the medical conditions affecting GWVs, and will ultimately help create programs that better meet the health care needs of all Veterans. For more information, visit: www.research.va.gov/programs/csp/585 or call 1-855-493-8387 (1-855-GWE-VETS).



Using Dietary Polyphenol Preparations for Treating Veterans with Gulf War Illness

DIFFICULTIES IN THINKING or lack of energy are hallmarks of GWI and can severely impact Veterans' ability to engage in day-to-day activities. Principal Investigator Dr. Drew Helmer, Director of the NJ WRIISC, in collaboration with Dr. Giulio Pasinetti at Mount Sinai School of Medicine in New York City, is launching a study that will look at whether natural chemicals (called polyphenols), found in a combination of grape seed extract and grape juice, are a safe and feasible for treatment of GWI. The study will be a randomized controlled trial where researchers compare different treatments assigned to participants using something like a coin flip (e.g., heads vs. tails). Preliminary evidence suggests that polyphenols may counteract damage to the brain caused by oxidative stress, such as from chemical exposures. GWVs participating in this study will undergo neuropsychological testing, and then will take daily doses of either the grape seed extract and grape juice or identical-appearing substitutes that do not contain the active substances (placebo) for 24 weeks. Dr. Helmer and his team will carefully collect and analyze test results to see whether Veterans were able to tolerate the higher intake of polyphenols and if thinking and fatigue improved. This project will determine whether grape seed extract and grape juice, readily available and safe products, could help improve the health and function of Veterans with GWI. [↗](#)

AT A GLANCE

Principal Investigator Glenn Wylie, DPhil, of the NJ WRIISC and the Kessler Rehabilitation Center, uses new neuroimaging techniques (functional MRI or fMRI) to allow us to better understand the brain and possible links to mental fatigue. This study is titled "Examination of Cognitive Fatigue in Gulf War Illness using Functional Magnetic Resonance Imaging." Detailed information about this study is located in the Spring/Summer 2014 edition of WRIISC Advantage on our website.



For more information on studies described in this edition of WRIISC Advantage, please contact us at your nearest WRIISC location or visit our website: www.WarRelatedIllness.va.gov.

Gulf War Veterans Enrolled in the Integrative Health and Wellness (IHW) Program at DC WRIISC

THE DC WRIISC conducted a study focused on GWVs enrolled in the Integrative Health and Wellness (IHW) Program. They compared GWVs to their non-GWV peers with respect to self-reported physical and mental health symptoms, and looked at their patterns of health and wellness service use within their first six months in the IHW Program. They focused on three services: group acupuncture, individual acupuncture, and meditation.

When comparing GW (n = 42) and non-GW (n = 184) Veterans on baseline symptom severity, GWVs reported more severe depression, insomnia, pain intensity, and pain-related disability. In spite of these differences in symptom severity, there were no differences in the use of specific services (ie., acupuncture, meditation) accessed. Of the

226 Veterans who enrolled in the IHW Program, 72% used at least one service during the first six months. Researchers also examined the number of sessions of each service that Veterans attended, and found that GWVs attended fewer sessions of group acupuncture. No other differences were observed.

This study provides insight into the factors that may drive GWVs to seek complementary and alternative medicine services. It also suggests that when selecting services, GWVs may prefer individual to group services when the option is available. It will be important for future studies of the IHW Program to examine whether participation in this program results in reduced physical and mental health symptoms. For more information regarding the study please see the recent publication: *Brooks Holliday, S.,*

Hull, A., Lockwood, C., Eickhoff, C., Sullivan, P., & Reinhard, M. (2014). Physical health, mental health, and utilization of complementary and alternative medicine services among Gulf War Veterans. Medical Care. 52 (12): 39-44.

Recent Research Highlights at CA WRIISC

CA WRIISC has been active in pursuing new post-deployment research opportunities for Veterans of all eras. Here are a few highlights:

- ▶ Dr. Peter Bayley will be starting a VA Rehabilitation Research Merit clinical trial to compare two treatments for Veterans with Post-Traumatic Stress Disorder (PTSD), a novel breathing technique called Sudarshan Kriya as compared to the standard VA treatment protocol.
- ▶ Dr. Maheen Adamson has been funded for a new clinical trial to study repetitive Transcranial Magnetic Stimulation (rTMS) as treatment for Veterans with traumatic brain injury through VA's Small Projects in Rehabilitation Research (SPiRE) award program.
- ▶ Dr. Linda Isaac, a WRIISC fellow, just published the article "The impact of depression on Veterans with PTSD and traumatic brain injury (TBI): A diffusion tensor imaging study" in *Biological Psychology (Biological Psychology 105 (2015) 20–28)*. The project looked at a group of Veterans with PTSD and TBI who were referred to the WRIISC clinical evaluation program to determine whether abnormalities found in brain white matter are further impacted by depression. Dr. Isaac reported that two areas of the brain, the uncinata fasciculus (UF) and the Cingulum fibre tracts, which are involved in mood and memory, are further impaired by depression in these Veterans. [↗](#)

Through this edition of **WRIISC Advantage**, we hope you have learned more about the exciting research we are doing on GWVs and GWI. As researchers and clinicians, we are honored to positively impact the future health of Veterans through our efforts!

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ATTENTION PROVIDERS: The updated **Management of Chronic Multisymptom Illness (CMI)** guideline (2014) describes critical decision points and comprehensive evidence-based recommendations for VA and DoD practitioners to improve patient outcomes: <http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp>.

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Do you want to learn more about our Clinical Services and Educational Offerings?

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