# DEPARTMENT OF VETERANS AFFAIRS

# ANNUAL REPORT TO CONGRESS

## Federally Sponsored Research on Gulf War Veterans' Illnesses for 2014

# Annual Report to Congress – FY 2014

**Federally Sponsored Research on Gulf War Veterans' Illnesses for 2014**

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TABLE OF CONTENTS

## EXECUTIVE SUMMARY

## I. INTRODUCTION

Section 707 of Public Law (P.L.) 102-585, as amended by section 104 of P.L. 105-368 and section 502 of P.L. 111-163, requires that an annual report be submitted to the Senate and House Veterans' Affairs Committees on the results, status, and priorities of research activities related to the health consequences of military service in the Gulf War (GW) in Operations Desert Shield and Desert Storm, 1990 and 1991. The Research Subcommittee of the interagency Deployment Health Working Group (DHWG) prepared the Annual Report to Congress on Federally Sponsored Research on Gulf War Veterans' Illnesses for 2014, which is the 21st report on Federal research and research activities. The DHWG tracks all federally-funded research projects related to GW Veterans' illnesses (GWVI).

As in previous annual reports to Congress, the material presented is divided into six sections and three appendices. Section I is an introduction; Section II summarizes the research priorities and organization of the Federal GW research portfolio; Section III highlights and summarizes research progress published since the last annual report to Congress; Section IV summarizes Federal funding trends for GW research during the 10-year period from fiscal year (FY) 2005 through FY 2014; Section V highlights new research projects and initiatives since the last report; Section VI contains literature references; and the Appendices contain listings of federally-funded research projects.

## II. RESEARCH PRIORITIES

The research priorities remain unchanged from last year. The 19 Research Topics (two of the original 21 topics were eliminated in the 2006 annual report to Congress) are grouped into five major Research Focus Areas. These Research Focus Areas are used to organize Sections III and V, as well as Appendix B (Project Listing by Research Focus Area). In November 2005, at the request of the Secretary of Veterans Affairs, the Department of Veterans Affairs (VA) Office of Research and Development (ORD) developed a set of criteria for inclusion of VA-funded projects in the GW research portfolio and then evaluated the entire VA research portfolio for projects meeting those criteria. The criteria used as the basis for the review are presented in Section II.

## III. PUBLISHED RESULTS AND STATUS OF THE FIELD IN 2014

Section III provides brief summaries of research articles on the health problems of GW Veterans published during calendar year (CY) 2014 or in CY 2013 after the previous annual report to Congress was submitted. Research results are grouped according to the five Research Focus Areas used to organize the 19 Research Topics (see Section II): Brain and Nervous System Function, Environmental Toxicology, Immune Function, Reproductive Health, and Symptoms and General Health Status. In this section, published research results are described followed by specific study abstracts taken from PubMed.

## IV. RESEARCH FUNDING TRENDS

VA, the Department of Defense (DoD), and Department of Health and Human Services (HHS) funded 450 distinct projects from FY 1992 through FY 2014 related to health problems affecting GW Veterans. The scope of the Federal research portfolio is broad, from small pilot studies to large-scale epidemiology studies involving large populations and major center-based research programs. Federal funding for research on GWVI totaled approximately $230 million for the period from FY 2005 through FY 2014. As of September 30, 2014, 380 projects (84 percent of the 450 projects) were completed, and 70 projects (16 percent) were new or ongoing.

## V. NEW RESEARCH PROJECTS AND INITIATIVES

Sixteen new projects were funded through the FY 2013 appropriation for the Gulf War Illness Research Program (GWIRP) managed by the Congressionally Directed Medical Research Programs (CDMRP) at DoD; these were not initiated until FY 2014. These projects focused on Brain and Nervous System Function (9), Immune Function (1), and Symptoms and General Health (6). Two ongoing DoD projects were funded for additional studies, one in Brain and Nervous System Function and one in Symptoms and General Health Status. VA funded eleven new projects in FY 2014. Seven of these projects focused on Brain and Nervous System Function, one focused on Reproductive Health, and three focused on Symptoms and General Health.

## I. INTRODUCTION

The Secretary of Veterans Affairs is required by section 707 of P.L. 102-585, as amended by section 104 of P.L. 105-368 and section 502 of P.L. 111-163, to submit an annual report on the results, status, and priorities of research activities related to the health consequences of military service in the GW to the Senate and House Committees on Veterans' Affairs. The Research Subcommittee of the interagency DHWG prepared this 2013 annual report to Congress, which is the 20th report on research and research activities (DHWG, 2004; DHWG, 2005; DHWG, 2006a; DHWG, 2006b; DHWG, 2007; DHWG, 2008; DHWG, 2009; DHWG, 2010; DHWG, 2011; DHWG, 2012; DHWG, 2013; DHWG, 2014; MVHCB, 2001; MVHCB, 2002; PGVCB, 1995; PGVCB, 1996b; PGVCB, 1997; PGVCB, 1998; PGVCB, 1999; PGVCB, 2001). The DHWG tracks all federally-funded research projects related to GWVI.

As in previous annual reports to Congress, the material presented is divided into six sections and three appendices. Section I is an introduction. Section II summarizes the research priorities and organization of the Federal GW research portfolio. Section III highlights and summarizes published research progress since the last report. Section IV summarizes Federal funding trends for GW research during the 10-year period from FY 2005 through FY 2014. Section V highlights new research projects and initiatives since the last annual report to Congress. Section VI contains literature references, and the Appendices contain listings of federally-funded research projects.

## II. RESEARCH PRIORITIES

### A. Nineteen Research Topics

The Persian Gulf Veterans Coordinating Board (PGVCB) was created in 1994 to coordinate research from VA, DoD, and HHS on GWVI. In 1995, the PGVCB devised a contextual framework for the results of completed and ongoing studies and also to develop an approach for the interpretation of research results. To that end, the PGVCB identified 19 major research questions and subsequently added two additional questions in 1996 (PGVCB, 1996a), to bring the total to 21. The comprehensive GW research portfolio has addressed each of these 21 questions, and relevant results have been published on each one. The Military and Veterans Health Coordinating Board (MVHCB), the successor organization to the PGVCB, conducted a comprehensive assessment of the progress made on each of these 21 questions in the 2000 annual report to Congress. The Research Subcommittee of the DHWG, which was established to address a broader range of deployment health issues, reviewed the 21 questions and replaced them with a corresponding list of 21 Research Topics for the 2004 annual report to Congress (DHWG, 2006a).

The original list of 21 questions has been reduced to 19. Based on the Institute of Medicine (IOM) of the National Academies review of the scientific literature on infectious diseases (Institute of Medicine, 2006b) and the state of our current scientific knowledge, the conclusion was reached in the 2006 annual report to Congress (DHWG, 2007) that there is no rationale to continue inclusion of infectious diseases as an area of research that

will provide answers to the causes or cure for these symptoms. Questions 2 and 19 have, therefore, been removed from the original list of 21 Questions and the third Research Focus Area has been refocused from Immune Function and Infectious Diseases to just Immune Function. Projects originally identified as "GW research" under these two questions will continue to be listed in Appendices A and B, but no funding amounts will be shown for FY 2007 or beyond.

Similarly, projects related to Posttraumatic Stress Disorder (PTSD) that were originally included in the Federal GW research portfolio were closed as of FY 2007 (i.e., no funds listed in Appendix C) if they did not directly study a population of ill GW Veterans or were not investigating treatments that may prove beneficial for ill GW Veterans.

The IOM report reviewing the available literature on amyotrophic lateral sclerosis (ALS) in Veterans (Institute of Medicine, 2006a) concluded there is limited and suggestive evidence of an association between military service and later development of ALS. This strengthens the decision to include ALS as a relevant topic in the Federal portfolio of GW research (DHWG, 2006b). ALS projects included in the GW portfolio are primarily focused on epidemiologic studies in GW Veterans and the development of new methodologies to identify and treat ALS.

## B. Research Portfolio Descriptors

VA maintains a research database of federally sponsored research on GWVI. This includes research conducted by Federal scientists, as well as that by non-Federal scientists supported by Federal research funds through grants, contracts, and cooperative agreements. It is not possible to accurately track research efforts that fall within the private sector or otherwise outside of the purview of the Federal government.

Nonetheless, the Research Subcommittee of the DHWG attempts to stay abreast of all research relevant to GWVI. This is accomplished by monitoring peer-reviewed published scientific literature, attending scientific meetings, and even using newspaper reports and personal accounts of researchers.

**Appendix A** lists the projects that VA, DoD, and HHS have funded to date. Research projects are grouped according to the department that is responsible for funding. Dual-funded projects are listed under both departments.

**Appendix B** lists all federally-funded GW research projects regardless of the department providing the funding. Three descriptors are used to categorize each funded project.

The first descriptor is the primary **Research Focus Area** of the project. The five Research Focus Areas are also used to organize the 19 Research Topics (see Section A, above).

- Brain and Nervous System Function (e.g., studies on neurological or psychological deficits and/or alterations)
  - Organic neuropsychological and neurological deficits (original Question 16)
  - Psychological symptoms and/or diagnoses (original Question 18)

- Environmental Toxicology (e.g., studies focused on specific environmental exposures such as pesticides, oil well fires, jet fuel, vaccines, medical prophylactic agents, etc.)
  - Petroleum products and combustion products (original Question 3)
  - Occupational/environmental hazards (original Question 4)
  - Organophosphorus nerve agent and/or sulfur mustard from bombing at Muhammadiyat or weapons bunker at Khamisiyah (original Question 5)
  - Chemical agents, other than at Khamisiyah (original Question 6)
  - Pyridostigmine bromide (PB) and other medical prophylaxes (e.g., vaccines and anti-malarials) (original Question 7)
  - Psychophysiological stressors (original Question 8)
  - Short-term, low level exposures to PB, N, N-diethyl-m-toluamide (DEET), or permethrin, alone or in combination as a cause of short-term and/or long-term neurological effects (original Question 17)

- Immune Function (e.g., studies on alterations in immune function or host defenses)
  - Altered immune function or host defense (original Question 10)

- Reproductive Health (e.g., studies on sexual and/or reproductive dysfunction)
  - Birth defects in offspring (original Question 11)
  - Lower reproductive success (original Question 12)
  - Sexual dysfunction (original Question 13)

- Symptoms and General Health (e.g., studies on mortality, pulmonary disease, cancer, chronic multisymptom illnesses, etc.)
  - Increased prevalence or severity of symptoms and/or illnesses (original Question 1)
  - Nonspecific symptoms and symptom complexes (e.g., chronic multisymptom illnesses (CMI)) (original Question 9)
  - Changes in lung function or airway reactivity (original Question 14)
  - Smaller baseline lung function or greater degree of nonspecific airway reactivity (original Question 15)
  - Development of cancers of any type (original Question 20)
  - Mortality rates (original Question 21)

Secondary and/or tertiary Research Focus Areas from the above list may also be assigned. Two additional Research Focus Areas may be used for secondary and tertiary assignments. This permits accounting for projects that cover multiple focus areas.

- Chemical weapons (e.g., sarin, sulfur mustard, etc.)
- PB and other medical prophylaxes (e.g., vaccines, PB, antimalarials, etc.)

The second descriptor is the **Project Focus**, categorized as follows:

- Diagnosis: studies that will improve the ability to diagnose previously unexplained conditions or to better refine diagnoses with new tools

- Exposure: studies that examine individual exposures and/or interactions of exposures (chemical, biological, pharmacological, physiological, etc.)
- Interactions: interactions of combined exposures (chemical, biological, pharmacological, physiological, etc.)
- Prevention: studies that will produce knowledge that could lead to disease prevention strategies
- Symptoms: prevalence and risk factors for symptoms and alterations in general health status
- Treatment: development or testing of new therapies

Each project is assigned up to three Project Focus areas as categorical descriptors. This allows accounting for projects that cover multiple focus areas. For example, a project on the neurophysiological effects of exposure to sarin in animals would have a focus on the brain and nervous system and a focus on chemical weapons. The number of focus areas (between one and three) assigned to a project depends on the project itself.

The third descriptor for each project is **Research Type**. Each research project on GWVI uses a method of approach to test a specific research hypothesis. Although precise categorization of research types can be difficult because of overlapping methodologies, research projects can be divided into the following general types:
MECHANISTIC: Research into underlying mechanisms of diseases and illnesses using in vitro and in vivo models.

CLINICAL: Application of an intervention, such as in a controlled drug trial, or use of methodologies such as case-control studies to define risk factors for disease.

EPIDEMIOLOGY: Study of the distribution and determinants of disease in human populations. It includes population-based studies focused on outcomes such as mortality, symptoms, hospitalizations, etc., using devices such as postal surveys, telephone interviews, and reviews of medical records.

DEVELOPMENT: In addition to tracking research on GWVI, the DHWG also tracks development activities. In general, development is the systematic use of the knowledge or understanding gained from research directed toward the production of materials; devices; systems; or methods, including design, development, and improvement of prototypes and new processes. Within the context of GWVI, the DHWG categorizes activities as development as an activity that satisfies the general definition of development described above and is directed toward new biologically based prevention, intervention, and treatment measures.

The research database on GWVI catalogs only research and development activities that either directly involve GW Veterans or answer specific questions about risk factors. An example of the latter is a research project using animal models to determine health effects of low-level chemical warfare agents. The database does not account for the vast accumulated knowledge derived from the Nation's investment in more generalized biomedical research over the past 50 years.

## C. Portfolio Criteria

In November 2005, at the request of the Secretary of Veterans Affairs, the VA ORD developed a set of criteria for inclusion of VA-funded projects in the GW research portfolio. The criteria and relevant references from that analysis are presented below. These criteria are now routinely used to identify relevant research projects. New projects selected for funding must meet these criteria and are presented in Section V.

1. Studies of CMI affecting GW Veterans, including case definitions for CMI in GW Veterans and the general population.
   a) Case definitions of multisymptom illnesses affecting GW Veterans
      (Fukuda et al., 1998; Haley et al., 1997a; Haley et al., 1997b; Haley et al., 2002; Wolfe et al., 2002)
   b) Chronic fatigue syndrome
      (Dunphy et al., 2003; Eisen et al., 2005; Gray et al., 2002; The Iowa Persian Gulf Study Group, 1997; Unwin et al., 1999)
   c) Fibromyalgia
      (Eisen et al., 2005; The Iowa Persian Gulf Study Group, 1997)
   d) Irritable bowel syndrome
      (Dunphy et al., 2003; Gray et al., 2002; The Iowa Persian Gulf Study Group, 1997)
   e) Multiple chemical sensitivity (MCS)
      (Fiedler et al., 2004; Gray et al., 2002; The Iowa Persian Gulf Study Group, 1997)

2. Conditions and/or symptoms occurring with higher prevalence in GW Veterans
   a) Fatigue
      (CDC, 1995; Coker et al., 1999; Doebbeling et al., 2000; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997b; The Iowa Persian Gulf Study Group, 1997; Unwin et al., 1999; Wolfe et al., 2002)
   b) Joint and muscle pain
      (CDC, 1995; Coker et al., 1999; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997a; Haley et al., 1997b; Haley, 2003; Kang et al., 2000; Pierce, 1997; Proctor et al., 1998; The Iowa Persian Gulf Study Group, 1997; Wolfe et al., 2002)
   c) Gastrointestinal complaints (dyspepsia, gastritis, diarrhea, etc.)
      (Blanchard et al., 2006; CDC, 1995; Coker et al., 1999; Eisen et al., 2005; Fukuda et al., 1998; Gray et al., 2002; Haley et al., 1997b; Kang et al., 2000; Proctor et al., 1998)
   d) Cognitive dysfunction (memory, attention, etc.)
      (CDC, 1995; Coker et al., 1999; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997b; Kang et al., 2000; Knoke et al., 2000; Proctor et al., 1998; The Iowa Persian Gulf Study Group, 1997; Wolfe et al., 2002)
   e) Sleep disturbances
      (CDC, 1995; Coker et al., 1999; Gray et al., 1999; Haley et al., 1997b; Kang et al., 2000; Knoke et al., 2000; Pierce, 1997; Proctor et al., 1998; Unwin et al., 1999; Wolfe et al., 2002)

f) Central Nervous System disorders (ALS, glioblastoma, imaging studies, etc.)
(Bullman et al., 2005; Haley, 2003; Horner et al., 2003; Weisskopf et al., 2005)
g) Headaches
(CDC, 1995; Coker et al., 1999; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997b; Kang et al., 2000; Knoke et al., 2000; Proctor et al., 1998; Unwin et al., 1999; Wolfe et al., 2002)
h) Dermatologic conditions
(CDC, 1995; Coker et al., 1999; Eisen et al., 2005; Fukuda et al., 1998; Gray et al., 1999; Kang et al., 2000; Knoke et al., 2000; Pierce, 1997; Proctor et al., 1998; Wolfe et al., 2002)

3. Long-term health effects of potentially hazardous substances, alone and in combination, to which GW Veterans may have been exposed to during deployment
   a) PB
   (Abou-Donia et al., 1996; Haley et al., 1997c; Wolfe et al., 2002; Abdel-Rahman et al., 2004)
   b) DEET
   (Abou-Donia et al., 1996; Haley et al., 1997c; Wolfe et al., 2002; Abdel-Rahman et al., 2004)
   c) Permethrin
   (Abou-Donia et al., 1996; Haley et al., 1997c; Wolfe et al., 2002; Abdel-Rahman et al., 2004)
   d) Oil well fire smoke
   (Poirier et al., 1998; Lange et al., 2002)
   e) Petroleum products (e.g., jet fuels) and combustion products
   (Peden-Adam et al., 2001; Bell et al., 2005)
   f) Multiple vaccinations and other medical prophylaxes
   (Rook et al., 1997; Hotopf et al., 2000; Kang et al., 2000)

4. Other topics from the 19 Topics forming the framework for the *Annual Report to Congress on Federally Sponsored Research on GW Veterans' Illnesses:*
   a) Altered immune function and/or host defense
   (Zhang et al., 1999; Peden-Adam et al., 2001)
   b) Physiological responses to biological stress
   (Abdel-Rahman et al., 2004; Fiedler et al., 2004)
   c) Sexual and/or reproductive dysfunction
   (Cowan et al., 1997; Doyle et al., 1997; The Iowa Persian Gulf Study Group, 1997)

## III. PUBLISHED RESULTS AND STATUS OF THE FIELD IN 2013

Since the last *Annual Report to Congress,* numerous research studies have provided new and detailed information on the health problems of GW Veterans. A PubMed search retrieved 35 relevant articles published in English in calendar year 2014 or in 2013 after the last report was submitted. These articles include federally and non-federally funded research, as well as international research. This section provides brief highlights of the

published research divided into the five Research Focus Areas described in Section II. B., above, followed by the PubMed abstracts.

## A. Brain and Nervous System Function

Studies relevant to Veterans of the 1990-1991 GW are presented in this section if they are related to brain and nervous system function. In 2014, most of these studies focused on psychological health and the effects of altered brain structure.

### General Brain Function and Exposure Research

Megahed et al. extended their studies of changes to the hippocampus to determine which changes are associated with cognitive impairments. They monitored gamma-amino butyric acid (GABA)-ergic interneurons after exposing rats to pyridostigmine bromide, pesticides, and restraint stress for four weeks. The rats had lower numbers of parvalbumin-expressing interneurons in the dentate gyrus and neuropeptide Y-expressing interneurons in the CA1 and CA3 hippocampal subfields; however, there were no changes in the somatostatin interneuron population. The authors suggested that these effects could be targets for improving cognitive problems (Megahed et al., 2015). In a study of mild to moderate traumatic brain injury (TBI) in Veterans of OEF, OIF, and the Gulf War (Operations Desert Shield/Desert Storm), Schiehser et al. concluded that these TBIs result in a worsened quality of life than in a comparison group and that they are associated with specifically with symptoms such as fatigue, depression,a nd sleep difficulties (Schiehser et al., 2014).

### Neuropsychological Functioning and Stress Response

Total cortical, lobar gray matter, and hippocampal volumes were measured in Gulf War Veterans and compared to their sleep quality. Poor sleep quality was correlated with PTSD and depression, but poor sleep was also correlated with reduced brain volumes independent of these comorbid psychological conditions (Chao et al., 2014b). In a pilot study of 20 GWVs, Bierer et al. found differences in the MRI diffusion tensor images (DTI) of those with and without PTSD. Lower mean diffusivity was found in the right cingulum bundle in patients with PTSD, but the effect was smaller in those who also met criteria for chronic multisymptom illness. The authors suggest that DTI results can be an indicator of current PTSD expression (Bierer et al., 2015). Inflammatory markers interleukin-6 (IL-6) and soluble receptor II for tumor necrosis factor (sTNF-RII) were compared with hippocampal volumes determined from MRI in 246 GWVs with and without PTSD. Increased levels of sTNF-RII, but not IL-6, were associated with reduced hippocampal volume, and the volume was not correlated with PTSD status. These authors suggest that inflammatory proteins can be used as markers of brain structure and function (O'Donovan et al., 2015). Shell et al. used two special amino acid-based nutrients to target specific neurotransmitter deficiencies associated with PTSD. They found reductions in PTSD symptoms and improved overall mental health (Shell et al., 2014).

The incidence of sexual assault during the Gulf War (1990-1991) was determined to be between 18% and 21% according to a survey of 1,700 Veterans, which is higher than the incidence in the civilian population. Deployment to the Gulf War was not associated with higher risk, but exposure to combat or being in a unit where sexual harassment was tolerated was correlated with higher risk (Murdoch et al., 2014).

Lai et al. investigated the effects of the Gulf War (1990-1991) on PTSD, anxiety, and depression in children and their parents. They found that parental distress was a risk factor for depression in children but not PTSD or anxiety (Lai et al., 2014). In a related study, PTSD and anxiety predicted poorer educational and occupational outcomes for these children, but the findings were not significant if a child's intelligence was considered. Depression was not predictive of either of these outcomes (Hadi et al., 2014).

## B. Environmental Toxicology

Environmental agents potentially toxic to GW Veterans in theater were the topics of numerous scientific reports in 2011. These agents can be grouped into three areas: (1) depleted uranium (DU), which is used in armor-piercing munitions; (2) chemical and anti-nerve agents (e.g., sarin, mustard gas, and PB); and (3) insecticides (e.g., permethrin, chlorpyrifos).

### DU

Kalinich and Kasper have reported that uranium from pellets implanted in rat leg muscle can migrate to the brain whereas other metals do not. They hypothesize that body burdens of metals can affect blood-brain barrier permeability and result in the release of inflammatory mediators (Kalinich and Kasper, 2014). In a study involving male rats, olfactory uptake of uranium was monitored after intranasal exposure to uranium containing solutions. After the exposure, uranium was located in the olfactory neuroepithelium and around olfactory nerve bundles. The authors suggest that uranium can migrate to the brain along the olfactory nerve and need not cross the blood-brain barrier (Ibanez et al., 2014). Zhivin et al. examined long-term effects of DU exposure in uranium-processing workers and in Veterans of the Gulf War and the Balkans War. They reviewed 27 articles and found limited evidence for increases in lung cancer in uranium-processing workers, but they were not able to find any evidence for uranium-related diseases in the Veterans (Zhivin et al., 2014).

### Nerve and Chemical Agents

Chao et al. conducted a study of apparent structural alterations in the hippocampal subfields of 56 Gulf War Veterans with suspected sarin/cyclosarin exposure to 56 "matched" unexposed Gulf War Veterans utilizing a 4T high-resolution magnetic resonance scanner by measuring the volumes of the CA1, CA2, CA3 and dentate gyrus (DG), and subiculum subfields. They found that exposed Veterans had smaller CA2 and CA3/DG subfield volumes. The findings suggest that low-level exposure to sarin and cyclosarin can have long-term deleterious effects on brain structure and brain function (Chao et al.,

2014a). Ferchmin et al. have suggested that the use of a cyclic diterpenoid compound, (1S,2E,4R,7E,11E)-cembra-2,7,11-triene-4,6-diol after exposure to diisopropylfluorophosphate (DFP) can reduce neurodegeneration in the hippocampus (Ferchmin et al., 2014). In another study, Rojas et al. developed an agonist for a prostaglandin receptor, known as TG6-10-1, which reduces the damage to the brain after seizures caused by DFP (Rojas et al., 2015).

### Insecticides and Pesticides

Pyridostigmine bromide (PB), pesticides like permethrin (PER) and chlorpyrifos (CPF), and insect repellents like DEET have been suggested as causative agents for the symptoms experienced by GW Veterans. Studies of mood and cognitive function following four weeks of exposure to Gulf War illness-related chemicals (including pyridostigmine bromide, permethrin, and DEET) with and without mild stress application have found reduced hippocampal volume and associated deficits in hippocampus-dependent spatial and object memory. Exposure to Gulf War illness-related chemicals and stress causes both hippocampus dependent and hippocampus independent memory impairments, and is also associated with decreased neurogenesis, partial loss of principal neurons, and mild inflammation. These studies suggest that treatment strategies that enhance neurogenesis and suppress inflammation may help alleviate mood and cognitive dysfunction (Hattiangady et al., 2014). In another study of rats exposed to PB/chlorpyrifos/permethrin, pain indicators were linked to changes in Na+ and K+ channels. The authors suggested that increases in the amplitudes of these channels could produce chronic deep tissue pain (Nutter and Cooper, 2014). When mice were exposed to CPF or CPF/PB/PER, there were changes in the hippocampus and other regions of the brain, and there were changes in immunoreactivity and and increase in brain acetylcholine levels. CPF/PB/PER exposure also showed microvascular changes (Ojo et al., 2014). Hernandez et al. investigated the effect of chlorpyrifos on axonal transport in rats using manganese-enhanced magnetic resonance imaging (MEMRI) of the optic nerve. The chlorpyrifos was shown to alter axonal transport to the brain, and this might be the reason for long-term neurological problems in exposed populations (Hernandez et al., 2015).

## C. Immune Dysfunction and Infectious Diseases

Khaiboullina et al. compared immune parameters in patients with either chronic fatigue syndrome or GWI. They measured 77 serum cytokines and determined that the two conditions have different immune profiles even though there are many symptoms in common.

## D. Reproductive Health

No pertinent articles dealing with reproductive health were published in 2014.

## E. Symptoms and General Health

### General Health

Murdoch et al. used three different surveys with increasing privacy levels in a randomized controlled trial (RCT) involving 324 Gulf War Veterans (1990-1991) to determine if there would be an impact on response rates. Greater privacy (and larger incentives) did not necessarily result in higher response (56.0% to 63.3%), but the use of "pre-merged" questionnaires helped to resolve some of the reluctance of Veterans to participate. (Murdoch et al., 2014). Kelsall et al. studied pain-related musculoskeletal disorders (MSDs) and psychological disorders in 1381 Australian Gulf War Veterans and a military comparison group of 1377. Similar numbers of GWVs (24.5%) and comparison group (22.4%) reported MSDs which were associated with depression and PTSD but not with alcohol abuse (Kelsall et al., 2014). In a follow-up article, they analyzed 18 studies that dealt with alcohol or substance use disorders in Veterans of the Gulf War (1990-1991), Afghanistan, (OEF), and Iraq (OIF) Wars. There is a slightly higher risk of alcohol use in these Veterans, but there have not been enough studies of substance abuse to draw conclusions as yet (Kelsall et al., 2015).

Beard and Kamel reviewed thirty publications through 2013 that dealt with the connection between amyotrophic lateral sclerosis (ALS) and military deployment. Some evidence suggests that ALS incidence is associated with service in the Gulf War; other evidence suggests any military service. The authors suggest that additional studies which include survival analyses, detailed clinical data, and sufficient statistical power are required (Beard and Kamel, 2015). Wallin et al. determined an overall relative risk of 0.69 (0.72 in men; 0.96 in women) of developing multiple sclerosis (MS) and other demyelinating diseases in Veterans of the Gulf War (1990-1991). There were 387 cases among 696,118 deployed and 1,454 cases among 1,786,215 non-deployed Veterans. There was not an increased risk across racial groups, age groups, or branch of military service.

### GWVI, Chronic Fatigue Syndrome, and Fibromyalgia

The relationship between GW Veterans' illnesses and autonomic dysfunction has been investigated. Ill GW Veterans reported post-exertional fatigue that had persisted for many years, so a group of 16 was compared to a control group of 12 patients. Conditions like orthostatic hypotension, postural orthostatic tachycardia syndrome (POTS), and various distal neuropathies were diagnosed in the study group but not in the controls. The authors point out that GW Veterans had objective autonomic test results that were significantly different from controls, and that this testing is necessary for evaluating GW Veterans (Li et al., 2014). Hayer et al. have begun a clinical trial using nasal irrigation with saline or nasal irrigation with xylitol to improve sinus symptoms and fatigue in GW Veterans. In addition to self-reported fatigue and overall quality of life, there will be laboratory analysis of pro-

inflammatory cytokines. In its early stages, the project has had very high rates of participant compliance (Hayer et al., 2015). In a study of complementary and alternative medicine (CAM) utilizing acupuncture and iRest yoga nidra, 42 of the 226 Veterans who participated were GW Veterans. While GW Veterans who enrolled in the program had more severe symptoms, those who actually participated had symptom severities similar to the other Veterans. More research is needed to elucidate the reasons for these observations (Holliday et al., 2014).

To assess mitochondrial dysfunction in a case-control study of seven deployed GW Veterans and seven non-deployed healthy controls, calf muscle phosphocreatine was evaluated by using P-31 magnetic resonance spectroscopy at rest, during a five-minute foot pedal depression exercise, and in recovery after exercise. Phosphocreatine recovery time was significantly longer in Gulf War illness cases, and this study suggests that mitochondrial dysfunction exists in these individuals (Koslik et al., 2014). In a randomized controlled trial, 46 GW Veterans with GWI received either 100mg per day of CoQ10, 300mg per day of CoQ10, or a placebo. The 100mg dose showed more improvement than the 300mg dose or the placebo in general self-reported health and in all symptoms except sleep problems (Golomb et al., 2014).

Chronic multisymptom illness (CMI) in GW Veterans was compared with similar symptoms reported by service members returning from Iraq and Afghanistan in between 2001 and 2008 (OIF and OEF). The overall reporting of symptoms was much less in the latter group than in GW Veterans, but there was a higher prevalence of CMI symptoms in the deployed than in the non-deployed groups from the more recent timeframe (Smith et al., 2014).

In a case-control study, Steele et al. assessed butyrylcholinesterase (BChE) activity and genotype in 304 GW Veterans (144 with GWI and 160 controls). Overall, BChE activity did not differ between the two groups, but when Veterans with the less common, less active BChE genotypes were compared with the control group, the odds ratio for developing GWI was 40.0. For the more common genotypes the odds ratio was 2.68. The authors concluded that the use of PB increased the risk for all Veterans but especially those with the less common genotypes (Steele et al., 2015). Using a systems biology approach and a discrete logic representation of endocrine and immune system function, Craddock et al. have predicted homeostatic states that are consistent with immune markers in male GW Veterans. Additional refinement is still necessary, but these kinds of calculations/predictions should be useful in designing clinical treatment trials to test the predictions (Craddock et al., 2014). The Institute of Medicine of the National Academy of Science reviewed the literature and held open discussions concerning case definitions for chronic multisymptom illness in GW Veterans (IOM, 2014a) and concerning long-term effects of blast injuries during the 1990-1991 Gulf War (IOM, 2014b). Each report included a number of recommendations for VA.

## F. Abstracts from Published Research

**Beard JD, Kamel F (2015) Military service, deployments, and exposures in relation to amyotrophic lateral sclerosis etiology and survival. Epidemiol Rev 37(1):55-70. doi: 10.1093/epirev/mxu001. (Epub 2014 Oct 31.)**

Rates of amyotrophic lateral sclerosis (ALS) have been reported to be higher among US military veterans, who currently number more than 21 million, but the causal factor(s) has not been identified. We conducted a review to examine the weight of evidence for associations between military service, deployments, and exposures and ALS etiology and survival. Thirty articles or abstracts published through 2013 were reviewed. Although the current evidence suggests a positive association with ALS etiology, it is too limited to draw firm conclusions regarding associations between military service and ALS etiology or survival. Some evidence suggests that deployment to the 1990-1991 Persian Gulf War may be associated with ALS etiology, but there is currently no strong evidence that any particular military exposure is associated with ALS etiology. Future studies should address the limitations of previous ones, such as reliance on mortality as a surrogate for incidence, a dearth of survival analyses, lack of clinical data, low statistical power, and limited exposure assessment. The Genes and Environmental Exposures in Veterans with Amyotrophic Lateral Sclerosis (GENEVA) Study is one such study, but additional research is needed to determine whether military-related factors are associated with ALS and to assess potential prevention strategies.

**Bierer LM, Ivanov I, Carpenter DM, Wong EW, Golier JA, Tang CY, Yehuda R (2015 Jan) White matter abnormalities in Gulf War veterans with posttraumatic stress disorder: A pilot study. Psychoneuroendocrinology 51:567-76. doi: 10.1016/j.psyneuen.2014.11.007. (Epub 2014 Nov 15.)**

BACKGROUND: Gulf War veterans were exposed to environmental toxins not present in other combat theaters resulting in a unique biological signature that only partially resembles that seen in other combat veterans with PTSD. Thus it is important to determine if brain abnormalities seen in non-Gulf War veterans with PTSD are also present in Gulf War veterans. In this pilot study, diffusion tensor imaging (DTI) tractography was used to assess the ultra-structural integrity of fronto-limbic white matter connections in Gulf War veterans with and without PTSD. The effects of chronic multisymptom illness on DTI measures was also evaluated. METHODS: Subjects were 20 previously studied Gulf War veterans on whom MRIs had been obtained. Mean diffusivity (MD) and fractional anisotropy (FA) were determined for left and right cingulum bundle by DTI tractography and compared in separate analyses for 12 veterans with, and 8 without PTSD. The effect of chronic multisymptom illness and it's interaction with PTSD, were similarly investigated using multivariate ACOVA. Partial correlations were used to test the associations of both DTI indices with PTSD severity and plasma cortisol, controlling for whole brain volume. RESULTS: Significantly lower MD was demonstrated in the right cingulum bundle among Gulf War veterans with PTSD. There were no significant differences in MD or FA in the left cingulum bundle. The presence of chronic multisymptom illness significantly attenuated the PTSD associated decrement in right cingulum MD. Clinician and self-rated PTSD symptom

severity scores were significantly associated with reduced MD and increased FA in the right cingulum. Similar associations were observed for 8am plasma cortisol in a subset of participants. CONCLUSIONS: The preliminary findings indicate increased structural integrity - supporting enhanced connectivity - between right amygdala and anterior cingulate cortex in PTSD. This effect was strongest among Gulf War veterans without chronic multisymptom illness. The association of both MD and FA in the right cingulum with PTSD severity, and with heightened glucocorticoid responsivity, suggests that these DTI findings are a reflection of current PTSD illness expression. Although based on a small sample, these microstructural observations are consistent with a functional model suggesting increased amygdala responsivity in association with anterior cingulate modulation in PTSD.

**Chao LL, Kriger S, Buckley S, Ng P, Mueller SG (2014a) Effects of low-level sarin and cyclosarin exposure on hippocampal subfields in Gulf War Veterans. Neurotoxicol 44:263-269. doi: 10.1016/j.neuro.2014.07.003. (Epub 2014 Jul 21.)**

BACKGROUND: More than 100,000 US troops were potentially exposed to chemical warfare agents sarin (GB) and cyclosarin (GF) when an ammunition dump at Khamisiyah, Iraq was destroyed during the 1991 Gulf War (GW). We previously reported reduced hippocampal volume in GW veterans with suspected GB/GF exposure relative to matched, unexposed GW veterans estimated from 1.5T magnetic resonance images (MRI). Here we investigate, in a different cohort of GW veterans, whether low-level GB/GF exposure is associated with structural alterations in specific hippocampal subfields, estimated from 4T MRI. METHODS: The Automatic Segmentation of Hippocampal Subfields (ASHS) technique was used to quantify CA1, CA2, CA3 and dentate gyrus (DG), and subiculum (SUB) subfields volumes from high-resolution T2-weighted images acquired on a 4T MR scanner in 56 GW veterans with suspected GB/GF exposure and 56 "matched" unexposed GW veterans (mean age 49±7 years). RESULTS: GB/GF exposed veterans had smaller CA2 ($p=0.003$) and CA3/DG ($p=0.01$) subfield volumes compared to matched, unexposed GW veterans. There were no group difference in total hippocampal volume, quantified with FreeSurfer, and no dose-response relationship between estimated levels of GB/GF exposure and total hippocampal or subfield volume. CONCLUSIONS: These findings extend our previous report of structural alterations in the hippocampi of GW veterans with suspected GB/GF exposure to volume changes in the CA2, CA3, and DG hippocampal subfields in a different cohort of GW veterans with suspected GB/GF exposure.

**Chao LL, Mohlenhoff BS, Weiner MW, Neylan TC (2014b) Associations between subjective sleep quality and brain volume in Gulf War Veterans. Sleep 37(3):445-452. doi: 10.5665/sleep.3472.**

STUDY OBJECTIVES: To investigate whether subjective sleep quality is associated with brain volume independent of comorbid psychiatric conditions. DESIGN: Cross-sectional. SETTING: Department of Veterans Affairs (VA) Medical Center. PARTICIPANTS: One hundred forty-four Gulf War Veterans (mean age 45 years; range: 31-70 years; 14% female). INTERVENTIONS: None. MEASUREMENTS AND RESULTS: Total cortical, lobar gray matter, and hippocampal volumes were quantified from 1.5 Tesla magnetic

resonance images using Freesurfer version 4.5. Subjective sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI). Multiple linear regressions were used to determine the association of sleep quality with total and regional brain volumes. The global PSQI score was positively correlated with lifetime and current posttraumatic stress disorder (PTSD) and current depressive symptoms ($P < 0.001$) and was higher in veterans with Gulf War Illness, trauma exposure, and those using psychotropic medication ($P \leq 0.03$). After adjusting for these comorbid variables, age, intracranial volume, and multiple comparisons, global PSQI was inversely associated with total cortical and frontal gray matter volume (adjusted $P \leq 0.03$). Within the frontal lobe, total PSQI was inversely associated with the superior and middle frontal, orbitofrontal, anterior cingulate, and frontal pole volumes (adjusted $P \leq 0.02$). Examination of the 3-factor structure of the PSQI revealed that the associations were driven by perceived sleep quality. CONCLUSIONS: Poorer subjective sleep quality was associated with reduced total cortical and regional frontal lobe volumes independent of comorbid psychiatric conditions. Future work will be needed to examine if effective treatment of disturbed sleep leads to improved structural and functional integrity of the frontal lobes.

**Craddock TJ, Fritsch P, Rice MA Jr, del Rosario RM, Miller DB, Fletcher MA, Klimas NG, Broderick G (2014) A role for homeostatic drive in the perpetuation of complex chronic illness: Gulf War Illness and chronic fatigue syndrome. PLoS One 9(1):e84839. doi: 10.1371/journal.pone.0084839.**

A key component in the body's stress response, the hypothalamic-pituitary-adrenal (HPA) axis orchestrates changes across a broad range of major biological systems. Its dysfunction has been associated with numerous chronic diseases including Gulf War Illness (GWI) and chronic fatigue syndrome (CFS). Though tightly coupled with other components of endocrine and immune function, few models of HPA function account for these interactions. Here we extend conventional models of HPA function by including feed-forward and feedback interaction with sex hormone regulation and immune response. We use this multi-axis model to explore the role of homeostatic regulation in perpetuating chronic conditions, specifically GWI and CFS. An important obstacle in building these models across regulatory systems remains the scarcity of detailed human in vivo kinetic data as its collection can present significant health risks to subjects. We circumvented this using a discrete logic representation based solely on literature of physiological and biochemical connectivity to provide a qualitative description of system behavior. This connectivity model linked molecular variables across the HPA axis, hypothalamic-pituitary-gonadal (HPG) axis in men and women, as well as a simple immune network. Inclusion of these interactions produced multiple alternate homeostatic states and sexually dimorphic responses. Experimental data for endocrine-immune markers measured in male GWI subjects showed the greatest alignment with predictions of a naturally occurring alternate steady state presenting with hypercortisolism, low testosterone and a shift towards a Th1 immune response. In female CFS subjects, expression of these markers aligned with an alternate homeostatic state displaying hypocortisolism, high estradiol, and a shift towards an anti-inflammatory Th2 activation. These results support a role for homeostatic drive in perpetuating dysfunctional cortisol levels through persistent interaction with the immune

system and HPG axis. Though coarse, these models may nonetheless support the design of robust treatments that might exploit these regulatory regimes.

**Ferchmin PA, Andino M, Reyes Salaman R, Alves J, Velez-Roman J, Cuadrado B, Carrasco M, Torres-Rivera W, Segarra A, Martins AH, Lee JE, Eterovic VA (2014) 4R-cembranoid protects against diisopropylfluorophosphate-mediated neurodegeneration. Neurotoxicology 44:80-90. doi: 10.1016/j.neuro.2014.06.001. (Epub 2014 Jun 10.)**

Many organophosphorous esters synthesized for applications in industry, agriculture, or warfare irreversibly inhibit acetylcholinesterase, and acute poisoning with these compounds causes life-threatening cholinergic overstimulation. Following classical emergency treatment with atropine, an oxime, and a benzodiazepine, surviving victims often suffer brain neurodegeneration. Currently, there is no pharmacological treatment to prevent this brain injury. Here we show that a cyclic diterpenoid, (1S,2E,4R,6R,7E,11E)-cembra-2,7,11-triene-4,6-diol (4R) ameliorates the damage caused by diisopropylfluorophosphate (DFP) in the hippocampal area CA1. DFP has been frequently used as a surrogate for the warfare nerve agent sarin. In rats, DFP is lethal at the dose used to cause brain damage. Therefore, to observe brain damage in survivors, the death rate was reduced by pre-administration of the peripherally acting antidotes pyridostigmine and methyl atropine or its analog ipratropium. Pyridostigmine bromide, methyl atropine nitrate, and ipratropium bromide were dissolved in saline and injected intramuscularly at 0.1mg/kg, 20mg/kg, and 23mg/kg, respectively. DFP (9mg/kg) dissolved in cold water was injected intraperitoneally. 4R (6mg/kg) dissolved in DMSO was injected subcutaneously, either 1h before or 5 or 24h after DFP. Neurodegeneration was assessed with Fluoro-Jade B and amino cupric silver staining; neuroinflammation was measured by the expression of nestin, a marker of activated astrocytes. Forty-eight hours after DFP administration, 4R decreased the number of dead neurons by half when injected before or after DFP. 4R also significantly decreased the number of activated astrocytes. These data suggest that 4R is a promising new drug that could change the therapeutic paradigm for acute poisoning with organophosphorous compounds by the implementation of a second-stage intervention after the classical countermeasure treatment.

**Golomb BA, Allison M, Koperski S, Koslik HJ, Devaraj S, Ritchie JB (2014) Coenzyme Q10 benefits symptoms in Gulf War veterans: results of a randomized double-blind study. Neural Comput 26(11):2594-651. doi: 10.1162/NECO_a_00659. (Epub 2014 Aug 22.)**

We sought to assess whether coenzyme Q10 (CoQ10) benefits the chronic multisymptom problems that affect one-quarter to one-third of 1990-1 Gulf War veterans, using a randomized, double-blind, placebo-controlled study. Participants were 46 veterans meeting Kansas and Centers for Disease Control criteria for Gulf War illness. Intervention was PharmaNord (Denmark) CoQ10 100 mg per day (Q100), 300 mg per day (Q300), or an identical-appearing placebo for 3.5 ± 0.5 months. General self-rated health (GSRH), the primary outcome, differed across randomization arms at baseline, and sex significantly predicted GSRH change, compelling adjustment for baseline GSRH and prompting sex-

stratified analysis. GSRH showed no significant benefit in the combined-sex sample. Among males (85% of participants), Q100 significantly benefited GSRH versus placebo and versus Q300, providing emphasis on Q100. Physical function (summary performance score, SPS) improved on Q100 versus placebo. A rise in CoQ10 approached significance as a predictor of improvement in GSRH and significantly predicted SPS improvement. Among 20 symptoms each present in half or more of the enrolled veterans, direction-of-difference on Q100 versus placebo was favorable for all except sleep problems; sign test 19:1, p=0.00004) with several symptoms individually significant. Significance for these symptoms despite the small sample underscores large effect sizes, and an apparent relation of key outcomes to CoQ10 change increases prospects for causality. In conclusion, Q100 conferred benefit to physical function and symptoms in veterans with Gulf War illness. Examination in a larger sample is warranted, and findings from this study can inform the conduct of a larger trial.

**Hadi F, Lai BS, Llabre MM (2014) Life outcomes influenced by war-related experiences during the Gulf crisis. Anxiety Stress Coping 27(2):156-75. doi: 10.1080/10615806.2013.832219. (Epub 2013 Sep 5.)**

This study examined the life outcomes of children exposed to the Gulf crisis in 1990-1991. We expected war-trauma exposure and psychological distress symptoms to predict poorer educational and occupational outcomes. Participants were 151 Kuwaiti citizens who were assessed during childhood (in 1993; M age = 10.6 years), and who were reassessed 10 years later in young adulthood (in 2003; M age = 21.2 years). Participants completed measures of intelligence, war-trauma exposure, posttraumatic stress symptoms, anxiety symptoms, depressive symptoms, intervening life events, and life outcomes. Results indicated that war-trauma exposure negatively impacted children's educational and occupational outcomes as young adults. Boys with higher levels of war-trauma exposure were less likely to attend University. Posttraumatic stress and anxiety symptoms also predicted poorer educational and occupational outcomes. However, this relationship was not significant when we accounted for children's intelligence. Depressive symptoms were not predictive of children's educational or occupational outcomes. Results suggest that war-trauma exposure may have life-altering effects on children. Tailored, early interventions are needed for children exposed to war traumas.

**Hattiangady B, Mishra V, Kodali M, Shuai B, Rao X, Shetty AK (2014) Object location and object recognition memory impairments, motivation deficits and depression in a model of Gulf War illness. Front Behav Neurosci 8:78. doi: 10.3389/fnbeh.2014.00078.**

Memory and mood deficits are the enduring brain-related symptoms in Gulf War illness (GWI). Both animal model and epidemiological investigations have indicated that these impairments in a majority of GW veterans are linked to exposures to chemicals such as pyridostigmine bromide (PB, an antinerve gas drug), permethrin (PM, an insecticide) and DEET (a mosquito repellant) encountered during the Persian Gulf War-1. Our previous study in a rat model has shown that combined exposures to low doses of GWI-related (GWIR) chemicals PB, PM, and DEET with or without 5-min of restraint stress (a mild

stress paradigm) causes hippocampus-dependent spatial memory dysfunction in a water maze test (WMT) and increased depressive-like behavior in a forced swim test (FST). In this study, using a larger cohort of rats exposed to GWIR-chemicals and stress, we investigated whether the memory deficiency identified earlier in a WMT is reproducible with an alternative and stress free hippocampus-dependent memory test such as the object location test (OLT). We also ascertained the possible co-existence of hippocampus-independent memory dysfunction using a novel object recognition test (NORT), and alterations in mood function with additional tests for motivation and depression. Our results provide new evidence that exposure to low doses of GWIR-chemicals and mild stress for 4 weeks causes deficits in hippocampus-dependent object location memory and perirhinal cortex-dependent novel object recognition memory. An open field test performed prior to other behavioral analyses revealed that memory impairments were not associated with increased anxiety or deficits in general motor ability. However, behavioral tests for mood function such as a voluntary physical exercise paradigm and a novelty suppressed feeding test (NSFT) demonstrated decreased motivation levels and depression. Thus, exposure to GWIR-chemicals and stress causes both hippocampus-dependent and hippocampus-independent memory impairments as well as mood dysfunction in a rat model.

**Hayer SD, Rabago DP, Amaza IP, Kille T, Zgierska A, Zakletskaia L, Krahn D, Obasi CN, Molander RC (2015 Jan 24) Effectiveness of Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Illness: Protocol for a Randomized Controlled Trial. Contemp Clin Trials. pii: S1551-7144(15)00020-8. doi: 10.1016/j.cct.2015.01.008. (Epub ahead of print.)**

INTRODUCTION: Gulf War Illness (GWI) affects 1 in 7 returned Persian Gulf War veterans. Quality-of-life impact is large; there is no cure. Chronic sinus symptoms and fatigue are common. Nasal irrigation with saline (NI-S) or xylitol (NI-X) improve sinus symptoms and fatigue in the general population. This trial will assess the effect of S-NI and X-NI on sinus and fatigue symptoms, economic outcomes and pro-inflammatory milieu among participants with GWI. METHODS: 75 participants (age 35 to 65years, 25 in each of three arms) with GWI will be recruited from the Veteran's Administration and the community. They will use routine care for sinus symptoms and fatigue and be randomized to continued usual care alone or additional therapy with NI-S or NI-X. Participants will be able to adjust specific elements of the NI procedure. The primary outcome (Sinonasal Outcome Test, SNOT-20) and other self-reported assessments will occur at baseline, 8 and 26weeks; lab assessment of pro-inflammatory cellular and cytokine profiles will occur at baseline and 26weeks. Other outcomes will include fatigue-specific and overall health-related quality of life, pro-inflammatory cellular and cytokine profiles, cost-effectiveness and participant satisfaction. RESULTS: Baseline demographic and clinical data from the first 10 participants show effective participant recruitment, enrollment, randomization, retention and data collection. CONCLUSION: Early study conduct suggests our participant-oriented approach will yield high rates of participant adherence and data capture, facilitating robust analysis. Results of this study will clarify the value of NI for chronic sinus symptoms and fatigue among patients with GWI.

**Hernandez CM, Beck WD, Naughton SX, Poddar I, Adam BL, Yanasak N, Middleton C, Terry AV Jr (2015 Jan 19) Repeated exposure to chlorpyrifos leads to prolonged impairments of axonal transport in the living rodent brain. Neurotoxicology. 47C:17-26. doi: 10.1016/j.neuro.2015.01.002. (Epub ahead of print.)**

The toxicity of the class of chemicals known as the organophosphates (OP) is most commonly attributed to the inhibition of the enzyme acetylcholinesterase. However, there is significant evidence that this mechanism may not account for all of the deleterious neurologic and neurobehavioral symptoms of OP exposure, especially those associated with levels that produce no overt signs of acute toxicity. In the study described here we evaluated the effects of the commonly used OP-pesticide, chlorpyrifos (CPF) on axonal transport in the brains of living rats using manganese (Mn2+)-enhanced magnetic resonance imaging (MEMRI) of the optic nerve (ON) projections from the retina to the superior colliculus (SC). T1-weighted MEMRI scans were evaluated at 6 and 24h after intravitreal injection of Mn2+. As a positive control for axonal transport deficits, initial studies were conducted with the tropolone alkaloid colchicine administered by intravitreal injection. In subsequent studies both single and repeated exposures to CPF were evaluated for effects on axonal transport using MEMRI. As expected, intravitreal injection of colchicine (2.5μg) produced a robust decrease in transport of Mn2+ along the optic nerve (ON) and to the superior colliculus (SC) (as indicated by the reduced MEMRI contrast). A single subcutaneous (s.c.) injection of CPF (18.0mg/kg) was not associated with significant alterations in the transport of Mn2+. Conversely, 14-days of repeated s.c. exposure to CPF (18.0mg/kg/day) was associated with decreased transport of Mn2+ along the ONs and to the SC, an effect that was also present after a 30-day (CPF-free) washout period. These results indicate that repeated exposures to a commonly used pesticide, CPF can result in persistent alterations in axonal transport in the living mammalian brain. Given the fundamental importance of axonal transport to neuronal function, these observations may (at least in part) explain some of the long term neurological deficits that have been observed in humans who have been repeatedly exposed to doses of OPs not associated with acute toxicity.

**Holliday SB, 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. Med Care 52(12 Suppl 5):S39-44. doi: 10.1097/MLR.0000000000000223.**

BACKGROUND: Gulf War veterans represent a unique subset of the veteran population. It has been challenging to identify interventions that result in improvements in physical and mental health for this population. Recently, there has been recognition of a potential role for complementary and alternative medicine (CAM) interventions. OBJECTIVES: This paper examines the characteristics of Gulf War and non-Gulf War veterans referred to a CAM clinic, and explores the utilization of services by this population. METHOD AND SUBJECTS: Participants included 226 veterans enrolled in a CAM clinic at a Veterans Affairs medical center, 42 of whom were Gulf War veterans. Self-report measures of physical/mental health were administered, and service utilization was obtained from participants' medical records for a 6-month period. RESULTS: Gulf War veterans enrolled

in the program reported more severe physical and mental health symptoms than non-Gulf War veterans. However, examining only veterans who participated in services in the 6 months following enrollment, the 2 groups reported similar symptom severity. Both groups were similar in their attendance of individual acupuncture and iRest yoga nidra, although Gulf War veterans attended fewer sessions of group acupuncture. CONCLUSIONS: Although Gulf War veterans who enroll in a CAM program may have more severe symptoms than non-Gulf War veterans, those who actually participate in services are similar to non-Gulf War veterans on these measures. These groups also differ in their pattern of service utilization. Future research should explore the reasons for these differences, and to identify ways to promote treatment engagement with this population.

**Ibanez C, Suhard D, Tessier C, Delissen O, Lestaevel P, Dublineau I, Gourmelon P (2014) Intranasal exposure to uranium results in direct transfer to the brain along olfactory nerve bundles. Neuropathol Appl Neurobiol 40(4):477-88. doi: 10.1111/nan.12061.**

AIMS: Uranium olfactory uptake after intranasal exposure raises some concerns for people potentially exposed to airborne radionuclide contamination as the brain could be a direct target for these contaminants. A model of nasal instillation was used to elucidate the transport mechanisms of uranium to the brain and to map its localization. METHODS: Increasing concentrations of depleted uranium containing solutions were instilled in the nasal cavity of adult male rats. Uranium concentrations were measured using inductively coupled plasma-mass spectrometry (ICP-MS) 4 h after instillation. Olfactory neuroepithelium cytoarchitecture was studied using immunohistochemistry experiments. Secondary ion mass spectrometry (SIMS) microscopy was performed to localize uranium in the olfactory system. RESULTS: ICP-MS analyses showed a frontal accumulation of uranium in the olfactory bulbs associated with a smaller increase in more caudal brain regions (frontal cortex, hippocampus and cerebellum). Uranium concentrations in the olfactory bulbs do not reach a saturation point. Olfactory nerve bundle integrity is not affected by uranium as revealed by immunohistochemistry. SIMS microscopy allowed us to show that uranium localization is mainly restricted to the olfactory neuroepithelium and around olfactory nerve bundles. It is subsequently detected in the olfactory nerve layer of the olfactory bulb. DISCUSSION: These results suggest the existence of a transcellular passage from the mucosa to the perineural space around axon bundles. Uranium bypasses the blood brain barrier and is conveyed to the brain via the cerebrospinal fluid along the olfactory nerve. Future studies might need to integrate this new contamination route to assess uranium neurotoxicity after nasal exposure.

**Institute of Medicine (2014a) Chronic Multisymptom Illness in Gulf War Veterans: Case Definitions Reexamined. Washington, DC: National Academies Press.**

Full text available: http://www.nap.edu/catalog.php?record_id=18623

**Institute of Medicine (2014b) Gulf War and Health, Volume 9: Long-Term Effects of Blast Exposures. Washington, DC: National Academies Press.**

Full text available: http://books.nap.edu/openbook.php?record_id=18253

**Kalinich JF, Kasper CE (2014)Do metals that translocate to the brain exacerbate traumatic brain injury? Med Hypotheses 82(5):558-62. doi: 10.1016/j.mehy.2014.02.011. (Epub 2014 Feb 17.)**

Metal translocation to the brain is strictly controlled and often prevented by the blood-brain barrier. For the most part, only those metals required to maintain normal function are transported into the brain where they are under tight metabolic control. From the literature, there are reports that traumatic brain injury disrupts the blood-brain barrier. This could allow the influx of metals that would normally have been excluded from the brain. We also have preliminary data showing that metal pellets, surgically-implanted into the leg muscle of a rat to simulate a shrapnel wound, solubilize and the metals comprising the pellet can enter the brain. Surprisingly, rats implanted with a military-grade tungsten alloy composed of tungsten, nickel, and cobalt also showed significantly elevated uranium levels in their brains as early as 1 month after pellet implantation. The only source of uranium was low levels that are naturally found in food and water. Conversely, rats implanted with depleted uranium pellets demonstrated elevated uranium levels in brain resulting from degradation of the implanted pellets. However, when cobalt levels were measured, there were no significant increases in the brain until the rats had reached old age. The only source of cobalt for these rats was the low levels found in their food and water. These data suggest that some metals or metal mixtures (i.e., tungsten alloy), when embedded into muscle, can enhance the translocation of other, endogenous metals (e.g., uranium) across the blood-brain barrier. For other embedded metals (i.e., depleted uranium), this effect is not observed until the animal is of advanced age. This raises the possibility that metal body-burdens can affect blood-brain barrier permeability in a metal-specific and age-dependent manner. This possibility is disconcerting when traumatic brain injury is considered. Traumatic brain injury has been called the "signature" wound of the conflicts in Iraq and Afghanistan, often, an embedded metal fragment wound occurs simultaneously. Since the blood-brain barrier can be disrupted by traumatic brain injury, this raises the possibility of free access to the brain for any metals found in the body. Therefore, we hypothesize that this influx of metals overwhelms normal brain homeostasis, depletes the brain's antioxidant defense systems, and activates microglial cells resulting in the release of inflammatory mediators that can potentially exacerbate the adverse effects of traumatic brain injury.

**Kelsall HL, McKenzie DP, Forbes AB, Roberts MH, Urquhart DM, Sim MR (2014) Pain-related musculoskeletal disorders, psychological comorbidity, and the relationship with physical and mental well-being in Gulf War Veterans. Pain 155(4):685-92. doi: 10.1016/j.pain.2013.12.025. (Epub 2013 Dec 19.)**

Occupational activities such as lifting loads, working in constrained spaces, and training increase the risk of pain-related musculoskeletal disorders (MSDs) in military veterans. Few studies have investigated MSD and psychological disorder in veterans, and previous studies had limitations. This cross-sectional study compared pain-related MSD and psychological comorbidity and well-being between 1381 male Australian 1990-1991 Gulf War veterans (veterans) and a military comparison group (n=1377, of whom 39.6% were

serving and 32.7% had previously deployed). At a medical assessment, 2000-2002, reported doctor-diagnosed arthritis or rheumatism, back or neck problems, joint problems, and soft tissue disorders were rated by medical practitioners as nonmedical, unlikely, possible, or probable diagnoses. Only probable MSDs were analysed. Psychological disorders in the past 12 months were measured using the Composite International Diagnostic Interview. The Short-Form Health Survey (SF-12) assessed 4-week physical and mental well-being. Almost one-quarter of veterans (24.5%) and the comparison group (22.4%) reported an MSD. Having any or specific MSD was associated with depression and posttraumatic stress disorder (PTSD), but not alcohol disorders. Physical and mental well-being was poorer in those with an MSD compared to those without, in both study groups (eg, veterans with any MSD, difference in SF-12 physical component summary scale medians = -10.49: 95% confidence interval -12.40, -8.57), and in those with MSD and psychological comorbidity compared with MSD alone. Comorbidity of any MSD and psychological disorder was more common in veterans, but MSDs were associated with depression, PTSD, and poorer well-being in both groups. Psychological comorbidity needs consideration in MSD management. Longitudinal studies are needed to assess directionality and causality.

**Kelsall HL, Wijesinghe MS, Creamer MC, McKenzie DP, Forbes AB, Page MJ, Sim MR (2015) Alcohol use and substance use disorders in Gulf War, Afghanistan, and Iraq War veterans compared with nondeployed military personnel. Epidemiol Rev 37(1):38-54. doi: 10.1093/epirev/mxu014. (Epub 2015 Jan 14.)**

Although recent veterans have been found to be at increased risk of psychiatric disorders, limited research has focused on alcohol or substance use disorders. This systematic review and meta-analysis examined whether alcohol or substance use disorders were more common in Gulf War, Afghanistan, and Iraq War veterans compared with military comparison groups nondeployed to the corresponding conflict, including never deployed personnel. Literature was searched (1990-2014) in multiple electronic databases. Studies were assessed for eligibility and quality, including risk of bias. Eighteen studies (1997-2014) met inclusion criteria. Pooled analysis based on a random-effects model yielded a summary odds ratio of 1.33 (95% confidence interval (CI): 1.22, 1.46) for alcohol (7 studies) and 2.13 (95% CI: 0.96, 4.72) for substance use (3 studies) disorders among Gulf War veterans, as well as 1.36 (95% CI: 1.11, 1.66) for alcohol (7 studies) and 1.14 (95% CI: 1.04, 1.25) for substance use (4 studies) disorders among Iraq/Afghanistan veterans; meta-regressions found no statistically significant association between theater of war and alcohol use or substance use disorders. Our findings indicate that Gulf and Iraq/Afghanistan war veterans are at higher alcohol use disorder risk than nondeployed veterans, but further studies with increased power are needed to assess substance use disorder risk in Gulf War veteran populations.

**Khaiboullina SF, DeMeirleir KL, Rawat S, Berk GS, Gaynor-Berk RS, Mijatovic T, Blatt N, Rizvanov AA, Young SG, Lombardi VC (2015) Cytokine expression provides clues to the pathophysiology of Gulf War illness and myalgic encephalomyelitis. Cytokine 72(1):1-8. doi: 10.1016/j.cyto.2014.11.019. (Epub 2014 Dec 13.)**

Gulf War illness (GWI) is a chronic disease of unknown etiology characterized by persistent symptoms such as cognitive impairment, unexplained fatigue, pervasive pain, headaches, and gastrointestinal abnormalities. Current reports suggest that as many as 200,000 veterans who served in the 1990-1991 Persian Gulf War were afflicted. Several potential triggers of GWI have been proposed including chemical exposure, toxins, vaccines, and unknown infectious agents. However, a definitive cause of GWI has not been identified and a specific biological marker that can consistently delineate the disease has not been defined. Myalgic encephalomyelitis (ME) is a disease with similar and overlapping symptomology, and subjects diagnosed with GWI typically fit the diagnostic criteria for ME. For these reasons, GWI is often considered a subgroup of ME. To explore this possibility and identify immune parameters that may help to understand GWI pathophysiology, we measured 77 serum cytokines in subjects with GWI and compared these data to that of subjects with ME as well as healthy controls. Our analysis identified a group of cytokines that identified ME and GWI cases with sensitivities of 92.5% and 64.9%, respectively. The five most significant cytokines in decreasing order of importance were IL-7, IL-4, TNF-α, IL-13, and IL-17F. When delineating GWI and ME cases from healthy controls, the observed specificity was only 33.3%, suggesting that with respect to cytokine expression, GWI cases resemble control subjects to a greater extent than ME cases across a number of parameters. These results imply that serum cytokines are representative of ME pathology to a greater extent than GWI and further suggest that the two diseases have distinct immune profiles despite their overlapping symptomology.

**Koslik HJ, Hamilton G, Golomb BA (2014) Mitochondrial dysfunction in Gulf War illness revealed by 31Phosphorus Magnetic Resonance Spectroscopy: a case-control study. PLoS One 9(3):e92887. doi: 10.1371/journal.pone.0092887.**

BACKGROUND: Approximately 1/3 of 1990-1 Gulf War veterans developed chronic multisymptom health problems. Implicated exposures bear mechanisms that adversely affect mitochondria. Symptoms emphasize fatigue, cognition and muscle (brain and muscle are aerobically demanding); with protean additional domains affected, compatible with mitochondrial impairment. Recent evidence supports treatments targeting cell bioenergetics (coenzyme10) to benefit Gulf War illness symptoms. However, no evidence has directly documented mitochondrial or bioenergetic impairment in Gulf War illness. OBJECTIVE: We sought to objectively assess for mitochondrial dysfunction, examining post-exercise phosphocreatine-recovery time constant (PCr-R) using (31)Phosphorus Magnetic Resonance Spectroscopy ((31)P-MRS), in Gulf War veterans with Gulf War illness compared to matched healthy controls. PCr-R has been described as a "robust and practical" index of mitochondrial status. DESIGN AND PARTICIPANTS: Case-control study from 2012-2013. Fourteen community-dwelling Gulf War veterans and matched controls from the San Diego area comprised 7 men meeting CDC and Kansas criteria for Gulf War illness, and 7 non-deployed healthy controls matched 1:1 to cases on age, sex, and ethnicity. OUTCOME MEASURE: Calf muscle phosphocreatine was evaluated by (31)P-MRS at rest, through 5 minutes of foot pedal depression exercise, and in recovery, to assess PCr-R. Paired t-tests compared cases to matched controls. RESULTS: PCr-R was significantly prolonged in Gulf War illness cases vs their matched controls: control values, mean ± SD, 29.0 ± 8.7 seconds; case values 46.1 ± 18.0 seconds; difference 17.1

± 14.9 seconds; p = 0.023. PCr-R was longer for cases relative to their matched controls for all but one pair; moreover while values clustered under 31 seconds for all but one control, they exceeded 35 seconds (with a spread up to 70 seconds) for all but one case. DISCUSSION: These data provide the first direct evidence supporting mitochondrial dysfunction in Gulf War illness. Findings merit replication in a larger study and/or corroboration with additional mitochondrial assessment tools.

**Lai BS, Hadi F, Llabre MM (2014) Parent and child distress after war exposure. Br J Clin Psychol 53(3):333-347. doi: 10.1111/bjc.12049. (Epub 2014 Apr 4.)**

OBJECTIVES: The purpose of this study was to examine multiple distress symptoms (i.e., post-traumatic stress [PTS], anxiety, depression) among parents and children exposed to the Gulf Crisis in 1990-1991. Profiles of parent distress were identified, and the relationship between parent distress and specific child distress symptoms was examined. DESIGN: Parents and children were assessed at one time point. METHODS: Participants included 151 children ($M_{age}$ = 10.62 years; 51% female) and 140 parents ($M_{age}$ = 40 years; 81% female). RESULTS: Utilizing latent profile analysis, three parallel profiles of parent distress were identified: low distress, moderate distress, and high distress. Parent distress was a risk factor for child depression, but it was not a risk factor for child PTS or anxiety. CONCLUSIONS: Findings support the importance of broadening the scope of research conducted after exposure to traumatic events to include the assessment of anxiety and depression, as well as PTS, among both parents and children. Additional implications for research and clinical work are discussed. PRACTITIONER POINTS: Findings support the importance of screening for multiple distress symptoms among both children and parents after war exposure. Based on our findings, clinicians may want to consider including parents in therapy for children reporting psychological distress, especially depression symptoms, after exposure to traumatic events. This study was cross-sectional. Thus, we are not able to infer direction or causality. The generalizability of our study should be interpreted with caution, as findings will need to be replicated across other populations and other cultures.

**Li M, Xu C, Yao W, Mahan CM, Kang HK, Sandbrink F, Zhai P, Karasik PA (2014) Self-reported post-exertional fatigue in Gulf War veterans: roles of autonomic testing. Front Neurosci 7:269. doi: 10.3389/fnins.2013.00269.**

To determine if objective evidence of autonomic dysfunction exists from a group of Gulf War veterans with self-reported post-exertional fatigue, we evaluated 16 Gulf War ill veterans and 12 Gulf War controls. Participants of the ill group had self- reported, unexplained chronic post-exertional fatigue and the illness symptoms had persisted for years until the current clinical study. The controls had no self-reported post-exertional fatigue either at the time of initial survey nor at the time of the current study. We intended to identify clinical autonomic disorders using autonomic and neurophysiologic testing in the clinical context. We compared the autonomic measures between the 2 groups on cardiovascular function at both baseline and head-up tilt, and sudomotor function. We identified 1 participant with orthostatic hypotension, 1 posture orthostatic tachycardia syndrome, 2 distal small fiber neuropathy, and 1 length dependent distal neuropathy

affecting both large and small fiber in the ill group; whereas none of above definable diagnoses was noted in the controls. The ill group had a significantly higher baseline heart rate compared to controls. Compound autonomic scoring scale showed a significant higher score (95% CI of mean: 1.72-2.67) among ill group compared to controls (0.58-1.59). We conclude that objective autonomic testing is necessary for the evaluation of self-reported, unexplained post-exertional fatigue among some Gulf War veterans with multi-symptom illnesses. Our observation that ill veterans with self-reported post-exertional fatigue had objective autonomic measures that were worse than controls warrants validation in a larger clinical series.

**Megahed T, Hattiangady B, Shuai B, Shetty AK (2015 Jan 8) Parvalbumin and neuropeptide Y expressing hippocampal GABA-ergic inhibitory interneuron numbers decline in a model of Gulf War illness. Front Cell Neurosci. 8:447. doi: 10.3389/fncel.2014.00447. eCollection 2014.**

Cognitive dysfunction is amongst the most conspicuous symptoms in Gulf War illness (GWI). Combined exposure to the nerve gas antidote pyridostigmine bromide (PB), pesticides and stress during the Persian Gulf War-1 (PGW-1) are presumed to be among the major causes of GWI. Indeed, our recent studies in rat models have shown that exposure to GWI-related (GWIR) chemicals and mild stress for 4 weeks engenders cognitive impairments accompanied with several detrimental changes in the hippocampus. In this study, we tested whether reduced numbers of hippocampal gamma-amino butyric acid (GABA)-ergic interneurons are among the pathological changes induced by GWIR-chemicals and stress. Animals were exposed to low doses of GWIR-chemicals and mild stress for 4 weeks. Three months after this exposure, subpopulations of GABA-ergic interneurons expressing the calcium binding protein parvalbumin (PV), the neuropeptide Y (NPY) and somatostatin (SS) in the hippocampus were stereologically quantified. Animals exposed to GWIR-chemicals and stress for 4 weeks displayed reduced numbers of PV-expressing GABA-ergic interneurons in the dentate gyrus and NPY-expressing interneurons in the CA1 and CA3 subfields. However, no changes in SS+ interneuron population were observed in the hippocampus. Furthermore, GABA-ergic interneuron deficiency in these animals was associated with greatly diminished hippocampus neurogenesis. Because PV+ and NPY+ interneurons play roles in maintaining normal cognitive function and neurogenesis, and controlling the activity of excitatory neurons in the hippocampus, reduced numbers of these interneurons may be one of the major causes of cognitive dysfunction and reduced neurogenesis observed in GWI. Hence, strategies that improve inhibitory neurotransmission in the hippocampus may prove beneficial for reversing cognitive dysfunction in GWI.

**Murdoch M, Polusny MA, Street A, Noorbaloochi S, Simon AB, Bangerter A, Grill J, Voller E (2014a) Sexual assault during the time of Gulf War I: a cross-sectional survey of U.S. service men who later applied for Department of Veterans Affairs PTSD disability benefits. Mil Med 179(3):285-293. doi: 10.7205/MILMED-D-12-00513.**

OBJECTIVES: To estimate the cumulative incidence of sexual assault during the time of Gulf War I among male Gulf War I Veterans who later applied for Department of Veterans

Affairs (VA) post-traumatic stress disorder disability benefits and to identify potential risk and protective factors for sexual assault within the population. METHOD: Mailed, national, cross-sectional survey supplemented with VA administrative and clinical data. RESULTS: Of 2,415 Veterans sampled, 1,700 (70%) responded. After adjusting for nonignorable missing data, the cumulative incidence of sexual assault during Gulf War I in this population ranged from 18% [95% confidence intervals (CI): 5.0%-51.9%] to 21% (95% CI: 20.0-22.0). Deployment was not associated with sexual assault [Odds Ratio (OR), 0.96; 95% CI: 0.75-1.23], but combat exposure was (OR, 1.80; 95% CI: 1.52-2.10). Other correlates of sexual assault within the population included working in a unit with greater tolerance of sexual harassment (OR, 1.80; 95% CI: 1.52-2.10) and being exposed to more sexual identity challenges (OR, 1.76; 95% CI: 1.55-2.00). CONCLUSIONS: The 9-month cumulative incidence of sexual assault in this particular population exceeded the lifetime cumulative incidence of sexual assault in U.S. civilian women. Although Persian Gulf deployment was not associated with sexual assault in this population, combat exposure was.

**Murdoch M, Simon AB, Polusny MA, Bangerter AK, Grill JP, Noorbaloochi S, Partin MR (2014b) Impact of different privacy conditions and incentives on survey response rate, participant representativeness, and disclosure of sensitive information: a randomized controlled trial. BMC Med Res Methodol 14(1):90. doi: 10.1186/1471-2288-14-90.**

BACKGROUND: Anonymous survey methods appear to promote greater disclosure of sensitive or stigmatizing information compared to non-anonymous methods. Higher disclosure rates have traditionally been interpreted as being more accurate than lower rates. We examined the impact of 3 increasingly private mailed survey conditions-ranging from potentially identifiable to completely anonymous-on survey response and on respondents' representativeness of the underlying sampling frame, completeness in answering sensitive survey items, and disclosure of sensitive information. We also examined the impact of 2 incentives ($10 versus $20) on these outcomes. METHODS: A 3X2 factorial, randomized controlled trial of 324 representatively selected, male Gulf War I era veterans who had applied for United States Department of Veterans Affairs (VA) disability benefits. Men were asked about past sexual assault experiences, childhood abuse, combat, other traumas, mental health symptoms, and sexual orientation. We used a novel technique, the pre-merged questionnaire, to link anonymous responses to administrative data. RESULTS: Response rates ranged from 56.0% to 63.3% across privacy conditions ($p = 0.49$) and from 52.8% to 68.1% across incentives ($p = 0.007$). Respondents' characteristics differed by privacy and by incentive assignments, with completely anonymous respondents and $20 respondents appearing least different from their non-respondent counterparts. Survey completeness did not differ by privacy or by incentive. No clear pattern of disclosing sensitive information by privacy condition or by incentive emerged. For example, although all respondents came from the same sampling frame, estimates of sexual abuse ranged from 13.6% to 33.3% across privacy conditions, with the highest estimate coming from the intermediate privacy condition ($p = 0.007$). CONCLUSION: Greater privacy and larger incentives do not necessarily result in higher disclosure rates of sensitive information than lesser privacy and lower incentives.

Furthermore, disclosure of sensitive or stigmatizing information under differing privacy conditions may have less to do with promoting or impeding participants' "honesty" or "accuracy" than with selectively recruiting or attracting subpopulations that are higher or lower in such experiences. Pre-merged questionnaires bypassed many historical limitations of anonymous surveys and hold promise for exploring non-response issues in future research.

**Nutter TJ, Cooper BY (2014) Persistent modification of Nav1.9 following chronic exposure to insecticides and pyridostigmine bromide. Toxicol Appl Pharmacol 277(3):298-309. doi: 10.1016/j.taap.2014.04.005. (Epub 2014 Apr 13.)**

Many veterans of the 1991 Gulf War (GW) returned from that conflict with a widespread chronic pain affecting deep tissues. Recently, we have shown that a 60day exposure to the insecticides permethrin, chlorpyrifos, and pyridostigmine bromide (NTPB) had little influence on nociceptor action potential forming Nav1.8, but increased Kv7 mediated inhibitory currents 8weeks after treatment. Using the same exposure regimen, we used whole cell patch methods to examine whether the influences of NTPB could be observed on Nav1.9 expressed in muscle and vascular nociceptors. During a 60day exposure to NTPB, rats exhibited lowered muscle pain thresholds and increased rest periods, but these measures subsequently returned to normal levels. Eight and 12weeks after treatments ceased, DRG neurons were excised from the sensory ganglia. Whole cell patch studies revealed little change in voltage dependent activation and deactivation of Nav1.9, but significant increases in the amplitude of Nav1.9 were observed 8weeks after exposure. Cellular studies, at the 8week delay, revealed that NTPB also significantly prolonged action potential duration and afterhyperpolarization (22°C). Acute application of permethrin (10μM) also increased the amplitude of Nav1.9 in skin, muscle and vascular nociceptors. In conclusion, chronic exposure to Gulf War agents produced long term changes in the amplitude of Nav1.9 expressed in muscle and vascular nociceptors. The reported increases in Kv7 amplitude may have been an adaptive response to increased Nav1.9, and effectively suppressed behavioral pain measures in the post treatment period. Factors that alter the balance between Nav1.9 and Kv7 could release spontaneous discharge and produce chronic deep tissue pain.

**O'Donovan A, Chao LL, Paulson J, Samuelson KW, Shigenaga JK, Grunfeld C, Weiner MW, Neylan TC (2015 Jan) Altered inflammatory activity associated with reduced hippocampal volume and more severe posttraumatic stress symptoms in Gulf War veterans. Psychoneuroendocrinology 51:557-66. doi: 10.1016/j.psyneuen.2014.11.010. (Epub 2014 Nov 18.)**

BACKGROUND: Inflammation may reduce hippocampal volume by blocking neurogenesis and promoting neurodegeneration. Posttraumatic stress disorder (PTSD) has been linked with both elevated inflammation and reduced hippocampal volume. However, few studies have examined associations between inflammatory markers and hippocampal volume, and none have examined these associations in the context of PTSD. METHODS: We measured levels of the inflammatory markers interleukin-6 (IL-6) and soluble receptor II for tumor necrosis factor (sTNF-RII) as well as hippocampal volume in 246 Gulf War veterans

with and without current and past PTSD as assessed with the Clinician Administered PTSD Scale (CAPS). Enzyme-linked immunosorbent assays were used to measure inflammatory markers, and 1.5Tesla magnetic resonance imaging (MRI) and Freesurfer version 4.5 were used to quantify hippocampal volume. Hierarchical linear regression and analysis of covariance models were used to examine if hippocampal volume and PTSD status would be associated with elevated levels of IL-6 and sTNF-RII. RESULTS: Increased sTNF-RII, but not IL-6, was significantly associated with reduced hippocampal volume (β=-0.14, p=0.01). The relationship between sTNF-RII and hippocampal volume was independent of potential confounds and covariates, including PTSD status. Although we observed no PTSD diagnosis-related differences in either IL-6 or sTNF-RII, higher PTSD severity was associated with significantly increased sTNF-RII (β=0.24, p=0.04) and reduced IL-6 levels (β=-0.24, p=0.04). CONCLUSIONS: Our results indicate that specific inflammatory proteins may be associated with brain structure and function as indexed by hippocampal volume and PTSD symptoms.

**Ojo JO, Abdullah L, Evans J, Reed JM, Montague H, Mullan MJ, Crawford FC (2014) Exposure to an organophosphate pesticide, individually or in combination with other Gulf War agents, impairs synaptic integrity and neuronal differentiation, and is accompanied by subtle microvascular injury in a mouse model of Gulf War agent exposure. Neuropathology 34(2):109-27. doi: 10.1111/neup.12061. (Epub 2013 Sep 30.)**

Gulf War illness (GWI) is a currently untreatable multi-symptom disorder experienced by 1990-1991 Persian Gulf War (GW) veterans. The characteristic hallmarks of GWI include cognitive dysfunction, tremors, migraine, and psychological disturbances such as depression and anxiety. Meta-analyses of epidemiological studies have consistently linked these symptomatic profiles to the combined exposure of GW agents such as organophosphate-based and pyrethroid-based pesticides (e.g. chlorpyrifos (CPF) and permethrin (PER) respectively) and the prophylactic use of pyridostigmine bromide (PB) as a treatment against neurotoxins. Due to the multi-symptomatic presentation of this illness and the lack of available autopsy tissue from GWI patients, very little is currently known about the distinct early pathological profile implicated in GWI (including its influence on synaptic function and aspects of neurogenesis). In this study, we used preclinical models of GW agent exposure to investigate whether 6-month-old mice exposed to CPF alone, or a combined dose of CPF, PB and PER daily for 10 days, demonstrate any notable pathological changes in hippocampal, cortical (motor, piriform) or amygdalar morphometry. We report that at an acute post-exposure time point (after 3 days), both exposures resulted in the impairment of synaptic integrity (reducing synaptophysin levels) in the CA3 hippocampal region and altered neuronal differentiation in the dentate gyrus (DG), demonstrated by a significant reduction in doublecortin positive cells. Both exposures also significantly increased astrocytic GFAP immunoreactivity in the piriform cortex, motor cortex and the basolateral amygdala and this was accompanied by an increase in (basal) brain acetylcholine (ACh) levels. There was no evidence of microglial activation or structural deterioration of principal neurons in these regions following exposure to CPF alone or in combination with PB and PER. Evidence of subtle microvascular injury was demonstrated by the reduction of platelet endothelial cell adhesion molecule (PECAM)-1

levels in CPF+PB+PER exposed group compared to control. These data support early (subtle) neurotoxic effects on the brain following exposure to GW agents.

**Rojas A, Ganesh T, Lelutiu N, Gueorguieva P, Dingledine R (2015 Feb) Inhibition of the prostaglandin EP2 receptor is neuroprotective and accelerates functional recovery in a rat model of organophosphorus induced status epilepticus. Neuropharmacology 3;93C:15-27. doi: 10.1016/j.neuropharm.2015.01.017. (Epub ahead of print.)**

Exposure to high levels of organophosphorus compounds (OP) can induce status epilepticus (SE) in humans and rodents via acute cholinergic toxicity, leading to neurodegeneration and brain inflammation. Currently there is no treatment to combat the neuropathologies associated with OP exposure. We recently demonstrated that inhibition of the EP2 receptor for PGE2 reduces neuronal injury in mice following pilocarpine-induced SE. Here, we investigated the therapeutic effects of an EP2 inhibitor (TG6-10-1) in a rat model of SE using diisopropyl fluorophosphate (DFP). We tested the hypothesis that EP2 receptor inhibition initiated well after the onset of DFP-induced SE reduces the associated neuropathologies. Adult male Sprague-Dawley rats were injected with pyridostigmine bromide (0.1 mg/kg, sc) and atropine methylbromide (20 mg/kg, sc) followed by DFP (9.5 mg/kg, ip) to induce SE. DFP administration resulted in prolonged upregulation of COX-2. The rats were administered TG6-10-1 or vehicle (ip) at various time points relative to DFP exposure. Treatment with TG6-10-1 or vehicle did not alter the observed behavioral seizures, however six doses of TG6-10-1 starting 80-150 min after the onset of DFP-induced SE significantly reduced neurodegeneration in the hippocampus, blunted the inflammatory cytokine burst, reduced microglial activation and decreased weight loss in the days after status epilepticus. By contrast, astrogliosis was unaffected by EP2 inhibition 4 d after DFP. Transient treatments with the EP2 antagonist 1 h before DFP, or beginning 4 h after DFP, were ineffective. Delayed mortality, which was low (10%) after DFP, was unaffected by TG6-10-1. Thus, selective inhibition of the EP2 receptor within a time window that coincides with the induction of cyclooxygenase-2 by DFP is neuroprotective and accelerates functional recovery of rats.

**Schiehser DM, Twamley EW, Liu L, Matevosyan A, Filoteo JV, Jak AJ, Orff HJ, Hanson KL, Sorg SF, Delano-Wood L (2014) The Relationship Between Postconcussive Symptoms and Quality of Life in Veterans With Mild to Moderate Traumatic Brain Injury. J Head Trauma Rehabil. 2014 Jun 11.**

OBJECTIVE: To assess the relationship between postconcussive symptoms and quality of life (QOL) in Veterans with mild to moderate traumatic brain injury (TBI). METHODS: Sixty-one Operation Enduring Freedom/Operation Iraqi Freedom/Persian Gulf War Veterans with a history of mild or moderate TBI, more than 6 months postinjury, and 21 demographically matched Veteran controls were administered self-report measures of QOL (World Health Organization Quality of Life-BREF) and postconcussive symptom severity (Neurobehavioral Symptom Inventory). RESULTS: Perceived QOL was significantly worse in Veterans with mild-moderate TBI than in controls. In the TBI group, QOL was predominantly associated with affective symptoms, and moderate to strong

correlations with fatigue and depression were evident across all QOL areas. Multivariate analyses revealed depression and fatigue to be the best predictors of Psychological, Social, and Environmental QOL, whereas sleep difficulty best predicted Physical QOL in mild-moderate TBI. CONCLUSION: Veterans with post-acute mild-moderate TBI evidence worse QOL than demographically matched Veteran controls. Affective symptoms, and specifically those of fatigue, depression, and sleep difficulty, appear to be the most relevant postconcussive symptoms predicting QOL in this population. These findings underscore the importance of examining specific symptoms as they relate to post-acute TBI QOL and provide guidance for treatment and intervention studies.

**Shell WE, Charuvastra M, Breitstein M, Pavlik SL, Charuvastra A, May L, Silver DS (2014) Administration of an amino Acid-based regimen for the management of autonomic nervous system dysfunction related to combat-induced illness. J Cent Nerv Syst Dis 6:93-8. doi: 10.4137/JCNSD.S13793. eCollection 2014.**

The etiology and pathophysiology of posttraumatic stress disorder (PTSD) remains poorly understood. The nutritional deficiencies associated with the altered metabolic processes of PTSD have not previously been studied in detail. This pilot study measured the reduction in symptoms in 21 military veterans reporting moderate to severe symptoms associated with PTSD. Two amino acid-based medical foods specifically formulated with biogenic amines and other nutrients were administered to study subjects targeting specific neurotransmitter deficiencies resulting from altered metabolic activity associated with PTSD. This study included the Physician Checklist - Military (PCL-M), Short Form General Health Survey (SF-36), and Epworth Sleepiness Scale to measure the change in each subject's score after 30 days of administration. An average decrease of 17 points was seen in the PCL-M, indicating a reduction in PTSD symptoms ($P < 0.001$). The mental health component of the SF-36 showed an average 57% increase in the subjects' mental health rating ($P < 0.001$). The results of this initial study demonstrate that addressing the increased dietary requirements of PTSD can improve symptoms of the disease while eliminating significant side effects. A larger, double-blind, randomized, placebo-controlled trial is warranted.

**Smith TC, Powell TM, Jacobson IG, Smith B, Hooper TI, Boyko EJ, Gackstetter GD. (2014) Chronic multisymptom illness: a comparison of Iraq and Afghanistan deployers with veterans of the 1991 Gulf War. Am J Epidemiol 180(12):1176-87. doi: 10.1093/aje/kwu240. (Epub 2014 Dec 2.)**

Symptoms and illnesses reported by veterans of the 1991 Gulf War era are a cause of potential concern for those military members who have deployed to the Gulf region in support of more recent contingency operations in Iraq and Afghanistan. In the present study, we quantified self-reported symptoms from participants in the Millennium Cohort Study, a prospective study representing all US service branches, including both active duty and Reserve/National Guard components (2001-2008). Self-reported symptoms were uniquely compared with those in a cohort of subjects from the 1991 Gulf War to gain context for the present report. Symptoms were then aggregated to identify cases of chronic multisymptom illness (CMI) based on the case definition from the Centers for Disease

Control and Prevention. The prevalence of self-reported CMI symptoms was compared with that collected in 1997-1999 from a study population of US Seabees from the 1991 Gulf War, as well as from deployed and nondeployed subgroups. Although overall symptom reporting was much less in the Millennium Cohort than in the 1991 Gulf War cohort, a higher prevalence of reported CMI was noted among deployed compared with nondeployed contemporary cohort members. An increased understanding of coping skills and resilience and development of well-designed screening instruments, along with appropriate clinical and psychological follow-up for returning veterans, might help to focus resources on early identification of potential long-term chronic disease manifestations.

**Steele L, Lockridge O, Gerkovich MM, Cook MR, Sastre A (2015 Jan 9) Butyrylcholinesterase genotype and enzyme activity in relation to Gulf War illness: preliminary evidence of gene-exposure interaction from a case-control study of 1991 Gulf War veterans. Environ Health 14(1):4. doi: 10.1186/1476-069X-14-4.**

BACKGROUND: Epidemiologic studies have implicated wartime exposures to acetylcholinesterase (AChE)-inhibiting chemicals as etiologic factors in Gulf War illness (GWI), the multisymptom condition linked to military service in the 1991 Gulf War. It is unclear, however, why some veterans developed GWI while others with similar exposures did not. Genetic variants of the enzyme butyrylcholinesterase (BChE) differ in their capacity for metabolizing AChE-inhibiting chemicals, and may confer differences in biological responses to these compounds. The current study assessed BChE enzyme activity and BChE genotype in 1991 Gulf War veterans to evaluate possible association of this enzyme with GWI. METHODS: This case-control study evaluated a population-based sample of 304 Gulf War veterans (144 GWI cases, meeting Kansas GWI criteria, and 160 controls). BChE enzyme activity levels and genotype were compared, overall, in GWI cases and controls. Potential differences in risk associated with cholinergic-related exposures in theater were explored using stratified analyses to compare associations between GWI and exposures in BChE genetic and enzyme activity subgroups. RESULTS: Overall, GWI cases and controls did not differ by mean BChE enzyme activity level or by BChE genotype. However, for the subgroup of Gulf War veterans with less common, generally less active, BChE genotypes (K/K, U/AK, U/A, A/F, AK/F), the association of wartime use of pyridostigmine bromide (PB) with GWI (OR = 40.00, p = 0.0005) was significantly greater than for veterans with the more common U/U and U/K genotypes (OR = 2.68, p = 0.0001). CONCLUSIONS: Study results provide preliminary evidence that military personnel with certain BChE genotypes who used PB during the 1991 Gulf War may have been at particularly high risk for developing GWI. Genetic differences in response to wartime exposures are potentially important factors in GWI etiology and should be further evaluated in conjunction with exposure effects.

**Wallin MT, Kurtzke JF, Culpepper WJ, Coffman P, Maloni H, Haselkorn JK, Mahan CM (2014) Multiple sclerosis in Gulf War era Veterans. 2. Military deployment and risk of multiple sclerosis in the first Gulf War. Neuroepidemiology 42(4):226-34. doi: 10.1159/000360701. (Epub 2014 May 25.)**

Background: Concern has been raised that US veterans of the 1990-1991 Gulf War (GW1) may be at increased risk to develop neurologic disease. Methods: An incident cohort of multiple sclerosis (MS) and other demyelinating disease (ODD) was assembled from the US military comprising the Gulf War era (1990-2007). Cases of MS and ODD meeting standard diagnostic criteria were matched to a database of all active duty personnel from the Department of Defense. Relative risk (RR) estimates for MS and all demyelinating disease based on onset, deployment status, and exposures were calculated. Results: For GW1, a total of 1,841 incident cases of definite MS and ODD were identified, with 387 among 696,118 deployed and 1,454 among 1,786,215 nondeployed personnel. The RR for MS alone among those deployed compared to those nondeployed was 0.69 (confidence interval, CI: 0.61-0.78), with 0.72 (CI: 0.62-0.83) in men and 0.96 (CI: 0.75-1.22) in women. Deployment was also nonsignificant or protective as an MS risk factor across racial groups, all age groups, and each military service. RRs for MS by service were: Air Force 0.71 (CI: 0.53-0.96), Army 0.80 (CI: 0.67-0.96), Marines 0.96 (CI: 0.63-1.47), and Navy 0.56 (CI: 0.43-0.74). Conclusion: Military deployment to GW1 was not a risk factor for developing MS.

**Zhivin S, Laurier D, Guseva Canu I (2014) Health effects of occupational exposure to uranium: do physicochemical properties matter? Int J Radiat Biol 90(11):1104-13. doi: 10.3109/09553002.2014.943849.**

PURPOSE: Physicochemical properties of uranium, including isotopic composition and solubility, are determinants of its toxicity. We reviewed epidemiological studies in civilian and military workers known to be exposed to uranium with different physicochemical properties to investigate its long-term effects, such as cancerous and circulatory diseases. MATERIALS AND METHODS: We systematically searched the Pubmed and the Scopus databases to identify studies of uranium- processing workers (published between 1980 and 2013) and veterans of the wars in the Persian Gulf and the Balkans (published between 1991 and 2013) in which defined outcomes, such as lung, lymphohematopoietic, kidney cancers, and circulatory diseases were examined. RESULTS from these studies in terms of risk of each health outcome (mortality or incidence) and analyses of dose-response relationship were examined to present the impact of uranium physicochemical properties on the observed results. RESULTS: Twenty-seven articles were reviewed. There is some evidence for increased lung cancer risk among uranium-processing workers. The evidence is less strong for lymphohematopoietic cancer. We found that most of the studies insufficiently assessed the physicochemical properties of uranium and some of them used proxies for the exposure assessment and risk estimation analyses. Studies of veterans of the wars in the Persian Gulf and the Balkans are uninformative in respect to internal uranium exposure. CONCLUSIONS: Existing epidemiological data on the physicochemical properties of uranium and associated health outcomes are inconclusive. Further studies among certain groups of uranium-processing workers (uranium-enrichment and fuel-fabrication workers) could contribute to our knowledge of the health effects of uranium with respect to its physicochemical properties.

## IV. RESEARCH FUNDING TRENDS

This section provides a quantitative overview of the current research portfolio on GWVI and the evolution of the portfolio since 1999. Topics that are covered include research expenditures by VA, DoD, and HHS from FY 2005-2014, and the number of research projects in which the Federal Government has invested.

The appropriated funds for FY 2005 through 2014, centrally obligated to each project, are shown in Appendix C and summarized in Table IV-1. Federal funding for GW research totaled approximately $230 million during this period. Funds obligated for these projects prior to FY 2005 are not shown in either Table IV-1 or Appendix C. Since many projects are multi-year efforts for which funds are obligated at the beginning of the project period, projects that received all of their funds prior to FY 2005 are listed with no associated obligation ($0) in Appendix C. Federal funds for these earlier projects were reported in prior annual reports to Congress.

**Table IV-1. 10-Year (FY 2005-2014) Funding Trends for GW Research in Millions of Dollars**

| Department | FY '05 | FY '06 | FY '07 | FY '08 | FY '09 | FY '10 | FY '11 | FY '12 | FY '13 | FY '14 | Total Costs FY '05-'14 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **DoD** | $ 10.1 | $ 10.1 | $ 3.4 | $ 11.7 | $ 10.4 | $ 10.4 | $ 10.3 | $ 11.7 | $ 19.5 | $ 4.1 | **$ 101.7** |
| **HHS** | $ 0.5 | $ 0.5 | $ 0.4 | $ 0.4 | $ 0 | $ 0 | $ 0 | $ 0 | $ 0 | $ 0 | **$ 1.8** |
| **VA** | $ 9.5 | $ 13.0 | $ 22.1 | $ 21.9 | $16.6 | $13.9 | $ 5.6 | $ 6.7 | $ 7.9 | $ 9.7 | **$ 126.9** |
| **Total** | **$ 20.1** | **$ 23.6** | **$25.9** | **$ 34.0** | **$ 27.0** | **$ 24.3** | **$ 15.9** | **$ 18.4** | **$ 27.4** | **$ 13.8** | **$ 230.4** |

The funding level for FY 2013 in the table above differs from the value reported in the 2013 annual report to Congress due to the delayed start of sixteen projects funded through the FY 2013 appropriation for the Gulf War Illness Research (GWIRP) managed by the Congressionally Directed Medical Research Programs (CDMRP) at DoD. DoD did not receive final approval until FY 2014. DoD funding listed for FY 2014 is only $2.5 million for the same reason and will be updated after the CDMRP projects selected for funding in FY 2014 have begun.

VA, DoD, and HHS sponsored a total of 450 distinct research projects on GWVI during the period of FY 1992 through FY 2014. Appendix A lists all of the research and development projects and programs supported now or in the past by each of the three Federal agencies. Nine projects have been dual-funded by VA and DoD, and each agency has given the project its own unique project number (DoD-115/VA-062; DoD-116/VA-063; DoD-116A/VA-063A; DoD-116B/VA-063B; D0D-118/VA-061; DoD-119/VA-055; DoD-125/VA-074; DoD-143/VA-078; and DoD-154/VA-088). In prior annual reports to Congress, the total

number of funded projects was corrected for the number of dual-funded projects. Starting with the 2005 annual report to Congress, this practice has been discontinued since VA and DoD may start or end funding of their portion of these projects independent of each other. Each dual-funded project is, therefore, treated as two distinct projects.

The numbers of new, ongoing, and completed projects for FY 2005 - FY 2014 are shown in Figure IV-1. As of September 30, 2014, 380 projects (84 percent of the 450 projects) were completed, and 70 projects (16 percent) were new or ongoing; the numbers of new, ongoing, and completed projects for each fiscal year are shown in Figure IV-1.

The annual distribution of new and ongoing projects within the five major Research Focus Areas is shown in Figure IV-2. From FY 2005 through 2014, new and ongoing research assigned to the Brain and Nervous System Function, Environmental Toxicology, and General Health and Symptoms categories have represented 96.4 ± 1.0 percent of all new and ongoing projects.

**Figure IV-1. Cumulative Number of Funded Projects (FY 2005 - FY 2014)**

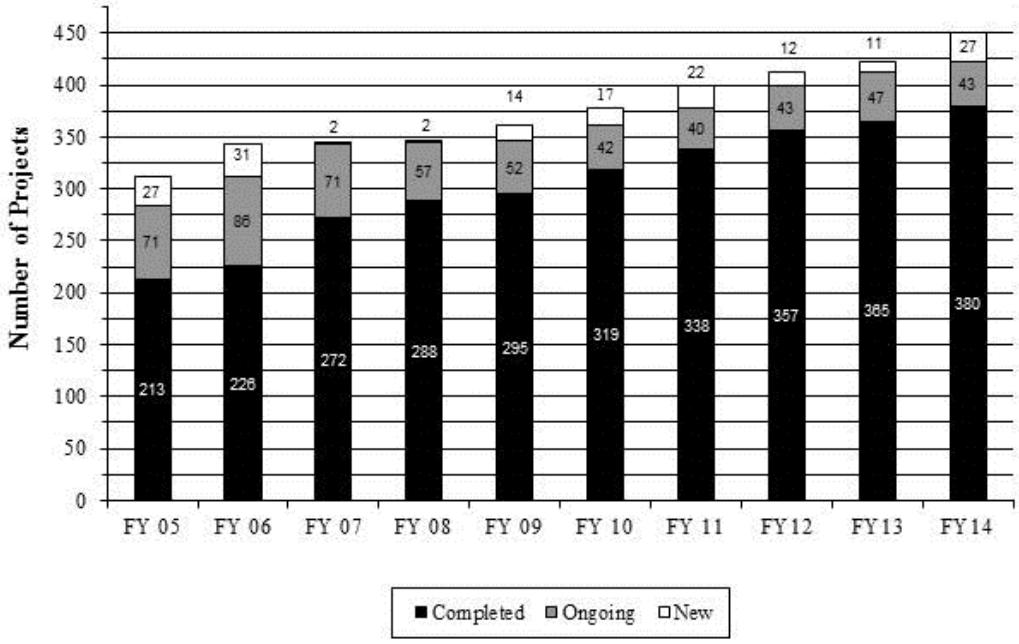
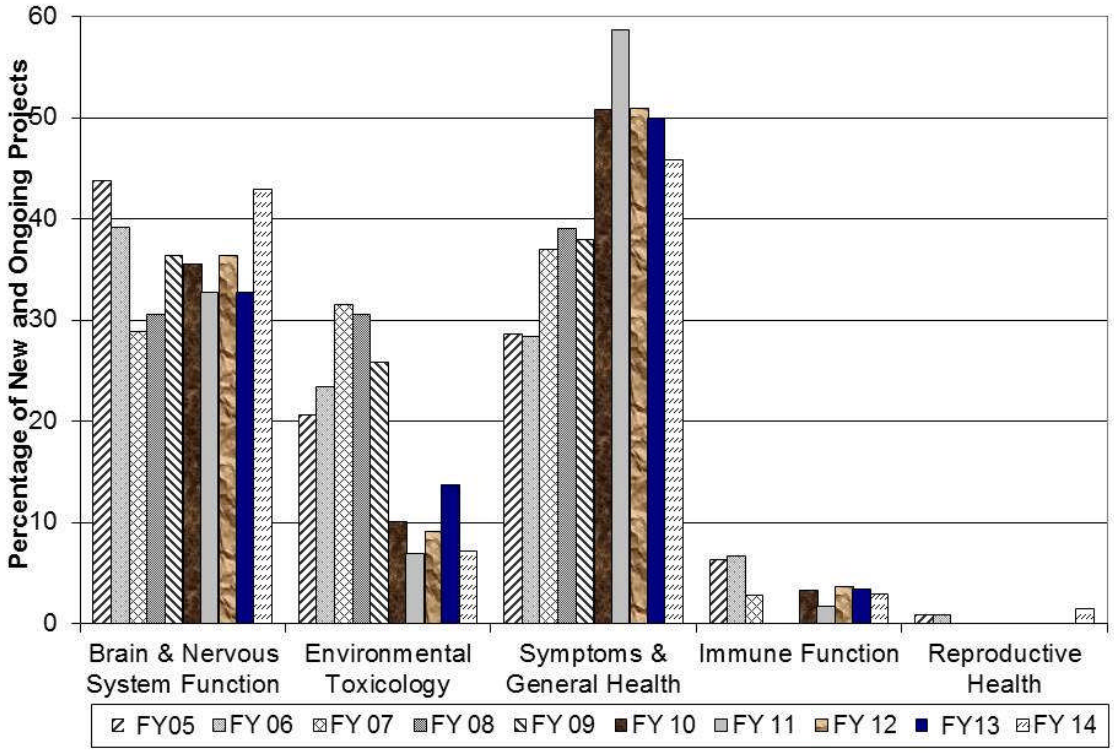


**Figure IV-2. Annual Distribution of Topic Areas for New and Ongoing Projects**




## V. NEW RESEARCH PROJECTS AND INITIATIVES

### A. New Initiatives

Requests for Applications (RFAs) were issued by both CDMRP and VA in FY 2014. Proposals received for review in response to these RFAs were reviewed, and projects selected for funding will begin in FY 2015. As more investigators engage in GW research, there has been an increase in applications for funding and increases in the number of newly-approved treatment trials and biomarker studies. In 2014, 27 new projects were added to the 43 ongoing projects.

In addition to the regularly-released RFAs, VA is planning special RFAs to address specific questions. An RFA in Health Services Research and Development asked researchers to propose ways of determining if GW Veterans are satisfied with their health care at VA and to propose solutions to any problems they identify. Thus far, two projects have been recommended for funding.

Two CDMRP-funded research consortia combine the talents and expertise of GW researchers who will focus on different aspects of GWI. One consortium will study brain-immune interactions to monitor neurotoxic and neuroinflammatory reactions as the

investigators try to understand the underlying causes of the health problems in GW Veterans. The other consortium will focus on a "systems biology" approach to combining basic research with clinical results to identify biomarkers and possible treatments for GW Veterans.

The Institute of Medicine (IOM) completed two studies for VA "Gulf War and Health, Volume 9: Long-Term Effects of Blast Exposures" was released on February 13, 2014, and "Consensus Case Definition for Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans" was released on March 12, 2014. Both reports provided useful recommendations for GW research.

### B. Portfolio Review

VA and DoD each review their portfolios of GW research on a regular basis in order to determine research gaps and to expand successful research topic areas. The Federal GW research portfolio is increasingly focused on identifying potential new treatments (clinical trials, including complementary medicine approaches) for ill GW Veterans and identifying new diagnostic markers of disease and potential therapeutic targets to develop new therapies. VA and DoD program managers meet regularly to share information regarding funded GW research projects and coordinate activities, whenever possible, to maximize combined program impact. To formalize this process, the GW research programs have been integrated into the ongoing Department-wide VA-DoD Joint Program Reviews. The first GW review was held in September 2013, and the next review will be during Summer 2015.

### C. New Projects

This section highlights the new research projects that have been approved since last year's 2013 annual report to Congress; these projects represent an investment of more than $30 million by the time they are completed. Projects preceded by an asterisk (*) were either funded using funds appropriated in prior years or approved for funding in prior fiscal years but not identified in previous annual reports to Congress. They are described below and incorporated into the tables in Appendices A, B, and C.

Two new treatment trials have begun. One uses transcranial magnetic stimulation to treat pain, and the other will use red and near infrared light to improve cognition in GW Veterans. Two new studies will use exercise to investigate the possibility that dysfunctional mitochondrial gene regulation or other mitochondrial disease is responsible for pain and fatigue. If they are successful, the ultimate outcomes could be biomarkers and new treatments for GW Veterans. Another project with the potential to develop biomarkers will test the involvement of microRNAs in neuroinflammation. These microRNAs could serve as biomarkers if they could be detected in blood. Two other projects involving neural membrane proteins and protein radicals will investigate the basis for neurological problems leading to pain and inflammation. Magnetic resonance of phosphorus-containing materials in the brain and muscle will be used to determine if reduced energy production in cells is related to fatigue and cognitive disorders. One final

project involves a review of existing information related to case definitions for chronic multisymptom illnesses in hopes that a consensus definition for use with GW Veterans can be formulated.

A number of clinical trials began in 2014. Yoga and acupuncture are being used to treat pain and other symptoms associated with GWVs, and cognitive rehabilitation therapy (CRT) is being applied to patients with difficulties associated with memory, attention, and judgement. Two studies are using steroids and three others are using nutritional supplements and botanicals to treat GW Veterans' symptoms. PET scans and MRI methods are useful for characterizing physiological changes which are surrogate biomarkers of illness, and genetic studies involving patients and model animals will help us understand individual susceptibility to symptoms.

## DoD Projects

Sixteen new projects were recommended for funding through the FY 2013 appropriation for the GWIRP managed by CDMRP, but were not finalized and funded until FY 2014. These projects focused on Brain and Nervous System Function (9), Immune Function (1), and Symptoms and General Health (6).

*DoD-227, "Monosodium Luminol for Improving Brain Function in Gulf War Illness" will use an animal model of Gulf War illness to rigorously test the efficacy of a drug called monosodium luminol-GVT (MSL-GVT, obtained from Bach Pharma) in easing cognitive dysfunction, depression, and anxiety. Thus, the major focus of this project is to develop a therapy for both improving the learning and memory function and reducing depression and anxiety in GW Veterans exhibiting GWI.

*DoD-228, "A Multimodal Evaluation of the Comparative Efficacy of Yoga versus a Patient-Centered Support Group for Treating Chronic Pain in Gulf War Illness" is designed to provide Veterans with GWI with a comprehensive yoga program that is both safe and effective in treating their pain. This treatment trial aims to determine some of the mechanisms of pain in GWI, especially dysfunction in the peripheral nervous system. If yoga is associated with improvement in pain, outcomes from this study would support performing a larger clinical trial of yoga for treating pain and other symptoms of GWI.

*DoD-229, "Bench to Bedside: Understanding Symptom Response to Acupuncture Treatment and Designing a Successful Acupuncture Treatment Program" will offer information on which GW Veterans respond to acupuncture, how they respond, and how to implement a program that will help others find relief. Differences in how Veterans respond to acupuncture treatment may help us understand how GWI works and help to find effective treatments for other Veteran health concerns.

*DoD-230, "An In Vivo Investigation of Brain Inflammation in Gulf War Illness with Integrated PET/MR Imaging" will use a new type of brain imaging technique that will, for the first time, allow comparisons of the degree of brain inflammation/microglial activation in

GW Veterans with GWI and in healthy GW Veteran controls. As a second comparison group, individuals with fibromyalgia (FM) will be studied to determine whether inflammation associated with this disorder is similar to that seen in GW Veterans. The ultimate goals of this study are to determine whether Veterans with GWI have brain inflammation, whether this inflammation is similar and in the same brain pathways as FM patients, and whether this inflammation is associated with increased rates of pain, fatigue, and cognitive symptoms experienced by GW Veterans.

*DoD-231, “Use of a Portable Stimulator to Treat GWI” will (1) examine how much vestibular damage is present in Veterans with GWI and (2) test the use of a portable stimulator that will deliver mild electrical stimulation to improve balance and reduce dizziness in GWI Veterans with verified balance problems. Preliminary data showed that low levels of electrical stimulation, delivered at levels that cannot be felt, can effectively improve balance. The next step is to develop a portable stimulator, similar to a hearing aid, that can be worn behind the ear and examine its effectiveness in improving balance and vestibular function over a 12-week trial.

*DoD-232, “Characterizing Treatable Causes of Small Fiber Polyneuropathy in Gulf War Veterans” is designed to evaluate Gulf War Veterans by neurological examination and other special tests to determine how many meet a case definition for small-fiber polyneuropathy (SFPN). Finding an association between SFPN and GWI has potential to point towards definitive testing and treatment options.

*DoD-233, “Assessment of MRI-Based Markers of Dopaminergic Integrity as a Biological Indicator of Gulf War Illness” will leverage existing brain imaging data from a well-characterized sample of 1990-1991 Gulf War Veterans to assess brain structures and processes of high interest for understanding GWI, but not previously studied in ill Gulf War Veterans.

*DoD-234, “A Prospective Open-Label Clinical Trial of Methylphenidate plus a GWI-Specific Nutrient Formula in Patients with Gulf War Illness and Concentration Disturbances” is designed to evaluate the safety and tolerability of methylphenidate hydrochloride in patients with GWI also taking a GWI-specific nutrient formula (GWI Nutrient Formula), a treatment shown to provide improvement to the fatigue and concentration disturbances associated with CFS. Primary aims are to evaluate the incidence of adverse events, clinical laboratory results, and other safety measures in Veterans taking methylphenidate hydrochloride and GWI Nutrient Formula. The secondary aims are to measure changes in fatigue, concentration disturbances, cognitive functioning, and pain level using validated response questionnaires, and to assess mitochondrial health function from subject blood samples.

*DoD-235, “Treating Gulf War Illness with Novel Anti-Inflammatories: A Screening of Botanical Microglia Modulators” will test nine different botanical microglia-modulators to identify the most promising botanical microglia anti-inflammatories for the treatment of GWI and secondarily identify biomarkers of GWI improvement. Forty individuals with GWI will

be recruited for this intensive longitudinal, cross-over, placebo-controlled, double-blind clinical trial.

*DoD-236, “Development of Dietary Polyphenol Preparations for Treating Veterans with Gulf War Illness” will test the potential efficacy of dietary supplementation with a combination of a flavonoid-rich preparation (FRP), comprised of two commercially available products, to alleviate clinical complications in Veterans with GWI. In particular, a randomized, double-blind, placebo-controlled study to test the feasibility and potential efficacy of FRP dietary supplementation to treat cognitive deficits and chronic fatigue in Veterans with GWI will be performed.

*DoD-237, “Direct Test for Neuroinflammation with [11C]DAP-713-PET Scanning” hypothesizes that excess cholinergic signaling further exacerbates neuroinflammation, ultimately contributing to the chronic syndrome of GWI. This working model will be tested directly in humans in vivo by using positron emission tomography (PET)-based neuroimaging to quantify inflammation and M2 receptor changes in the brains of clinically well-characterized Gulf War Veterans. Specifically, ten Gulf War Veterans and ten healthy control participants will each undergo two PET scans, including [11C]DPA-713 PET to test for an increase in translocator protein (TSPO), a marker of brain inflammation, and [18F]FP-TZTP PET to test M2 receptor function.

*DoD-238, “Restoring the Brain's Lipid Homeostasis as a Therapeutic Avenue for Treating the CNS Symptoms of Gulf War Illness” will test whether therapeutic modulation of biochemical pathways involved in de novo phosphatidylcholine (PC) synthesis and peroxisomal function and replenishing lipid metabolites are potential approaches for treating GWI. Two drugs will be tested to restore lipid homeostasis in the brain and improve neurobehavioral deficits and astroglia dysfunction in GW agent-exposed mice. By the end of the 3-year project, at least one drug should be identified as a lead compound for further testing in support of an FDA clinical trial application.

*DoD-239, “Mitochondrial and Nuclear Genetics in Gulf War Illness” will compare 40 Veterans with GWI 40 matched healthy controls, to see if ill Veterans are more likely to have unfavorable variants of the genes involved in detoxification (the main outcome); to see if they differ in mt patterns ("haplogroups"); also, to see if they have more mtDNA deletions and duplications; and to see if Gulf exposures, genetics of exposure detoxification, and, possibly, mt genetics work together to predict whether GWI occurred, how severe it is, and its pattern of improvement vs stability vs progression.

*DoD-240, “Novel Therapeutic Approaches for the Treatment of Depression and Cognitive Deficits in a Rodent Model of Gulf War Veterans' Illness” will test the hypothesis that "chronic alterations in the ER CICR system underlie depression and cognitive deficits in GWI and that it is possible to interfere with this signaling system using FDA approved drugs and effectively treat and possibly 'cure' depression and memory impairments associated with GWI." The specific aims of this project are (1) to develop a rat model of OP exposure mimicking different OP levels seen by Gulf War Veterans and manifesting the hippocampal damage and chronic morbidities associated with chronic GWI, (2) to

demonstrate that alterations in components of CICR systems cause chronic changes in Ca2+ signaling that represent, in part, a molecular mechanism underlying these GWI morbidities, and (3) to elucidate innovative treatments for GWI morbidities by identifying pharmacological agents that target the altered CICR molecular components in this rat model of GWI.

*DoD-241, “Gulf War Illness Inflammation Reduction Trial” is a clinical trial whose goal is to determine if reducing inflammation is an effective treatment for GWI. In a pilot study , blood samples from Gulf War Veterans with and without GWI were compared and strong evidence of chronic inflammation in Veterans with GWI was found. The proposed study is a randomized, two-group, double-blind, placebo-controlled clinical trial of delayed-release prednisone versus matching placebo. A total of 100 Veterans with GWI will be enrolled in the trial. Prednisone was chosen as the study drug because of its well-established pleiotropic anti-inflammatory properties.

*DoD-242, “Epigenetic Mediation of Endocrine and Immune Response in an Animal Model of Gulf War Illness” will test whether DNA methylation and chromatin modifications produce stable changes in transcriptional signaling as a result of environmental exposure under stress, which may contribute significantly to a neuro-immune hypersensitivity in GWI driving symptom severity. The specific aims of this study are to examine the epigenomic response to DFP, a sarin surrogate, and associated changes to the immune and endocrine response to LPS challenge in a C57Bl6/J mouse model of GWI.

**VA Funded Projects**

VA initiated funding for eleven new projects during FY 2013. These five projects focused on Brain and Nervous System Function (7), Reproductive Health (1), and Symptoms and General Health (3).

VA-183, “Examination of Cognitive Fatigue in Gulf War Illness Using fMRI” will attempt to establish the network of brain areas underlying cognitive fatigue (i.e., fatigue that is exacerbated by everyday mental and physical demands) in Veterans with GWI. This will be done by looking at cognitive fatigue as a trait of GWI, and by looking at cognitive fatigue as a state that individuals with GWI are more prone to than are healthy Veteran controls. One goal is to establish fMRI as an objective measure of cognitive fatigue in GWVs with GWI. To induce cognitive fatigue, GWVs with GWI will be subjected to sustained performance of an attention task while in the MRI scanner. Diffusion Tensor Imaging (DTI) methods will also be used to study white matter tract integrity.

VA-184, “Longitudinal Assessment of Gulf War Veterans with Suspected Sarin Exposure” is designed to extend previous findings of structural and functional brain changes in a larger, non-overlapping sample of 150 GW Veterans suspected of having been exposed to the nerve agents sarin and cyclosarin. These GWVs exhibited reduced brain volume, hippocampal atrophy, and impaired cognitive function. Changes in hippocampal subfields in exposed Veterans will be examined, and diffusion tensor imaging (DTI) will be used to

examine the effects of suspected sarin/cyclosarin exposure on white matter microstructure integrity.

VA-185, “Identification of Plasma Biomarkers of Gulf War Illness Using "omic" Technology” is designed to generate plasma proteomic, lipidomic, and metabolomic profiles of GWI in mouse models, enabling characterization of biomarkers associated with the particular exposure experienced by Gulf War Veterans. These profiles will be correlated to problems of the central nervous system. Once the correlations in mice are made, human GWI plasma will be analyzed for analogous biomarkers. Biomarkers developed from these analyses will identify clinical subgroups for which appropriate treatments can be developed.

VA-186, “Gulf War Exposures and the Molecular Mechanisms of Paternal Reproductive Risk” will investigate whether environmental exposures resulting in aryl hydrocarbon receptor (AHR) activation can result in reproductive problems in males. C57BL6 mice and aryl hydrocarbon receptor knockout mice will be exposed to a complex mixture of polyaromatic hydrocarbons (PAHs) and particulate matter (PM). Endpoints will include fertilization rates, blastocyst rates; embryo day 16.5 and term litter size, weight, length, structural assessment, and internal organ defects through the use of genetic, genomic, and proteomic assays.

VA-187, “Multimodal Biological Assessment of Gulf War Illness” incorporates advances in neuroimaging, genetics, pain and sleep physiology, neuroendocrinology and neurodegeneration biomarker development in a multidisciplinary approach to defining neurobiological abnormalities underlying GWVI symptomatology. The project will (1) characterize abnormalities in brain structural and functional integrity relevant to cognition, (2) develop cebrospinal fluid (CSF) biomarkers associated with neurodegeneration, (3) identify abnormalities in central and peripheral systems regulating pain perception, fatigue, and sleep, and (4) identify genetic variants and/or epigenetic alterations associated with neurodegeneration and impaired pain processing.

VA-188, “Complementary Neurosteroid Intervention in Gulf War Veterans’ Illnesses” will use pregnenolone to determine if its pleiotropic actions are advantageous for the diverse clinical manifestations in GWVI in a randomized controlled trial (RCT) involving Gulf War Veterans with a history of deployment and symptoms of GWVI. There will also be neurosteroid biomarker investigations, using mass spectrometry to characterize the metabolic profile of pregnenolone, to obtain valuable pharmacokinetic data, and to determine optimal therapeutic efficacy and potential neurosteroid predictors of clinical response.

VA-189, “CAM in Veterans with Gulf War Illnesses” is a prospective, randomized controlled clinical trial (RCT) to determine whether complementary and alternative medicine (CAM) will lead to improved general health in GWVs with Gulf War Veterans’ Illnesses (GWVIs) compared to Health Education. The primary hypothesis is that deployed GWVs who meet CDC criteria for chronic multisymptom illness and receive combined auricular acupuncture and iRest® Yoga Nidra will exhibit greater improvements in physical health functioning,

reductions in pain, fatigue, cognitive deficits and sleep disturbance than the comparison group.

VA-190, “Cognitive Rehabilitation for Gulf War Illness” is a study designed to target a specific component of GWI, namely problem-solving ability, known to be associated with disability. This impairment is also related to poorer adherence to medical regimes, making it difficult for GWVs to manage other aspects of GWI. The approach will be to treat this deficit using a state-of-the-art evidence-based approach to cognitive rehabilitation called Problem-Solving Therapy (PST) in a multi-site, randomized controlled trial of telephone-delivered PST versus telephone-delivered Health Education.

VA-191, “Novel neurotrophic therapies in an optimized mouse model of GWVI” is aimed at designing a treatment modality that can restore the normal functioning of cholinergic neurons and their targets in patients with GWVI. To stimulate production of brain-derived neurotrophic factor (BDNF) after exposure of transgenic mice to the GWVI-associated chemicals (PB, permethrin, and DEET), 7,8-dihydroxyflavone (7,8-DHF) will be administered along with moderate exercise. This intervention is expected to cause a recovery of brain function in a mouse model optimized for studies of cholinergic neurons, and the model can be used to test therapeutics relevant to patients with GWVI.

VA-192, “Women vs. Men with GWI: Differences in Computational Models and Therapeutic Targets” is designed to understand the underlying mechanisms of GWI and to target treatments more effectively in men and women. This model involves challenging a patient with exercise and drawing blood at multiple times to map out mediators of genomic, cellular and chemical response. In a preliminary study involving 50 men and 10 women with GWI, the data show that the condition is mediated differently in men and women, but the small sample size prevents modeling the mediators of persistent illness in women to the point of identifying therapeutic targets. The current study is designed to increase the number of women to outline further differences in response between genders.

VA-193, “Neuroinflammation, Oxidative Stress, and Hippocampal Defects in Gulf War Illness” is a pilot study designed to ascertain the delayed and persistent effects of various Gulf War agents on hippocampal functions and the involvement of neuroinflammation and oxidative stress. Wild type mice and mice with higher levels of the antioxidant enzyme, extracellular superoxide dismutase (EC-SOD), will be used as the model system, and the mice will be exposed to various Gulf War agents alone or in combination to simulate conditions during the Gulf War. The level of inflammatory cytokines and glucocorticoid hormone will be monitored to ascertain the level of acute and chronic inflammation.

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# Appendices

## Federally Funded Research Projects

# Appendix A

## Project Index By Department

## DEPARTMENT OF DEFENSE PROJECTS

| | |
|---|---|
| DoD-001 | Naval Health Study Program |
| DoD-001A | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees |
| DoD-001B | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not |
| DoD-001C | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among GW Veterans and other active-duty personnel |
| DoD-001D | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in GW Veterans |
| DoD-001E | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study |
| DoD-001F | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: GWV vs. NDV |
| DoD-001G | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian GW Veterans |
| DoD-002 | Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET |
| DoD-004 | The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey |
| DoD-007A | Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling |
| DoD-007B | Carcinogenicity of Depleted Uranium Fragments |
| DoD-008A | Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL) |
| DoD-008B | Development of a Leishmania Skin Test Antigen (LSTA) |
| DoD-009 | Identification of the Genetic Factors Which Control Tropism in Leishmania |
| DoD-010 | Pyridostigmine Synergistic Toxicity Study |
| DoD-011 | Male/Female Differential Tolerances to Pyridostigmine Bromide |
| DoD-013 | Effects of Persian Gulf War Service on Military Working Dogs |
| DoD-014 | Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry |
| DoD-015 | Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm |

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| DoD-016 | Kuwait Oil Fire Health Risk Assessment |
| DoD-017 | Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning |
| DoD-018 | Kuwait Oil Fires Troop Exposure Assessment Model (TEAM) |
| DoD-019 | Persian Gulf Veterans Health Tracking System |
| DoD-021 | Study of Variability in Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals with Symptoms Following Participation in Operation Desert Storm |
| DoD-022 | Chronic Organophosphorus Exposure and Cognition |
| DoD-023 | Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families |
| DoD-030 | Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study |
| DoD-031 | Dysregulation of the Stress Response in the Persian Gulf Syndrome |
| DoD-032 | Neuropsychological Functioning in Persian Gulf Era Veterans |
| DoD-033 | Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity |
| DoD-034 | Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents |
| DoD-035 | Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War |
| DoD-036 | Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms |
| DoD-037 | Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats |
| DoD-038 | Diagnostic Antigens of Leishmania tropica |
| DoD-039 | A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces |
| DoD-040 | Psychological and Neurobiological Consequences of the Gulf War Experience |
| DoD-041 | Evaluation of Muscle Function in Persian Gulf Veterans |
| DoD-042 | The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment |
| DoD-044 | Investigation of Seminal Plasma Hypersensitivity Reactions |
| DoD-045 | Air Force Women's Health Surveillance Study |
| DoD-046 | Exploratory Data Analysis with the CCEP Database |
| DoD-047 | Study of Mycoplasmal Infections in GW Veterans |

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| DoD-048 | Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs. Selected Control Groups |
| DoD-049 | Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts |
| DoD-050 | Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways |
| DoD-051 | Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses |
| DoD-052 | Female Gender and Other Potential Predictors of Functional Health Status Among Persian GW Veterans |
| DoD-053 | Long-Term Effects of Subclinical Exposures to Sarin |
| DoD-054 | Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure |
| DoD-055 | Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects |
| DoD-056 | Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine |
| DoD-057 | Physiologic Effects of Stress in GW Veterans |
| DoD-058 | Illness Among Persian GW Veterans: Case Validation Studies |
| DoD-059 | Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis |
| DoD-060 | Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness |
| DoD-061 | Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid |
| DoD-062 | Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice |
| DoD-063 | PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity |
| DoD-064 | Individual Differences in Neurobehavioral Effects of Pyridostigmine |
| DoD-065 | Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment |
| DoD-066 | Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction |
| DoD-067 | Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria |
| DoD-069 | Five-Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents |
| DoD-070 | War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes |
| DoD-071 | A Comparison of Post Deployment Hospitalization Between Vietnam and GW Veterans |

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| DoD-072 | Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals |
| DoD-073 | Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes |
| DoD-074 | Relationship of Stress Exposures to Health in GW Veterans |
| DoD-075 | Toxic Interactions of Prophylactic Drugs and Pesticides |
| DoD-076 | Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel |
| DoD-077 | Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War |
| DoD-078 | Experimental Models of Gulf War Syndrome |
| DoD-079 | Time Course of Stress-induced Impairment of Blood Brain Barrier |
| DoD-080 | Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells |
| DoD-081 | Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress |
| DoD-082 | Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs |
| DoD-083 | Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism |
| DoD-084 | Psychobiologic Alterations in Persian GW Veterans with and without PTSD |
| DoD-085 | CNS Cytokines and CRH in GW Veterans with Multiple Unexplained Symptoms |
| DoD-086 | Effects of Combat Stress on Structure and Function of the Hippocampus |
| DoD-087 | Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related Quality of Life among PGWVs |
| DoD-088 | Clinical Relevance of Novel Immunological Markers in PTSD |
| DoD-089 | Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder |
| DoD-090 | SPECT Benzodiazepine Receptor and MR Imaging in PTSD |
| DoD-091 | Neurological and Circadian Substrates of PTSD-like Behaviors |
| DoD-092 | Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder |
| DoD-093 | Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up |
| DoD-094 | Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. GW Veterans |
| DoD-095 | Development of Diagnostic tools and alternative treatment drugs for Leishmania |
| DoD-096 | Deployment Health Center |
| DoD-097 | Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and |

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| | Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis |
| DoD-098 | Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans |
| DoD-099 | DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: Hospitalizations |
| DoD-100 | Antibodies to Squalene |
| DoD-101 | Mechanisms in Chronic Multisymptom Illnesses |
| DoD-102 | Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans |
| DoD-103 | Human Metabolism and Interactions of Deployment-related Chemicals |
| DoD-104 | Clinical Evaluation of a Proposed New Gulf War Syndrome |
| DoD-105 | Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala |
| DoD-106 | The Role of Th1/Th2 cytokine balance in Gulf War-related illness |
| DoD-107 | Stress, Organophosphates and Blood Brain Barrier Integrity |
| DoD-108 | Health Status of Current National Guard Members |
| DoD-109 | Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms |
| DoD-110 | Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy |
| DoD-111 | Autonomic Dysfunction in GW Veterans |
| DoD-112 | Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease? |
| DoD-113 | Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects |
| DoD-114 | A Re-examination of Neuropsychological Functioning in Persian GW Veterans |
| DoD-115 | A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D) |
| DoD-116 | VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V) |
| DoD-116A | Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA) |
| DoD-116B | Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly VA/DoD- 2DB) |
| DoD-117 | Patterns of Pre-Persian Gulf War Illness and Health Care Seeking |
| DoD-118 | An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also VA-61) |

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| DoD-119 | Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also VA-55) |
| DoD-120 | Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents |
| DoD-121 | Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development |
| DoD-122 | Carcinogenic Potential of Depleted Uranium and Tungsten Alloys |
| DoD-123 | Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys |
| DoD-124 | Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin |
| DoD-125 | A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74) |
| DoD-126 | Blood-Brain Barrier Transport of Uranium |
| DoD-127 | Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man |
| DoD-128 | Multifactorial Assessment of Depleted Uranium Neurotoxicity |
| DoD-129 | Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness |
| DoD-130 | Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents |
| DoD-131 | Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses |
| DoD-132 | Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness |
| DoD-133 | Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome |
| DoD-134 | Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin |
| DoD-135 | Biochemical Markers for Exposure to Low Doses of Organophosphorus Exposure |
| DoD-136 | A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure |
| DoD-137 | Low Level Exposure to Sulfur Mustard: Development of a SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin |
| DoD-138 | Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents |
| DoD-139 | Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses |
| DoD-140 | US DOD Surveillance for Neoplasms in Infancy |
| DoD-141 | Physical, Mental, Social, and Family Health Outcomes of GW Veterans |
| DoD-142 | Illnesses Among Persian GW Veterans: Case Validation Studies (Iowa / Great Britain) |

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| DoD-143 | Millennium Cohort Study (See also VA-78) |
| DoD-144 | Psychological Health Screening: Methods and Metrics for Deployed Forces |
| DoD-145 | Early Intervention Research Program to Enhance Soldier Resilience |
| DoD-146 | Assessment of Toxicology Assays Methods & Chemical Exposures Among a Cohort of US Marines |
| DoD-147 | Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications |
| DoD-148 | Predicting operational readiness for deployed Army National Guard and Army Reserve soldiers and families |
| DoD-149 | Longitudinal Health Study of GW Veterans |
| DoD-150 | Validation Study of Gulf War Deployment Files |
| DoD-151 | Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in GW Veterans |
| DoD-152 | Characterization of Intracellular Signaling Pathways Activated by Nerve Agents |
| DoD-153 | Gulf War Illness Research |
| DoD-154 | Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-88) |
| DoD-155 | Neuropsychological Functioning in GW Veterans Exposed to Pesticides and Pyridostigmine Bromide |
| DoD-156 | The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant |
| DoD-157 | Novel Leishmania and Malaria Potassium Channels: Candidate Therapeutic Targets |
| DoD-158 | Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission of Genetic Damage to Offspring |
| DoD-159 | Neurotoxicity from Chronic Exposure to Depleted Uranium |
| DoD-160 | Characterization of the Reproductive Toxicity of Depleted Uranium |
| DoD-161 | Glutamate Receptor Aptamers and ALS |
| DoD-162 | Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function |
| DoD-163 | Neuroimmune Effects of Inhaling Low Dose Sarin |
| DoD-164 | Efficacy of Adjunct Sleep Interventions for PTSD (EASI-PTSD) |
| DoD-165 | Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military – BALSAM |
| DoD-166 | A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance |

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| DoD-167 | Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure |
| DoD-168 | Developing Biomarkers for Fibromyalgia |
| DoD-169 | Development of Novel Therapy for Chronic Neuropathic Pain |
| DoD-170 | Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I |
| DoD-171 | Q10 for GW Veterans |
| DoD-172 | CNDP1 Polymorphisms and Carnosine Therapy in GWI |
| DoD-173 | A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in GW Veterans with Chronic Multisymptom Illness |
| DoD-174 | Autonomic Biomarkers and Treatment for Gulf War Illness |
| DoD-175 | Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium |
| DoD-176 | Studies on Axonal Transport in an Animal Model for Gulf War Syndrome |
| DoD-177 | Randomized Trial of an Environmental Medicine Approach to GW Veterans' Illness |
| DoD-178 | Analysis of Paraoxonase Status among US Navy GW Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions |
| DoD-179 | Mechanisms of Mitochondrial Defects in Gulf War Syndrome |
| DoD-180 | Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of Fatigue |
| DoD-181 | Effectiveness of Acupuncture in the Treatment of Gulf War Illness |
| DoD-182 | Trial of Naltrexone and Dextromethorphan for GW Veterans' Illness |
| DoD-183 | Biomarkers of GW Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation |
| DoD-184 | Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the GW Veterans' Illnesses |
| DoD-185 | Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model |
| DoD-186 | Small Intestinal Microbial Community in Gulf War Illness |
| DoD-187 | The Use of Comprehensive Molecular Profiling with Network and Control Theory to Better Understand GWI and Model Therapeutic Strategies |
| DoD-188 | Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War Illness |
| DoD-189 | Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers |
| DoD-190 | Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness |

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| DoD-191 | Neuroimmune Interactions, Low-Dose Sarin Inhalation, and Gulf War Syndrome |
| DoD-192 | Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome |
| DoD-193 | Genome Instability: A Common Link in Gulf War Illness Patients |
| DoD-194 | Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome |
| DoD-195 | Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness |
| DoD-196 | Probiotic (Bifidobacterium Infantis) for Gulf War Illness |
| DoD-197 | Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness? |
| DoD-198 | Oxidative Stress |
| DoD-199 | Gulf War Illness: Evaluation of an Innovative Detoxification Program |
| DoD-200 | XMRV and GWI: Is There an Association? |
| DoD-201 | Synergistic Actions of Pyridostigmine Bromide and Insecticides on Muscle and Vascular Nociceptors |
| DoD-202 | Brain-Immune Interactions as Basis of Gulf War Illness: Consortium Development |
| DoD-203 | Redefining Gulf War Illness Using Longitudinal Health Data: The Devens Cohort |
| DoD-204 | Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Syndrome |
| DoD-205 | The HPA Axis and Metabolic Outcomes in GW Veterans |
| DoD-206 | Investigating Clinical Benefits of a Novel Sleep-Focused, Mind-Body Program on Gulf War Illness Symptoms: An Exploratory Randomized Controlled Trial |
| DoD-207 | Gulf War Illness Research Development Consortium (GWIC) |
| DoD-208 | Genome-Wide Association Study of a Validated Case Definition of Gulf War Illness in a Population-Representative Sample |
| DoD-209 | Proteomic Immune Profiling for the Therapeutic Modulation of Cognitive Impairment in a Novel GWI Mouse Model |
| DoD-210 | Assessment of Diverse Biological Indicators in Gulf War Illness: Are They Replicable? Are They Related? |
| DoD-211 | Detection of Xenotropic Murine Leukemia Virus-Related Virus (XMRV) in Gulf War Illness: Role in Pathogenesis or Biomarker? |
| DoD-212 | Integrative Physiology of Gulf War Illness: Role of Autonomic Function, Central Neural Processing, and Sleep |
| DoD-213 | Effectiveness of Acupressure Treatment for Pain Management and Fatigue Relief in GW Veterans |
| DoD-214 | Abnormalities in Human Brain Creatine Metabolism in Gulf War Illness Probed with MRS |
| DoD-215 | Identifying Immune Drivers of Gulf War Illness Using a Novel Daily Sampling Approach |

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| DoD-216 | Intranasal Insulin: A Novel Treatment for Gulf War Multisymptom Illness |
| DoD-217 | Efficacy of Treatments Tried: A Survey of GW Veterans |
| DoD-218 | Establishing a 1991 Veterans Research Network to ImproveCharacterization of Gulf War Illness and Provide a National Resource for Veterans and Investigators |
| DoD-219 | Organophosphate-Related Alterations in Myelin and Axonal Transport in the Living Mammalian Brain |
| DoD-220 | Biomarker Discovery in GW Veterans: Development of a War Illness Diagnostic Panel |
| DoD-221 | Role of microRNAs in the Pathobiology of Gulf War Illness: Identification of Potential Novel Therapeutic Targets |
| DoD-222 | Brain Immune Interactions as the Basis of Gulf War Illness: Gulf War Illness Consortium (GWIC) |
| DoD-223 | Persistent Neural Membrane Protein Misregulation Following Neurotoxicant Exposure |
| DoD-224 | Understanding Gulf War Illness: An Integrative Modeling Approach |
| DoD-225 | The Role of Protein Radicals in Chronic Neuroimmune Dysfunction and Neuropathology in Response to a Multiple-Hit Model of Gulf War Exposures |
| DoD-226 | Gulf War Illness: Assessment of Bioenergetics in Brain and Muscle |
| DoD-227 | Monosodium Luminol for Improving Brain Function in Gulf War Illness |
| DoD-228 | A Multimodal Evaluation of the Comparative Efficacy of Yoga versus a Patient-Centered Support Group for Treating Chronic Pain in Gulf War Illness |
| DoD-229 | Bench to Bedside: Understanding Symptom Response to Acupuncture Treatment and Designing a Successful Acupuncture Treatment Program |
| DoD-230 | An in Vivo Investigation of Brain Inflammation in Gulf War Illness with Integrated PET/MR Imaging |
| DoD-231 | Use of a Portable Stimulator to Treat GWI |
| DoD-232 | Characterizing Treatable Causes of Small Fiber Polyneuropathy in Gulf War Veterans |
| DoD-233 | Assessment of MRI-Based Markers of Dopaminergic Integrity as a Biological Indicator of Gulf War Illness |
| DoD-234 | A Prospective Open-Label Clinical Trial of Methylphenidate plus a GWI-Specific Nutrient Formula in Patients with Gulf War Illness and Concentration Disturbances |
| DoD-235 | Treating Gulf War Illness with Novel Anti-Inflammatories: A Screening of Botanical Microglia Modulators |
| DoD-236 | Development of Dietary Polyphenol Preparations for Treating Veterans with Gulf War Illness |
| DoD-237 | Direct Test for Neuroinflammation with [11C]DAP713-PET Scanning |
| DoD-238 | Restoring the Brain's Lipid Homeostasis as a Therapeutic Avenue for Treating the CNS Symptoms of Gulf War Illness |
| DoD-239 | Mitochondrial and Nuclear Genetics in Gulf War Illness |

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| DoD-240 | Novel Therapeutic Approaches for the Treatment of Depression and Cognitive Deficits in a Rodent Model of Gulf War Veterans' Illness |
| DoD-241 | Gulf War Illness Inflammation Reduction Trial |
| DoD-242 | Epigenetic Mediation of Endocrine and Immune Response in an Animal Model for Gulf War Illness |

## DEPARTMENT OF HEALTH AND HUMAN SERVICES PROJECTS

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| HHS-001 | Health Assessment of Persian GW Veterans from Iowa |
| HHS-002 | Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18 |
| HHS-003 | Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and Blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires |
| HHS-004 | Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian GW Veterans in Mississippi |
| HHS-005 | Cognitive Function and Symptom Patterns in Persian Gulf Veterans |
| HHS-006 | Defining Gulf War Illness |
| HHS-007 | Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid |
| HHS-008 | Strategy to Identify Non-Additive Response to Chemical Mixtures |
| HHS-009 | Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments |
| HHS-010 | Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline |
| HHS-011 | Deployment to the Gulf War and the Subsequent Development of Cancer |
| HHS-012 | Genetic Epidemiology of ALS in Veterans |

## DEPARTMENT OF VETERANS AFFAIRS PROJECTS

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| VA-001 | Mortality Follow-up Study of Persian Gulf Veterans |
| VA-002 | National Health Survey of Persian Gulf Veterans |
| VA-002A | VA National Survey of Persian Gulf Veterans - Phase I |
| VA-002B | VA National Survey of Persian Gulf Veterans - Phase II |
| VA-002C | VA National Survey of Persian Gulf Veterans - Phase III |
| VA-003 | Use of Roster of Veterans Who Served in Persian Gulf Area |
| VA-004 | Boston Environmental Hazards Research Center Program |
| VA-004A | Evaluation of Cognitive Functioning of Persian Gulf Veterans |
| VA-004B | Evaluation of Neurological Functioning in Persian Gulf Veterans |
| VA-004C | Gulf War and Vietnam Veterans Cancer Incidence Surveillance |
| VA-004D | Evaluation of Respiratory Dysfunction Among GW Veterans |
| VA-004E | The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility |
| VA-004F | Validity of Computerized Tests |
| VA-005 | East Orange Environmental Hazards Research Center Program |
| VA-005A | Health and Exposure Survey of Persian Gulf Veterans |
| VA-005B | Physiological and Psychological Assessments of Persian Gulf Veterans |
| VA-005C | Effects of Exertion and Chemical Stress on Persian Gulf Veterans |
| VA-005D | Effects of Genetics and Stress on Responses to Environmental Toxins |
| VA-006 | Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research |
| VA-006A | Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I) |
| VA-006B | Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II) |
| VA-006C | Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III) |
| VA-006D | DNA Damage from Chemical Agents and Its Repair (Project IV) |
| VA-006E | Clinical and Epidemiology Leishmania Research |
| VA-007 | Desert Storm Reunion Survey |
| VA-008 | Psychological Test Data of GW Veterans Over Time |

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| VA-009 | Evaluation of Cognitive Functioning in Persian GW Veterans Reporting War-related Health Problems |
| VA-010 | Memory and Attention in PTSD |
| VA-011 | Neuropsychological Functioning in Veterans |
| VA-012 | Psychological Assessment of Operation Desert Storm Returnees |
| VA-013 | Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot Study |
| VA-015 | Vaccine-Mediated Immunity Against Leishmaniasis |
| VA-016 | Protective Immunity in Experimental Visceral Leishmaniasis |
| VA-017 | Immunological Evaluation of Persian Gulf Veterans |
| VA-018 | Chronic Gastrointestinal Illness in Persian Gulf Veterans |
| VA-020 | Psychological Adjustment in Operation Desert Shield/Storm Veterans |
| VA-021 | A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in ODS |
| VA-036 | Stress Symptoms and Their Causal Attribution in Desert Storm Veterans |
| VA-040 | Musculoskeletal Symptoms in Gulf War Syndrome |
| VA-046 | Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder |
| VA-047 | Retrospective Verification of Mustard Gas Exposure |
| VA-048 | Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance |
| VA-049 | Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction |
| VA-050 | Neuropsychological findings in a sample of Operation Desert Storm Veterans |
| VA-051 | Psychobiological Assessment of Desert Storm Veterans |
| VA-053 | Spouses and Children Program |
| VA-054 | Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress |
| VA-055 | Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also DoD-119) |
| VA-056 | Birmingham's GW Veterans' Illness Demonstration Clinic (13) |
| VA-057 | Case Management and Residential Rehabilitation for Persian GW Veterans (13) |
| VA-058 | Implementation and Evaluation of GW Veterans' Demonstration Project (13) |
| VA-059 | Demonstration Treatment Program for GW Veterans with Unexplained Physical Symptoms (13) |
| VA-060 | Identification and Management of Sleep Disorders in GW Veterans |

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| VA-061 | An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also DoD-118) |
| VA-062 | A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V) |
| VA-063 | VA/DoD Core Funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D) |
| VA-063A | Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also DoD-116A; formerly VA/DoD-2VA/2DA) |
| VA-063B | Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB) |
| VA-064 | Boston Environmental Hazards Research Center |
| VA-064A | Functional Neuroimaging in Lead Exposed Adults |
| VA-064B | Quantification and Validation of Structure-Function Relationships Through Visuospatial Test Performance |
| VA-064C | Development of a Structured Neurotoxicant Assessment Checklist (SNAC) for Clinical use in Veteran Populations |
| VA-065 | San Antonio Environmental Hazards Research Center |
| VA-065A | Does a Variant of the Human SOD2 Gene Increase Sensitivity to Hazards? |
| VA-065B | The Contribution of FEN-1 to Genetic Integrity Subsequent to Oxidative Stress |
| VA-065C | The Importance of Hydrogen Peroxide Detoxification in Cellular Protection |
| VA-065D | Do Defective Gpx1 and ALDH2 Genes Increase Sensitivity to Environmental Hazards? |
| VA-066 | Physiological Responding in Posttraumatic Stress Disorder |
| VA-067 | Olfactory Functioning in GW Veterans |
| VA-068 | Family Study of Fibromyalgia |
| VA-069 | Cardiovascular Hyporeactivity and Fatiguing Illness in GW Veterans |
| VA-070 | A Clinical Evaluation of the Health Status of Persian GW Veterans in VISN 8 |
| VA-071 | Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome |
| VA-072 | Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses |
| VA-073 | Pain Sensitivity in GW Veterans with Medically Unexplained Musculoskeletal Pain |
| VA-074 | A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125) |
| VA-075 | ALS and Veterans: Are Veterans at Increased Risk? |
| VA-076 | Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD |

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| VA-077 | HPA Axis Reactivity in Men and Women with Chronic PTSD |
| VA-078 | Millennium Cohort Study (See also DoD-143) |
| VA-080 | Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress |
| VA-081 | Stress, Pro-Inflammatory Cytokines and Coping Behavior |
| VA-082 | Pituitary Adrenal Function in People with Fatiguing Illness |
| VA-083 | Neuropsychological Assessment of a Population-Based Sample of Persian GW Veterans and Controls |
| VA-084 | Neurobiology of Severe Psychological Trauma in Women |
| VA-085 | Associative Learning in Veterans with and without Combat Experience |
| VA-086 | A Clinical Trial of Magnetic Stimulation in Depression |
| VA-087 | Improving Outcomes of Depression in Primary Care |
| VA-088 | Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also DoD-154) |
| VA-089 | National Registry of Veterans with Amyotrophic Lateral Sclerosis |
| VA-090 | Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness |
| VA-090A | Neuronal Hyperexcitability and Motor Neuron Regeneration |
| VA-090B | Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders |
| VA-090C | Developmental Differences in Alcohol Withdrawal Sensitivity |
| VA-090D | Seizures and Neuroplasticity: Physiology and Biochemistry |
| VA-091 | The Role of Dietary Choline in Neuroprotection |
| VA-092 | Acetylcholinesterase Activity in GW Veterans |
| VA-093 | HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans |
| VA-094 | The Immunology of Chronic Cutaneous Leishmaniasis |
| VA-095 | The Role of Signal Regulatory Proteins in Astrocytomas |
| VA-096 | Functional Imaging of Pain in Veterans with Unexplained Muscle Pain |
| VA-097 | Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas |
| VA-098 | Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas |
| VA-099 | Vaccination Against Visceral Leishmaniasis with a Multi-Epitope Vaccine |
| VA-100 | Studies of the Blood-Brain Barrier and it's Manipulation |

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| VA-101 | Biomarkers Discovery in ALS |
| VA-102 | Cholinergic and Monoaminergic Influences on Sleep |
| VA-103 | Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal |
| VA-104 | Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome |
| VA-105 | Expression of the Major Surface Protease of Leishmania Chagasi |
| VA-106 | Interoceptive Stressor Conditioning: A Model for Gulf War Illness |
| VA-107 | Evaluation of Stress Response Systems in GW Veterans with CMI |
| VA-108 | Telemedicine Treatment for Veterans with Gulf War Illness |
| VA-109 | Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics |
| VA-110 | Pain Among GW Veterans: Secondary Analysis of CSP#458 Data |
| VA-111 | T-Cell Responses to Multiple Immunizations and Stress |
| VA-112 | National VA Amyotrophic Lateral Sclerosis Research Consortium |
| VA-113 | Novel Cause of Motor Neuron Disease |
| VA-114 | Strategies in Therapeutic Development of Neurodegenerative Diseases |
| VA-115 | Autonomic System Changes Cause Intestinal Symptoms in GW Veterans |
| VA-116 | Quantitative Trait Genes Controlling Circadian and Sleep Behaviors |
| VA-117 | Estimates of Cancer Prevalence in Gulf Veterans Using State Registries |
| VA-118 | Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004 |
| VA-119 | Patterns of Microarray Gene Expression in Gulf War Illness |
| VA-120 | Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis |
| VA-121 | Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders |
| VA-122 | Role of Mitochondrial Oxidative Stress in ALS |
| VA-123 | Interactions Between Maternal Care, Stress and Pyridostigmine Bromide |
| VA-124 | Early Life Determinants of Vulnerability to Pyridostigmine Bromide |
| VA-125 | Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla |
| VA-126 | Structural Magnetic Resonance Imaging in Gulf War-Era Veterans |
| VA-127 | Interactions of the Leishmania sp. with Mammalian Cells |
| VA-128 | MR Tracking of Stem Cells for Replacement Therapy in ALS |

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| VA-129 | Glucocorticoid Responsivity in GW Veterans |
| VA-130 | Tissue Factor and Gulf War-Associated Chronic Coagulopathies |
| VA-131 | Neuroendocrine Regulators and Proteomics in GW Veterans with CMI |
| VA-132 | Immunologic Mechanisms and Biomarkers in Gulf War Illness |
| VA-133 | Longitudinal Study of Gene Expression and Gene Products in Veterans with Gulf War Illness |
| VA-134 | Autonomic Functions of GW Veterans with Unexplained Illnesses |
| VA-135 | Motor Neuron Function of GW Veterans with Excessive Fatigue |
| VA-136 | Central Mechanisms Modulating Visceral Sensitivity |
| VA-137 | Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans |
| VA-138 | Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP |
| VA-139 | Sleep Neurobiology and Circuitry |
| VA-140 | Integrated Neuroimaging and Neuropathological Analysis of the Effects of Physical Activity on Progression and Therapy in ALS |
| VA-141 | Genetic Analysis of an Invertebrate Model of Amyotrophic Lateral Sclerosis |
| VA-142 | VA Gulf War Biorepository Trust |
| VA-143 | The Role of Protein Oxidation in the Progression of ALS |
| VA-144 | Testing the Role of Permethrin on the Progression of ALS |
| VA-145 | Proteomic Analysis of Cellular Response to Biological Warfare Agents |
| VA-146 | Direct Delivery of Neurotoxins to the Brain by an Intranasal Route |
| VA-147 | The Diagnosis and Pathogenesis of Occult Leishmaniasis |
| VA-148 | Profile of GW Veterans Who Applied for Undiagnosed Illness Compensation |
| VA-149 | Behavior of Neural Stem Cells in a Rat Model of GWS |
| VA-150 | GW Veterans Illnesses' Research IDIQ Contract with UTSW |
| VA-151 | Genetic Epidemiology of ALS |
| VA-152 | Multiple Sclerosis in GW Veterans |
| VA-153 | Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex |
| VA-154 | Imaging Pain Modulation in GW Veterans with Chronic Muscle Pain |
| VA-155 | Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis |

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| VA-156 | Gulf War Era Cohort and Biorepository (CSP 585) |
| VA-157 | A Clinical Demonstration of an EEG Brain-Computer Interface for ALS Patients (CSP 567) |
| VA-158 | Testing the Feasibility of MC CBT for Veterans with IBS |
| VA-159 | Somatic hypersensitivity in Veterans with IBS |
| VA-160 | Lipoic Acid Therapy for Experimental Autoimmune Encephalomyelitis |
| VA-161 | Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease |
| VA-162 | Transcription factors regulating sensory gene expression and pain pathways |
| VA-163 | Immunoregulation of Myelin Specific T Lymphocytes |
| VA-164 | Central Mechanisms Modulating Visceral Sensitivity (renewal of VA-136) |
| VA-165 | A Pilot Study of CPAP Adherence Promotion by Peer Buddies with Sleep Apnea |
| VA-166 | A Randomized Controlled Trial of a Mindfulness-Based Intervention for Gulf War Syndrome |
| VA-167 | Neuroprotection and Myelin Repair Mechanisms in Multiple Sclerosis |
| VA-168 | Sleep Neurobiology and Circuitry |
| VA-169 | Prevention of Hippocampal Neurodegeneration Due to Age and Apnea |
| VA-170 | Epigenetic Mechanisms Relevant to the Pathogenesis of ALS |
| VA-171 | Nanoparticle Coupled Antioxidants for Respiratory Illness in Veterans |
| VA-172 | Understanding Pain of Gastrointestinal Origin in Women that Serve in OEF/OIF |
| VA-173 | Impact of Exercise Training on Pain and Brain Function in GW Veterans |
| VA-174 | VA GW Veterans' Illnesses Biorepository |
| VA-175 | Memory and Mood Enhancing Therapiesfor Gulf War Illness |
| VA-176 | MEG Synchronous Neural Interactions (SNI) in GW Veterans |
| VA-177 | Somatic Hypersensitivity in Veterans with IBS |
| VA-178 | rTMS for the Treatment of Chronic Pain in GW1 Veterans |
| VA-179 | Vascular and Skeletal Muscle Function in Gulf War Veterans Illness |
| VA-180 | Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with GWI |
| VA-181 | Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI |
| VA-182 | Consensus Case Definition for Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans |
| VA-183 | Examination of Cognitive Fatigue in Gulf War Illness Using fMRI |

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| VA-184 | Longitudinal Assessment of Gulf War Veterans with Suspected Sarin Exposure |
| VA-185 | Identification of Plasma Biomarkers of Gulf War Illness Using “omic” Technology |
| VA-186 | Gulf War Exposures and the Molecular Mechanisms of Paternal Reproductive Risk |
| VA-187 | Multimodal Biological Assessment of Gulf War Illness |
| VA-188 | Complementary Neurosteroid Intervention in Gulf War Veterans’ Illnesses |
| VA-189 | CAM in Veterans with Gulf War Illnesses |
| VA-190 | Cognitive Rehabilitation for Gulf War Illness |
| VA-191 | Novel Neurotrophic Therapies in an Optimized Mouse Model of GWVI |
| VA-192 | Women vs. Men with GWI: Differences in Computational Models and Therapeutic Targets |
| VA-193 | Neuroinflammation, Oxidative Stress, and Hippocampal Defects in Gulf War Illness |

# Appendix B

## Project List by Research Focus Areas

## Brain and Nervous System Function

### Clinical

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Diagnosis | DoD-165 | Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military – BALSAM |
| | Diagnosis | DoD-230 | An in Vivo Investigation of Brain Inflammation in Gulf War Illness with Integrated PET/MR Imaging |
| | Diagnosis | DoD-232 | Characterizing Treatable Causes of Small Fiber Polyneuropathy in Gulf War Veterans |
| | Diagnosis | DoD-233 | Assessment of MRI-Based Markers of Dopaminergic Integrity as a Biological Indicator of Gulf War Illness |
| | Diagnosis | DoD-237 | Direct Test for Neuroinflammation with [11C]DAP713-PET Scanning |
| | Symptoms | VA-142 | VA Gulf War Biorepository Trust |
| | Treatment | VA-157 | A Clinical Demonstration of an EEG Brain-Computer Interface for ALS Patients (CSP 567) |
| | Treatment | VA-188 | Complementary Neurosteroid Intervention in Gulf War Veterans' Illnesses |
| | Treatment | VA-190 | Cognitive Rehabilitation for Gulf War Illness |
| | Treatment | DoD-228 | A Multimodal Evaluation of the Comparative Efficacy of Yoga versus a Patient-Centered Support Group for Treating Chronic Pain in Gulf War Illness |
| | Treatment; Symptoms | DoD-166 | A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance |
| Environmental Toxicology | Symptoms; Exposure | VA-064 A | Functional Neuroimaging in Lead Exposed Adults |
| Environmental Toxicology; | Symptoms; Chemical Weapons | DoD-063 | PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity |
| Immune Function; Symptoms and General Health | Symptoms | VA-005 B | Physiological and Psychological Assessments of Persian Gulf Veterans |
| Symptoms and General Health | Diagnosis | DoD-032 | Neuropsychological Functioning in Persian Gulf Era Veterans |
| Symptoms and General Health | Symptoms | DoD-040 | Psychological and Neurobiological Consequences of the Gulf War Experience |
| Symptoms and General Health | Prevention | DoD-083 | Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism |
| Symptoms and General Health | Symptoms | DoD-084 | Psychobiologic Alterations in Persian GW Veterans with and without PTSD |
| Symptoms and General Health | Symptoms | DoD-086 | Effects of Combat Stress on Structure and Function of the Hippocampus |
| Symptoms and General Health | Symptoms | DoD-089 | Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder |

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| Symptoms and General Health | Diagnosis | DoD-090 | SPECT Benzodiazepine Receptor and MR Imaging in PTSD |
| Symptoms and General Health | Symptoms | DoD-132 | Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness |
| Symptoms and General Health | Diagnosis | DoD-147 | Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications |
| Symptoms and General Health | Treatment | DoD-212 | Integrative Physiology of Gulf War Illness: Role of Autonomic Functi on, Central Neural Processing, and Sleep |
| Symptoms and General Health | Symptoms | HHS-005 | Cognitive Function and Symptom Patterns in Persian Gulf Veterans |
| Symptoms and General Health | Symptoms | VA-004 | Boston Environmental Hazards Research Center Program |
| Symptoms and General Health | Symptoms | VA-004 A | Evaluation of Cognitive Functioning of Persian Gulf Veterans |
| Symptoms and General Health | Symptoms | VA-004 B | Evaluation of Neurological Functioning in Persian Gulf Veterans |
| Symptoms and General Health | Diagnosis | VA-004 F | Validity of Computerized Tests |
| Symptoms and General Health | Symptoms | VA-005 | East Orange Environmental Hazards Research Center Program |
| Symptoms and General Health | Symptoms | VA-006 A | Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I) |
| Symptoms and General Health | Symptoms | VA-007 | Desert Storm Reunion Survey |
| Symptoms and General Health | Symptoms | VA-009 | Evaluation of Cognitive Functioning in Persian Gulf War Veterans Reporting War-related Health Problems |
| Symptoms and General Health | Symptoms | VA-010 | Memory and Attention in PTSD |
| Symptoms and General Health | Symptoms | VA-011 | Neuropsychological Functioning in Veterans |
| Symptoms and General Health | Symptoms | VA-012 | Psychological Assessment of Operation Desert Storm Returnees |
| Symptoms and General Health | Symptoms | VA-013 | Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot Study |
| Symptoms and General Health | Symptoms | VA-020 | Psychological Adjustment in Operation Desert Shield/Storm Veterans |
| Symptoms and General Health | Symptoms | VA-021 | A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in ODS |
| Symptoms and General Health | Symptoms | VA-050 | Neuropsychological findings in a sample of Operation Desert Storm Veterans |
| Symptoms and General Health | Symptoms | VA-051 | Psychobiological Assessment of Desert Storm Veterans |
| Symptoms and General Health | Symptoms | VA-054 | Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress |
| Symptoms and General Health | Symptoms | VA-064 | Boston Environmental Hazards Research Center |
| Symptoms and General Health | Symptoms | VA-066 | Physiological Responding in Posttraumatic Stress Disorder |
| Symptoms and General Health | Symptoms | VA-072 | Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses |
| Symptoms and General Health | Symptoms | VA-076 | Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD |

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| Symptoms and General Health | Symptoms | VA-077 | HPA Axis Reactivity in Men and Women with Chronic PTSD |
| Symptoms and General Health | Symptoms | VA-083 | Neuropsychological Assessment of a Population-Based Sample of Persian GW Veterans and Controls |
| Symptoms and General Health | Symptoms | VA-084 | Neurobiology of Severe Psychological Trauma in Women |
| Symptoms and General Health | Symptoms | VA-085 | Associative Learning in Veterans with and without Combat Experience |
| Symptoms and General Health | Treatment | VA-089 | National Registry of Veterans with Amyotrophic Lateral Sclerosis |
| Symptoms and General Health | Symptoms | VA-093 | HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans |
| Symptoms and General Health | Treatment | VA-112 | National VA Amyotrophic Lateral Sclerosis Research Consortium |
| Symptoms and General Health | Diagnosis | VA-125 | Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla |
| Symptoms and General Health | Diagnosis | DoD-238 | Restoring the Brain's Lipid Homeostasis as a Therapeutic Avenue for Treating the CNS Symptoms of Gulf War Illness |
| Symptoms and General Health | Treatment | VA-181 | Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI |
| Symptoms and General Health | Treatment | DoD-240 | Novel Therapeutic Approaches for the Treatment of Depression and Cognitive Deficits in a Rodent Model of Gulf War Veterans' Illness |
| Symptoms and General Health | Symptoms; Diagnosis | DoD-065 | Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment |
| Symptoms and General Health | Symptoms; Exposure | DoD-057 | Physiologic Effects of Stress in GW Veterans |
| Symptoms and General Health | Symptoms; Exposure | DoD-133 | Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome |
| Symptoms and General Health | Diagnosis; Symptoms | DoD-087 | Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related Quality of Life among PGWVs |
| Symptoms and General Health | Treatment; Symptoms | DoD-125 | A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74) |
| Symptoms and General Health | Diagnosis; Symptoms | DoD-131 | Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses |
| Symptoms and General Health | Diagnosis; Symptoms | DoD-144 | Psychological Health Screening: Methods and Metrics for Deployed Forces |
| Symptoms and General Health | Diagnosis; Symptoms | DoD-153 | Gulf War Illness Research |
| Symptoms and General Health | Treatment; Symptoms | DoD-164 | Efficacy of Adjunct Sleep Interventions for PTSD (EASI- PTSD) |
| Symptoms and General Health | Treatment; Symptoms | VA-060 | Identification and Management of Sleep Disorders in Gulf War Veterans |
| Symptoms and General Health | Diagnosis; Symptoms | VA-064 B | Quantification and Validation of Structure-Function relationships through visuospatial test performance |
| Symptoms and General Health | Diagnosis; Symptoms | VA-067 | Olfactory Functioning in GW Veterans |
| Symptoms and General Health | Treatment; Symptoms | VA-074 | A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125) |

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| Symptoms and General Health | Treatment; Symptoms | VA-086 | A Clinical Trial of Magnetic Stimulation in Depression |
| Symptoms and General Health | Treatment | VA-087 | Improving Outcomes of Depression in Primary Care |
| | Symptoms | | |
| Symptoms and General Health | Treatment; Symptoms | VA-138 | Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP |
| Symptoms and General Health; | Symptoms; Environmental Toxicology | VA-008 | Psychological Test Data of GW Veterans Over Time |
| Symptoms and General Health; | Symptoms; Diagnosis | DoD-197 | Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness? |

## Development

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Diagnosis | HHS-013 | ALS Biomarkers in the Cerebrospinal Fluid |
| | Diagnosis | VA-184 | Longitudinal Assessment of Gulf War Veterans with Suspected Sarin Exposure |
| | Treatment | DoD-189 | Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers |
| | Treatment | VA-160 | Lipoic Acid Therapy for Experimental Autoimmune Encephalomyelitis |
| | Treatment | DoD-231 | Use of a Portable Stimulator to Treat GWI |
| | Symptoms | VA-183 | Examination of Cognitive Fatigue in Gulf War Illness Using fMRI |
| Environmental Toxicology | Treatment; Exposure; Symptoms | DoD-184 | Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the GW Veterans' Illnesses |
| Symptoms and General Health | Diagnosis | VA-113 | Novel Cause of Motor Neuron Disease |
| Symptoms and General Health | Treatment; Prevention | VA-097 | Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas |
| Symptoms and General Health | Diagnosis; Symptoms | VA-101 | Biomarkers Discovery in ALS |
| Symptoms and General Health | Treatment; Symptoms | VA-128 | MR Tracking of Stem Cells for Replacement Therapy in ALS |

## Epidemiology

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| Symptoms and General Health | Symptoms | DoD-023 | Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families |
| Symptoms and General Health | Symptoms | DoD-082 | Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs |
| Symptoms and General Health | Symptoms | DoD-114 | A Re-examination of Neuropsychological Functioning in Persian GW Veterans |
| Symptoms and General Health | Symptoms | DoD-118 | An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also VA-61) |

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| Symptoms and General Health | Symptoms | HHS-006 | Defining Gulf War Illness |
| Symptoms and General Health | Diagnosis | HHS-012 | Genetic Epidemiology of ALS in Veterans |
| Symptoms and General Health | Symptoms | VA-036 | Stress Symptoms and Their Causal Attribution in Desert Storm Veterans |
| Symptoms and General Health | Symptoms | VA-061 | An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also DoD-118) |
| Symptoms and General Health | Symptoms | VA-068 | Family Study of Fibromyalgia |
| Symptoms and General Health | Symptoms | VA-075 | ALS and Veterans: Are Veterans at Increased Risk? |
| Symptoms and General Health | Symptoms | VA-110 | Pain Among GW Veterans: Secondary Analysis of CSP#458 Data |
| Symptoms and General Health | Symptoms | VA-150 | GW Veterans Illnesses' Research IDIQ Contract |
| Symptoms and General Health | Diagnosis | VA-151 | Genetic Epidemiology of ALS Veterans |
| Symptoms and General Health | Symptoms | VA-152 | Multiple Sclerosis in GW Veterans |
| Symptoms and General Health | Symptoms | DoD-227 | Monosodium Luminol for Improving Brain Function in Gulf War Illness |
| Symptoms and General Health | Symptoms; Diagnosis | DoD-104 | Clinical Evaluation of a Proposed New Gulf War Syndrome |
| Symptoms and General Health | Treatment; Prevention | DoD-145 | Early Intervention Research Program to Enhance Soldier Resilience |
| Symptoms and General Health | Diagnosis; Symptoms | DoD-052 | Female Gender and Other Potential Predictors of Functional Health Status Among Persian GW Veterans |
| Symptoms and General Health | Diagnosis; Symptoms | DoD-154 | Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-088) |
| Symptoms and General Health | Diagnosis; Symptoms | HHS-002 | Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18 |
| Symptoms and General Health | Diagnosis; Symptoms | VA-088 | Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also DoD-154) |

## Mechanistic

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Diagnosis | VA-174 | VA GW Veterans' Illnesses Biorepository |
| | Diagnosis | VA-176 | MEG Synchronous Neural Interactions (SNI) in GW Veterans |
| | Diagnosis | VA-187 | Multimodal Biological Assessment of Gulf War Illness |
| | Diagnosis | VA-193 | Neuroinflammation, Oxidative Stress, and Hippocampal Defects in Gulf War Illness |
| | Symptoms | VA-091 | The Role of Dietary Choline in Neuroprotection |
| | Symptoms | VA-120 | Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis |

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| | Symptoms | VA-139 | Sleep Neurobiology and Circuitry |
| | Symptoms | VA-141 | Genetic Analysis of an Invertebrate Model of Amyotrophic Lateral Sclerosis |
| | Treatment | DoD-161 | Glutamate Receptor Aptamers and ALS |
| | Treatment | VA-140 | Integrated Neuroimaging and Neuropathological Analysis of the Effects of Physical Activity on Progression and Therapy in ALS |
| | Treatment | VA-163 | Immunoregulation of Myelin Specific T Lymphocytes |
| | Treatment | VA-191 | Novel Neurotrophic Therapies in an Optimized Mouse Model of GWVI |
| | Treatment; Symptoms | VA-161 | Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease |
| Environmental Toxicology | Exposure; Interactions; Treatment | VA-175 | Memory and Mood Enhancing Therapies for Gulf War Illness |
| Environmental Toxicology | Symptoms | VA-126 | Structural Magnetic Resonance Imaging in Gulf War-Era Veterans |
| Environmental Toxicology | Symptoms; Exposure | DoD-176 | Studies on Axonal Transport in an Animal Model for Gulf War Syndrome |
| Environmental Toxicology | Exposure; Symptoms | DoD-190 | Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness |
| Environmental Toxicology Chemical Weapons | Exposure; Symptoms | DoD-219 | Organophosphate-Related Alterations in Myelin and Axonal Transport in the Living Mammalian Brain |
| Environmental Toxicology; | Treatment; Exposure; Immune Function | DoD-185 | Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model |
| Environmental Toxicology; Symptoms and General Health | Symptoms; Exposure | DoD-170 | Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I |
| Environmental Toxicology; Symptoms and General Health | Symptoms; Exposure | DoD-198 | Oxidative Stress |
| Symptoms and General Health | Symptoms | DoD-080 | Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells |
| Symptoms and General Health | Symptoms | DoD-091 | Neurological and Circadian Substrates of PTSD-like Behaviors |
| Symptoms and General Health | Symptoms | DoD-092 | Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder |
| Symptoms and General Health | Symptoms | DoD-105 | Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala |
| Symptoms and General Health | Treatment; Diagnosis | DoD-205 | The HPA Axis and Metabolic Outcomes in GW Veterans |
| Symptoms and General Health | Symptoms | VA-081 | Stress, Pro-Inflammatory Cytokines and Coping Behavior |
| Symptoms and General Health | Symptoms | VA-090 | Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness |
| Symptoms and General Health | Symptoms | VA-090A | Neuronal Hyperexcitability and Motor Neuron Regeneration |
| Symptoms and General Health | Symptoms | VA-090B | Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders |
| Symptoms and General Health | Symptoms | VA-090C | Developmental Differences in Alcohol Withdrawal Sensitivity |
| Symptoms and General Health | Symptoms | VA-090D | Seizures and Neuroplasticity: Physiology and Biochemistry |
| Symptoms and General Health | Symptoms | VA-092 | Acetylcholinesterase Activity in GW Veterans |

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| Symptoms and General Health | Symptoms | VA-095 | The Role of Signal Regulatory Proteins in Astrocytomas |
| Symptoms and General Health | Symptoms | VA-098 | Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas |
| Symptoms and General Health | Symptoms | VA-103 | Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal |
| Symptoms and General Health | Symptoms | VA-109 | Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics |
| Symptoms and General Health | Treatment | VA-114 | Strategies in Therapeutic Development of Neurodegenerative Diseases |
| Symptoms and General Health | Symptoms | VA-116 | Quantitative Trait Genes Controlling Circadian and Sleep Behaviors |
| Symptoms and General Health | Symptoms | VA-121 | Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders |
| Symptoms and General Health | Symptoms | VA-122 | Role of Mitochondrial Oxidative Stress in ALS |
| Symptoms and General Health | Symptoms | VA-129 | Glucocorticoid Responsivity in GW Veterans |
| Symptoms and General Health | Diagnosis; Symptoms | DoD-214 | Abnormalities in Human Brain Creatine Metabolism in Gulf War Illness Probed with MRS |
| Symptoms and General Health | Treatment; Symptoms | VA-100 | Studies of the Blood-Brain Barrier and its Manipulation |
| Symptoms and General Health | Prevention; Symptoms | VA-102 | Cholinergic and Monoaminergic Influences on Sleep |
| Symptoms and General Health | Treatment | VA-167 | Neuroprotection and Myelin Repair Mechanisms in Multiple Sclerosis |
| Symptoms and General Health | Treatment | VA-168 | Sleep Neurobiology and Circuitry |
| Symptoms and General Health | Treatment; Prevention | VA-169 | Prevention of Hippocampal Neurodegeneration Due to Age and Apnea |
| Symptoms and General Health | Diagnosis; Prevention | VA-170 | Epigenetic Mechanisms Relevant to the Pathogenesis of ALS |
| Immune Function | Treatment | DoD-202 | Brain-Immune Interactions as Basis of Gulf War Illness: Consortium Development |
| Immune Function | Diagnosis; Symptoms | DoD-222 | Brain Immune Interactions as the Basis of Gulf War Illness: Gulf War Illness Consortium (GWIC) |

## Environmental Toxicology

### Clinical

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| Brain and Nervous System Function | Interactions; Exposure; Symptoms | VA-048 | Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance |
| Brain and Nervous System Function; Symptoms and General Health | Exposure; Symptoms | VA-005 C | Effects of Exertion and Chemical Stress on Persian Gulf Veterans |
| Chemical Weapons | Symptoms | DoD-060 | Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness |
| Chemical Weapons | Exposure | DoD-146 | Assessment of Toxicology Assay Methods and Chemical Exposures Among a Cohort of US Marines Deployed in the Gulf War |
| Pyridostigmine Bromide | Exposure; Prevention | DoD-011 | Male/Female Differential Tolerances to Pyridostigmine Bromide |

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| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-124 | Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure Interactions | DoD-155 | Neuropsychological Functioning in GW Veterans Exposed to Pesticides and Pyridostigmine Bromide Symptoms |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Symptoms | DoD-064 | Individual Differences in Neurobehavioral Effects of Pyridostigmine |
| Symptoms and General Health | Exposure; Symptoms | VA-004 D | Evaluation of Respiratory Dysfunction Among GW Veterans |
| Symptoms and General Health; Brain and Nervous System Function | Exposure; Symptoms | DoD-156 | The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant |

## Development

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Interactions; Exposure | DoD-034 | Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents |
| | Diagnosis; Exposure | DoD-134 | Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin |
| | Exposure; Interactions | HHS-008 | Strategy to Identify Non-Additive Response to Chemical Mixtures |
| Brain and Nervous System Function; Symptoms and General Health | Diagnosis; Exposure; Symptoms | VA-064 C | Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in Veteran populations |
| Chemical Weapons | Diagnosis | DoD-049 | Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts |
| Chemical Weapons | Exposure; Diagnosis | DoD-138 | Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents |
| Chemical Weapons | Diagnosis; Exposure | DoD-050 | Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways |
| Chemical Weapons | Diagnosis; Exposure | DoD-137 | Low Level Exposure to Sulfur Mustard: Development of an SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin |
| Chemical Weapons | Diagnosis; Exposure | DoD-167 | Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure |
| Symptoms and General Health | Diagnosis; Exposure | DoD-018 | Kuwait Oil Fires Troop Exposure Assessment Model (TEAM) |
| Symptoms and General Health | Diagnosis; Exposure | DoD-019 | Persian Gulf Veterans Health Tracking System |
| Symptoms and General Health | Diagnosis; Exposure | DoD-100 | Antibodies to Squalene |
| Symptoms and General Health | Diagnosis; Exposure; Symptoms | DoD-016 | Kuwait Oil Fire Health Risk Assessment |
| Symptoms and General Health | Diagnosis | DoD-221 | Role of microRNAs in the Pathobiology of Gulf War Illness: Identification of Potential Novel Therapeutic Targets |

## Epidemiology

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| Chemical Weapons | Exposure; Symptoms | DoD-116 A | Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA) |
| Chemical Weapons | Exposure; Symptoms | VA-063 A | Follow-Up Investigation of troops exposed to nerve agents at Aberdeen Proving Ground (Pilot Study) (See also DoD-116A; formerly VA/DoD-2VA/2DA) |
| Chemical Weapons; Symptoms and General Health | Exposure; Symptoms | DoD-069 | Five Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents |
| Chemical Weapons; Symptoms and General Health | Exposure; Symptoms | DoD-093 | Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up |
| Pyridostigmine Bromide | Exposure | DoD-017 | Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent |
| Pyridostigmine Bromide | Prevention; Exposure | DoD-021 | Study of Variability in Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals with Symptoms Following Participation in Operation Desert Storm |
| Symptoms and General Health | Symptoms | DoD-013 | Effects of Persian Gulf War Service on Military Working Dogs |
| Symptoms and General Health | Exposure; Symptoms | DoD-094 | Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. GW Veterans |
| Symptoms and General Health | Exposure; Symptoms | DoD-099 | DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: Hospitalizations |
| Symptoms and General Health | Exposure; Symptoms | VA-003 | Use of Roster of Veterans Who Served in Persian Gulf Area |
| Symptoms and General Health | Exposure; Symptoms | VA-006 | Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research |

## Mechanistic

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Exposure; Interactions | DoD-103 | Human Metabolism and Interactions of Deployment-related Chemicals |
| | Exposure; Interactions | VA-145 | Proteomic Analysis of Cellular Response to Biological Warfare Agents |
| | Exposure; Prevention | HHS-003 | Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires |
| | Exposure; Prevention | VA-004 E | The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility |
| | Exposure; Prevention | VA-171 | Nanoparticle Coupled Antioxidants for Respiratory Illness in Veterans |
| | Exposure; Symptoms | DoD-223 | Persistent Neural Membrane Protein Misregulation Following Neurotoxicant Exposure |

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| Brain and Nervous System Function | Exposure | DoD-175 | Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium |
| Brain and Nervous System Function | Interactions; Exposure; Symptoms | DoD-178 | Analysis of Paraoxonase Status among US Navy GW Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions |
| Brain and Nervous System Function | Exposure; Interactions | VA-146 | Direct Delivery of Neurotoxins to the Brain by an Intranasal Route |
| Brain and Nervous System Function | Exposure; Prevention | DoD-159 | Neurotoxicity from Chronic Exposure to Depleted Uranium |
| Brain and Nervous System Function | Exposure; Symptoms | VA-144 | Testing the Role of Permethrin on the Progression of ALS |
| Brain and Nervous System Function | Exposure; Symptoms | VA-149 | Behavior of Neural Stem Cells in a Rat Model of GWS |
| Brain and Nervous System Function; Chemical Weapons | Exposure; Symptoms | DoD-022 | Chronic Organophosphorus Exposure and Cognition |
| Brain and Nervous System Function; Immune Function | Exposure; Interactions; Symptoms | DoD-037 | Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats |
| Brain and Nervous System Function; | Exposure | DoD-126 | Blood-Brain Barrier Transport of Uranium |
| Brain and Nervous System Function; | Exposure; Symptoms | DoD-128 | Multifactorial Assessment of Depleted Uranium Neurotoxicity |
| Brain and Nervous System Function; | Exposure; Symptoms | DoD-129 | Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness |
| Brain and Nervous System Function; Pyridostigmine Bromide | Exposure; Interactions | DoD-201 | Synergistic Actions of Pyridostigmine Bromide and Insecticides on Muscle and Vascular Nociceptors |
| Brain and Nervous System Function; Pyridostigmine Bromide | Exposure; Symptoms | VA-143 | The Role of Protein Oxidation in the Progression of ALS |
| Brain and Nervous System Function; Symptoms and General Health | Exposure; Symptoms | DoD-007 A | Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling |
| Brain and Nervous System Function | Exposure; Interactions | DoD-225 | The Role of Protein Radicals in Chronic Neuroimmune Dysfunction and Neuropathology in Response to a Multiple-Hit Model of Gulf War Exposures |
| Chemical Weapons | Exposure; Diagnosis | DoD-136 | A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure |
| Chemical Weapons; Brain and Nervous System Function | Exposure | VA-006 D | DNA Damage from Chemical Agents and Its Repair (Project IV) |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Diagnosis | DoD-135 | Biochemical Markers for Exposure to Low Doses of Organophosphorus Exposure |
| Chemical Weapons; Brain and Nervous System Function | Prevention; Exposure | DoD-051 | Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-054 | Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-055 | Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-056 | Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine |

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| Chemical Weapons;<br>Brain and Nervous System Function | Exposure;<br>Interactions;<br>Symptoms | DoD-061 | Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid |
| Chemical Weapons;<br>Brain and Nervous System Function | Exposure;<br>Interactions; Symptoms | DoD-062 | Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice |
| Chemical Weapons;<br>Brain and Nervous System Function | Exposure;<br>Interactions; Symptoms | DoD-072 | Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals |
| Chemical Weapons;<br>Brain and Nervous System Function | Exposure;<br>Interactions; Symptoms | DoD-113 | Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects |
| Chemical Weapons;<br>Brain and Nervous System Function | Exposure;<br>Symptoms | DoD-053 | Long-Term Effects of Subclinical Exposures to Sarin |
| Chemical Weapons;<br>Brain and Nervous System Function | Exposure;<br>Symptoms | DoD-152 | Characterization of Intracellular Signaling Pathways Activated by Nerve Agents |
| Immune Function | Exposure;<br>Interactions | HHS-007 | Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid |
| Immune Function | Exposure; Symptoms | DoD-163 | Neuroimmune Effects of Inhaling Low Dose Sarin |
| Immune Function and Infectious Diseases | Exposure;<br>Symptoms | DoD-191 | Neuroimmune Interactions, Low-Dose Sarin Inhalation, and Gulf War Syndrome |
| Immune Function | Exposure | DoD-123 | Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys |
| Immune Function<br>Pyridostigmine Bromide | Exposure;<br>Interactions | DoD-077 | Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War |
| Immune Function<br>Symptoms and General Health | Exposure;<br>Symptoms | DoD-130 | Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents |
| Pyridostigmine Bromide | Prevention;<br>Exposure | DoD-033 | Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity |
| Pyridostigmine Bromide | Exposure;<br>Interactions | DoD-010 | Pyridostigmine Synergistic Toxicity Study |
| Pyridostigmine Bromide;<br>Brain and Nervous System Function | Exposure;<br>Interactions | DoD-002 | Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET |
| Pyridostigmine Bromide;<br>Brain and Nervous System Function | Exposure;<br>Interactions | DoD-075 | Toxic Interactions of Prophylactic Drugs and Pesticides |
| Pyridostigmine Bromide;<br>Brain and Nervous System Function | Exposure;<br>Interactions | DoD-107 | Stress, Organophosphates and Blood Brain Barrier Integrity |
| Pyridostigmine Bromide;<br>Brain and Nervous System Function | Exposure;<br>Interactions; Symptoms | DoD-078 | Experimental Models of Gulf War Syndrome |
| Pyridostigmine Bromide;<br>Brain and Nervous System Function | Exposure;<br>Interactions; Symptoms | DoD-079 | Time Course of Stress-induced Impairment of Blood Brain Barrier |
| Pyridostigmine Bromide;<br>Brain and Nervous System Function | Exposure;<br>Interactions; Symptoms | DoD-139 | Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses |
| Pyridostigmine Bromide;<br>Brain and Nervous System Function | Exposure;<br>Interactions; Symptoms | VA-006 C | Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III) |
| Pyridostigmine Bromide;<br>Brain and Nervous System Function | Exposure;<br>Interactions; Symptoms | VA-080 | Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress |

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| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Symptoms | DoD-059 | Pyridostigmine-induced Neurodegeneration: Role of Neuronal Apoptosis |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Symptoms | VA-049 | Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Symptoms | VA-106 | Interoceptive Stressor Conditioning: A Model for Gulf War Illness |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Symptoms | VA-123 | Interactions Between Maternal Care, Stress and Pyridostigmine Bromide |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Symptoms | VA-124 | Early Life Determinants of Vulnerability to Pyridostigmine Bromide |
| Pyridostigmine Bromide; Symptoms and General Health | Exposure; Interactions; Symptoms | VA-005 D | Effects of Genetics and Stress on Responses to Environmental Toxins |
| Reproductive Health; | Exposure; Symptoms | DoD-121 | Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development |
| Symptoms and General Health | Exposure | VA-065 | San Antonio Environmental Hazards Research Center |
| Symptoms and General Health | Exposure | VA-065 A | Does a variant of the human SOD2 gene increase sensitivity to hazards? |
| Symptoms and General Health | Exposure | VA-065 B | The contribution of FEN-1 to genetic integrity subsequent to oxidative stress |
| Symptoms and General Health | Exposure | VA-065 C | The importance of hydrogen peroxide detoxification in cellular protection |
| Symptoms and General Health | Exposure | VA-065 D | Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental hazards? |
| Symptoms and General Health | Symptoms | VA-155 | Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis |
| Symptoms and General Health | Exposure; Symptoms | DoD-160 | Characterization of the Reproductive Toxicity of Depleted Uranium |
| Symptoms and General Health | Exposure; Symptoms | DoD-192 | Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome |
| Symptoms and General Health; | Exposure | DoD-007 B | Carcinogenicity of Depleted Uranium Fragments |
| Symptoms and General Health; | Exposure; Symptoms | DoD-122 | Carcinogenic Potential of Depleted Uranium and Tungsten Alloys |
| Symptoms and General Health; | Exposure; Symptoms | DoD-127 | Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man |

## Immune Function and Infectious Diseases

### Clinical

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Diagnosis | DoD-047 | Study of Mycoplasmal Infections in GW Veterans |
| | Symptoms | DoD-048 | Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs. Selected Control |

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| | Diagnosis | VA-147 | The Diagnosis and Pathogenesis of Occult Leishmaniasis |
| | Diagnosis; Treatment | VA-006 E | Clinical and Epidemiology Leishmania Research |
| Brain and Nervous System Function | Symptoms | DoD-088 | Clinical Relevance of Novel Immunological Markers in PTSD |
| Brain and Nervous System Function | Symptoms | VA-017 | Immunological Evaluation of Persian Gulf Veterans |
| Environmental Toxicology | Exposure; Interactions; Symptoms | DoD-106 | The Role of Th1/Th2 cytokine balance in Gulf War-related illness |
| Symptoms and General Health | Treatment; Diagnosis | DoD-067 | Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria |
| Symptoms and General Health | Symptoms; Exposure | VA-006 B | Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II) |
| Symptoms and General Health | Exposure; Interactions | DoD-162 | Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function |
| Symptoms and General Health | Exposure; Symptoms | DoD-042 | The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment |
| Symptoms and General Health | Treatment; Symptoms | DoD-119 | Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also VA-55) |
| Symptoms and General Health | Treatment; Symptoms | VA-055 | Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also DoD-119) |

## Development

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Diagnosis | DoD-008 A | Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL) |
| | Diagnosis | DoD-008 B | Development of a Leishmania Skin Test Antigen (LSTA) |
| | Diagnosis | DoD-038 | Diagnostic Antigens of Leishmania tropica |
| | Diagnosis | DoD-066 | Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction |
| | Diagnosis; Treatment | DoD-095 | Development of Diagnostic tools and alternative treatment drugs for Leishmania |
| Symptoms and General Health | Diagnosis | DoD-097 | Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis |
| Symptoms and General Health | Prevention; Symptoms | VA-099 | Vaccination Against Visceral Leishmaniasis with a multi-epitope vaccine |

## Mechanistic

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Treatment | DoD-009 | Identification of the Genetic Factors Which Control Tropism in Leishmania |
| | Treatment | DoD-157 | Novel Leishmania and Malaria Potassium Channels: Candidate Therapeutic Targets |
| | Prevention | VA-015 | Vaccine-Mediated Immunity Against Leishmaniasis |
| | Prevention | VA-016 | Protective Immunity in Experimental Visceral Leishmaniasis |

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| | Symptoms | VA-127 | Interactions of the Leishmania sp. with Mammalian Cells |
| | Symptoms | DoD-215 | Identifying Immune Drivers of Gulf War Illness Using a Novel Daily Sampling Approach |
| | Prevention; Treatment | VA-094 | The Immunology of Chronic Cutaneous Leishmaniasis |
| Brain and Nervous System Function | Symptoms | DoD-195 | Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness |
| Environmental Toxicology | Diagnosis | DoD-242 | Epigenetic Mediation of Endocrine and Immune Response in an Animal Model for Gulf War Illness |
| Environmental Toxicology | Exposure | DoD-151 | Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in GW Veterans |
| Environmental Toxicology | Exposure; Interactions | DoD-112 | Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease? |
| Environmental Toxicology; Pyridostigmine Bromide | Exposure; Interactions | DoD-076 | Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel |
| Environmental Toxicology; Pyridostigmine Bromide | Exposure; Interactions; Symptoms | DoD-081 | Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress |
| Symptoms and General Health | Symptoms | VA-111 | T Cell Responses to Multiple Immunizations and Stress |
| Symptoms and General Health | Treatment; Symptoms | VA-105 | Expression of the Major Surface Protease of Leishmania Chagasi |

# Reproductive Health

## Clinical

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Exposure | VA-186 | Gulf War Exposures and the Molecular Mechanisms of Paternal Reproductive Risk |
| | Symptoms | VA-053 | Spouses and Children Program |
| Environmental Toxicology; Chemical Weapons | Symptoms | VA-047 | Retrospective Verification of Mustard Gas Exposure |
| Immune Function | Symptoms | DoD-044 | Investigation of Seminal Plasma Hypersensitivity Reactions |

## Epidemiology

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Prevention | DoD-001 C | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among Gulf War Veterans and other active-duty personnel |
| | Prevention | DoD-001 D | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in GW Veterans |

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| | Symptoms | DoD-001 G | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian GW Veterans |
| | Prevention; Symptoms | DoD-035 | Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War. |
| | Prevention; Symptoms | HHS-004 | Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian GW Veterans in Mississippi |

### Mechanistic

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| Environmental Toxicology | Exposure; Symptoms | DoD-158 | Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission of Genetic Damage to Offspring |

## Symptoms and General Health

### Clinical

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Symptoms | DoD-001 A | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees |
| | Diagnosis | DoD-109 | Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms |
| | Symptoms | VA-018 | Chronic Gastrointestinal Illness in Persian Gulf Veterans |
| | Symptoms | VA-040 | Musculoskeletal Symptoms in Gulf War Syndrome |
| | Treatment; Diagnosis; Symptoms | DoD-172 | CNDP1 Polymorphisms and Carnosine Therapy in GWI |
| | Treatment; Symptoms | DoD-171 | Q10 for GW Veterans |
| | Treatment; Symptoms | DoD-181 | Effectiveness of Acupuncture in the Treatment of Gulf War Illness |
| | Treatment; Symptoms | DoD-186 | Small Intestinal Microbial Community in Gulf War Illness |
| | Treatment | DoD-204 | Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Syndrome |
| | Treatment | VA-189 | CAM in Veterans with Gulf War Illnesses |
| | Treatment | DoD-229 | Bench to Bedside: Understanding Symptom Response to Acupuncture Treatment and Designing a Successful Acupuncture Treatment Program |
| | Treatment | DoD-234 | A Prospective Open-Label Clinical Trial of Methylphenidate plus a GWI-Specific Nutrient Formula in Patients with Gulf War Illness and Concentration Disturbances |
| | Treatment | DoD-235 | Treating Gulf War Illness with Novel Anti-Inflammatories: A Screening of Botanical Microglia Modulators |
| | Treatment | DoD-236 | Development of Dietary Polyphenol Preparations for Treating Veterans with Gulf War Illness |
| | Treatment | DoD-241 | Gulf War Illness Inflammation Reduction Trial |

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| | Treatment; Symptoms | DoD-206 | Investigating Clinical Benefits of a Novel Sleep-Focused, Mind-Body Program on Gulf War Illness Symptoms: An Exploratory Randomized Controlled Trial |
| | Treatment; Symptoms | DoD-216 | Intranasal Insulin: A Novel Treatment for Gulf War Multisymptom Illness |
| | Treatment; Symptoms | VA-056 | Birmingham's GW Veterans' Illness Demonstration Clinic |
| | Treatment; Symptoms | VA-058 | Implementation and Evaluation of GW Veterans' Demonstration Project |
| | Diagnosis; Symptoms | VA-104 | Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome |
| | Treatment; Symptoms | VA-137 | Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans |
| | Treatment; Symptoms | VA-153 | Bacterial Overgrowth Associated with Chronic Multi- Symptom Illness Complex |
| | Treatment; Symptoms | VA-158 | Testing the Feasibility of MC CBT for Veterans with IBS |
| | Treatment | VA-165 | A Pilot Study of CPAP Adherence Promotion by Peer Buddies with Sleep Apnea |
| Brain and Nervous System Function | Symptoms | DoD-036 | Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms |
| Brain and Nervous System Function | Symptoms | DoD-041 | Evaluation of Muscle Function in Persian Gulf Veterans |
| Brain and Nervous System Function | Symptoms | DoD-058 | Illness Among Persian GW Veterans: Case Validation Studies |
| Brain and Nervous System Function | Symptoms | DoD-085 | CNS Cytokines and CRH in GW Veterans with Multiple Unexplained Symptoms |
| Brain and Nervous System Function | Symptoms | DoD-101 | Mechanisms in Chronic Multisymptom Illnesses |
| Brain and Nervous System Function | Symptoms | VA-069 | Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans |
| Brain and Nervous System Function | Symptoms | VA-071 | Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome |
| Brain and Nervous System Function | Symptoms | VA-073 | Pain Sensitivity in GW Veterans with Medically Unexplained Musculoskeletal Pain |
| Brain and Nervous System Function | Symptoms | VA-082 | Pituitary Adrenal Function in People with Fatiguing Illness |
| Brain and Nervous System Function | Symptoms | VA-096 | Functional Imaging of Pain in Veterans with Unexplained Muscle Pain |
| Brain and Nervous System Function | Symptoms | VA-107 | Evaluation of Stress Response Systems in GW Veterans with CMI |
| Brain and Nervous System Function | Symptoms | VA-134 | Autonomic Functions of GW Veterans with Unexplained Illnesses |
| Brain and Nervous System Function | Symptoms | VA-135 | Motor Neuron Function of GW Veterans with Excessive Fatigue |
| Brain and Nervous System Function | Symptoms | VA-154 | Imaging Pain Modulation in GW Veterans with Chronic Muscle Pain |
| Brain and Nervous System Function | Symptoms; Diagnosis | DoD-180 | Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of Fatigue |
| Brain and Nervous System Function | Diagnosis; Symptoms | DoD-111 | Autonomic Dysfunction in GW Veterans |
| Brain and Nervous System Function | Treatment; Symptoms | DoD-115 | A Randomized, Multi-Center, Controlled Trial of Multi- Modal Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D) |

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| Brain and Nervous System Function | Treatment; Symptoms | DoD-173 | A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in GW Veterans with Chronic Multisymptom Illness |
| Brain and Nervous System Function | Treatment; Symptoms | DoD-182 | Trial of Naltrexone and Dextromethorphan for GW Veterans' Illness |
| Brain and Nervous System Function | Treatment; Symptoms | VA-057 | Case Management and Residential Rehabilitation for Persian Gulf War Veterans |
| Brain and Nervous System Function | Treatment; Symptoms | VA-059 | Demonstration Treatment Program for GW Veterans With Unexplained Physical Symptoms (13) |
| Brain and Nervous System Function | Treatment; Symptoms | VA-062 | A Randomized, Multi-Center, Controlled Trial of Multi- Modal Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V) |
| Brain and Nervous System Function | Treatment; Symptoms | VA-108 | Telemedicine Treatment for Veterans with Gulf War Illness |
| Brain and Nervous System Function | Treatment | VA-166 | A Randomized Controlled Trial of a Mindfulness-Based Intervention for Gulf War Syndrome |
| Brain and Nervous System Function | Treatment | VA-173 | Impact of Exercise Training on Pain and Brain Function in Gulf War Veterans |
| Brain and Nervous System Function; | Diagnosis; Symptoms | DoD-031 | Dysregulation of the Stress Response in the Persian Gulf Syndrome |
| Brain and Nervous System Function | Treatment; Symptoms | DoD-199 | Gulf War Illness: Evaluation of an Innovative Detoxification Program |
| Brain and Nervous System | Treatment | VA-178 | rTMS for the Treatment of Chronic Pain in GW1 Veterans |
| Environmental Toxicology | Treatment | DoD-177 | Randomized Trial of an Environmental Medicine Approach to Gulf War Veterans' Illness |
| Immune Function | Symptoms | DoD-187 | The Use of Comprehensive Molecular Profiling with Network and Control Theory to Better Understand GWI and Model Therapeutic Strategies |
| Immune Function | Symptoms | DoD-188 | Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War Illness |
| Other Topics | Treatment; Symptoms | DoD-196 | Probiotic (Bifidobacterium Infantis) for Gulf War Illness |

## Development

| Research Focus | Project Focus | Project | Project Title |
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| | Treatment; Symptoms | DoD-169 | Development of Novel Therapy for Chronic Neuropathic Pain |
| | Diagnosis | DoD-210 | Assessment of Diverse Biological Indicators in Gulf War Illness: Are They Replicable? Are They Related? |
| | Diagnosis | VA-182 | Consensus Case Definition for Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans |
| Brain and Nervous System Function | Diagnosis; Symptoms | DoD-168 | Developing Biomarkers for Fibromyalgia |
| Brain and Nervous System Function | Diagnosis; Treatment | DoD-209 | Proteomic Immune Profiling for the Therapeutic Modulation of Cognitive Impairment in a Novel GWI Mouse Model |
| Immune Function | Symptoms; Diagnosis | DoD-183 | Biomarkers of GW Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation |

## Epidemiology

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Symptoms | DoD-001 B | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not. |
| | Symptoms | DoD-001 E | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study |
| | Symptoms | DoD-001 F | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: GWV vs. NDV |
| | Symptoms | DoD-004 | The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey |
| | Symptoms | DoD-014 | Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry |
| | Symptoms | DoD-046 | Exploratory Data Analysis with the CCEP Database |
| | Symptoms | DoD-070 | War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes |
| | Symptoms | DoD-071 | A Comparison of Post Deployment Hospitalization between Vietnam and GW Veterans |
| | Symptoms | DoD-098 | Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans |
| | Prevention | DoD-110 | Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy |
| | Symptoms | DoD-116 B | Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly VA/DoD-2DB) |
| | Symptoms | DoD-120 | Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents |
| | Diagnosis | DoD-140 | US DOD Surveillance for Neoplasms in Infancy |
| | Symptoms | DoD-148 | Predicting Operational Readiness for Deployed Army National Guard and Army Reserve Soldiers and Families |
| | Symptoms | DoD-150 | Validation Study of Gulf War Deployment Files |
| | Symptoms | DoD-203 | Redefining Gulf War Illness Using Longitudinal Health Data: The Devens Cohort |
| | Symptoms | HHS-001 | Health Assessment of Persian GW Veterans from Iowa |
| | Prevention | HHS-009 | Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments |
| | Symptoms | HHS-011 | Deployment to the Gulf War and the Subsequent Development of Cancer |
| | Symptoms | VA-002 | National Health Survey of Persian Gulf Veterans |

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| | Symptoms | VA-002 A | VA National Survey of Persian Gulf Veterans - Phase I |
| | Symptoms | VA-002 B | VA National Survey of Persian Gulf Veterans - Phase II |
| | Symptoms | VA-004 C | Gulf War and Vietnam Veterans Cancer Incidence Surveillance |
| | Symptoms | VA-046 | Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder |
| | Symptoms | VA-063 B | Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB) |
| | Symptoms | VA-070 | A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8 |
| | Symptoms | VA-117 | Estimates of Cancer Prevalence in Gulf Veterans Using State Registries |
| | Symptoms | DoD-218 | Establishing a 1991 Veterans Research Network To Improve Characterization of Gulf War Illness and Provide a National Resource for Veterans and Investigators |
| | Symptoms; Exposure | DoD-073 | Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes |
| | Diagnosis; Exposure | DoD-208 | Genome-Wide Association Study of a Validated Case Definition of Gulf War Illness in a Population-Representative Sample |
| | Prevention; Symptoms | DoD-108 | Health Status of Current National Guard Members |
| | Prevention; Symptoms | DoD-117 | Patterns of Pre-Persian Gulf War Illness and Health Care Seeking |
| | Prevention; Treatment | HHS-010 | Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline |
| | Symptoms | DoD-015 | Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm |
| | Prevention | DoD-102 | Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans |
| | Symptoms | VA-001 | Mortality Follow-up Study of Persian Gulf Veterans |
| | Symptoms | VA-148 | Profile of GW Veterans Who Applied for Undiagnosed Illness Compensation |
| | Symptoms | DoD-217 | Efficacy of Treatments Tried: A Survey of GW Veterans |
| Brain and Nervous System Function | Symptoms | DoD-039 | A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces |
| Brain and Nervous System Function | Symptoms | DoD-141 | Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans |
| Brain and Nervous System Function | Symptoms | DoD-142 | Illnesses Among Persian GW Veterans: Case Validation Studies (Iowa / Great Britain) |
| Brain and Nervous System Function | Symptoms | DoD-143 | Millennium Cohort Study |
| Brain and Nervous System Function | Symptoms | DoD-149 | Longitudinal Health Study of GW Veterans |
| Brain and Nervous System Function | Symptoms | VA-002 C | VA National Survey of Persian Gulf Veterans - Phase III |
| Brain and Nervous System Function | Symptoms | VA-005 A | Health and Exposure Survey of Persian Gulf Veterans |

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| Brain and Nervous System Function | Symptoms | VA-078 | Millenium Cohort Study |
| Brain and Nervous System Function | Symptoms | VA-118 | Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004 |
| Brain and Nervous System Function | Symptoms; Exposure | VA-156 | Gulf War Era Cohort and Biorepository (CSP 585) |
| Brain and Nervous System Function; Reproductive Health | Symptoms | DoD-045 | Air Force Women's Health Surveillance Study |
| Environmental Toxicology | Symptoms | VA 156 | Gulf War Era Cohort and Biorepository (CSP 585) |
| Environmental Toxicology | Symptoms; Exposure | DoD-074 | Relationship of Stress Exposures to Health in GW Veterans |
| Environmental Toxicology; Chemical Weapons | Exposure; Symptoms | DoD-116 | VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V) |
| Environmental Toxicology; Chemical Weapons | Exposure; Symptoms | VA-063 | VA/DoD Core funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D) |
| Reproductive Health | Symptoms | DoD-030 | Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study |
| Reproductive Health | Symptoms; Diagnosis; Prevention | DoD-096 | Deployment Health Center |
| Reproductive Health | Symptoms; Prevention | DoD-001 | Naval Health Study Program |

## Mechanistic

| Research Focus | Project Focus | Project | Project Title |
|---|---|---|---|
| | Diagnosis | DoD-193 | Genome Instability: A Common Link in Gulf War Illness Patients |
| | Diagnosis | DoD-220 | Biomarker Discovery in GW Veterans: Development of a War Illness Diagnostic Panel |
| | Diagnosis | VA-185 | Identification of Plasma Biomarkers of Gulf War Illness Using “omic” Technology |
| | Diagnosis | DoD-239 | Mitochondrial and Nuclear Genetics in Gulf War Illness |
| | Diagnosis; Symptoms | VA-179 | Vascular and Skeletal Muscle Function in Gulf War Veterans Illness |
| | Diagnosis: Symptoms | VA-180 | Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with GWI |
| | Diagnosis; Treatment | DoD-224 | Understanding Gulf War Illness: An Integrative Modeling Approach |
| | Symptoms | DoD-179 | Mechanisms of Mitochondrial Defects in Gulf War Syndrome |
| | Symptoms | VA-130 | Tissue Factor and Gulf War-Associated Chronic Coagulopathies |
| | Symptoms | VA-131 | Neuroendocrine Regulators and Proteomics in GW Veterans with CMI |
| | Symptoms | VA-136 | Central Mechanisms Modulating Visceral Sensitivity |
| | Symptoms | VA-159 | Somatic hypersensitivity in Veterans with IBS |
| | Symptoms | VA-162 | Transcription factors regulating sensory gene expression and pain pathways |
| | Symptoms | VA-177 | Somatic hypersensitivity in Veteraans with IBS |
| | Symptoms; Treatment | VA-164 | Central Mechanisms Modulating Visceral Sensitivity (renewal of VA-136) |

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| | Symptoms; Treatment | VA-172 | Understanding Pain of Gastrointestinal Origin in Women that Serve in OEF/OIF |
| | Treatment | VA-192 | Women vs. Men with GWI: Differences in Computational Models and Therapeutic Targets |
| Brain and Nervous System Function | Symptoms | VA-115 | Autonomic System Changes Cause Intestinal Symptoms in Gulf War Veterans |
| Brain and Nervous System Function | Symptoms | VA-119 | Patterns of Microarray Gene Expression in Gulf War Illness |
| Brain and Nervous System Function | Symptoms | DoD-194 | Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome |
| Brain and Nervous System Function | Symptoms; Treatment | DoD-213 | Effectiveness of Accupressure Treatment for Pain Management and Fatigue Relief in GW Veterans |
| Brain and Nervous System Function | Treatment | DoD-207 | Gulf War Illness Research Development Consortium (GWIC) |
| Brain and Nervous System Function | Diagnosis; Symptoms | DoD-226 | Gulf War Illness: Assessment of Bioenergetics in Brain and Muscle |
| Environmental Toxicology | Exposure; Symptoms | DoD-174 | Autonomic Biomarkers and Treatment for Gulf War Illness |
| Immune Function | Diagnosis | DoD-200 | XMRV and GWI: Is There an Association? |
| Immune Function | Diagnosis Symptoms | DoD-211 | Detection of Xenotropic Murine Leukemia Virus-Related Virus (XMRV) in Gulf War Illness: Role in Pathogenesis or Biomarker? |
| Immune Function | Symptoms | VA-132 | Immunologic Mechanisms and Biomarkers in Gulf War Illness |
| Immune Function | Symptoms | VA-133 | Longitudinal Study of Gene Expression and Gene Products in Veterans with Gulf War Illness |

# Appendix C
# Project Funding

**(As of September 30, 2014)**

# NOTES ON REVISED TABLE OF SPENDING FOR GULF WAR VETERANS' ILLNESSES RESEARCH FROM FY 2005-2014

**General Notes**

1. All entries for research funding reflect money centrally obligated to researchers (both intramural and extramural) to carry out the specific projects. These funds also cover operational costs for administration, infrastructure, etc. Each department allocates these costs in slightly different ways, making it difficult to completely account for these funds. For example, in VA the research appropriation does not pay for clinician/investigator salaries. By law those funds must come from the patient care appropriation. These salary costs are not included in the obligated costs listed in the table.
2. A "blank" funding entry generally reflects years in which a project was not active (e.g., it had not started or it had come to an end).
3. Some multiyear projects receive all of their funding in the fiscal year of the authorization and appropriation. For those, the dollars authorized and obligated are shown for that fiscal year. The remaining funding entries show $0 for the years that the project is active.
4. Although all projects funded from FY 1992-2014 are listed, only the financial data for FY 2005-2014 (a 10-year window) are shown in Appendix C; Totals for FY 2005-2014 do not include funds obligated in FY 1992-2004. Projects that received all of their obligated funds prior to FY 2005 will, therefore, appear in the table as having no funding.
5. Some intramural projects/programs are supported out of operational costs. For those projects, $0 is entered for the funds in the fiscal years that the project is active.
6. Programs consisting of multiple projects are represented in one of two ways depending on how funds are centrally obligated:
   a**. Funds centrally obligated to the program**: These programs are shown in the table as a main program indicated by project designation such as DoD-1, and projects within the program as DoD-1A, DoD-1B, etc. All funds are shown under the main program. Blank funding entries are shown for the individual projects.
   b. **Funds centrally obligated to projects within a program**: The funds for these programs are only indicated by their projects without a main program identifier, for example, VA-2A and VA-2B.

**Specific Notes**

1. DoD-4 is part of a larger US Army study conducted at Walter Reed Army Institute of Research. Funding for this project has been combined into project DoD-23. In addition, projects DoD-8A and 8B are part of a larger US Army study in which all funding has been combined and is shown under program DoD-8.
2. HHS-3 was funded from the FY'91 appropriation, which is not included in this accounting.
3. HHS-4 was funded from the FY'93 appropriation, which is not included in this accounting.
4. Funds for VA-1 for FY'94 through FY'97 represent an aggregate of funds for both the VA Mortality Study and the VA National Survey of Persian Gulf Veterans. Beginning in FY'98, VA-1 reflects continuation of the VA Mortality Study. Beginning in FY'98, VA–2A, 2B, and 2C reflect funding for separate components of the VA National Survey of Persian Gulf Veterans.
5. In nine instances (DoD-115 & VA-062, DoD-116 & VA-063, DoD-116A & VA-063A, DoD-116B & VA-063B, DoD-118 & VA-061, DoD-119 &VA-055, DoD-125 & VA-074, DoD-143 & VA-078 ,and DoD154 & VA-88), two different designations represent the same project because both DoD and VA funded them jointly. The total funding appropriated for each of these nine projects is broken down and reported separately by funding agency.

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-001 | Naval Health Study Program | C | | | | | | | | | | | $0 |
| DoD-001 A | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees | C | | | | | | | | | | | $0 |
| DoD-001 B | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not. | C | | | | | | | | | | | $0 |
| DoD-001 C | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among GW Veterans and other active-duty personnel | C | | | | | | | | | | | $0 |
| DoD-001 D | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in GW Veterans | C | | | | | | | | | | | $0 |
| DoD-001 E | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study | C | | | | | | | | | | | $0 |
| DoD-001 F | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: GWV vs. NDV | C | | | | | | | | | | | $0 |
| DoD-001 G | Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian GW Veterans | C | | | | | | | | | | | $0 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-002 | Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET | C | | | | | | | | | | | $0 |
| DoD-004 | The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey | C | | | | | | | | | | | $0 |
| DoD-007 A | Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling | C | | | | | | | | | | | $0 |
| DoD-007 B | Carcinogenicity of Depleted Uranium Fragments | C | | | | | | | | | | | $0 |
| DoD-008 | Program DoD-8. | C | | | | | | | | | | | $0 |
| DoD-008 A | Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL) | C | | | | | | | | | | | $0 |
| DoD-008 B | Development of a Leishmania Skin Test Antigen (LSTA) | C | | | | | | | | | | | $0 |
| DoD-009 | Identification of the Genetic Factors Which Control Tropism in Leishmania | C | | | | | | | | | | | $0 |
| DoD-010 | Pyridostigmine Synergistic Toxicity Study | C | | | | | | | | | | | $0 |
| DoD-011 | Male/Female Differential Tolerances to Pyridostigmine Bromide | C | | | | | | | | | | | $0 |
| DoD-013 | Effects of Persian Gulf War Service on Military Working Dogs | C | | | | | | | | | | | $0 |
| DoD-014 | Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry | C | | | | | | | | | | | $0 |
| DoD-015 | Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm | C | | | | | | | | | | | $0 |
| DoD-016 | Kuwait Oil Fire Health Risk Assessment | C | | | | | | | | | | | $0 |
| DoD-017 | Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning | C | | | | | | | | | | | $0 |
| DoD-018 | Kuwait Oil Fires Troop Exposure Assessment Model (TEAM) | C | | | | | | | | | | | $0 |
| DoD-019 | Persian Gulf Veterans Health Tracking System | C | | | | | | | | | | | $0 |

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*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-021 | Study of Variability In Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals With Symptoms Following Participation in Operation Desert Storm | C | | | | | | | | | | | $0 |
| DoD-022 | Chronic Organophosphorus Exposure and Cognition | C | | | | | | | | | | | $0 |
| DoD-023 | Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families | C | | | | | | | | | | | $0 |
| DoD-030 | Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study | C | | | | | | | | | | | $0 |
| DoD-031 | Dysregulation of the Stress Response in the Persian Gulf Syndrome | C | | | | | | | | | | | $0 |
| DoD-032 | Neuropsychological Functioning in Persian Gulf Era Veterans | C | | | | | | | | | | | $0 |
| DoD-033 | Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity | C | | | | | | | | | | | $0 |
| DoD-034 | Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents | C | | | | | | | | | | | $0 |
| DoD-035 | Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War. | C | | | | | | | | | | | $0 |
| DoD-036 | Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms | C | | | | | | | | | | | $0 |
| DoD-037 | Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats | C | | | | | | | | | | | $0 |
| DoD-038 | Diagnostic Antigens of Leishmania tropica | C | | | | | | | | | | | $0 |
| DoD-039 | A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces | C | | | | | | | | | | | $0 |
| DoD-040 | Psychological and Neurobiological Consequences of the Gulf War Experience | C | | | | | | | | | | | $0 |
| DoD-041 | Evaluation of Muscle Function in Persian Gulf Veterans | C | | | | | | | | | | | $0 |

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## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-042 | The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment | C | | | | | | | | | | | $0 |
| DoD-044 | Investigation of Seminal Plasma Hypersensitivity Reactions | C | | | | | | | | | | | $0 |
| DoD-045 | Air Force Women's Health Surveillance Study | C | | | | | | | | | | | $0 |
| DoD-046 | Exploratory Data Analysis with the CCEP Database | C | | | | | | | | | | | $0 |
| DoD-047 | Study of Mycoplasmal Infections in GW Veterans | C | | | | | | | | | | | $0 |
| DoD-048 | Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs. Selected Control Groups | C | | | | | | | | | | | $0 |
| DoD-049 | Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts | C | | | | | | | | | | | $0 |
| DoD-050 | Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways | C | | | | | | | | | | | $0 |
| DoD-051 | Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses | C | | | | | | | | | | | $0 |
| DoD-052 | Female Gender and Other Potential Predictors of Functional Health Status Among Persian GW Veterans | C | | | | | | | | | | | $0 |
| DoD-053 | Long-Term Effects of Subclinical Exposures to Sarin | C | | | | | | | | | | | $0 |
| DoD-054 | Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure | C | | | | | | | | | | | $0 |
| DoD-055 | Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects | C | | | | | | | | | | | $0 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-056 | Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine | C | | | | | | | | | | | $0 |
| DoD-057 | Physiologic Effects of Stress in GW Veterans | C | | | | | | | | | | | $0 |
| DoD-058 | Illness Among Persian GW Veterans: Case Validation Studies | C | | | | | | | | | | | $0 |
| DoD-059 | Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis | C | | | | | | | | | | | $0 |
| DoD-060 | Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness | C | | | | | | | | | | | $0 |
| DoD-061 | Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid | C | | | | | | | | | | | $0 |
| DoD-062 | Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice | C | | | | | | | | | | | $0 |
| DoD-063 | PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity | C | | | | | | | | | | | $0 |
| DoD-064 | Individual Differences in Neurobehavioral Effects of Pyridostigmine | C | | | | | | | | | | | $0 |
| DoD-065 | Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment | C | | | | | | | | | | | $0 |
| DoD-066 | Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction | C | | | | | | | | | | | $0 |
| DoD-067 | Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria | C | | | | | | | | | | | $0 |
| DoD-069 | Five Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents | C | $0 | $0 | | | | | | | | | $0 |
| DoD-070 | War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes | C | | | | | | | | | | | $0 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-071 | A Comparison of Post Deployment Hospitalization Between Vietnam and GW Veterans | C | | | | | | | | | | | $0 |
| DoD-072 | Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals | C | | | | | | | | | | | $0 |
| DoD-073 | Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes | C | | | | | | | | | | | $0 |
| DoD-074 | Relationship of Stress Exposures to Health in GW Veterans | C | | | | | | | | | | | $0 |
| DoD-075 | Toxic Interactions of Prophylactic Drugs and Pesticides | C | | | | | | | | | | | $0 |
| DoD-076 | Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel | C | | | | | | | | | | | $0 |
| DoD-077 | Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War | C | | | | | | | | | | | $0 |
| DoD-078 | Experimental Models of Gulf War Syndrome | C | | | | | | | | | | | $0 |
| DoD-079 | Time Course of Stress-induced Impairment of Blood Brain Barrier | C | | | | | | | | | | | $0 |
| DoD-080 | Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells | C | | | | | | | | | | | $0 |
| DoD-081 | Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress | C | | | | | | | | | | | $0 |
| DoD-082 | Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs | C | | | | | | | | | | | $0 |
| DoD-083 | Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism | C | | | | | | | | | | | $0 |
| DoD-084 | Psychobiologic Alterations in Persian GW Veterans with and without PTSD | C | | | | | | | | | | | $0 |
| DoD-085 | CNS Cytokines and CRH in GW Veterans with Multiple Unexplained Symptoms | C | | | | | | | | | | | $0 |
| DoD-086 | Effects of Combat Stress on Structure and Function of the Hippocampus | C | | | | | | | | | | | $0 |
| DoD-087 | Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related | C | | | | | | | | | | | $0 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | Quality of Life among PGWVs | | | | | | | | | | | | |
| DoD-088 | Clinical Relevance of Novel Immunological Markers in PTSD | C | | | | | | | | | | | $0 |
| DoD-089 | Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder | C | | | | | | | | | | | $0 |
| DoD-090 | SPECT Benzodiazepine Receptor and MR Imaging in PTSD | C | | | | | | | | | | | $0 |
| DoD-091 | Neurological and Circadian Substrates of PTSD-like Behaviors | C | | | | | | | | | | | $0 |
| DoD-092 | Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder | C | | | | | | | | | | | $0 |
| DoD-093 | Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up | C | | | | | | | | | | | $0 |
| DoD-094 | Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. GW Veterans | C | | | | | | | | | | | $0 |
| DoD-095 | Development of Diagnostic tools and alternative treatment drugs for Leishmania | C | | | | | | | | | | | $0 |
| DoD-096 | Deployment Health Center | C | $0 | | | | | | | | | | $0 |
| DoD-097 | Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis | C | | | | | | | | | | | $0 |
| DoD-098 | Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans | C | $0 | $0 | $0 | $0 | $0 | | | | | | $0 |
| DoD-099 | DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: | C | | | | | | | | | | | $0 |

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## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | Hospitalizations | | | | | | | | | | | | |
| DoD-100 | Antibodies to Squalene | C | $0 | $0 | $0 | | | | | | | | $0 |
| DoD-101 | Mechanisms in Chronic Multisymptom Illnesses | C | $2,429,999 | $0 | $0 | $0 | $0 | | | | | | $2,429,999 |
| DoD-102 | Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans | C | | | | | | | | | | | $0 |
| DoD-103 | Human Metabolism and Interactions of Deployment-related Chemicals | C | $160,000 | $326,570 | $166,570 | $0 | $0 | | | | | | $653,140 |
| DoD-104 | Clinical Evaluation of a Proposed New Gulf War Syndrome | C | | | | | | | | | | | $0 |
| DoD-105 | Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala | C | | | | | | | | | | | $0 |
| DoD-106 | The Role of Th1/Th2 cytokine balance in Gulf War-related illness | C | | | | | | | | | | | $0 |
| DoD-107 | Stress, Organophosphates and Blood Brain Barrier Integrity | C | | | | | | | | | | | $0 |
| DoD-108 | Health Status of Current National Guard Members | C | $0 | | | | | | | | | | $0 |
| DoD-109 | Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms | C | | | | | | | | | | | $0 |
| DoD-110 | Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy | C | | | | | | | | | | | $0 |
| DoD-111 | Autonomic Dysfunction in GW Veterans | C | $0 | | | | | | | | | | $0 |
| DoD-112 | Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease? | C | | | | | | | | | | | $0 |
| DoD-113 | Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects | C | $0 | | | | | | | | | | $0 |
| DoD-114 | A Re-examination of Neuropsychological Functioning in Persian GW Veterans | C | | | | | | | | | | | $0 |
| DoD-115 | A Randomized, Multi-Center, Controlled Trial of Multi-Model | C | | | | | | | | | | | $0 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D) | | | | | | | | | | | | |
| DoD-116 | VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V) | C | | | | | | | | | | | $0 |
| DoD-116 A | Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA) | C | | | | | | | | | | | $0 |
| DoD-116 B | Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly VA/DoD- 2DB) | C | | | | | | | | | | | $0 |
| DoD-117 | Patterns of Pre-Persian Gulf War Illness and Health Care Seeking | C | | | | | | | | | | | $0 |
| DoD-118 | An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also VA-61) | C | | | | | | | | | | | $0 |
| DoD-119 | Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also VA-55) | C | | | | | | | | | | | $0 |
| DoD-120 | Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents | C | | | | | | | | | | | $0 |
| DoD-121 | Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development | C | | | | | | | | | | | $0 |
| DoD-122 | Carcinogenic Potential of Depleted Uranium and Tungsten Alloys | C | | | | | | | | | | | $0 |
| DoD-123 | Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys | C | | | | | | | | | | | $0 |
| DoD-124 | Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin | C | $0 | $0 | | | | | | | | | $0 |
| DoD-125 | A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74) | C | $0 | $0 | | | | | | | | | $0 |
| DoD-126 | Blood-Brain Barrier Transport of Uranium | C | $0 | $0 | $0 | $0 | $0 | | | | | | $0 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-127 | Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man | C | | | | | | | | | | | $0 |
| DoD-128 | Multifactorial Assessment of Depleted Uranium Neurotoxicity | C | $89,055 | $0 | $0 | $0 | $0 | | | | | | $89,055 |
| DoD-129 | Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness | C | $0 | $0 | $0 | $0 | $0 | | | | | | $0 |
| DoD-130 | Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents | C | $0 | $0 | $0 | $0 | $0 | | | | | | $0 |
| DoD-131 | Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses | C | $0 | $0 | $0 | $0 | $0 | | | | | | $0 |
| DoD-132 | Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness | C | $0 | $0 | $0 | | | | | | | | $0 |
| DoD-133 | Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome | C | $0 | $0 | $0 | | | | | | | | $0 |
| DoD-134 | Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin | C | $0 | $0 | $0 | | | | | | | | $0 |
| DoD-135 | Biochemical Markers for Exposure to Low Doses of Organophosphorus Exposure | C | $0 | | | | | | | | | | $0 |
| DoD-136 | A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure | C | $0 | | | | | | | | | | $0 |
| DoD-137 | Low Level Exposure to Sulfur Mustard: Development of a SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin | C | $0 | $0 | | | | | | | | | $0 |
| DoD-138 | Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents | C | $0 | $0 | $0 | | | | | | | | $0 |
| DoD-139 | Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses | C | | | | | | | | | | | $0 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-140 | US DOD Surveillance for Neoplasms in Infancy | C | $0 | $0 | | | | | | | | | $0 |
| DoD-141 | Physical, Mental, Social, and Family Health Outcomes of GW Veterans | C | | | | | | | | | | | $0 |
| DoD-142 | Illnesses Among Persian GW Veterans: Case Validation Studies (Iowa / Great Britain) | C | $0 | | | | | | | | | | $0 |
| DoD-143 | Millennium Cohort Study | O | $2,880,000 | $2,893,000 | $3,251,000 | $3,160,000 | $3,145,000 | $3,306,000 | $3,347,000 | $3,676,000 | $3,535,000 | $4,073,000 | $33,266,000 |
| DoD-144 | Psychological Health Screening: Methods and Metrics for Deployed Forces | C | $0 | $0 | $0 | $0 | $0 | | | | | | $0 |
| DoD-145 | Early Intervention Research Program to Enhance Soldier Resilience | C | $0 | $0 | $0 | $0 | $0 | $0 | | | | | $0 |
| DoD-146 | Assessment of Toxicology Assay Methods and Chemical Exposures Among a Cohort of US Marines Deployed in the Gulf War | C | | | | | | | | | | | $0 |
| DoD-147 | Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications | C | $0 | $0 | | | | | | | | | $0 |
| DoD-148 | Predicting Operational Readiness for Deployed Army National Guard and Army Reserve Soldiers and Families | C | | | | | | | | | | | $0 |
| DoD-149 | Longitudinal Health Study of GW Veterans | C | $0 | $0 | | | | | | | | | $0 |
| DoD-150 | Validation Study of Gulf War Deployment Files | C | | | | | | | | | | | $0 |
| DoD-151 | Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in GW Veterans | C | $0 | $0 | | | | | | | | | $0 |
| DoD-152 | Characterization of Intracellular Signaling Pathways Activated by Nerve Agents | C | $0 | $0 | $0 | $0 | $0 | | | | | | $0 |
| DoD-153 | Gulf War Illness Research | C | $928,000 | $0 | | | | | | | | | $928,000 |
| DoD-154 | Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study | C | $604,372 | $0 | $0 | $0 | $0 | $0 | | | | | $604,372 |
| DoD-155 | Neuropsychological Functioning in GW Veterans Exposed to Pesticides and Pyridostigmine Bromide | C | $0 | $0 | $0 | $0 | | | | | | | $0 |

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*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-156 | The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| DoD-157 | Novel Leishmania And Malaria Potassium Channels: Candidate Therapeutic Targets | C | $0 | | | | | | | | | | $0 |
| DoD-158 | Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission Of Genetic Damage To Offspring | C | $0 | | | | | | | | | | $0 |
| DoD-159 | Neurotoxicity from Chronic Exposure to Depleted Uranium | C | $0 | | | | | | | | | | $0 |
| DoD-160 | Characterization of the Reproductive Toxicity of Depleted Uranium | C | $0 | | | | | | | | | | $0 |
| DoD-161 | Glutamate Receptor Aptamers and ALS | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| DoD-162 | Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| DoD-163 | Neuroimmune Effects of Inhaling Low Dose Sarin | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| DoD-164 | Efficacy of Adjunct Sleep Interventions For PTSD (EASI-PTSD) | C | $999,623 | $0 | $0 | $0 | | | | | | | $999,623 |
| DoD-165 | Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military - BALSAM | C | $1,000,799 | $0 | $0 | $0 | | | | | | | $1,000,799 |
| DoD-166 | A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance | C | $1,000,000 | $0 | $0 | $0 | | | | | | | $1,000,000 |
| DoD-167 | Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure | C | | $637,848 | $0 | $0 | $0 | | | | | | $637,848 |
| DoD-168 | Developing Biomarkers for Fibromyalgia | C | | $936,067 | $0 | $0 | $0 | | | | | | $936,067 |
| DoD-169 | Development of Novel Therapy for Chronic Neuropathic Pain | C | | $840,574 | $0 | $0 | $0 | | | | | | $840,574 |
| DoD-170 | Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I | C | | $208,353 | $0 | $0 | $0 | | | | | | $208,353 |
| DoD-171 | Q10 for GW Veterans | C | | $718,261 | $0 | $0 | $0 | | | | | | $718,261 |
| DoD-172 | CNDP1 Polymorphisms and | C | | $831,200 | $0 | $0 | $0 | | | | | | $831,200 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | Carnosine Therapy in GWI | | | | | | | | | | | | |
| DoD-173 | A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in GW Veterans with Chronic Multisymptom Illness | C | | $650,279 | $0 | $0 | $0 | | | | | | $650,279 |
| DoD-174 | Autonomic Biomarkers and Treatment for Gulf War Illness | C | | $687,530 | $0 | $0 | $0 | | | | | | $687,530 |
| DoD-175 | Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium | C | | $767,061 | $0 | $0 | $0 | | | | | | $767,061 |
| DoD-176 | Studies on Axonal Transport in an Animal Model for Gulf War Syndrome | C | | $112,500 | $0 | $0 | $0 | | | | | | $112,500 |
| DoD-177 | Randomized Trial of an Environmental Medicine Approach to GW Veterans' Illness | C | | $445,865 | $0 | $0 | $0 | | | | | | $445,865 |
| DoD-178 | Analysis of Paraoxonase Status among US Navy GW Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions | C | | $73,153 | $0 | $0 | $0 | | | | | | $73,153 |
| DoD-179 | Mechanisms of Mitochondrial Defects in Gulf War Syndrome | C | | | | $440,674 | $0 | $0 | $0 | | | | $440,674 |
| DoD-180 | Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of Fatigue | C | | | | $921,000 | $0 | $0 | $0 | | | | $921,000 |
| DoD-181 | Effectiveness of Acupuncture in the Treatment of Gulf War Illness | C | | | | $1,015,733 | $0 | $0 | $0 | | | | $1,015,733 |
| DoD-182 | Trial of Naltrexone and Dextromethorphan for GW Veterans' Illness | C | | | | $1,063,641 | $0 | $0 | $0 | | | | $1,063,641 |
| DoD-183 | Biomarkers of GW Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation | C | | | | $653,460 | $0 | $0 | $0 | | | | $653,460 |
| DoD-184 | Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the GW Veterans' Illnesses | C | | | | $311,135 | $0 | $0 | $0 | | | | $311,135 |
| DoD-185 | Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model | C | | | | $718,326 | $0 | $0 | $0 | | | | $718,326 |
| DoD-186 | Small Intestinal Microbial Community in Gulf War Illness | C | | | | $634,142 | $0 | $0 | $0 | | | | $634,142 |

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## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-187 | The Use of Comprehensive Molecular Profiling with Network and Control Theory to Better Understand GWI and Model Therapeutic Strategies | C | | | | $715,456 | $0 | $0 | $0 | | | | $715,456 |
| DoD-188 | Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War Illness | C | | | | $842,400 | $0 | $0 | $0 | | | | $842,400 |
| DoD-189 | Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers | C | | | | $303,000 | $0 | $0 | $0 | | | | $303,000 |
| DoD-190 | Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness | C | | | | $894,000 | $0 | $0 | $0 | | | | $894,000 |
| DoD-191 | Neuroimmune Interactions, Low-Dose Sarin Inhalation, and Gulf War Syndrome | C | | | | | $1,247,995 | $0 | $0 | $0 | | | $1,247,995 |
| DoD-192 | Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome | C | | | | | $742,296 | $0 | $0 | $0 | | | $742,296 |
| DoD-193 | Genome Instability: A Common Link in Gulf War Illness Patients | C | | | | | $904,364 | $0 | $0 | $0 | | | $904,364 |
| DoD-194 | Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome | C | | | | | $705,654 | $0 | $0 | $0 | | | $705,654 |
| DoD-195 | Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness | C | | | | | $678,953 | $0 | $0 | $0 | | | $678,953 |
| DoD-196 | Probiotic (Bifidobacterium Infantis) for Gulf War Illness | C | | | | | $466,260 | $0 | $0 | $0 | | | $466,260 |
| DoD-197 | Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness? | C | | | | | $929,224 | $0 | $0 | $0 | | | $929,224 |
| DoD-198 | Oxidative Stress | C | | | | | $927,000 | $0 | $0 | $0 | | | $927,000 |
| DoD-199 | Gulf War Illness: Evaluation of an Innovative Detoxification Program | C | | | | | $633,677 | $0 | $0 | $0 | | | $633,677 |
| DoD-200 | XMRV and GWI: Is There an Association? | O | | | | | | $565,794 | $0 | $0 | $0 | $0 | $565,794 |
| DoD-201 | Synergistic Actions of Pyridostigmine Bromide and Insecticides on Muscle and Vascular Nociceptors | C | | | | | | $852,157 | $0 | $0 | $0 | | $852,157 |
| DoD-202 | Brain-Immune Interactions as Basis | C | | | | | | $262,052 | $0 | $0 | $0 | | $262,052 |

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## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | of Gulf War Illness: Consortium Development | | | | | | | | | | | | |
| DoD-203 | Redefining Gulf War Illness Using Longitudinal Health Data: The Devens Cohort | O | | | | | | $708,169 | $0 | $0 | $0 | $0 | $708,169 |
| DoD-204 | Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Syndrome | O | | | | | | $668,072 | $0 | $0 | $0 | $0 | $668,072 |
| DoD-205 | The HPA Axis and Metabolic Outcomes in GW Veterans | O | | | | | | $699,933 | $0 | $0 | $0 | $0 | $699,933 |
| DoD-206 | Investigating Clinical Benefits of a Novel Sleep-Focused, Mind-Body Program on Gulf War Illness Symptoms: An Exploratory Randomized Controlled Trial | O | | | | | | $606,496 | $0 | $0 | $0 | $0 | $606,496 |
| DoD-207 | Gulf War Illness Research Development Consortium (GWIC) | C | | | | | | $251,475 | $0 | $0 | $0 | | $251,475 |
| DoD-208 | Genome-Wide Association Study of a Validated Case Definition of Gulf War Illness in a Population-Representative Sample | C | | | | | | $140,357 | $0 | $0 | $0 | | $140,357 |
| DoD-209 | Proteomic Immune Profiling for the Therapeutic Modulation of Cognitive Impairment in a Novel GWI Mouse Model | O | | | | | | $925,368 | $0 | $0 | $0 | $0 | $925,368 |
| DoD-210 | Assessment of Diverse Biological Indicators in Gulf War Illness: Are They Replicable? Are They Related? | O | | | | | | $741,013 | $0 | $0 | $0 | $0 | $741,013 |
| DoD-211 | Detection of Xenotropic Murine Leukemia Virus-Related Virus (XMRV) in Gulf War Illness: Role in Pathogenesis or Biomarker? | C | | | | | | $403,050 | $0 | $0 | $0 | | $403,050 |
| DoD-212 | Integrative Physiology of Gulf War Illness: Role of Autonomic Function, Central Neural Processing, and Sleep | C | | | | | | $254,295 | $0 | $0 | $0 | | $254,295 |
| DoD-213 | Effectiveness of Acupressure Treatment for Pain Management and Fatigue Relief in GW Veterans | O | | | | | | | $677,280 | $0 | $0 | $0 | $677,280 |
| DoD-214 | Abnormalities in Human Brain Creatine Metabolism in Gulf War Illness Probed with MRS | O | | | | | | | $878,051 | $0 | $0 | $0 | $878,051 |
| DoD-215 | Identifying Immune Drivers of Gulf War Illness Using a Novel Daily Sampling Approach | O | | | | | | | $900,642 | $0 | $0 | $0 | $900,642 |
| DoD-216 | Intranasal Insulin: A Novel Treatment | O | | | | | | | $1,492,571 | $0 | $0 | | $1,492,571 |

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*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | for Gulf War Multisymptom Illness | | | | | | | | | | | $0 | |
| DoD-217 | Efficacy of Treatments Tried: A Survey of GW Veterans | O | | | | | | | $527,365 | $0 | $0 | $0 | $527,365 |
| DoD-218 | Establishing a 1991 Veterans Research Network To Improve Characterization of Gulf War Illness and Provide a National Resource for Veterans and Investigators | O | | | | | | | $814,165 | $0 | $0 | $0 | $814,165 |
| DoD-219 | Organophosphate-Related Alterations in Myelin and Axonal Transport in the Living Mammalian Brain | O | | | | | | | $859,673 | $0 | $0 | $0 | $859,673 |
| DoD-220 | Biomarker Discovery in GW Veterans: Development of a War Illness Diagnostic Panel | O | | | | | | | $784,175 | $0 | $0 | $0 | $784,175 |
| DoD-221 | Role of microRNAs in thePathobiology of Gulf War Illness: Identification of Potential Novel Therapeutic Targets | O | | | | | | | | $339,305 | $0 | $0 | $339,305 |
| DoD-222 | Brain Immune Interactions as the Basis of Gulf War Illness: Gulf War Illness Consortium (GWIC) | O | | | | | | | | $2,642,203 | $2,141,930 | $0 | $4,784,133 |
| DoD-223 | Persistent Neural Membrane Protein Misregulation Following Neurotoxicant Exposure | O | | | | | | | | $881,479 | $0 | $0 | $881,479 |
| DoD-224 | Understanding Gulf War Illness: An Integrative Modeling Approach | O | | | | | | | | $2,361,185 | $1,741,342 | $0 | $4,102,527 |
| DoD-225 | The Role of Protein Radicals in Chronic Neuroimmune Dysfunction and Neuropathology in Response to a Multiple-Hit Model of Gulf War Exposures | O | | | | | | | | $884,129 | $0 | $0 | $884,129 |
| DoD-226 | Gulf War Illness: Assessment of Bioenergetics in Brain and Muscle | O | | | | | | | | $930,000 | $0 | $0 | $930,000 |
| DoD-227 | Monosodium Luminol for Improving Brain Function in Gulf War Illness | O | | | | | | | | | $872,357 | | $872,357 |
| DoD-228 | A Multimodal Evaluation of the Comparative Efficacy of Yoga versus a Patient-Centered Support Group for Treating Chronic Pain in Gulf War Illness | O | | | | | | | | | $603,663 | | $603,663 |
| DoD-229 | Bench to Bedside: Understanding Symptom Response to Acupuncture Treatment and Designing a Successful Acupuncture Treatment Program | O | | | | | | | | | $395,880 | | $395,880 |

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## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-230 | An In Vivo Investigation of Brain Inflammation in Gulf War Illness with Integrated PET/MR Imaging | O | | | | | | | | | $1,026,352 | | $1,026,352 |
| DoD-231 | Use of a Portable Stimulator to Treat GWI | O | | | | | | | | | $553,095 | | $553,095 |
| DoD-232 | Characterizing Treatable Causes of Small Fiber Polyneuropathy in Gulf War Veterans | O | | | | | | | | | $1,031,355 | | $1,031,355 |
| DoD-233 | Assessment of MRI-Based Markers of Dopaminergic Integrity as a Biological Indicator of Gulf War Illness | O | | | | | | | | | $425,471 | | $425,471 |
| DoD-234 | A Prospective Open-Label Clinical Trial of Methylphenidate plus a GWI-Specific Nutrient Formula in Patients with Gulf War Illness and Concentration Disturbances | O | | | | | | | | | $580,981 | | $580,981 |
| DoD-235 | Treating Gulf War Illness with Novel Anti-Inflammatories: A Screening of Botanical Microglia Modulators | O | | | | | | | | | $652,496 | | $652,496 |
| DoD-236 | Development of Dietary Polyphenol Preparations for Treating Veterans with Gulf War Illness | O | | | | | | | | | $540,039 | | $540,039 |
| DoD-237 | Direct Test for Neuroinflammation with [11C]DAP-713-PET Scanning | O | | | | | | | | | $849,827 | | $849,827 |
| DoD-238 | Restoring the Brain's Lipid Homeostasis as a Therapeutic Avenue for Treating the CNS Symptoms of Gulf War Illness | O | | | | | | | | | $954,000 | | $954,000 |
| DoD-239 | Mitochondrial and Nuclear Genetics in Gulf War Illness | O | | | | | | | | | $930,000 | | $930,000 |
| DoD-240 | Novel Therapeutic Approaches for the Treatment of Depression and Cognitive Deficits in a Rodent Model of Gulf War Veterans' Illness | O | | | | | | | | | $884,066 | | $884,066 |
| DoD-241 | Gulf War Illness Inflammation Reduction Trial | O | | | | | | | | | $1,044,682 | | $1,044,682 |
| DoD-242 | Epigenetic Mediation of Endocrine and Immune Response in an Animal Model of Gulf War Illness | O | | | | | | | | | $774,746 | | $774,746 |
| | | | | | | | | | | | | | |
| | **DoD Totals** | | $10,091,848 | $10,128,261 | $3,417,570 | $11,672,967 | $10,380,423 | $10,384,231 | $10,280,922 | $11,714,301 | $19,537,282 | $4,073,000 | $101,680,805 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

*Status: C=Complete; O=Ongoing*

## Department of Health and Human Services Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| HHS-001 | Health Assessment of Persian GW Veterans from Iowa | C | | | | | | | | | | | $0 |
| HHS-002 | Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18 | C | | | | | | | | | | | $0 |
| HHS-003 | Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires | C | | | | | | | | | | | $0 |
| HHS-004 | Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian GW Veterans In Mississippi | C | | | | | | | | | | | $0 |
| HHS-005 | Cognitive Function and Symptom Patterns in Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| HHS-006 | Defining Gulf War Illness | C | | | | | | | | | | | $0 |
| HHS-007 | Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid | C | | | | | | | | | | | $0 |
| HHS-008 | Strategy to Identify Non-Additive Response to Chemical Mixtures | C | | | | | | | | | | | $0 |
| HHS-009 | Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments | C | $0 | $0 | $0 | | | | | | | | $0 |
| HHS-010 | Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline | C | $0 | $0 | $0 | | | | | | | | $0 |
| HHS-011 | Deployment to the Gulf War and the Subsequent Development of Cancer | C | $0 | $0 | $0 | | | | | | | | $0 |
| HHS-012 | Genetic Epidemiology of ALS in Veterans | C | $466,481 | $455,587 | $441,974 | $433,467 | $0 | $0 | $0 | | | | $1,797,509 |
| | | | | | | | | | | | | | |
| | **HHS Totals** | | $466,481 | $455,587 | $441,974 | $433,467 | $0 | $0 | $0 | $0 | $0 | $0 | $1,797,509 |

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*Status: C=Complete; O=Ongoing*

## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-001 | Mortality Follow-up Study of Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| VA-002 | National Health Survey of Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| VA-002 A | VA National Survey of Persian Gulf Veterans - Phase I | C | | | | | | | | | | | $0 |
| VA-002 B | VA National Survey of Persian Gulf Veterans - Phase II | C | | | | | | | | | | | $0 |
| VA-002 C | VA National Survey of Persian Gulf Veterans - Phase III | C | | | | | | | | | | | $0 |
| VA-003 | Use of Roster of Veterans Who Served in Persian Gulf Area | C | | | | | | | | | | | $0 |
| VA-004 | Boston Environmental Hazards Research Center Program | C | | | | | | | | | | | $0 |
| VA-004 A | Evaluation of Cognitive Functioning of Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| VA-004 B | Evaluation of Neurological Functioning in Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| VA-004 C | Gulf War And Vietnam Veterans Cancer Incidence Surveillance | C | | | | | | | | | | | $0 |
| VA-004 D | Evaluation of Respiratory Dysfunction Among GW Veterans | C | | | | | | | | | | | $0 |
| VA-004 E | The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility | C | | | | | | | | | | | $0 |
| VA-004 F | Validity of Computerized Tests | C | | | | | | | | | | | $0 |
| VA-005 | East Orange Environmental Hazards Research Center Program | C | | | | | | | | | | | $0 |
| VA-005 A | Health and Exposure Survey of Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| VA-005 B | Physiological and Psychological Assessments of Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| VA-005 C | Effects of Exertion and Chemical Stress on Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| VA-005 D | Effects of Genetics and Stress on Responses to Environmental Toxins | C | | | | | | | | | | | $0 |
| VA-006 | Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research | C | | | | | | | | | | | $0 |
| VA-006 A | Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I) | C | | | | | | | | | | | $0 |

**Department of Veterans Affairs Gulf War Research Funding**

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-006 B | Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II) | C | | | | | | | | | | | $0 |
| VA-006 C | Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III) | C | | | | | | | | | | | $0 |
| VA-006 D | DNA Damage from Chemical Agents and Its Repair (Project IV) | C | | | | | | | | | | | $0 |
| VA-006 E | Clinical and Epidemiology Leishmania Research | C | | | | | | | | | | | $0 |
| VA-007 | Desert Storm Reunion Survey | C | | | | | | | | | | | $0 |
| VA-008 | Psychological Test Data of GW Veterans Over Time | C | | | | | | | | | | | $0 |
| VA-009 | Evaluation of Cognitive Functioning in Persian GW Veterans Reporting War-related Health Problems | C | | | | | | | | | | | $0 |
| VA-010 | Memory and Attention in PTSD | C | | | | | | | | | | | $0 |
| VA-011 | Neuropsychological Functioning in Veterans | C | | | | | | | | | | | $0 |
| VA-012 | Psychological Assessment of Operation Desert Storm Returnees | C | | | | | | | | | | | $0 |
| VA-013 | Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot Study | C | | | | | | | | | | | $0 |
| VA-015 | Vaccine-Mediated Immunity Against Leishmaniasis | C | | | | | | | | | | | $0 |
| VA-016 | Protective Immunity in Experimental Visceral Leishmaniasis | C | | | | | | | | | | | $0 |
| VA-017 | Immunological Evaluation of Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| VA-018 | Chronic Gastrointestinal Illness in Persian Gulf Veterans | C | | | | | | | | | | | $0 |
| VA-020 | Psychological Adjustment in Operation Desert Shield/Storm Veterans | C | | | | | | | | | | | $0 |
| VA-021 | A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in ODS | C | | | | | | | | | | | $0 |
| VA-036 | Stress Symptoms and Their Causal Attribution in Desert Storm Veterans | C | | | | | | | | | | | $0 |
| VA-040 | Musculoskeletal Symptoms in Gulf War Syndrome | C | | | | | | | | | | | $0 |
| VA-046 | Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder | C | | | | | | | | | | | $0 |

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## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-047 | Retrospective Verification of Mustard Gas Exposure | C | | | | | | | | | | | $0 |
| VA-048 | Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance | C | | | | | | | | | | | $0 |
| VA-049 | Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction | C | | | | | | | | | | | $0 |
| VA-050 | Neuropsychological findings in a sample of Operation Desert Storm Veterans | C | | | | | | | | | | | $0 |
| VA-051 | Psychobiological Assessment of Desert Storm Veterans | C | | | | | | | | | | | $0 |
| VA-053 | Spouses and Children Program | C | | | | | | | | | | | $0 |
| VA-054 | Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress | C | | | | | | | | | | | $0 |
| VA-055 | Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also DoD-119) | C | | | | | | | | | | | $0 |
| VA-056 | Birmingham's GW Veterans' Illness Demonstration Clinic (13) | C | | | | | | | | | | | $0 |
| VA-057 | Case Management and Residential Rehabilitation for Persian GW Veterans (13) | C | | | | | | | | | | | $0 |
| VA-058 | Implementation and Evaluation of GW Veterans' Demonstration Project (13) | C | | | | | | | | | | | $0 |
| VA-059 | Demonstration Treatment Program for GW Veterans With Unexplained Physical Symptoms (13) | C | | | | | | | | | | | $0 |
| VA-060 | Identification and Management of Sleep Disorders in GW Veterans | C | | | | | | | | | | | $0 |
| VA-061 | An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also DoD-118) | C | | | | | | | | | | | $0 |
| VA-062 | A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V) | C | | | | | | | | | | | $0 |
| VA-063 | VA/DoD Core funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D) | C | $250,000 | $250,000 | $250,000 | | | | | | | | $750,000 |

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**Department of Veterans Affairs Gulf War Research Funding**

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-063 A | Follow-Up Investigation of troops exposed to nerve agents at Aberdeen Proving Ground (Pilot Study) (See also DoD-116A; formerly VA/DoD-2VA/2DA) | C | | | | | | | | | | | $0 |
| VA-063 B | Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB) | C | | | | | | | | | | | $0 |
| VA-064 | Boston Environmental Hazards Research Center | C | $337,200 | $337,200 | | | | | | | | | $674,400 |
| VA-064 A | Functional Neuroimaging in Lead Exposed Adults | C | | | | | | | | | | | $0 |
| VA-064 B | Quantification and Validation of Structure-Function relationships through visuospatial test performance | C | | | | | | | | | | | $0 |
| VA-064 C | Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in Veteran populations | C | | | | | | | | | | | $0 |
| VA-065 | San Antonio Environmental Hazards Research Center | C | | | | | | | | | | | $0 |
| VA-065 A | Does a variant of the human SOD2 gene increase sensitivity to hazards? | C | | | | | | | | | | | $0 |
| VA-065 B | The contribution of FEN-1 to genetic integrity subsequent to oxidative stress | C | | | | | | | | | | | $0 |
| VA-065 C | The importance of hydrogen peroxide detoxification in cellular protection | C | | | | | | | | | | | $0 |
| VA-065 D | Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental hazards? | C | | | | | | | | | | | $0 |
| VA-066 | Physiological Responding in Posttraumatic Stress Disorder | C | | | | | | | | | | | $0 |
| VA-067 | Olfactory Functioning in GW Veterans | C | | | | | | | | | | | $0 |
| VA-068 | Family Study of Fibromyalgia | C | | | | | | | | | | | $0 |
| VA-069 | Cardiovascular Hyporeactivity and Fatiguing Illness in GW Veterans | C | | | | | | | | | | | $0 |
| VA-070 | A Clinical Evaluation of the Health Status of Persian GW Veterans in VISN 8 | C | | | | | | | | | | | $0 |
| VA-071 | Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome | C | | | | | | | | | | | $0 |

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## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-072 | Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses | C | | | | | | | | | | | $0 |
| VA-073 | Pain Sensitivity in GW Veterans with Medically Unexplained Musculoskeletal Pain | C | | | | | | | | | | | $0 |
| VA-074 | A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125) | C | | | | | | | | | | | $0 |
| VA-075 | ALS and Veterans: Are Veterans at Increased Risk? | C | | | | | | | | | | | $0 |
| VA-076 | Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD | C | | | | | | | | | | | $0 |
| VA-077 | HPA Axis Reactivity in Men and Women with Chronic PTSD | C | | | | | | | | | | | $0 |
| VA-078 | Millenium Cohort Study | C | | | | | | | | | | | $0 |
| VA-080 | Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress | C | $248,458 | $253,277 | $252,602 | | | | | | | | $754,337 |
| VA-081 | Stress, Pro-Inflammatory Cytokines and Coping Behavior | C | | | | | | | | | | | $0 |
| VA-082 | Pituitary Adrenal Function in People with Fatiguing Illness | C | $276,112 | $121,842 | | | | | | | | | $397,954 |
| VA-083 | Neuropsychological Assessment of a Population-Based Sample of Persian GW Veterans and Controls | C | | | | | | | | | | | $0 |
| VA-084 | Neurobiology of Severe Psychological Trauma in Women | C | | | | | | | | | | | $0 |
| VA-085 | Associative Learning in Veterans with and without Combat Experience | C | | | | | | | | | | | $0 |
| VA-086 | A Clinical Trial of Magnetic Stimulation in Depression | C | | | | | | | | | | | $0 |
| VA-087 | Improving Outcomes of Depression in Primary Care | C | | | | | | | | | | | $0 |
| VA-088 | Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study | C | | | | | | | | | | | $0 |
| VA-089 | National Registry of Veterans with Amyotrophic Lateral Sclerosis | C | $799,104 | $863,951 | | | | | | | | | $1,663,055 |
| VA-090 | Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness | C | $281,000 | $449,990 | $449,990 | $0 | $0 | $0 | $281,000 | $70,250 | | | $1,532,230 |

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## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-090A | Neuronal Hyperexcitability and Motor Neuron Regeneration | C | | | | | | | | | | | $0 |
| VA-090B | Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders | C | | | | | | | | | | | $0 |
| VA-090C | Developmental Differences in Alcohol Withdrawal Sensitivity | C | | | | | | | | | | | $0 |
| VA-090D | Seizures and Neuroplasticity: Physiology and Biochemistry | C | | | | | | | | | | | $0 |
| VA-091 | The Role of Dietary Choline in Neuroprotection | C | | | | | | | | | | | $0 |
| VA-092 | Acetylcholinesterase Activity In GW Veterans | C | | | | | | | | | | | $0 |
| VA-093 | HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans | C | $163,205 | $127,405 | | | | | | | | | $290,610 |
| VA-094 | The Immunology of Chronic Cutaneous Leishmaniasis | C | $157,360 | $202,320 | | | | | | | | | $359,680 |
| VA-095 | The Role of Signal Regulatory Proteins in Astrocytomas | C | $238,239 | $178,679 | | | | | | | | | $416,918 |
| VA-096 | Functional Imaging of Pain in Veterans with Unexplained Muscle Pain | C | $128,698 | $70,302 | $135,127 | $95,382 | | | | | | | $429,509 |
| VA-097 | Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas | C | $241,957 | $246,355 | $134,628 | | | | | | | | $622,940 |
| VA-098 | Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas | C | $168,600 | $168,600 | | | | | | | | | $337,200 |
| VA-099 | Vaccination Against Visceral Leishmaniasis with a multi-epitope vaccine | C | $118,863 | $117,908 | | | | | | | | | $236,771 |
| VA-100 | Studies of the Blood-Brain Barrier and its Manipulation | C | $151,740 | $151,740 | | | | | | | | | $303,480 |
| VA-101 | Biomarkers Discovery in ALS | C | $227,130 | $151,555 | $112,009 | $299,165 | $274,432 | | | | | | $1,064,291 |
| VA-102 | Cholinergic and Monoaminergic Influences on Sleep | C | $175,814 | $134,328 | | | | | | | | | $310,142 |
| VA-103 | Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal | C | $307,253 | $317,845 | | | | | | | | | $625,098 |
| VA-104 | Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome | C | $168,600 | $84,300 | | | | | | | | | $252,900 |
| VA-105 | Expression of the Major Surface Protease of Leishmania Chagasi | C | $119,535 | $92,817 | | | | | | | | | $212,352 |
| VA-106 | Interoceptive Stressor Conditioning: A Model for Gulf War Illness | C | $193,440 | $198,161 | | | | | | | | | $391,601 |

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## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-107 | Evaluation of Stress Response Systems in GW Veterans with CMI | C | $192,766 | $117,412 | $210,637 | $173,321 | $93,226 | $0 | | | | | $787,362 |
| VA-108 | Telemedicine Treatment for Veterans with Gulf War Illness | C | $185,714 | $238,616 | $224,916 | $11,100 | | | | | | | $660,346 |
| VA-109 | Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics | C | $158,372 | $306,912 | $317,503 | $321,148 | $241,520 | | | | | | $1,345,455 |
| VA-110 | Pain Among GW Veterans: Secondary Analysis of CSP#458 Data | C | $96,439 | $48,557 | | | | | | | | | $144,996 |
| VA-111 | T Cell Responses to Multiple Immunizations and Stress | C | $112,399 | $112,399 | | | | | | | | | $224,798 |
| VA-112 | National VA Amyotrophic Lateral Sclerosis Research Consortium | C | $1,171,208 | $734,590 | | | | | | | | | $1,905,798 |
| VA-113 | Novel Cause of Motor Neuron Disease | C | $166,352 | $110,152 | $110,152 | $110,152 | $0 | | | | | | $496,808 |
| VA-114 | Strategies in Therapeutic Development of Neurodegenerative Diseases | C | $266,950 | $370,920 | | | | | | | | | $637,870 |
| VA-115 | Autonomic System Changes Cause Intestinal Symptoms in GW Veterans | C | $275,623 | $275,623 | | | | | | | | | $551,246 |
| VA-116 | Quantitative Trait Genes Controlling Circadian and Sleep Behaviors | C | $125,888 | $228,734 | | | | | | | | | $354,622 |
| VA-117 | Estimates of Cancer Prevalence in Gulf Veterans Using State Registries | C | $42,206 | $151,740 | $115,772 | $66,597 | $0 | | | | | | $376,315 |
| VA-118 | Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004 | C | $42,262 | $160,535 | $119,453 | | | | | | | | $322,250 |
| VA-119 | Patterns of Microarray Gene Expression in Gulf War Illness | C | $192,204 | $168,600 | $168,600 | | | | | | | | $529,404 |
| VA-120 | Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis | C | $90,988 | $165,116 | | | | | | | | | $256,104 |
| VA-121 | Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders | C | $295,938 | $441,612 | | | | | | | | | $737,550 |
| VA-122 | Role of Mitochondrial Oxidative Stress in ALS | C | $55,188 | $271,896 | | | | | | | | | $327,084 |
| VA-123 | Interactions Between Maternal Care, Stress and Pyridostigmine Bromide | C | $60,134 | $48,332 | $178,447 | | | | | | | | $286,913 |
| VA-124 | Early Life Determinants of Vulnerability to Pyridostigmine Bromide | C | $213,110 | $195,688 | | | | | | | | | $408,798 |
| VA-125 | Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla | C | $322,532 | $479,892 | $743,778 | $653,747 | $560,455 | $5,135,117 | | | | | $7,895,521 |
| VA-126 | Structural Magnetic Resonance Imaging in Gulf War-Era Veterans | C | $159,552 | $165,565 | $165,565 | | | | | | | | $490,682 |

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| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-127 | Interactions of the Leishmania sp. with Mammalian Cells | C | $101,216 | $166,464 | | | | | | | | | $267,680 |
| VA-128 | MR Tracking of Stem Cells for Replacement Therapy in ALS | C | $236,730 | $236,730 | | | | | | | | | $473,460 |
| VA-129 | Glucocorticoid Responsivity in GW Veterans | C | $168,600 | $167,164 | $168,600 | | | | | | | | $504,364 |
| VA-130 | Tissue Factor and Gulf War-Associated Chronic Coagulopathies | C | | $194,826 | $217,055 | $248,741 | $273,861 | $158,089 | $161,644 | | | | $1,254,216 |
| VA-131 | Neuroendocrine Regulators and Proteomics in GW Veterans with CMI | C | | $60,767 | $163,579 | | | | | | | | $224,346 |
| VA-132 | Immunologic Mechanisms and Biomarkers in Gulf War Illness | C | | $64,630 | $112,400 | $112,400 | $56,200 | $56,200 | | | | | $401,830 |
| VA-133 | Longitudinal Study of Gene Expression and Gene Products in Veterans with Gulf War Illness | C | | $112,400 | $112,400 | | | | | | | | $224,800 |
| VA-134 | Autonomic Functions of GW Veterans with Unexplained Illnesses | C | | $8,880 | $0 | $0 | $25,880 | $101,863 | $72,667 | | | | $209,290 |
| VA-135 | Motor Neuron Function of GW Veterans with Excessive Fatigue | C | | $6,744 | $0 | $0 | $79,242 | $103,549 | $25,712 | | | | $215,247 |
| VA-136 | Central Mechanisms Modulating Visceral Sensitivity | C | | $83,288 | $81,715 | $121,055 | | | | | | | $286,058 |
| VA-137 | Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans | C | | $161,968 | $224,294 | $217,325 | $0 | $104,982 | | | | | $708,569 |
| VA-138 | Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP | C | | $226,773 | $235,240 | $258,136 | $9,819 | | | | | | $729,968 |
| VA-139 | Sleep Neurobiology and Circuitry | C | | $33,720 | | | | | | | | | $33,720 |
| VA-140 | Integrated Neuroimaging and Neuropathological Analysis of the Effects of Physical Activity on Progression and Therapy in ALS | C | | $232,553 | | | | | | | | | $232,553 |
| VA-141 | Genetic Analysis of an Invertebrate Model of Amyotrophic Lateral Sclerosis | C | | $243,779 | | | | | | | | | $243,779 |
| VA-142 | VA Gulf War Biorepository Trust | C | | $991,510 | $991,510 | $1,091,547 | $5,664,976 | $754,942 | $948,168 | $592,544 | $471,756 | | $11,506,953 |
| VA-143 | The Role of Protein Oxidation in the Progression of ALS | C | | $112,400 | $112,400 | | | | | | | | $224,800 |
| VA-144 | Testing the Role of Permethrin on the Progression of ALS | C | | $112,400 | $112,400 | | | | | | | | $224,800 |
| VA-145 | Proteomic Analysis of Cellular Response to Biological Warfare Agents | C | | $129,260 | $224,800 | $224,800 | $112,400 | $67,752 | | | | | $759,012 |

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## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-146 | Direct Delivery of Neurotoxins to the Brain by an Intranasal Route | C | | $161,687 | $256,159 | $245,295 | $195,214 | | | | | | $858,355 |
| VA-147 | The Diagnosis and Pathogenesis of Occult Leishmaniasis | C | | $98,350 | | | | | | | | | $98,350 |
| VA-148 | Profile of GW Veterans Who Applied for Undiagnosed Illness Compensation | C | | $24,307 | $71,008 | | | | | | | | $95,315 |
| VA-149 | Behavior of Neural Stem Cells in a Rat Model of GWS | C | | | $129,861 | $268,901 | $273,801 | $136,900 | | | | | $809,463 |
| VA-150 | GW Veterans Illnesses' Research IDIQ Contract with UTSW | C | | | $15,000,000 | $15,000,000 | $6,972,481 | $2,288,755 | $31,472 | | | | $39,292,708 |
| VA-151 | Genetic Epidemiology of ALS Veterans (CSP #500B) | C | | | | $2,116,602 | $377,557 | $377,557 | $242,775 | | | | $3,114,491 |
| VA-152 | Multiple Sclerosis in GW Veterans | C | | | | $122,010 | $137,791 | $120,866 | | | | | $380,667 |
| VA-153 | Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex | O | | | | | $8,377 | $168,600 | $94,681 | $158,219 | $43,278 | $49,504 | $522,659 |
| VA-154 | Imaging Pain Modulation in GW Veterans with Chronic Muscle Pain (renewal of VA-096) | C | | | | | $300,782 | $258,076 | $259,657 | $262,184 | | | $1,080,699 |
| VA-155 | Bacterial Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis | O | | $71,486 | $156,461 | $176,790 | $165,790 | $165,790 | $222,552 | $168,600 | $168,600 | $168,600 | $1,464,669 |
| VA-156 | Gulf War Era Cohort and Biorepository (CSP #585) | O | | | | | | $28,361 | $5,110 | $2,157,664 | $2,155,789 | $2,292,081 | $6,639,005 |
| VA-157 | A Clinical Demonstration of an EEG Brain-Computer Interface for ALS Patients (CSP #567) | C | | | | | | $2,368,460 | $965,519 | $26,296 | $84,236 | | $3,444,511 |
| VA-158 | Testing the Feasibility of MC CBT for Veterans with IBS | C | | | | | | $17,953 | $93,153 | | | | $111,106 |
| VA-159 | Somatic hypersensitivity in Veterans with IBS | C | | | | | $56,200 | $112,400 | $112,400 | $56,200 | | | $337,200 |
| VA-160 | Lipoic Acid Therapy for Experimental Autoimmune Encephalomyelitis | C | | | | | | $224,126 | $168,600 | $168,600 | $168,600 | | $729,926 |
| VA-161 | Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease | O | | | | | | $332,743 | $168,600 | $168,600 | $168,600 | $84,300 | $922,843 |
| VA-162 | Transcription factors regulating sensory gene expression and pain pathways | C | | | | | $94,416 | $168,600 | | | | | $263,016 |
| VA-163 | Immunoregulation of Myelin Specific T Lymphocytes | O | | | | | $371,209 | $361,972 | $168,600 | $168,600 | $42,150 | $168,600 | $1,281,131 |
| VA-164 | Central Mechanisms Modulating Visceral Sensitivity (renewal of VA-136) | O | | | | | $255,170 | $267,687 | $119,256 | $90,574 | $112,982 | $168,600 | $1,014,269 |

*****Totals for FY '05 -'14 do not include funds obligated in FY 1992 -2004

*Status: C=Complete; O=Ongoing*

## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-165 | A Pilot Study of CPAP Adherence Promotion by Peer Buddies with Sleep Apnea | C | | | | | | | $94,838 | | | | $94,838 |
| VA-166 | A Randomized Controlled Trial of a Mindfulness-Based Intervention for Gulf War Syndrome | C | | | | | | | $106,898 | $112,394 | | | $219,292 |
| VA-167 | Neuroprotection anf Myelin Repair Mechanisms in Multiple Sclerosis | O | | | | | | | $267,287 | $259,707 | $259,707 | $259,707 | $1,046,408 |
| VA-168 | Sleep Neurobiology and Circuitry | O | | | | | | | $244,063 | $303,406 | $168,600 | $168,600 | $884,669 |
| VA-169 | Prevention of Hippocampal Neurodegeneration Due to Age and Apnea | O | | | | | | | $202,742 | $270,322 | $270,322 | $270,322 | $1,013,708 |
| VA-170 | Epigenetic Mechanisms Relevant to the Pathogenesis of ALS | O | | | | | | | $182,650 | $168,600 | $168,600 | $168,600 | $688,450 |
| VA-171 | Nanoparticle Coupled Antioxidants for Respiratory Illness in Veterans | O | | | | | | | $140,500 | $168,600 | $168,600 | $168,600 | $646,300 |
| VA-172 | Understanding Pain of Gastrointestinal Origin in Women that Serve in OEF/OIF | O | | | | | | | $84,300 | $168,600 | $168,600 | $123,640 | $545,140 |
| VA-173 | Impact of Exercise Training on Pain and Brain Function in GW Veterans | O | | | | | | | $104,167 | $202,910 | $386,948 | $371,321 | $1,065,346 |
| VA-174 | GW Veterans' Illnesses Biorepository | O | | | | | | | | $237,878 | $263,848 | $197,250 | $698,976 |
| VA-175 | Memory and Mood Enhancing Therapies for Gulf War Illness | O | | | | | | | | $266,950 | $281,000 | $281,000 | $828,950 |
| VA-176 | MEG Synchronous Neural Interactions (SNI) in GW Veterans | O | | | | | | | | $406,888 | $397,334 | $397,334 | $1,201,556 |
| VA-177 | Somatic Hypersensitivity in Veterans with IBS (renewal of VA-159) | O | | | | | | | | $68,970 | $197,998 | $159,121 | $426,089 |
| VA-178 | rTMS for the Treatment of Chronic Pain in GW1 Veterans | O | | | | | | | | | $309,100 | $309,100 | $618,200 |
| VA-179 | Vascular and Skeletal Muscle Function in Gulf War Veterans Illness | O | | | | | | | | | $111,330 | $168,257 | $279,587 |
| VA-180 | Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with GWI | O | | | | | | | | | $92,453 | $174,769 | $267,222 |
| VA-181 | Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI | O | | | | | | | | | $427,447 | $774,029 | $1,201,476 |
| VA-182 | Consensus Case Definition for Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans | C | | | | | | | | | $850,000 | | $850,000 |
| VA-183 | Examination of Cognitive Fatigue in Gulf War Illness Using fMRI | O | | | | | | | | | | $279,149 | $279,149 |

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*Status: C=Complete; O=Ongoing*

**Department of Veterans Affairs Gulf War Research Funding**

| PROJECT NO | PROJECT TITLE | STATUS | FY 2005 | FY 2006 | FY2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | FY 2014 | TOTALS FY 05-14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VA-184 | Longitudinal Assessment of Gulf War Veterans with Suspected Sarin Exposure | O | | | | | | | | | | $268,201 | $268,201 |
| VA-185 | Identification of Plasma Biomarkers of Gulf War Illness Using "omic" Technology | O | | | | | | | | | | $511,947 | $511,947 |
| VA-186 | Gulf War Exposures and the Molecular Mechanisms of Paternal Reproductive Risk | O | | | | | | | | | | $300,433 | $300,433 |
| VA-187 | Multimodal Biological Assessment of Gulf War Illness | O | | | | | | | | | | $477,509 | $477,509 |
| VA-188 | Complementary Neurosteroid Intervention in Gulf War Veterans' Illnesses | O | | | | | | | | | | $230,005 | $230,005 |
| VA-189 | CAM in Veterans with Gulf War Illnesses | O | | | | | | | | | | $140,533 | $140,533 |
| VA-190 | Cognitive Rehabilitation for Gulf War Illness | O | | | | | | | | | | $142,910 | $142,910 |
| VA-191 | Novel neurotrophic therapies in an optimized mouse model of GWVI | O | | | | | | | | | | $195,947 | $195,947 |
| VA-192 | Women vs. Men with GWI: Differences in Computational Models and Therapeutic Targets | O | | | | | | | | | | $189,365 | $189,365 |
| VA-193 | Neuroinflammation, Oxidative Stress, and Hippocampal Defects in Gulf War Illness | O | | | | | | | | | | $70,250 | $70,250 |
| | | | | | | | | | | | | | |
| | **VA Totals** | | $9,484,679 | $13,013,552 | $22,059,061 | $21,934,214 | $16,600,799 | $13,881,340 | $5,569,011 | $6,723,556 | $7,937,878 | $9,729,584 | $126,933,674 |

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