# DEPARTMENT OF VETERANS AFFAIRS

# ANNUAL REPORT TO CONGRESS

## Federally Sponsored Research on Gulf War Veterans' Illnesses for 2013

# Annual Report to Congress – FY 2013

**Federally Sponsored Research on Gulf War Veterans' Illnesses for 2013**

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## 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; August 2, 1990 – July 31, 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 2013, which is the 20th 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) 2004 through FY 2013; 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 2013

Section III provides brief summaries of research articles on the health problems of GW Veterans published during calendar year (CY) 2013 or in CY 2012 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 423 distinct projects from FY 1992 through FY 2013 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 $220 million for the period from FY 2004 through FY 2013. As of September 30, 2013, 365 projects (86 percent of the 423 projects) were completed, and 58 projects (14 percent) were new or ongoing.

## V. NEW RESEARCH PROJECTS AND INITIATIVES

Six new projects were funded through the FY 2012 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 2013. These projects focused on Brain and Nervous System Function (1), Environmental Toxicology (3), and Symptoms and General Health (2). VA funded five new projects in FY 2013. One of these projects focused on Brain and Nervous System Function, and three focused on Symptoms and General Health. The fifth focused on developing a commonly-accepted definition of Chronic Multisymptom Illness in 1990-1991 Gulf War Era Veterans.

## 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; 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 2004 through FY 2013. 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 60 relevant articles published in English in calendar year 2013 or in 2012 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 2013, most of these studies focused on psychological health and the effects of altered brain structure.

#### General Brain Function and Exposure Research

Healthy (n = 14) and ill (n = 33) GW Veterans were compared using a face-name associative memory test during fMRI. The ill Veterans exhibited decreased memory performance relative to the healthy controls, and fMRI data indicated differences between the two groups in the left hippocampus (Odegard et al., 2013). In another study of memory using fMRI, 15 ill GW Veterans and 11 controls were evaluated before and after two bicycle exercise stress tests. Eight of the GW Veterans increased their memory scores after the exercise, and seven had lower scores. This phenomenon was not observed in the control subjects. The GW Veterans with lower memory scores were found to have significantly elevated lactate concentrations in the prefrontal area of the brain (left anterior cingulated cortex). This might be a useful biomarker for one subgroup of GW Veterans

(Rayhan et al., 2013a). A follow-up exercise test focused on changes in pain, autonomic function, and memory in ill GW Veterans. The 28 GW Veterans and 10 controls were subjected to fMRI scans before and after two exercise stress tests. One group of GW Veterans (n = 10) was diagnosed with orthostatic tachycardia (increased heart rate and reduced blood flow to the brain upon changing position), and the other group (n = 18) with exercise-induced hyperalgesia (increased sensitivity to pain). These changes, not observed in controls, could be helpful in understanding post-exertional malaise in GW Veterans (Rayhan et al., 2013c). Ill GW Veterans (n = 31) and controls (n = 20) were also subjected to fMRI scans with diffusion tensor imaging (DTI). DTI is important in determining the connectivity between different parts of the brain, and in the GW Veterans, there was a correlation between DTI data for the right inferior fronto-occipital fasciculus of the brain and symptoms like fatigue, pain, and hyperalgesia (Rayhan et al., 2013d). The DTI data for changes in the brain could be a biomarker for chronic multisymptom illness in GW Veterans (Rayhan et al., 2013d; Roehr, 2013). GW Veterans were also evaluated for headache types. Of the 50 GW Veterans in the study, 64 percent had migraines, compared with 82 percent of chronic fatigue syndrome (CFS) patients and 13 percent in controls. Other measures of pain, fatigue, and other symptoms were the same in GW Veterans and CFS patients. It is suggested that migraine prevalence should be added to the evaluation of GW Veterans (Rayhan et al., 2013b).

**Neuropsychological Functioning and Stress Response**

The most common psychological health issue to arise from the GW was posttraumatic stress disorder (PTSD). In a study to monitor trends in treatments for PTSD and other mental disorders, Hermes et al. compared VA workload for the time periods 1997-2005 and 2005-2010. They found that the number of patients treated and the treatment intensity increased over the study's timeframe (Hermes et al., 2012). A group of 317 GW Veterans was evaluated for exposure to warzone activities, posttraumatic stress symptoms, and physical health. Posttraumatic stress symptoms were found to be associated with general post-deployment health, but the correlation was stronger for GW Veterans who reported less warzone exposure. Men and women were included in the study, but there were no gender differences in the correlations (Wachen et al., 2013). Wright et al. investigated the connection between PTSD in Veterans (GW and others) and posttrauma support mechanisms. Factors like low unit cohesion, low social support, and low family support correlated with the development of PTSD. Pre-trauma vulnerability and pre-existing psychiatric problems were also associated with PTSD. The study suggests points at which interventions can mitigate PTSD symptoms (Wright et al., 2013). Delayed neurological problems such as Alzheimer's disease (AD) are linked to military service, so Veitch et al. estimated that there will be 140,000 excess cases of AD in Veterans (GW and others) by 2020. They suggest that management of military-specific risk factors such as tobacco use, traumatic brain injury (TBI), depression, and PTSD is one way to reduce the number of cases (Veitch et al., 2013).

In a study of visual hyperarousal, subjects were shown images associated with the 1991 GW. Healthy GW Veterans constituted the control group, and ill Veterans were categorized as Syndromes 1, 2, and 3 of the Haley case definition. The ill GW Veterans

reported hyperarousal significantly more frequently than did the controls, so it was concluded that this is due to damage to the cholinergic, dopaminergic, and white brain matter rather than warzone stress (Tillman et al., 2013).

A study comparing pain-related musculoskeletal disorders (MSD) and psychological comorbidity/well-being was conducted on 1381 male Australian GW Veterans and 1377 non-GW Veterans. MSDs such as arthritis or rheumatism, back or neck problems, joint problems, and soft tissue disorders were diagnosed in 24.5 percent of GW Veterans and 22.4 percent of the comparison group. Participants with MSDs were more likely to have depression, PTSD, and poorer well-being regardless of whether they were GW Veterans or not (Kelsall et al., 2013). Kuwaiti children (average age 10.6 years) and their parents (81 percent female, average age 36.5 years; 19 percent male, average age 41 years) who were in Kuwait during the 1990-1991 Gulf War were assessed in 1993. Psychological distress observed in children and parents during a 2003 follow-up was attributed to exposure to the trauma of war. The parents reported more distress than did the children, but the children's distress did not resolve over the 10-year period. The authors suggest that early intervention is key to minimizing the effects of war trauma in children (Llabre et al., 2013; Hadi et al., 2013). In response to the findings of these studies, VA amended two regulations dealing with GW Veterans. One provides for medical care for GW Veterans who developed a mental illness within 2 years after their service and within 2 years after the end of the Gulf War (VA, 2013a). The other identifies five illnesses which are considered to be secondary to a service-connected TBI (VA, 2013b).

## 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., mustard gas and PB); and (3) insecticides (e.g., permethrin, chlorpyrifos).

### DU

Urine monitoring and health surveillance of GW Veterans with embedded metal fragments continues. In a study of GW Veterans with embedded DU fragments and/or inhalation exposure, chromosomes from peripheral blood were analyzed using fluorescence in-situ hybridization. There was no evidence that exposure to DU caused significant chromosome damage (Bakhmutsky et al., 2013). The pulmonary health of GW Veterans with high levels of urine uranium was compared to that of Veterans with low levels of urine uranium. The authors evaluated respiratory symptoms, pulmonary function tests, and chest computed tomography (CT) scans, and concluded that DU exposure did not cause long-term pulmonary problems (Hines et al., 2013). Urine concentrations of uranium and other metals (toxic metals or those likely to be in embedded fragments) were measured in GW Veterans and compared to markers of kidney function, pulmonary tests, and patient questionnaires. There was no correlation between uranium concentrations and any adverse health effects, but there was some evidence of kidney injury in patients with

elevated concentrations of multiple metals. Imaging studies (PET-CT and ultrasound) were also conducted to determine if there were tissue reactions to the embedded fragments (McDiarmid et al., 2013). DU has also been measured in semen samples from six GW Veterans. Uranium levels range from "undetectable" (< 0.8 pg/g) to "very high" (3350 pg/g) and correlate with the body burden of uranium in the individuals tested as a result of retained DU fragments (Todorov et al., 2013). DU in the form of uranyl nitrate was used to expose rats to low and extremely high levels of DU for various lengths of time to test liver and kidney toxicity. In vitro studies also tested whether DU had any effects on cell cultures or on enzymes that help metabolize foreign materials. The activity of selected enzymes decreased by as much as 40 percent, but the in vivo and cell culture experiments showed no direct effect of the DU. It was proposed that there are adaptive mechanisms that compensate for the enzyme effects (Gueguen et al., 2013). In rat brain mitochondria, DU in the form of uranyl acetate induced production of mitochondrial reactive oxygen species (ROS), lipid peroxidation, glutathione oxidation, and inhibition of mitochondrial complex activity. The authors suggest that this mitochondrial oxidative stress may be an important factor in DU neurotoxicity (Shaki et al., 2013). In a theoretical study of the interaction of background gamma radiation with 10-micrometer DU particles in which the DU would be induced to emit extra electrons, it was determined that the energies of these electrons would be too small to cause an increase in cancer risk (Pattison, 2013). Dutch Veterans who deployed to the Balkans between 1993 and 2001 could have been exposed to DU, but cancer incidence in that group was 17 percent less than in Veterans who were deployed to other areas. This finding was contrary to suggestions that DU was related to increased cancer risk (Bogers et al., 2013). In Iraq, however, increases in cancer incidences have been observed in Baghdad, Basra, and Mosul, and it has been inferred that DU is responsible (Fathi et al., 2013). There was concern in southwestern Iran that sandstorms might transport DU-contaminated soil from Iraq, but air (n = 22) and soil (n = 20) samples collected in the area show no evidence of DU (Yousefi and Najafi, 2013). A number of sites in Hawaii had been used for training army personnel in the use of DU-containing ordnance, but it was determined that the general population near these sites would not have been exposed to DU (Eckerd, 2013). Zunic identified the lupus erythematosus cell (LEC) in cytology samples from 47 of 225 bronchoalveolar lavage (BAL) specimens obtained from children in Serbia between 1992 and 2002. It was noted that LECs increased after periods of bombing, presumably by DU-containing munitions. It was suggested that the observed non-specific changes could be indicative of "radiation alveolitis" possibly from DU (Zunic, 2013a; Zunic, 2013b).

**Nerve and Chemical Agents**

It has been proposed that nerve agent plumes were sent into the upper atmosphere when Iraqi chemical weapons storage facilities were bombed early in the Gulf War, then traveled south and exposed U.S. troops and set off chemical detectors (Tuite and Haley, 2013). This claim has been challenged on the basis of a number of meteorological issues (Chang, 2013). Nonetheless, it has been suggested that epidemiological studies of GW Veterans need to be reevaluated to include alarms as a surrogate measure of exposure to nerve agents (Tuite and Haley, 2013). As a follow-up study, 8,020 GW-era Veterans were asked about chemical alarms, and they were evaluated for possible exposure to chemical

weapons destroyed at Khamisiyah, Iraq. It was concluded that the symptoms in ill GW Veterans were more likely to be associated with the chemical alarms (odds ratio, 4.13) than with the Khamisiyah plume (odds ratio, 1.21) (Haley and Tuite, 2013).

### 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. In a study of the effects of PB and PER on lipid concentrations in the brain, it was found that phosphatidylcholine and sphingomyelin levels were higher and lyso-platelet activating factors were lower in exposed mice. Detection of these materials in blood plasma could lead to useful biomarkers (Abdullah et al., 2013). 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., 2013). Rats exposed to PB/DEET/PER exhibited depressive- and anxiety-like behavior and problems with learning and memory. Applying mild physical stress made these symptoms worse. Physiologically there were changes in the hippocampus and reduced neural stem cell activity (Parihar et al., 2013). In another study of rats exposed to PB/CPF/PER, pain indicators were linked to changes in the Na+ and K+ channels. Treatment with linopirdine helped the symptoms to resolve (Nutter et al., 2013).

## C. Immune Dysfunction and Infectious Diseases

Broderick, et al. compared ill and healthy GW Veterans and patients with chronic fatigue syndrome before, during, and after an exercise test. Microarray gene expression profiling, enzyme-linked immunosorbent assay (ELISA) tests, and flow cytometry were used to measure neuroendocrine-immune signaling and inflammatory activity. GW Veterans were determined to exhibit overexpression of exercise response mechanism and neuro-inflammatory response (Broderick, et al., 2013). An exercise study of cytokine expression patterns in male and female GW Veterans indicates that some markers were the same for males and females, but IL-23, Th17, and IL-17 are more gender-specific (Smylie et al., 2013).

Moss has suggested that sodium chloride can increase the risk of autoimmune diseases in GW Veterans in the same way as that proposed for pyridostigmine bromide (Moss, 2013). Maloney, et al. presented a latent viral immune inflammatory response (LVIIR) model to explain CMI. The basis for this model is an inflammatory response to viral antigens that has deleterious effects on the nervous system. The model also suggests that omega-3 fatty acids may decrease inflammation (Maloney et al., 2013). Shoenfeld and coworkers describe an “autoimmune (or autoinflammatory) syndrome induced by adjuvants” (ASIA) as the explanation for GW Veterans’ symptoms because of vaccinations (Cruz-Tapias et al, 2013; Vera-Lastra et al, 2013).

## D. Reproductive Health

Arnetz et al. studied a range of adverse birth outcomes in Iraqis who emigrated to the United States before (n = 122) and after (n = 185) the 1991 Gulf War. Participants in the study were asked about chemical and non-chemical exposures, and both were higher after the Gulf War. The authors concluded that increased adverse birth outcomes are related to GW chemical exposures (Arnetz et al., 2013). Another study reports that increased numbers of Iraqi children with birth defects were living in areas where naturally occurring contaminants and those related to war activities were located (Alborz, 2013).

## E. Symptoms and General Health

### General Health

Twelve large epidemiologic studies and two registries that contain information collected from GW Veterans were reviewed to determine how best to use the existing data and collect data in the future. It was found that questions regarding exposures in the Gulf were very similar in the previous studies whereas neurocognitive and psychological questions varied widely. Future longitudinal studies which build on existing data could be useful in improving the health of Veterans (McNeil et al., 2013). In a retrospective study of war-related vascular injuries in Kuwait in 1990 and 1991, the authors concluded that a vascular surgeon is necessary in a military surgical team (Jawas et al., 2013). Since it has been suggested that GW Veterans, soccer players, and other physically active groups are at increased risk of developing amyotrophic lateral sclerosis (ALS), Huisman et al. administered questionnaires to 636 ALS patients and 2,166 controls. They determined that ALS patients had significantly higher levels of activity during leisure time, but there was no association between ALS and occupational physical activity. It was suggested that either genetic factors or a “lifestyle promoting physical fitness” increase ALS risk (Huisman et al., 2013). In a study of 101 multiple sclerosis (MS) cases in Kuwait, three factors were found to be correlated to increased risk of MS: (1) a family history of MS; (2) head trauma; and (3) being present in Kuwait during the 1990-1991 Gulf War (Al-Afasy et al., 2013). Auxéméry reiterated that the health problems in GW Veterans were real and need to be addressed (Auxéméry, 2013).

An analysis of a recent survey of 2773 GW Veterans indicates that they have poorer health status than and do not use VA health care benefits as much as other Veteran groups (Smith-Osborne, 2013). In a National Survey of Women Veterans (n = 3611), the cost of health care was a major concern of GW Veterans and OEF/OIF Veterans. It was also determined that primary care, reproductive health, and mental health care need to be integrated for women Veterans of all eras (Washington, et al., 2013).

### 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). In another study, autonomic system profile scales, sudomotor function, and high-frequency heart rate variability of patients categorized in Syndromes 1, 2, and 3 of the Haley case definition were also significantly different from controls (Haley et al., 2013). It has also been suggested that stress must be included along with environmental exposure and genetic susceptibility in discussing autonomic dysfunction in a group such as GW Veterans (Freeman, 2013).

Platelet function was compared in ill (n = 43) and healthy (n = 21) GW Veterans. Ill patients had elevated platelet counts and C-reactive protein, spontaneous platelet aggregation, and enhanced thrombin receptor agonist peptide 6 (TRAP 6)-induced ATP secretion, all of which the authors attribute to an underlying inflammatory process (Johnson et al., 2013). Smith et al. revisited the CDC case definition for chronic multisymptom illness in GW Veterans (Fukuda et al., 1998) in a study of 311 GW Veterans. They found that 33.8 percent of the cohort met the case definition criteria but that these patients had many different groups of symptoms. That said, the authors suggested that this definition is still useful for assessing illness in GW Veterans (Smith et al., 2013).

It has been suggested that recruitment of suitable participants is the most significant problem in conducting clinical trials on GW Veterans. Of the many different approaches used to reach GW Veterans, directed media was clearly the best (accounting for 52 percent of those recruited), but the authors emphasize the need to have a diverse plan for recruiting (Erickson et al., 2013). In a randomized controlled clinical trial using the antioxidant L-carnosine to treat 25 ill GW Veterans, Baraniuk et al. found that cognitive function was improved and diarrhea associated with irritable bowel syndrome was reduced. Even though there was no effect on fatigue, pain, and other symptoms, carnosine might be a valuable treatment for two of the symptoms reported by GW Veterans (Baraniuk et al., 2013). 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 reviewed the literature concerning treatments for chronic multisymptom illness in GW Veterans and concluded that a “one size fits all” approach to treating GW Veterans illnesses is not appropriate. A number of recommendations were also provided in the report (IOM, 2013).

## F. Abstracts from Published Research

**Abdullah L, Evans JE, Montague H, Reed JM, Moser A, Crynen G, Gonzalez A, Zakirova Z, Ross I, Mullan C, Mullan M, Ait-Ghezala G, Crawford F (2013) Chronic elevation of phosphocholine containing lipids in mice exposed to Gulf War agents**

**pyridostigmine bromide and permethrin. Neurotoxicol Teratol. 40:74-84. (Epub 2013 Oct 17.)**

For two decades, 25 percent of the Veterans who served in the 1991 Gulf War (GW) have been living with Gulf War Illness (GWI), a chronic multisymptom illness. Evidence suggests that brain structures involved in cognitive function may be affected in GWI. Gulf War agents such as the acetylcholinesterase (AChE) inhibitor pyridostigmine bromide (PB) and the pesticide permethrin (PER) are considered key etiogenic factors in GWI. We therefore developed a mouse model of GW agent exposure by co-administering PB and PER and showed that this model exhibits cognitive impairment and anxiety, and increased astrogliosis at chronic post-exposure time-points. Since GW agents inhibit AChE, we hypothesized that PB+PER exposure will modulate phosphatidylcholine (PC) and sphingomyelin (SM), which are reservoirs of phosphocholine required for endogenous ACh synthesis. Lipidomic analyses showed that PC and SM were elevated in the brains of exposed compared to control mice. Brain ether PC (ePC) species were increased but lyso-platelet activating factors (lyso-PAF) that are products of ePC were decreased in exposed animals compared to controls. Catalase expression (a marker for peroxisomes) was increased in GW agent exposed mice compared to controls. Ether PC and lyso-PAF modulation was also evident in the plasma of GW agent exposed mice compared to controls. These studies suggest peroxisomal and lysosomal dysfunction in the brain at a chronic post-exposure timepoint following GW agent exposure. Our studies provide a new direction for GWI research, which will be useful for developing suitable therapies for treating GWI.

**Al-Afasy HH, Al-Obaidan MA, Al-Ansari YA, Al-Yatama SA, Al-Rukaibi MS, Makki NI, Suresh A, Akhtar S (2013) Risk factors for multiple sclerosis in Kuwait: a population-based case-control study. Neuroepidemiology 40(1):30-35. (Epub 2012 Oct 11.)**

Multiple sclerosis (MS) is a chronic and progressively disabling inflammatory autoimmune disorder of the central nervous system. MS has a multifactorial etiology and is triggered by environmental factors in individuals with complex genetic risk profiles. The epidemiology of MS changes with the spatial and temporal distribution of these genetic and nongenetic risk factors. This population-based matched case-control study aimed to determine the risk factors for MS in Kuwait. From May 2 to 9, 2010, we enrolled 101 confirmed MS cases using the list frame maintained by the Multiple Sclerosis Association of Kuwait. For each case, two population controls individually matched for age (±2 years), gender and nationality were selected. Data on demographic, socioeconomic variables, potential genetic and environmental factors were collected using a structured questionnaire. For a each case, the questions were directed to the period that preceded the recognition of the disease, while for each of the two matched controls, a date of 'pseudodiagnosis' of MS was established, i.e. the date on which the control subject was of the same age as his/her matched case was at MS diagnosis and accordingly questions were directed to the preceding period. The multivariable conditional logistic regression model showed that compared with controls, the cases were significantly more likely to have a family history of MS [matched odds ratio (OR)(adj) = 6.7; 95 percent confidence interval (95 percent CI): 2.5-18.0; $p < 0.001$] or have suffered from a head trauma in the past before MS diagnosis

(matched OR(adj) = 2.6; 95 percent CI: 1.2-5.5; p = 0.014). Furthermore, compared with controls, cases were significantly more likely to have stayed in Kuwait during the Iraqi invasion of 1990 (matched OR (adj) = 1.8; 95 percent CI: 1.1-3.5; p = 0.022). This study showed that a family history of MS, a history of head injury, and presence in Kuwait at the time of the Iraqi invasion of 1990 were associated with a significantly increased MS risk. Future retrospective cohort studies by using existing biological and epidemiological databases may provide a clue to MS etiology.

**Alborz A (2013) Environmental characteristics and prevalence of birth defects among children in post-war Iraq: implications for policies on rebuilding the Iraqi education system. Med Confl Surviv. 29(1):26-44.**

This article explores the relationship between the prevalence of 'birth defects' and environmental characteristics, and considers implications for targeting resources to establish the educational inclusion of children affected. A household survey in four governorates across Iraq in 2010, conducted under the auspices of [the Council for Assisting Refugee Academics], achieved interviews with 6,032 households and collected data on more than 10,000 children and young people. Analyses suggested an association between reported presence of potential sources of contamination in local environments from human and domestic waste, and to some extent from naturally occurring contaminants and the detritus of warfare, with higher numbers of resident children having 'birth defects'. Children living in Basra were found to be most significantly impacted. This finding adds to a growing literature on associations between potential sources of environmental contaminants and impact on the health of children living in affected localities.

**Arnetz B, Drutchas A, Sokol R, Kruger M, Jamil H (2013) 1991 Gulf War exposures and adverse birth outcomes. US Army Med Dep J. 2013 Apr-Jun:58-65.**

We studied 1991 Gulf War (GW)-related environmental exposures and adverse birth outcomes in Iraqis. A random cross-sectional sample of 307 Iraqi families that immigrated to the United States responded to a structured interview covering socioeconomics, lifestyle, environmental exposures, and birth outcome. Data per each family were collected either from the man or the woman in the respective family. The respondents were divided into those that resided in Iraq during and following the GW (post-GW, n=185) and those that had left before (pre-GW, n=122). The primary outcome was lifetime prevalence of adverse birth outcomes, i.e., congenital anomalies, stillbirth, low birth weight, and preterm delivery and its relationship to GW exposures. Mean number of adverse birth outcomes increased from 3.43 (SD=2.11) in the pre-GW to 4.63 (SD=2.63) in the post-GW group (P<.001). Mean chemical (Ch) and nonchemical (NCh) environmental exposure scores increased from pre-GW scores of 0.38 units (SD=1.76) and 0.43 (SD=1.86), respectively, to post-GW scores of 5.65 units (SD=6.23) and 7.26 (SD=5.67), P<.001 between groups for both exposures. There was a significant dose-response relationship between Ch environmental exposure (P=.001), but not NCh exposure, and number of adverse birth outcomes. Exposure to burning oil pits and mustard gas increased the risks for specific adverse birth outcomes by 2 to 4 times. Results indicate that Gulf War Ch, but

not NCh exposures are related to adverse birth outcomes. Pregnancies in women with a history of war exposures might benefit from more intensive observation.

**Auxéméry Y (2013) The Gulf War Syndrome twenty years on. Encephale 39(5):332-338. (Epub 2013 Jan 23.) French.**

INTRODUCTION: After Operation Desert Storm which took place in Iraq from August 1990 to July 1991 involving a coalition of 35 countries and a 700,000 strong contingent of mainly American men, some associations of war Veterans, the media and researchers described a new diagnostic entity: the Gulf War Syndrome (GWS).

LITERATURE FINDINGS: GWS seems to be a new disorder which associates a litany of functional symptoms integrating the musculoskeletal, digestive, tegumentary and neurosensory systems. The symptoms presented do not allow a syndrome already known to be considered and the aetiology of the clinical picture remains unexplained, an increasing cause for concern resulting from the extent of the phenomenon and its media coverage. It quickly appears that there is no consensus amongst the scientific community concerning a nosographic description of GWS: where can all these functional complaints arise from? Different aetiopathogenic hypotheses have been studied by the American administration who is attempting to incriminate exposure to multiple risks such as vaccines and their adjuvants, organophosphorous compounds, pyridostigmine (given to the troops for the preventive treatment of the former), impoverished uranium, and the toxic emanations from oil well fires. But despite extremely in-depth scientific investigations, 10 years after the end of the war, no objective marker of physical suffering has been retained to account for the disorders presented. It would appear that the former soldiers are in even better objective health than the civil population whereas their subjective level of health remains low. Within this symptomatic population, some authors have begun to notice that the psychological disorders appear and persist associating: asthenia, fatigability, mood decline, sleep disorders, cognitive disorders and posttraumatic stress disorder (PTSD). Within the nosological framework, does GWS cause functional disorders or somatisation? Finally, 20 years after the end of the fighting, only PTSD has been causally attributed to military deployment.

CLINICAL FINDINGS: Certain functional symptoms of GWS occur during the latent phase of a future reexperiencing syndrome, latent phase which is the locus of non-specific symptoms. The psychotraumatised subject does not express himself spontaneously and waits to be invited to do so: if the social context does not allow this expression, the suffering can remain lodged in a few parts of the body. How can the inexpressible part of the trauma be recounted, particularly if the social context does not allow it? For civil society, calling into question "the somatic word" of Veterans is difficult: why were they sent to face these hardships? What could we learn from these soldiers we do not wish to listen to: the horror of the war, the aggressive impulse of men, and the confrontation with death? Another obstacle to this reflection is the reference to stress as a prevalent aetiopathogenic model of the psychological trauma. A model like this, considering that PTSD is a normal reaction to an abnormal situation, finally discredits the subject and society and disempowers them by freezing them in a passive status of victim.

DISCUSSION: However, as GWS affects approximately a quarter of subjects deployed, it is not very likely that all these symptoms are caused by a psychotraumatic reaction. Many Veterans suffering from GWS have themselves rejected the diagnosis of PTSD, arguing that they do not suffer repetition nightmares. What the Veterans rightly tell us here is that the notions of stress and trauma cannot strictly be superimposed. A subject may have been intensely stressed without ever establishing traumatic flashbacks and likewise; a psychological trauma can be experienced without stress and without fear but in a moment of terror. This clarification is in line with the first criterion of the DSM-IV-TR which necessarily integrates the objective and subjective dimensions as determinants of PTSD. Yet, scientific studies relating to GWS are struggling to establish opposition or continuity links between the objective external exposure (smoke from petrol wells, impoverished uranium, biological agents, chemicals) and the share of inner emotion albeit reactive and characterised by a subjective stress. There were no lack of stress factors for the troops deployed: repeated alerts of chemical attacks, hostility of the environment with its sandstorms and venomous animals, climatic conditions making long hours of backup and static observation difficult, collecting bodies, lack of knowledge of the precise geography of their movements and uncertainty of the duration of the conflict. The military anti-nuclear-bacteriological-chemical uniform admittedly provided protective confinement, shutting out the hostile world from which the threat would come but, at the same time, this isolation increases the fear of a hypothetical risk whilst the internal perceptions are increased and can open the way to future somatisations. In a context like this, the somatic manifestations of anxiety (palpitations, sweating, paresthesia…) are willingly associated with somatised functional disorders to which can also be assigned over-interpretations of bodily feelings according to a hypochondriacal mechanism. The selective attention to somatic perceptions in the absence of mentalisations, the request for reassurance reiterated and the excessive use of the treatment system will be diagnostic indices of these symptoms caused by the stress. Rather than toxic exposure to such and such a substance, the non-specific syndrome called "Gulf War Syndrome" is the result of exposure to the eponymous operational theatre. But if the psychological and psychosomatic suffering occurring in Veterans is immutable throughout history, the expression of these difficulties has specificities according to the past cultural, political and scientific context. In the example of GWS, the diffusion of the fear of a pathology resulting from chemical weapons has promoted this phenomenon. To spare the bother of a group psychological reflection, the scientific and political authorities chose to investigate the implication of environmental factors in the genesis of the disorder. At individual as well as social level, rather than accept a psychogenic origin, a common defence mechanism is to assign the suffering to an external cause. With the perspective of preventing the risk of diffusion of other unexplained syndromes, which could occur following future armed conflicts, new epidemiological diagnostic models must be defined. The media also has considerable responsibility for the diffusion of epidemic psychological reactions but at the same time, they can inform the population about certain individual or group psychopathological mechanisms.

CONCLUSION: The GWS exists: it is not an "imaginary illness" but a serious public health issue which has led to tens of thousands of complaints and swallowed up millions of

dollars. To reply to human suffering, a new nosographic entity can spread through society taking the epidemic expression of a somatised disorder via identification, imitation and suggestion mechanisms. This possibility questions not only mental health but also the sociology and politics. It is necessary to inform the leaders and the general population of the possibility of this type of mass reaction, which can take the shape of a highly contagious complex functional syndrome.

**Bakhmutsky MV, Squibb K, McDiarmid M, Oliver M, Tucker JD (2013) Long-term exposure to depleted uranium in Gulf-War Veterans does not induce chromosome aberrations in peripheral blood lymphocytes. Mutat Res. 757(2):132-139. (Epub 2013 Aug 8.)**

Depleted uranium (DU) is a high-density heavy metal that has been used in munitions since the 1991 Gulf War. DU is weakly radioactive and chemically toxic, and long-term exposure may cause adverse health effects. This study evaluates genotoxic effects of exposure to DU by measuring chromosome damage in peripheral blood lymphocytes with fluorescence in situ hybridization whole-chromosome painting. Study participants are Gulf War-I Veterans with embedded DU fragments and/or inhalation exposure due to involvement in friendly-fire incidents; they are enrolled in a long-term health surveillance program at the Baltimore Department of Veterans Affairs Medical Center. Blood was drawn from 35 exposed male Veterans aged 39 to 62 years. Chromosomes 1, 2, and 4 were painted red and chromosomes 3, 5, and 6 were simultaneously labeled green. At least 1800 metaphase cells per subject were scored. Univariate regression analyses were performed to evaluate the effects of log (urine uranium), age at time of blood draw, log(lifetime X-rays), pack-years smoked and alcohol use, against frequencies of cells with translocated chromosomes, dicentrics, acentric fragments, color junctions and abnormal cells. No significant relationships were observed between any cytogenetic endpoint and log(urine uranium) levels, smoking, or log(lifetime X-rays). Age at the time of blood draw showed significant relationships with all endpoints except for cells with acentric fragments. Translocation frequencies in these Veterans were all well within the normal range of published values for healthy control subjects from around the world. These results indicate that chronic exposure to DU does not induce significant levels of chromosome damage in these Veterans.

**Baraniuk JN, El-Amin S, Corey R, Rayhan R, Timbol C (2013) Carnosine treatment for Gulf War illness: a randomized controlled trial. Glob J Health Sci. 5(3):69-81.**

About 25 percent of 1990-1991 Persian Gulf War Veterans experience disabling fatigue, widespread pain, and cognitive dysfunction termed Gulf War illness (GWI) or Chronic Multisymptom Illness (CMI). A leading theory proposes that wartime exposures initiated prolonged production of reactive oxygen species (ROS) and central nervous system injury. The endogenous antioxidant L-carnosine (B-alanyl-L-histidine) is a potential treatment since it is a free radical scavenger in nervous tissue. To determine if nutritional supplementation with L-carnosine would significantly improve pain, cognition and fatigue in GWI, a randomized double blind placebo controlled 12 week dose escalation study involving 25 GWI subjects was employed. L-carnosine was given as 500, 1000, and 1500

mg increasing at 4 week intervals. Outcomes included subjective fatigue, pain and psychosocial questionnaires, and instantaneous fatigue and activity levels recorded by ActiWatch Score devices. Cognitive function was evaluated by WAIS-R digit symbol substitution test. Carnosine had 2 potentially beneficial effects: WAIS-R scores increased significantly, and there was a decrease in diarrhea associated with irritable bowel syndrome. No other significant incremental changes were found. Therefore, 12 weeks of carnosine (1500 mg) may have beneficial cognitive effects in GWI. Fatigue, pain, hyperalgesia, activity, and other outcomes were resistant to treatment.

**Bogers RP, van Leeuwen FE, Grievink L, Schouten LJ, Kiemeney LA, Schram-Bijkerk D (2013) Cancer incidence in Dutch Balkan Veterans. Cancer Epidemiol. 37(5):550-555. (Epub 2013 May 22.)**

Suspicion has been raised about an increased cancer risk among Balkan Veterans because of alleged exposure to depleted uranium. The authors conducted a historical cohort study to examine cancer incidence among Dutch Balkan Veterans. Male military personnel (n=18,175, median follow-up 11 years) of the Army and Military Police who had been deployed to the Balkan region (1993-2001) was compared with their peers not deployed to the Balkans (n=135,355, median follow-up 15 years) and with the general Dutch population of comparable age and sex. The incidence of all cancers and 4 main cancer subgroups was studied in the period 1993-2008. The cancer incidence rate among Balkan deployed military men was 17 percent lower than among non-Balkan deployed military men (hazard ratio 0.83 (95 percent confidence interval 0.69, 1.00)). For the 4 main cancer subgroups, hazard ratios were statistically non-significantly below 1. Also compared to the general population cancer rates were lower in Balkan deployed personnel (standardised incidence rate ratio (SIR) 0.85 (0.73, 0.99). The SIR for leukaemia was 0.63 (0.20, 1.46). The authors conclude that earlier suggestions of increased cancer risks among Veterans are not supported by empirical data. The lower risk of cancer might be explained by the 'healthy warrior effect'.

**Broderick G, Ben-Hamo R, Vashishtha S, Efroni S, Nathanson L, Barnes Z, Fletcher MA, Klimas N (2013) Altered immune pathway activity under exercise challenge in Gulf War Illness: an exploratory analysis. Brain Behav Immun 28:159-169. (Epub 2012 Nov 29.)**

Though potentially linked to the basic physiology of stress response we still have no clear understanding of GWI, a debilitating illness presenting with a complex constellation of immune, endocrine and neurological symptoms. Here we compared male GWI (n=20) with healthy Veterans (n=22) and subjects with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) (n=7). Blood was drawn during a Graded eXercise Test (GXT) prior to exercise, at peak effort (VO2 max) and 4-h post exercise. Affymetrix HG U133 plus 2.0 microarray gene expression profiling in peripheral blood mon onuclear cells (PBMCs) was used to estimate activation of over 500 documented pathways. This was cast against ELISA-based measurement of 16 cytokines in plasma and flow cytometric assessment of lymphocyte populations and cytotoxicity. A 2-way ANOVA corrected for multiple comparisons (q statistic <0.05) indicated significant increases in neuroendocrine-

immune signaling and inflammatory activity in GWI, with decreased apoptotic signaling. Conversely, cell cycle progression and immune signaling were broadly subdued in CFS. Partial correlation networks linking pathways with symptom severity via changes in immune cell abundance, function and signaling were constructed. Central to these were changes in IL-10 and CD2+ cell abundance and their link to two pathway clusters. The first consisted of pathways supporting neuronal development and migration whereas the second was related to androgen-mediated activation of NF-κB. These exploratory results suggest an over-expression of known exercise response mechanisms as well as illness-specific changes that may involve an overlapping stress-potentiated neuro-inflammatory response.

**Chang JC (2013) Comments on a recent article on meteorological and intelligence evidence of long-distance transit of chemical weapons fallout from bombing early in the 1991 Persian Gulf War. Neuroepidemiology. 41(3-4):183-184. (Epub 2013 Sep 18.)**

Full text available: http://www.karger.com/Article/FullText/354163

**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.**

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.

**Cruz-Tapias P, Agmon-Levin N, Israeli E, Anaya JM, Shoenfeld Y (2013) Autoimmune (auto-inflammatory) syndrome induced by adjuvants (ASIA)--animal models as a proof of concept. Curr Med Chem. 20(32):4030-4036.**

ASIA syndrome, "Autoimmune (Auto-inflammatory) Syndromes Induced by Adjuvants" includes at least four conditions which share a similar complex of signs and symptoms and have been defined by hyperactive immune responses: siliconosis, macrophagic myofasciitis syndrome, Gulf War syndrome and post-vaccination phenomena. Exposure to adjuvants has been documented in these four medical conditions, suggesting that the common denominator to these syndromes is a trigger entailing adjuvant activity. An important role of animal models in proving the ASIA concept has been established. Experimentally animal models of autoimmune diseases induced by adjuvants are currently widely used to understand the mechanisms and etiology and pathogenesis of these diseases and might thus promote the development of new diagnostic, predictive and therapeutic methods. In the current review we wish to unveil the variety of ASIA animal models associated with systemic and organ specific autoimmune diseases induced by adjuvants. We included in this review, animal models for rheumatoid arthritis-like disease, for systemic lupus erythematosus-like disease, autoimmune thyroid disease-like disease, antiphospholipid syndrome, myocarditis and others. All these models support the concept of ASIA, as the Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants.

**de Silva VA, Jayasekera NE, Hanwella R (2013) Multiple physical symptoms in a military population: a cross-sectional study. Ann Gen Psychiatry 12(1):24.**

BACKGROUND: Medically unexplained symptoms have been reported among both civilians and military personnel exposed to combat. A large number of military personnel deployed to the Gulf War in 1991 reported non-specific symptoms. These symptoms did not constitute a clearly defined syndrome. Post-traumatic stress disorder (PTSD) and to a lesser degree exposure to combat are associated with physical symptoms.

METHODS: This is a cross-sectional study of representative samples of Sri Lanka Navy Special Forces and regular forces deployed in combat areas continuously during a 1-year period. Multiple physical symptoms were elicited using a checklist of 53 symptoms. Cases were defined as individuals with ten or more symptoms. Symptoms of common mental disorder were identified using the General Health Questionnaire 12 (GHQ-12). PTSD was diagnosed using the 17-item National Centre for PTSD checklist civilian version.

RESULTS: Prevalence of multiple physical symptoms was 10.4 percent (95 percent CI 8.11-12.75). Prevalence was significantly less in the Special Forces (5.79 percent) than in the regular forces (13.35 percent). The mean number of symptoms reported by those who met the criteria for PTSD was 12.19 (SD 10.58), GHQ caseness 7.87 (SD 7.57) and those without these conditions 2.84 (SD 3.63). After adjusting for socio-demographic and

service variables, 'thought I might be killed,' 'coming under small arms fire,' and 'coming under mortar, missile and artillery fire' remained significant. Multiple physical symptoms were associated with functional impairment and poor perceived general health.

CONCLUSIONS: Prevalence of multiple physical symptoms was significantly lower in the Special Forces despite high exposure to potentially traumatic events. More multiple physical symptoms were reported by personnel with PTSD and common mental disorders. Multiple physical symptoms were associated with functional impairment.

**Department of Veterans Affairs (2013b) Secondary service connection for diagnosable illnesses associated with traumatic brain injury. Final rule. Fed Regist. 78(242):76196-209.**

VA amends its adjudication regulations concerning service connection. This final rule acts upon a report of the National Academy of Sciences, Institute of Medicine (IOM), Gulf War and Health, Volume 7: Long-Term Consequences of Traumatic Brain Injury, regarding the association between traumatic brain injury (TBI) and five diagnosable illnesses. This amendment establishes that if a veteran who has a service-connected TBI also has one of these diagnosable illnesses, then that illness will be considered service connected as secondary to the TBI.

**Department of Veterans Affairs. (2013a) Tentative eligibility determinations; presumptive eligibility for psychosis and other mental illness. Final rule. Fed Regist. 78(93):28140-28143.**

This document amends (VA regulation authorizing tentative eligibility determinations to comply with amended statutory authority concerning minimum active-duty service requirements. This document also codifies in regulation statutory presumptions of medical care eligibility for Veterans of certain wars and conflicts who developed psychosis within specified time periods and for Persian Gulf War Veterans who developed a mental illness other than psychosis within 2 years after service and within 2 years after the end of the Persian Gulf War period.

**Eckerd J (2013) Insights in public health: the facts about depleted uranium in Hawai'i. Hawaii J Med Public Health 72(11):404-405.**

Full text available: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3831570/

**Erickson LC, Ritchie JB, Javors JM, Golomb BA (2013) Recruiting a special sample with sparse resources: lessons from a study of Gulf War Veterans. Clin Trials 10(3):473-482. (Epub 2013 Jan 16.)**

BACKGROUND: Recruitment is the most common failure point for clinical studies, with recruitment failure adversely affecting science, dollar costs, human capital, and the ethical risk-benefit trade-off to study participants. Added problems attend recruitment of special and/or challenging candidate populations, particularly in settings of sparse recruitment

resources. Obstacles to study recruitment and participation of ill Gulf War Veterans (GWV) include health barriers, work and family obligations, mistrust of the medical/scientific community, and challenges to identifying/reaching potential participants.

PURPOSE: We sought to identify and implement a minimal-cost multipronged recruitment approach for a small single-site (<50 participants) study of a special group, ill GWVs, with approaches substantially applicable to other recruitment settings and larger multisite studies.

METHODS: Categories of recruitment approach included directed as well as general media, collaborations with support groups/interest groups, local free advertising resources (Craigslist and Backpage), physician outreach, Internet-based approaches, and referrals from study participants and screenees. We describe the subcategories and yield of each approach within each approach.

RESULTS: Each approach contributed candidates to the final recruitment tally, with the largest fractional contribution by directed media (52 percent). Among the remainder, no other individual approach was clearly dominant (largest contribution: 13 percent). LIMITATIONS: Special population subsamples present special challenges; all approaches cited may not be useful in all settings and subpopulations.

CONCLUSIONS: A multipronged suite of minimal-cost approaches led to successful recruitment to target for this single-site clinical trial for a special population with significant recruitment challenges. It additionally yielded a nation-wide corpus of several hundred individuals interested in participation in future studies of GWVs. While certain approaches produced disproportionate yield, it was not possible to predict these a priori. We suggest that this model, which incorporates a suite of approaches, and delineates backup approaches in the event of recruitment shortfall, may provide a template applicable to recruitment of other special samples in settings of limited resources and also is germane to cost-effective recruitment in studies more generally.

**Fathi RA, Matti LY, Al-Salih HS, Godbold D (2013) Environmental pollution by depleted uranium in Iraq with special reference to Mosul and possible effects on cancer and birth defect rates. Med Confl Surviv. 29(1):7-25.**

Iraq is suffering from depleted uranium (DU) pollution in many regions and the effects of this may harm public health through poisoning and increased incidence of various cancers and birth defects. DU is a known carcinogenic agent. About 1200 tonnes of ammunition were dropped on Iraq during the Gulf Wars of 1991 and 2003. As a result, contamination occurred in more than 350 sites in Iraq. Currently, Iraqis are facing about 140,000 cases of cancer, with 7,000 to 8,000 new ones registered each year. In Baghdad cancer incidences per 100,000 population have increased, just as they have also increased in Basra. The overall incidence of breast and lung cancer, Leukaemia and Lymphoma, has doubled even tripled. The situation in Mosul city is similar to other regions. Before the Gulf Wars Mosul had a higher rate of cancer, but the rate of cancer has further increased since the Gulf Wars.

**Freeman R (2013) Objective evidence of autonomic dysfunction and the role of stress in the Gulf War syndrome. JAMA Neurol. 70(2):158-159.**

Full text available: http://archneur.jamanetwork.com/article.aspx?articleid=1397607

**Gueguen Y, Rouas C, Monin A, Manens L, Stefani J, Delissen O, Grison S, Dublineau I (2013) Molecular, cellular, and tissue impact of depleted uranium on xenobiotic-metabolizing enzymes. Arch Toxicol. 2013 Oct 23.**

Enzymes that metabolize xenobiotics (XME) are well recognized in experimental models as representative indicators of organ detoxification functions and of exposure to toxicants. As several in vivo studies have shown, uranium can alter XME in the rat liver or kidneys after either acute or chronic exposure. To determine how length or level of exposure affects these changes in XME, we continued our investigation of chronic rat exposure to depleted uranium (DU, uranyl nitrate). The first study examined the effect of duration (1-18 months) of chronic exposure to DU, the second evaluated dose dependence, from a level close to that found in the environment near mining sites (0.2 mg/L) to a supra-environmental dose (120 mg/L, 10 times the highest level naturally found in the environment), and the third was an in vitro assessment of whether DU exposure directly affects XME and, in particular, CYP3A. The experimental in vivo models used here demonstrated that CYP3A is the enzyme modified to the greatest extent: high gene expression changed after 6 and 9 months. The most substantial effects were observed in the liver of rats after 9 months of exposure to 120 mg/L of DU: CYP3A gene and protein expression and enzyme activity all decreased by more than 40 percent. Nonetheless, no direct effect of DU by itself was observed after in vitro exposure of rat microsomal preparations, HepG2 cells, or human primary hepatocytes. Overall, these results probably indicate the occurrence of regulatory or adaptive mechanisms that could explain the indirect effect observed in vivo after chronic exposure.

**Hadi F, Lai BS, Llabre MM (2013) Life outcomes influenced by war-related experiences during the Gulf crisis. Anxiety Stress Coping. 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.

**Haley RW, Charuvastra E, Shell WE, Buhner DM, Marshall WW, Biggs MM, Hopkins SC, Wolfe GI, Vernino S (2013) Cholinergic autonomic dysfunction in Veterans with Gulf War illness: confirmation in a population-based sample. JAMA Neurol. 70(2):191-200. (Epub 2012 Nov 26.)**

BACKGROUND: The authors of prior small studies raised the hypothesis that symptoms in Veterans of the 1991 Gulf War, such as chronic diarrhea, dizziness, fatigue, and sexual dysfunction, are due to cholinergic autonomic dysfunction.

OBJECTIVE: To perform a confirmatory test of this prestated hypothesis in a larger, representative sample of GW Veterans.

DESIGN: Nested case-control study.

SETTING: Clinical and Translational Research Center, University of Texas Southwestern Medical Center, Dallas.

PARTICIPANTS: Representative samples of GW Veterans meeting a validated case definition of Gulf War illness with 3 variants (called syndromes 1-3) and a control group, all selected randomly from the U.S. Military Health Survey.

MAIN OUTCOME MEASURES: Validated domain scales from the Autonomic Symptom Profile questionnaire, the Composite Autonomic Severity Score, and high-frequency heart rate variability from a 24-hour electrocardiogram.

RESULTS: The Autonomic Symptom Profile scales were significantly elevated in all 3 syndrome groups ($P < .001$), primarily due to elevation of the orthostatic intolerance, secretomotor, upper gastrointestinal dysmotility, sleep dysfunction, urinary, and autonomic diarrhea symptom domains. The Composite Autonomic Severity Score was also higher in the 3 syndrome groups ($P = .045$), especially in syndrome 2, primarily due to a significant reduction in sudomotor function as measured by the Quantitative Sudomotor Axon Reflex Test, most significantly in the foot; the score was intermediate in the ankle and upper leg and was nonsignificant in the arm, indicating a peripheral nerve length-related deficit. The normal increase in high-frequency heart rate variability at night was absent or blunted in all 3 syndrome groups ($P < .001$).

CONCLUSION: Autonomic symptoms are associated with objective, predominantly cholinergic autonomic deficits in the population of GW Veterans.

**Haley RW, Tuite JJ (2012) Epidemiologic Evidence of Health Effects from Long-Distance Transit of Chemical Weapons Fallout from Bombing Early in the 1991 Persian Gulf War. Neuroepidemiology 40(3):178-189.**

BACKGROUND: Military intelligence data published in a companion paper explain how chemical fallout from U.S. and Coalition bombing of Iraqi chemical weapons facilities early in the air campaign transited long distance, triggering nerve agent alarms and exposing U.S. troops. We report the findings of a population-based survey designed to test competing hypotheses on the impact on chronic GWI of nerve agent from early-war bombing versus post-war demolition.

METHODS: The U.S. Military Health Survey performed computer-assisted telephone interviews of a stratified random sample of GW-era Veterans (n = 8,020). Early-war exposure was measured by having heard nerve agent alarms and post-war exposure, by the computer-generated plume from the Khamisiyah demolition. GWI was measured by two widely published case definitions.

RESULTS: The OR (95 percent CI) for the association of alarms with the Factor case definition was 4.13 (95 percent CI 2.51-6.80) compared with 1.21 (95 percent CI 0.86-1.69) for the Khamisiyah plume. There was a dose-related trend for the number of alarms ($p(\text{trend}) < 0.001$) but not for the number of days in the Khamisiyah plume ($p(\text{trend}) = 0.17$).

CONCLUSIONS: Exposure to low-level sarin nerve agent in fallout from bombing early in the air campaign contributed more to chronic illness than post-war demolition.

**Hines SE, Gucer P, Kligerman S, Breyer R, Centeno J, Gaitens J, Oliver M, Engelhardt S, Squibb K, McDiarmid M (2013) Pulmonary health effects in Gulf War I service members exposed to depleted uranium. J Occup Environ Med. 55(8):937-944.**

OBJECTIVE: In a population of Gulf War I Veterans who sustained inhalational exposure to depleted uranium during friendly fire incidents in 1991, we evaluated whether those with high body burdens of uranium were more likely to have pulmonary health abnormalities than those with low body burdens.

METHODS: We compared self-reported respiratory symptoms, mean pulmonary function values, and prevalence of low-dose chest computed tomography abnormalities between high and low urine uranium groups.

RESULTS: We found no significant differences in respiratory symptoms, abnormal pulmonary function values, or prevalence of chest computed tomography abnormalities between high and low urine uranium groups. Overall, the cohort's pulmonary function values fell within the expected clinical range.

CONCLUSIONS: Our results support previous estimates that the depleted uranium levels inhaled during the 1991 friendly fire incidents likely do not cause long-term adverse pulmonary health effects.

**Huisman MH, Seelen M, de Jong SW, Dorresteijn KR, van Doormaal PT, van der Kooi AJ, de Visser M, Schelhaas HJ, van den Berg LH, Veldink JH (2013) Lifetime physical activity and the risk of amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry 84(9):976-981. (Epub 2013 Feb 16.)**

BACKGROUND: It has been hypothesised that physical activity is a risk factor for developing amyotrophic lateral sclerosis (ALS), fuelled by observations that professional soccer players and Gulf War Veterans are at increased risk. In a population based study, we determined the relation between physical activity and risk of sporadic ALS, using an objective approach for assessing physical activity.

METHODS: 636 sporadic ALS patients and 2166 controls, both population based, completed a semistructured questionnaire on lifetime history of occupations, sports and hobbies. To objectively compare the energy cost of a lifetime history of occupational and leisure time physical activities and to reduce recall bias, metabolic equivalent scores were assigned to each activity based on the Compendium of Physical Activities.

RESULTS: ALS patients had significantly higher levels of leisure time physical activity compared with controls (OR 1.08, 95 percent CI 1.02 to 1.14, p=0.008). No significant difference was found between patients and controls in the level of vigorous physical activities, including marathons and triathlons, or in occupational activity. Cumulative measures of physical activity in quartiles did not show a dose-response relationship.

CONCLUSIONS: An increased risk of ALS with higher levels of leisure time physical activity was found in the present study. The lack of association with occupational physical activity and the absence of a dose-response relationship strengthen the hypothesis that not increased physical activity per se but rather a genetic profile or lifestyle promoting physical fitness increases ALS susceptibility.

**Institute of Medicine (2013) Gulf War and Health. Treatment for Chronic Multisymptom Illness. Washington, DC: The National Academies Press.**

Full text available: http://www.nap.edu/catalog.php?record_id=13539

**Jawas A, Abbas AK, Nazzal M, Albader M, Abu-Zidan FM (2013) Management of war-related vascular injuries: experience from the second gulf war. World J Emerg Surg. 8(1):22.**

AIM: To study the biomechanism, pattern of injury, management, and outcome of major vascular injuries treated at Mubarak Al-Kabeer Teaching Hospital, Kuwait during the Second Gulf War.

METHODS: This is a descriptive retrospective study. War-related injured patients who had major vascular injuries and were treated at Mubarak Al-Kabeer Teaching Hospital from August 1990 to September 1991 were studied. Studied variables included age, gender,

anatomical site of vascular injury, mechanism of injury, associated injuries, type of vascular repair, and clinical outcome.

RESULTS: 36 patients having a mean (SD) age of 29.8 (10.2) years were studied. 32 (89 percent) were males and 21 (58 percent) were civilians. Majority of injuries were caused by bullets (47.2 percent) and blast injuries (47.2 percent). Eight patients (22 percent) presented with shock. There were 31 arterial injuries, common and superficial femoral artery injuries were most common (10/31). Arterial repair included interposition saphenous vein graft in seven patients, thrombectomy with end-to-end / lateral repair in 12 patients, vein patch in two patients, and arterial ligation in four patients. Six patients had arterial ligation as part of primary amputation. 3/21 (14.3 percent) patients had secondary amputation after attempted arterial vascular repair of an extremity. There were a total of 17 venous injuries, 13 managed by lateral suture repair and 4 by ligation. The median (range) hospital stay was 8 (1-76) days. 5 patients died (14 percent).

CONCLUSIONS: Major vascular injuries occurred in 10 percent of hospitalized war-related injured patients. Our secondary amputation rate of extremities was 14 percent. The presence of a vascular surgeon within a military surgical team is highly recommended. Basic principles and techniques of vascular repair remain an essential part of training general surgeons because it may be needed in unexpected wars.

**Johnson GJ, Leis LA, Slater BC, Bach RR (2013) Elevated platelet count, C-reactive protein and thromboxane analog-induced platelet aggregation in patients with Gulf War Veterans' illnesses: evidence of a chronic inflammatory state? Blood Coagul Fibrinolysis 24(7):736-741.**

A previous study of Gulf War veteran's illnesses (GWVI) observed evidence of platelet activation in a majority of patients with GWVI. To further characterize platelet function, we studied 43 patients (40 men) with GWVI (GWVI+) and 21 Veterans who served concurrently in the Gulf War but who lacked criteria for GWVI (GWVI-). All participants were free of infection and known inflammatory diseases. Studies performed included platelet count, immature platelet fraction (IPF), plasma thrombopoietin (TPO), C-reactive protein (CRP), platelet aggregation and ATP secretion in response to six agonists, and spontaneous aggregation. Platelet counts and CRP were significantly elevated in GWVI+ compared to GWVI- patients without elevation in IPF or TPO. Platelet aggregation did not differ between GWVI+ and GWVI- patients except for spontaneous aggregation that was significantly greater in GWVI+ patients. Platelet ATP secretion was similar in the two groups, except the response to 50 μmol/l thrombin receptor agonist peptide 6 (TRAP 6) was significantly greater in GWVI+ patients. When platelet aggregation was analyzed in relation to CRP, the response to 0.5 μmol/l U46619 was significantly greater in patients whose CRP was at least 2 μg/ml. Therefore, GWVI+ patients had elevated platelet counts, spontaneous aggregation, TRAP 6-induced secretion, and CRP, but no impairment of platelet function. The increased platelet counts and U46619-induced aggregation appear to be consequences of an underlying inflammatory state in GWVI.

**Kelsall HL, McKenzie DP, Forbes AB, Roberts MH, Urquhart DM, Sim MR (2013) Pain-related musculoskeletal disorders, psychological comorbidity, and the relationship with physical and mental well-being in Gulf War Veterans. Pain S0304-3959(13)00688-X.**

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 percent were serving and 32.7 percent 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 12months 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 percent) and the comparison group (22.4 percent) 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 (e.g., Veterans with any MSD, difference in SF-12 physical component summary scale medians = -10.49: 95 percent 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.

**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. (Epub 2014 Jan 7.)**

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 percent 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.

**Llabre MM, Hadi F, La Greca AM, Lai BS (2013) Psychological Distress in Young Adults Exposed to War-Related Trauma in Childhood. J Clin Child Adolesc Psychol. 2013 Aug 26.**

We tested a conceptual model of the effect of war-trauma exposure in childhood on psychological distress in young adulthood. Participants included 151 urban Kuwaiti children (51 percent female; M age = 10.62 years) exposed to the 1990-1991 Gulf crisis (assessed in 1993); participants also included 140 parents (81 percent female; M age mothers = 36.50 years; M age fathers = 41 years). In 2003, 120 participants were reassessed as young adults (50 percent female; M age = 21.19 years). The conceptual model was evaluated with structural equations. War-trauma exposure was associated with psychological distress in children and parents, but parents reported larger effects than children. Parents' psychological distress did not contribute to children's psychological distress. Children's psychological distress did not dissipate over time. Social support may function as a potential mediator of the effect of war-trauma exposure on psychological distress. Findings support the importance of early detection and treatment of children exposed to war trauma. Findings also implicate social support as a factor to consider in clinical interventions for children exposed to war trauma.

**Maloney CD, Jensen S, Gil-Rivas V, Goolkasian P (2013) Latent viral immune inflammatory response model for chronic multisymptom illness. Med Hypotheses 80(3):220-229. (Epub 2012 Dec 21.)**

A latent viral immune inflammatory response (LVIIR) model is presented which integrates factors that contribute to chronic multisymptom illness (CMI) in both the veteran and civilian populations. The LVIIR model for CMI results from an integration of clinical experience with a review of the literature in four distinct areas: (1) studies of idiopathic multisymptom illness in the Veteran population including two decades of research on Gulf War I Veterans with CMI; (2) new evidence supporting the existence of chronic inflammatory responses to latent viral antigens and the effect these responses may have on the nervous system; (3) recent discoveries concerning the role of vitamin D in maintaining normal innate and adaptive immunity including suppression of latent viruses and regulation of the immune inflammatory response; and (4) the detrimental effects of extreme chronic repetitive stress (ECRS) on the immune and nervous systems. The LVIIR model describes the pathophysiology of a pathway to CMI and presents a new direction for the clinical assessment of CMI that includes the use of neurological signs from a physical exam, objective laboratory data, and a new proposed latent viral antigen-antibody imaging technique for the peripheral and central nervous system. The LVIIR model predicts that

CMI can be treated by a focus on reversal of immune system impairment, suppression of latent viruses and their antigens, and healing of nervous system tissue damaged by chronic inflammation associated with latent viral antigens and by ECRS. In addition, the LVIIR model suggests that maintaining optimal serum 25 OH vitamin D levels will maximize immune system suppression of latent viruses and their antigens and will minimize immune system inflammation. This model also emphasizes the importance of decreasing ECRS to improve immune system function and to minimize nervous system injury from excess serum glucocorticoid levels. The proposed model supports growing evidence that increasing omega 3 essential fatty acid levels in nervous system tissues may decrease inflammation in the nervous system and improve neural plasticity and recovery from neuronal injury.

**McDiarmid MA, Gaitens JM, Hines S, Breyer R, Wong-You-Cheong JJ, Engelhardt SM, Oliver M, Gucer P, Kane R, Cernich A, Kaup B, Hoover D, Gaspari AA, Liu J, Harberts E, Brown L, Centeno JA, Gray PJ, Xu H, Squibb KS (2013) The Gulf War depleted uranium cohort at 20 years: bioassay results and novel approaches to fragment surveillance. Health Phys. 104(4):347-361.**

During the 1991 Gulf War, U.S. Servicemembers were exposed to depleted uranium (DU) through friendly-fire incidents involving DU munitions and vehicles protected by DU armor. Routes of exposure to DU involved inhalation of soluble and insoluble DU oxide particles, wound contamination, and retained embedded DU metal fragments that continue to oxidize in situ and release DU to the systemic circulation. A biennial health surveillance program established for this group of Veterans by the U.S. Department of Veterans Affairs has shown continuously elevated urine DU concentrations in the subset of Veterans with embedded fragments for over 20 years. While the 2011 assessment was comprehensive, few clinically significant U-related health effects were observed. This report is focused on health outcomes associated with two primary target organs of concern for long term effects of this combat-related exposure to DU. Renal biomarkers showed minimal DU-related effects on proximal tubule function and cytotoxicity, but significant biomarker results were observed when urine concentrations of multiple metals also found in fragments were examined together. Pulmonary tests and questionnaire results indicate that pulmonary function after 20 years remains within the clinical normal range. Imaging of DU embedded fragment-associated tissue for signs of inflammatory or proliferative reactions possibly associated with foreign body transformation or with local alpha emissions from DU was also conducted using PET-CT and ultrasound. These imaging tools may be helpful in guiding decisions regarding removal of fragments.

**McNeil RB, Thomas CM, Coughlin SS, Hauser E, Huang GD, Goldstein KM, Johnson MR, Dunn-Thomas T, Provenzale DT (2013) An assessment of survey measures used across key epidemiologic studies of United States Gulf War I Era Veterans. Environ Health 12:4.**

Over the past two decades, 12 large epidemiologic studies and 2 registries have focused on U.S. Veterans of the 1990-1991 Gulf War Era. We conducted a review of these studies' research tools to identify existing gaps and overlaps of efforts to date, and to

advance development of the next generation of Gulf War Era survey tools. Overall, we found that many of the studies used similar instruments. Questions regarding exposures were more similar across studies than other domains, while neurocognitive and psychological tools were the most variable. Many studies focused on self-reported survey results, with a range of validation practices. However, physical exams, biomedical assessments, and specimen storage were not common. This review suggests that while research may be able to pool data from past surveys, future surveys need to consider how their design can yield data comparable with previous surveys. Additionally, data that incorporate recent technologies in specimen and genetic analyses would greatly enhance such survey data. When combined with existing data on deployment-related exposures and post-deployment health conditions, longitudinal follow-up of existing studies within this collaborative framework could represent an important step toward improving the health of Veterans.

**Moss JI. (2013) Gulf War illnesses are autoimmune illnesses caused by increased activity of the p38/MAPK pathway in CD4+ immune system cells, which was caused by nerve agent prophylaxis and adrenergic load. Med Hypotheses 81(6):1002-1003. (Epub 2013 Sep 17.)**

Sodium chloride intake might increase the risk for the development of autoimmune diseases by increasing the activity of the p38/MAPK pathway in CD4+ cells thereby producing pathogenic TH17 cells which are inflammatory. Two factors (muscarinic and beta adrenergic stimulation), already shown to potentiate each other's toxic effects in whole mice, and have combined amplified sub lethal effects on mouse T cells, can have the same effect on CD4+ signaling pathways as sodium chloride. Sick 1991 Gulf War Veterans express elevated Th17 cytokine activity, and therefore may have autoimmune illnesses caused directly by the above mentioned exposures.

**Nutter TJ, Jiang N, Cooper BY (2013) Persistent Na+ and K+ channel dysfunctions after chronic exposure to insecticides and pyridostigmine bromide. Neurotoxicology 39:72-83. (Epub 2013 Aug 29.)**

Many soldiers that served in the 1991 Gulf War developed widespread chronic pain. Exposure to insecticides and the nerve gas prophylactic pyridostigmine bromide (PB) was identified as risk factors by the Research Advisory Committee on Gulf War Veterans' Illnesses (GWI). We examined whether a 60 day exposure to neurotoxicants/PB (NTPB) produced behavioral, molecular and cellular indices of chronic pain in the rat. Male rats were exposed to chlorpyrifos (120mg/kg; SC), permethrin (2.6mg/kg; topical), and PB (13.0mg/kg; oral) or their respective vehicles (corn oil, ethanol, and water). Permethrin can exert profound influences on voltage activated Na(+) channel proteins; while chlorpyrifos and PB can increase absorption and/or retard metabolism of permethrin as well as inhibit cholinesterases. During and after exposure to these agents, we assessed muscle pressure pain thresholds and activity (distance and rest time). Eight and 12 weeks after treatments ceased, we used whole cell patch electrophysiology to examine the physiology of tissue specific DRG nociceptor channel proteins expressed in muscle and putative vascular nociceptors (voltage dependent, activation, inactivation, and

deactivation). Behavioral indices were unchanged after treatment with NTPB. Eight weeks after treatments ended, the peak and average conductance of Kv7 mediated K(+) currents were significantly increased in vascular nociceptors. When a specific Kv7 inhibitor was applied (linopirdine, 10μM) NTPB treated vascular nociceptors emitted significantly more spontaneous APs than vehicle treated neurons. Changes to Kv7 channel physiology were resolved 12 weeks after treatment. The molecular alterations to Kv7 channel proteins and the specific susceptibility of the vascular nociceptor population could be important for the etiology of GWI pain.

**Odegard TN, Cooper CM, Farris EA, Arduengo J, Bartlett J, Haley R (2012) Memory impairment exhibited by Veterans with Gulf War Illness. Neurocase (Epub 2012 Apr 23, ahead of print.)**

Roughly 26-32 percent of U.S. Veterans, who served in the first GW, report suffering from chronic health problems ( Golomb, 2008, Proceedings of the National Academies of Science, 105, 4295). The present study investigated the memory deficits reported by these ill GW Veterans (GWV) using a face-name associative memory paradigm administered during functional magnetic resonance imaging (fMRI). The fMRI data confirmed memory performance on the memory task to be related to the amount of activation in the left hippocampus observed during the study. In addition, ill-GWV demonstrated decreased memory performance relative to unaffected GWV on this memory test, providing evidence of memory deficits using an objective measure of memory.

**Ojo JO, Abdullah L, Evans J, Reed JM, Montague H, Mullan MJ, Crawford FC (2013) 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 2013 Sep 30. doi: 10.1111/neup.12061.**

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.

**Parihar VK, Hattiangady B, Shuai B, Shetty AK (2013) Mood and memory deficits in a model of Gulf War illness are linked with reduced neurogenesis, partial neuron loss, and mild inflammation in the hippocampus. Neuropsychopharmacology 38(12):2348-2362. (Epub 2013 Jun 28.)**

Impairments in mood and cognitive function are the key brain abnormalities observed in Gulf War Illness (GWI), a chronic multisymptom health problem afflicting ~25 percent of Veterans who served in the Persian Gulf War-1. Although the precise cause of GWI is still unknown, combined exposure to a nerve gas prophylaxis drug pyridostigmine bromide (PB) and pesticides DEET and permethrin during the war has been proposed as one of the foremost causes of GWI. We investigated the effect of 4 weeks of exposure to Gulf War illness-related (GWIR) chemicals in the absence or presence of mild stress on mood and cognitive function, dentate gyrus neurogenesis, and neurons, microglia, and astrocytes in the hippocampus. Combined exposure to low doses of GWIR chemicals PB, DEET, and permethrin induced depressive and anxiety-like behavior and spatial learning and memory dysfunction. Application of mild stress in the period of exposure to chemicals exacerbated the extent of mood and cognitive dysfunction. Furthermore, these behavioral impairments were associated with reduced hippocampal volume and multiple cellular alterations such as chronic reductions in neural stem cell activity and neurogenesis, partial loss of principal neurons, and mild inflammation comprising sporadic occurrence of activated microglia and significant hypertrophy of astrocytes. The results show the first evidence of an association between mood and cognitive dysfunction and hippocampal pathology epitomized by decreased neurogenesis, partial loss of principal neurons, and mild inflammation in a model of GWI. Hence, treatment strategies that are efficacious for enhancing neurogenesis and suppressing inflammation may be helpful for alleviation of mood and cognitive dysfunction observed in GWI.

**Pattison JE (2013) The interaction of natural background gamma radiation with depleted uranium micro-particles in the human body. J Radiol Prot. 33(1):187-198. (Epub 2013 Jan 7.)**

In this study, some characteristics of the photo-electrons produced when natural background gamma radiation interacts with micron-sized depleted uranium (DU) particles in the human body have been estimated using Monte Carlo simulations. In addition, an estimate has been made of the likelihood of radiological health effects occurring due to such an exposure. Upon exposure to naturally occurring background gamma radiation,

DU particles in the body will produce an enhancement of the dose to the tissue in the immediate vicinity of the particles due to the photo-electric absorption of the radiation in the particle. In this study, the photo-electrons produced by a 10 μm-size particle embedded in tissue at the centre of the human torso have been investigated. The mean energies of the photo-electrons in the DU particle and in the two consecutive immediately surrounding 2 μm-wide tissue shells around the particle were found to be 38, 49 and 50 keV, respectively, with corresponding ranges of 1.3, 38 and 39 μm, respectively. The total photo-electron fluence-rates in the two consecutive 2 μm-wide tissue layers were found to be 14 percent and 7 percent of the fluence-rate in the DU particle, respectively. The estimated dose enhancement due to one 10 μm-sized DU particle in 1 cm(3) of tissue was less than 2 in 10 million of the dose received by the tissue without a particle being present. The increase in risk of death from cancer due to this effect is consequently insignificant.

**Rayhan RU, Raksit MP, Timbol CR, Adewuyi O, Vanmeter JW, Baraniuk JN (2013a) Prefrontal lactate predicts exercise-induced cognitive dysfunction in Gulf War Illness. Am J Transl Res. 5(2):212-223. (Epub 2013 Mar 28.)**

BACKGROUND: 25 percent to 30 percent of Veterans deployed to the 1990 to 1991 Persian Gulf War exhibit an idiopathic syndrome of chronic fatigue, exertional exhaustion, pain, hyperalgesia, cognitive, and affective dysfunction known as Gulf War Illness (GWI).

METHODS: Gulf War Veterans (n=15) and sedentary veteran and civilian controls (n=11) completed a 2-back working memory test in an fMRI before and after two bicycle exercise stress test. We performed single voxel (1) H MRS to evaluate brain metabolic differences in the left anterior cingulate cortex and the changes associated with exercise.

RESULTS: Eight GWI subjects increased their 2-back scores after exercise (labelled increasers) and seven GWI subjects decreased their 2-back scores after exercise (labelled decreasers). These phenotypic responses were absent for controls. Decreasers had significantly elevated prefrontal lactate levels compared to Increasers prior to completion of the exercise stress tests. Evaluation of prefrontal lactate levels prior to exercise demonstrated predictability ROC analysis) of the two diametrically opposed subgroups.

CONCLUSION: Prefrontal lactate levels may be a potential biomarker for exercise-induced subgroups in GWI. The alterations in brain energetics may be in part responsible for a subgroup of GWI and underlie some of the symptoms present in the patient population.

**Rayhan RU, Ravindran MK, Baraniuk JN (2013b) Migraine in gulf war illness and chronic fatigue syndrome: prevalence, potential mechanisms, and evaluation. Front Physiol. 4:181. doi: 10.3389/fphys.2013.00181.**

OBJECTIVE: To assess the prevalence of headache subtypes in Gulf War Illness (GWI) and Chronic Fatigue Syndrome (CFS) compared to controls.

BACKGROUND: Approximately, 25 percent of the military personnel who served in the 1990-1991 Persian Gulf War have developed GWI. Symptoms of GWI and CFS have considerable overlap, including headache complaints. Migraines are reported in CFS. The type and prevalence of headaches in GWI have not been adequately assessed.

METHODS: 50 GWI, 39 CFS and 45 controls had structured headache evaluations based on the 2004 International Headache Society criteria. All subjects had history and physical examinations, fatigue and symptom related questionnaires, measurements of systemic hyperalgesia (dolorimetry), and assessments for exclusionary conditions.

RESULTS: Migraines were detected in 64 percent of GWI (odds ratio = 11.6 [4.1-32.5]) (mean [±95 percent CI]) and 82 percent of CFS subjects (odds ratio = 22.5 [7.8-64.8]) compared to only 13 percent of controls. There was a predominance of females in the CFS compared to GWI and controls. However, migraine status was independent of gender in GWI and CFS groups (x (2) = 2.7; P = 0.101). Measures of fatigue, pain, and other ancillary criteria were comparable between GWI and CFS subjects with and without headache.

CONCLUSION: The high prevalence of migraine in CFS was confirmed and extended to GWI subjects. GWI and CFS may share dysfunctional central pathophysiological pathways that contribute to migraine and subjective symptoms. The high migraine prevalence warrants the inclusion of a structured headache evaluation in GWI and CFS subjects, and treatment when present.

**Rayhan RU, Stevens BW, Raksit MP, Ripple JA, Timbol CR, Adewuyi O, VanMeter JW, Baraniuk JN (2013c) Exercise challenge in Gulf War Illness reveals two subgroups with altered brain structure and function. PLoS One 8(6):e63903.**

Nearly 30 percent of the approximately 700,000 military personnel who served in Operation Desert Storm (1990-1991) have developed Gulf War Illness, a condition that presents with symptoms such as cognitive impairment, autonomic dysfunction, debilitating fatigue and chronic widespread pain that implicate the central nervous system. A hallmark complaint of subjects with Gulf War Illness is post-exertional malaise; defined as an exacerbation of symptoms following physical and/or mental effort. To study the causal relationship between exercise, the brain, and changes in symptoms, 28 Gulf War Veterans and 10 controls completed an fMRI scan before and after two exercise stress tests to investigate serial changes in pain, autonomic function, and working memory. Exercise induced two clinical Gulf War Illness subgroups. One subgroup presented with orthostatic tachycardia (n=10). This phenotype correlated with brainstem atrophy, baseline working memory compensation in the cerebellar vermis, and subsequent loss of compensation after exercise. The other subgroup developed exercise induced hyperalgesia (n=18) that was associated with cortical atrophy and baseline working memory compensation in the basal ganglia. Alterations in cognition, brain structure, and symptoms were absent in controls. Our novel findings may provide an understanding of the relationship between the brain and post-exertional malaise in Gulf War Illness.

**Rayhan RU, Stevens BW, Timbol CR, Adewuyi O, Walitt B, VanMeter JW, Baraniuk JN (2013d) Increased brain white matter axial diffusivity associated with fatigue, pain and hyperalgesia in Gulf War illness. PLoS One 8(3):e58493. (Epub 2013 Mar 20.)**

BACKGROUND: Gulf War exposures in 1990 and 1991 have caused 25 percent to 30 percent of deployed personnel to develop a syndrome of chronic fatigue, pain, hyperalgesia, cognitive, and affective dysfunction.

METHODS: Gulf War Veterans (n=31) and sedentary veteran and civilian controls (n=20) completed fMRI scans for diffusion tensor imaging. A combination of dolorimetry, subjective reports of pain and fatigue were correlated to white matter diffusivity properties to identify tracts associated with symptom constructs.

RESULTS: Gulf War Illness subjects had significantly correlated fatigue, pain, hyperalgesia, and increased axial diffusivity in the right inferior fronto-occipital fasciculus. ROC generated thresholds and subsequent binary regression analysis predicted CMI classification based upon axial diffusivity in the right inferior fronto-occipital fasciculus. These correlates were absent for controls in dichotomous regression analysis.

CONCLUSION: The right inferior fronto-occipital fasciculus may be a potential biomarker for Gulf War Illness. This tract links cortical regions involved in fatigue, pain, emotional and reward processing, and the right ventral attention network in cognition. The axonal neuropathological mechanism(s) explaining increased axial diffusivity may account for the most prominent symptoms of Gulf War Illness.

**Roehr B. (2013) Researchers identify possible physical marker of Gulf War illness. BMJ. 346:f1958.**

Full text available: http://www.bmj.com/content/346/bmj.f1958

**Shaki F, Hosseini MJ, Ghazi-Khansari M, Pourahmad J (2013) Depleted uranium induces disruption of energy homeostasis and oxidative stress in isolated rat brain mitochondria. Metallomics 5(6):736-744.**

Depleted uranium (DU) is emerging as an environmental pollutant primarily due to its military applications. Gulf War Veterans with embedded DU showed cognitive disorders that suggest that the central nervous system is a target of DU. Recent evidence has suggested that DU could induce oxidative stress and mitochondrial dysfunction in brain tissue. However, the underlying mechanisms of DU toxicity in brain mitochondria are not yet well understood. Brain mitochondria were obtained using differential centrifugation and were incubated with different concentrations (50, 100 and 200 μM) of uranyl acetate (UA) as a soluble salt of U(238) for 1 h. In this research, mitochondrial ROS production, collapse of mitochondrial membrane potential and mitochondrial swelling were examined by flow cytometry following the addition of UA. Meanwhile, mitochondrial sources of ROS formation were determined using specific substrates and inhibitors. Complex II and IV

activity and also the extent of lipid peroxidation and glutathione (GSH) oxidation were detected via spectroscopy. Furthermore, we investigated the concentration of ATP and ATP/ADP ratio using luciferase enzyme and cytochrome c release from mitochondria which was detected by ELISA kit. UA caused concentration-dependent elevation of succinate-linked mitochondrial ROS production, lipid peroxidation, GSH oxidation and inhibition of mitochondrial complex II. UA also induced mitochondrial permeability transition, ATP production decrease and increase in cytochrome c release. Pre-treatment with antioxidants significantly inhibited all the above mentioned toxic effects of UA. This study suggests that mitochondrial oxidative stress and impairment of oxidative phosphorylation in brain mitochondria may play a key role in DU neurotoxicity as reported in Gulf War Syndrome.

**Smith BN, Wang JM, Vogt D, Vickers K, King DW, King LA (2013) Gulf war illness: symptomatology among Veterans 10 years after deployment. J Occup Environ Med. 55(1):104-110.**

OBJECTIVE: To further elucidate the nature of illness in Veterans of the 1990 to 1991 Gulf War (GW) by examining the GW Illness (GWI) definition advanced by the Centers for Disease Control and Prevention, which specified caseness as having at least one symptom from two of the three factors: fatigue, mood-cognition, and musculoskeletal.

METHODS: A total of 311 male and female GW Veterans drawn from across the Nation were assessed in a survey-based study approximately 10 years after deployment.

RESULTS: A total of 33.8 percent of the probability-weighted sample met GWI criteria. Multiple symptom profiles were found, with more than half of GWI cases endorsing a symptom on all the three factors, and almost all cases endorsing at least one mood-cognition symptom.

CONCLUSION: Although the Centers for Disease Control and Prevention definition has some limitations that should be considered, it remains a useful tool for assessing the presence of illness in GW Veterans.

**Smith-Osborne A (2013) Veterans Administration health care policies as a protective mechanism supporting an expected life trajectory after military service. Soc Work Public Health 28(2):81-96.**

Changes in the American military since the end of military conscription, as well as the increasing number of service-connected disabilities, suggest the need for increased consideration of the effects of health policies when assessing the impact of military service on young Americans' life course. This study analyzes data from the most recent National Survey of Veterans to investigate the health status, health benefits, and health care utilization of 2,773 Gulf War Veterans, in association with resumption of their civilian life trajectory. Findings suggest that this sample of Veterans may have poorer health status than previous Veteran cohorts and did not fully utilize Veterans' health care benefits to which they were entitled. This article examines whether Veterans may usefully be

considered a group at risk for health disparities, in that they have greater health risks and potentially poorer health status and access than mainstream Americans.

**Smylie AL, Broderick G, Fernandes H, Razdan S, Barnes Z, Collado F, Sol C, Fletcher MA, Klimas N (2013) A comparison of sex-specific immune signatures in Gulf War illness and chronic fatigue syndrome. BMC Immunol. 14:29.**

BACKGROUND: Though potentially linked to the basic physiology of stress response we still have no clear understanding of Gulf War Illness (GWI), a debilitating condition presenting complex immune, endocrine and neurological symptoms. Here we compared male (n = 20) and female (n = 10) Veterans with GWI separately against their healthy counterparts (n = 21 male, n = 9 female) as well as subjects with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) (n = 12 male, n = 10 female).

METHODS: Subjects were assessed using a Graded eXercise Test (GXT) with blood drawn prior to exercise, at peak effort (VO2 max) and 4-hours post exercise. Using chemiluminescent imaging we measured the concentrations of IL-1a, 1b, 2, 4, 5, 6, 8, 10, 12 (p70), 13, 15, 17 and 23, IFNγ, TNFα and TNFβ in plasma samples from each phase of exercise. Linear classification models were constructed using stepwise variable selection to identify cytokine co-expression patterns characteristic of each subject group.

RESULTS: Classification accuracies in excess of 80 percent were obtained using between 2 and 5 cytokine markers. Common to both GWI and CFS, IL-10 and IL-23 expression contributed in an illness and time-dependent manner, accompanied in male subjects by NK and Th1 markers IL-12, IL-15, IL-2 and IFNγ. In female GWI and CFS subjects IL-10 was again identified as a delineator but this time in the context of IL-17 and Th2 markers IL-4 and IL-5. Exercise response also differed between sexes: male GWI subjects presented characteristic cytokine signatures at rest but not at peak effort whereas the opposite was true for female subjects.

CONCLUSIONS: Though individual markers varied, results collectively supported involvement of the IL-23/Th17/IL-17 axis in the delineation of GWI and CFS in a sex-specific way.

**Tillman GD, Calley CS, Green TA, Buhl VI, Biggs MM, Spence JS, Briggs RW, Haley RW, Kraut MA, Hart J Jr. (2013) Visual event-related potentials as markers of hyperarousal in Gulf War illness: Evidence against a stress-related etiology. Psychiatry Res 211(3):257-267. (Epub 2012 Nov 11.)**

An exaggerated response to emotional stimuli is among the many symptoms widely reported by Veterans of the 1991 Persian Gulf War. These symptomologies have been attributed to damage and dysfunction associated with deployment-related exposures. We collected event-related potential data from 22 Veterans meeting Haley criteria for GW Syndromes 1-3 and from 8 matched GW Veteran controls, who were deployed but not symptomatic, while they performed a visual three-condition oddball task where images authenticated to be associated with the 1991 Persian Gulf War were the distractor stimuli.

Hyperarousal reported by ill Veterans was significantly greater than that by control Veterans, but this was not paralleled by higher amplitude P3a in their ERP responses to GW-related distractor stimuli. Whereas previous studies of PTSD patients have shown higher amplitude P3b responses to target stimuli that are placed amid trauma-related nontarget stimuli, ill Veterans in this study showed P3b amplitudes to target stimuli-placed amid GW-related nontarget stimuli – that were significantly lower than those of the control group. Hyperarousal scores reliably predicted P3b, but not P3a, amplitudes. Although many factors may contribute to P3b amplitude differences – most notably depression and poor sleep quality, symptoms that are prevalent in the GW syndrome groups – our findings in context of previous studies on this population are consistent with the contention that dysfunction in cholinergic and dopaminergic neurotransmitter systems, and in white matter and basal ganglia may be contributing to impairments in GW Veterans.

**Todorov TI, Ejnik JW, Guandalini G, Xu H, Hoover D, Anderson L, Squibb K, McDiarmid MA, Centeno JA (2013) Uranium quantification in semen by inductively coupled plasma mass spectrometry. J Trace Elem Med Biol 27(1):2-6. (Epub 2012 Sep 1.)**

In this study, we report uranium analysis for human semen samples. Uranium quantification was performed by inductively coupled plasma mass spectrometry. No additives, such as chymotrypsin or bovine serum albumin, were used for semen liquefaction, as they showed significant uranium content. For method validation we spiked 2g aliquots of pooled control semen at three different levels of uranium: low at 5 pg/g, medium at 50 pg/g, and high at 1000 pg/g. The detection limit was determined to be 0.8 pg/g uranium in human semen. The data reproduced within 1.4-7 percent RSD and spike recoveries were 97-100 percent. The uranium level of the unspiked, pooled control semen was 2.9 pg/g of semen (n=10). In addition six semen samples from a cohort of Veterans exposed to depleted uranium (DU) in the 1991 Gulf War were analyzed with no knowledge of their exposure history. U ranium levels in the Veterans' semen samples ranged from undetectable (<0.8 pg/g) to 3350 pg/g. This wide concentration range for uranium in semen is consistent with known differences in current DU body burdens in these individuals, some of whom have retained embedded DU fragments.

**Tuite JJ, Haley RW (2012) Meteorological and Intelligence Evidence of Long-Distance Transit of Chemical Weapons Fallout from Bombing Early in the 1991 Persian Gulf War. Neuroepidemiology 40(3):160-177.**

BACKGROUND: Coalition bombings on the night of January 18-19, 1991, early in the GW, targeted the Iraqi chemical weapons infrastructure. On January 19, 1991, nerve agent alarms sounded within coalition positions hundreds of kilometers to the south, and the trace presence of sarin vapor was identified by multiple technologies. Considering only surface dispersion of plumes from explosions, officials concluded that the absence of casualties around bombed sites precluded long-distance transit of debris to U.S. troop positions to explain the alarms and detections. Consequently, they were discounted as false positives, and low-level nerve agent exposure early in the air war was disregarded in epidemiologic investigations of chronic illnesses.

INTELLIGENCE DATA: Newly assembled evidence indicates that plumes from those nighttime bombings of Iraqi chemical facilities would have traversed the stable nocturnal boundary layer and penetrated the residual layer where they would be susceptible to rapid transit by supergeostrophic winds. This explanation is supported by plume height predictions, available weather charts, weather satellite images showing transit of a hot air mass, effects of solar mixing of atmospheric layers, and observations of a stationary weather front and thermal inversion in the region.

CONCLUSIONS: Current evidence supports long-distance transit. Epidemiologic studies of chronic postwar illness should be reassessed using Veterans' reports of hearing nerve agent alarms as the measure of exposure.

**Veitch DP, Friedl KE, Weiner MW (2013) Military risk factors for cognitive decline, dementia and Alzheimer's disease. Curr Alzheimer Res. 10(9):907-30.**

Delayed neurological health consequences of environmental exposures during military service have been generally underappreciated. The rapidly expanding understanding of Alzheimer's disease (AD) pathogenesis now makes it possible to quantitate some of the likely long-term health risks associated with military service. Military risk factors for AD include both factors elevated in military personnel such as tobacco use, traumatic brain injury (TBI), depression, and post-traumatic stress disorder (PTSD) and other nonspecific risk factors for AD including, vascular risk factors such as obesity and obesity-related diseases (e.g., metabolic syndrome), education and physical fitness. The degree of combat exposure, Vietnam era Agent Orange exposure and Gulf War Illness may also influence risk for AD. Using available data on the association of AD and specific exposures and risk factors, the authors have conservatively estimated 423,000 new cases of AD in Veterans by 2020, including 140,000 excess cases associated with specific military exposures. The cost associated with these excess cases is approximately $5.8 billion to $7.8 billion. Mitigation of the potential impact of military exposures on the cognitive function of Veterans and management of modifiable risk factors through specifically designed programs will be instrumental in minimizing the impact of AD in Veterans in the future decades.

**Vera-Lastra O, Medina G, Cruz-Dominguez Mdel P, Jara LJ, Shoenfeld Y (2013) Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome): clinical and immunological spectrum. Expert Rev Clin Immunol. 9(4):361-373.**

An adjuvant is a substance that enhances the antigen-specific immune response, induces the release of inflammatory cytokines, and interacts with Toll-like receptors and the NALP3 inflammasome. The immunological consequence of these actions is to stimulate the innate and adaptive immune response. The activation of the immune system by adjuvants, a desirable effect, could trigger manifestations of autoimmunity or autoimmune disease. Recently, a new syndrome was introduced, autoimmune/inflammatory syndrome induced by adjuvants (ASIA), that includes postvaccination phenomena, macrophagic myofasciitis, Gulf War syndrome and siliconosis. This syndrome is characterized by

nonspecific and specific manifestations of autoimmune disease. The main substances associated with ASIA are squalene (Gulf War syndrome), aluminum hydroxide (postvaccination phenomena, macrophagic myofasciitis) and silicone with siliconosis. Mineral oil, guaiacol and iodine gadital are also associated with ASIA. The following review describes the wide clinical spectrum and pathogenesis of ASIA including defined autoimmune diseases and nonspecific autoimmune manifestations, as well as the outlook of future research in this field.

**Wachen JS, Shipherd JC, Suvak M, Vogt D, King LA, King DW (2013) Posttraumatic stress symptomatology as a mediator of the relationship between warzone exposure and physical health symptoms in men and women. J Trauma Stress 26(3):319-28. (Epub 2013 May 20.)**

The mediating role of posttraumatic stress symptomatology (PSS) on the association between warzone exposure and physical health symptoms in 7 bodily systems (cardiovascular, dermatological, gastrointestinal, genitourinary, musculoskeletal, neurological, and pulmonary) was examined. We also examined if mediation effects varied as a function of sex. A sample of 317 U.S. GW Veterans was assessed for warzone exposure, PSS, and physical health symptoms 10 years after deployment. PSS was significantly associated with postdeployment physical health in all symptom categories when accounting for predeployment health (with effect sizes ranging from a 1.27-1.64 increase in the likelihood of postdeployment physical health symptoms with a 1 standard deviation increase in the PSS symptoms). PSS severity mediated the relationship between warzone exposure and postdeployment symptoms in all physical health domains (with percent mediation ranging 44 percent-75 percent). A significant Warzone Exposure × PSS interaction emerged for 5 outcomes such that the effect of PSS on physical health was stronger for Veterans reporting lower warzone exposure. No significant interactions with sex emerged. These findings suggest the important influence of PSS on physical health symptoms for both men and women.

**Washington DL, Bean-Mayberry B, Hamilton AB, Cordasco KM, Yano EM (2013) Women Veterans' healthcare delivery preferences and use by military service era: findings from the National Survey of Women Veterans. J Gen Intern Med. 28 Suppl 2:S571-S576.**

BACKGROUND: The number of women Veterans (WVs) utilizing the Veterans Health Administration (VA) has doubled over the past decade, heightening the importance of understanding their healthcare delivery preferences and utilization patterns. Other studies have identified healthcare issues and behaviors of WVs in specific military service eras (e.g., Vietnam), but delivery preferences and utilization have not been examined within and across eras on a population basis.

OBJECTIVE: To identify healthcare delivery preferences and healthcare use of WVs by military service era to inform program design and patient-centeredness.

DESIGN AND PARTICIPANTS: Cross-sectional 2008-2009 survey of a nationally representative sample of 3,611 WVs, weighted to the population.

MAIN MEASURES: Healthcare delivery preferences measured as importance of selected healthcare features; types of healthcare services and number of visits used; use of VA or non-VA; all by military service era.

KEY RESULTS: Military service era differences were present in types of healthcare used, with World War II and Korea era WVs using more specialty care, and Vietnam era to present WVs using more women's health and mental health care. Operations Enduring Freedom, Iraqi Freedom, New Dawn (OEF/OIF/OND) WVs made more healthcare visits than WVs of earlier military eras. The greatest healthcare delivery concerns were location convenience for Vietnam and earlier WVs, and cost for Gulf War and OEF/OIF/OND WVs. Co-located gynecology with general healthcare was also rated important by a sizable proportion of WVs from all military service eras.

CONCLUSIONS: Our findings point to the importance of ensuring access to specialty services closer to home for WVs, which may require technology-supported care. Younger WVs' higher mental health care use reinforces the need for integration and coordination of primary care, reproductive health and mental health care.

**Wright BK, Kelsall HL, Sim MR, Clarke DM, Creamer MC (2013) Support mechanisms and vulnerabilities in relation to PTSD in Veterans of the Gulf War, Iraq War, and Afghanistan deployments: a systematic review. J Trauma Stress 26(3):310-318. (Epub 2013 May 13.)**

Pretrauma factors of psychiatric history and neuroticism have been important in highlighting vulnerability to posttraumatic stress disorder (PTSD), whereas posttrauma support mechanisms have been associated with positive health and well-being outcomes, particularly in Veterans. The relationship between these factors and PTSD has not been the subject of a systematic review in Veterans. An online search was conducted, supplemented by reference list and author searches. Two investigators systematically and independently examined eligible studies. From an initial search result of 2,864, 17 met inclusion criteria. A meta-analysis of unit cohesion involving 6 studies found that low unit cohesion was associated with PTSD, standardised mean difference of -1.62, 95 percent confidence interval (CI) [-2.80, -0.45]. A meta-analysis of social support involving 7 studies found that low social support was associated with PTSD, standardised mean difference of - 12.40, 95 percent CI [-3.42, -1.38]. Three of 5 studies found a significant relationship between low-family support and PTSD; insufficient data precluded a meta-analysis. Regarding pretrauma vulnerability, 2 studies on psychiatric history and 1 on neuroticism found positive relationships with PTSD. Posttrauma factors of low support were associated with higher reporting of PTSD. Cross-sectional methodology may be inadequate to capture complex relationships between support and PTSD; more longitudinal research is required.

**Yousefi H, Najafi A (2013) Assessment of depleted uranium in South-Western Iran. J Environ Radioact. 124:160-162. (Epub 2013 Jun 20.)**

Depleted uranium (DU) has been used in a number of conflicts most notably during the Gulf War in Iraq and existence of it has been reported in Kuwait by IAEA experts. Due to heavy sand storms prevailing into the direction to South West of Iran transporting sand originating from Iraq, the probability that DU could be moved is considered high. Therefore, it was decided to take some air and soil samples near border line and some nearest cities. The study was focused on finding DU in air and soil of these south-west provinces. Twenty-two (22) air samples and 20 soil samples were collected and analyzed on their contents of uranium isotopes by alpha, beta and gamma spectrometry. The air and soil samples have been measured by use of an alpha-beta counter and by a gamma spectrometer, respectively. Results showed that there is no radiation impact from DU and so no DU has been transported via sand storms since all results were obtained below the detection limit.

**Zunic S (2013) Cytological characteristics of lung washings from children in depleted uranium stroked region. J Biol Regul Homeost Agents 27(4):961-967.**

The study was based on theoretical interpretation of authentic findings of Lupus Erythematosus Cells (LEC) in bronchoalveolar lavage (BAL) samples of children who underwent flexible bronchoscopy for clinical symptoms and radiological changes consistent with persistent pulmonary infiltrates during the first year after the bombing of Serbia in 1999. Differential cell counts were compared and statistical significance of differences for estimated cell population percentages calculated in groups of LEC positive (LEC+) and LEC negative (LEC-) BAL specimens. Significant increase of percentages of neutrophils and eosinophils and decreased percentages of macrophages were found in the group of LEC+ in comparison with LEC- BAL specimens (p less than 0.05, p less than 0.001, p less than 0.001, respectively). Presence of decreased percentages of cells of monocyte-macrophage lineage with consequent expansion of white blood cells in BAL, argue for understanding the nature of LEC+ alveolitis as a possible nonspecific finding of radiation-induced biological response of pulmonary tissue. LEC phenomenon may be understood as an early radio adaptive tissue response. Depleted uranium (DU) radiotoxic effect with concomitant alpha particles radiation has been associated with unpredictable and everlasting biological effects. The emission of radiation in the course of several decades due to corrosion of scattered remnants of DU armaments, which has been potentiated by the repeated bombing of the regions within range of the transfer of radioactive particles by air, strikes a broad territory and numerous populations, and unavoidably leads to in vivoPetkau effect. Except the war, peacetime nuclear disasters in various parts of the world, such as Fukushima, Chernobyl and others, contribute to this effect too. In this way, the Petkau effect is a challenge for science to declare the future health strategy with the main goal focused on minimizing the early, as well as delayed in vivo effects of depleted uranium.

**Zunic S (2013) Lupus erythematosus cell phenomenon in pediatric bronchoalveolar lavages: possible manifestation of early radioadaptive response in radiation induced alveolitis. J Biol Regul Homeost Agents 27(2):389-398.**

A 10-year (December 1992 - December 2002) evaluation of 225 pediatric bronchoalveolar lavage (BAL) differential cell counts showed appearance of the cells corresponding to the cytological entity - lupus erythematosus cell (LEC) in 47 specimens of which not a single case was associated with the coexistent autoimmune disease. There was a significant increase in the percentage of LEC in BAL samples of the examinees during the first 6 months after the bombing of targets in Serbia (July-December 1999) in comparison to the period 1992 to March 24, 1999, and after the bombing of targets in Serbia (2000-2002). Maintaining the character of occurrence of LEC in BAL as nonspecific (Zunic et al. 1996), the devastating power of alpha particles (originated from uranium decay) gives an opportunity to discuss this phenomenon more comprehensibly and perceive a new vista related to the pathogenesis of LEC phenomenon in BAL. Since the period after 1991 corresponds to the time after the first Gulf War, and later the bombing of targets in Bosnia, the possibility of occurrence of LEC in BAL as a manifestation of radiation alveolitis due to contamination by air transferred depleted uranium (DU) particles could not be excluded.

## 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 2004-2013, and the number of research projects in which the Federal Government has invested.

The appropriated funds for FY 2004 through 2013, centrally obligated to each project, are shown in Appendix C and summarized in Table IV-1. Federal funding for GW research totaled approximately $220 million during this period. Funds obligated for these projects prior to FY 2004 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 2004 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 2004-2013) Funding Trends for GW Research in Millions of Dollars**

| Department | FY '04 | FY '05 | FY '06 | FY '07 | FY '08 | FY '09 | FY '10 | FY '11 | FY '12 | FY '13 | Total Costs FY '04-'13 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **DoD** | $ 11.1 | $ 10.1 | $ 10.1 | $ 3.4 | $ 11.7 | $ 10.4 | $ 10.4 | $ 10.3 | $ 11.7 | $ 3.5 | **$ 92.7** |
| **HHS** | $ 0.5 | $ 0.5 | $ 0.5 | $ 0.4 | $ 0.4 | $ 0 | $ 0 | $ 0 | $ 0 | $ 0 | **$ 2.3** |
| **VA** | $ 7.6 | $ 9.5 | $ 13.0 | $ 22.1 | $21.9 | $16.6 | $ 13.9 | $ 5.6 | $ 6.7 | $ 7.9 | **$ 124.8** |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Total** | **$ 19.2** | **$ 20.1** | **$23.6** | **$ 25.9** | **$ 34.0** | **$ 27.0** | **$ 24.3** | **$ 15.9** | **$ 18.4** | **$ 11.4** | **$ 219.8** |

The funding level for FY 2012 in the table above differs from the value reported in the 2012 annual report to Congress due to the delayed start of six projects funded through the FY 2012 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 2013. DoD funding for FY 2013 is only $3.5 million for the same reason and will be updated in the 2014 annual report to Congress after the CDMRP projects selected for funding in FY 2013 have begun.

VA, DoD, and HHS sponsored a total of 423 distinct research projects on GWVI during the period of FY 1992 through FY 2013. 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 2004 - FY 2013 are shown in Figure IV-1. As of September 30, 2013, 365 projects (86 percent of the 423 projects) were completed, and 58 projects (14 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 2004 through 2013, new and ongoing research assigned to the Brain and Nervous System Function, Environmental Toxicology, and General Health and Symptoms categories have represented 95.7 ± 1.1 percent of all new and ongoing projects.

**Figure IV-1. Cumulative Number of Funded Projects (FY 2003 - FY 2013)**

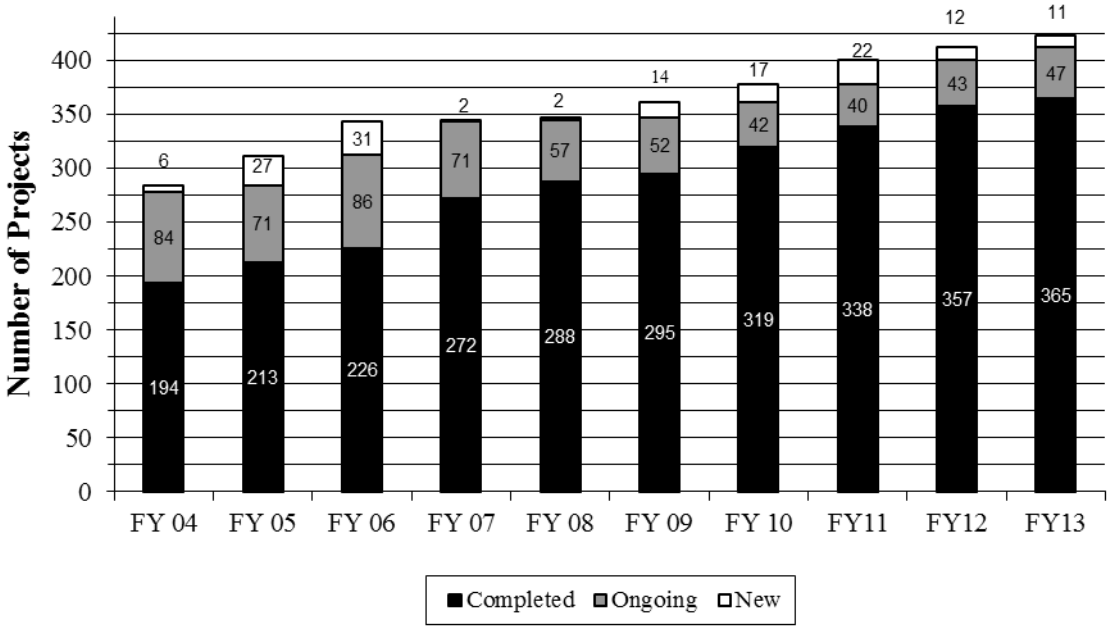
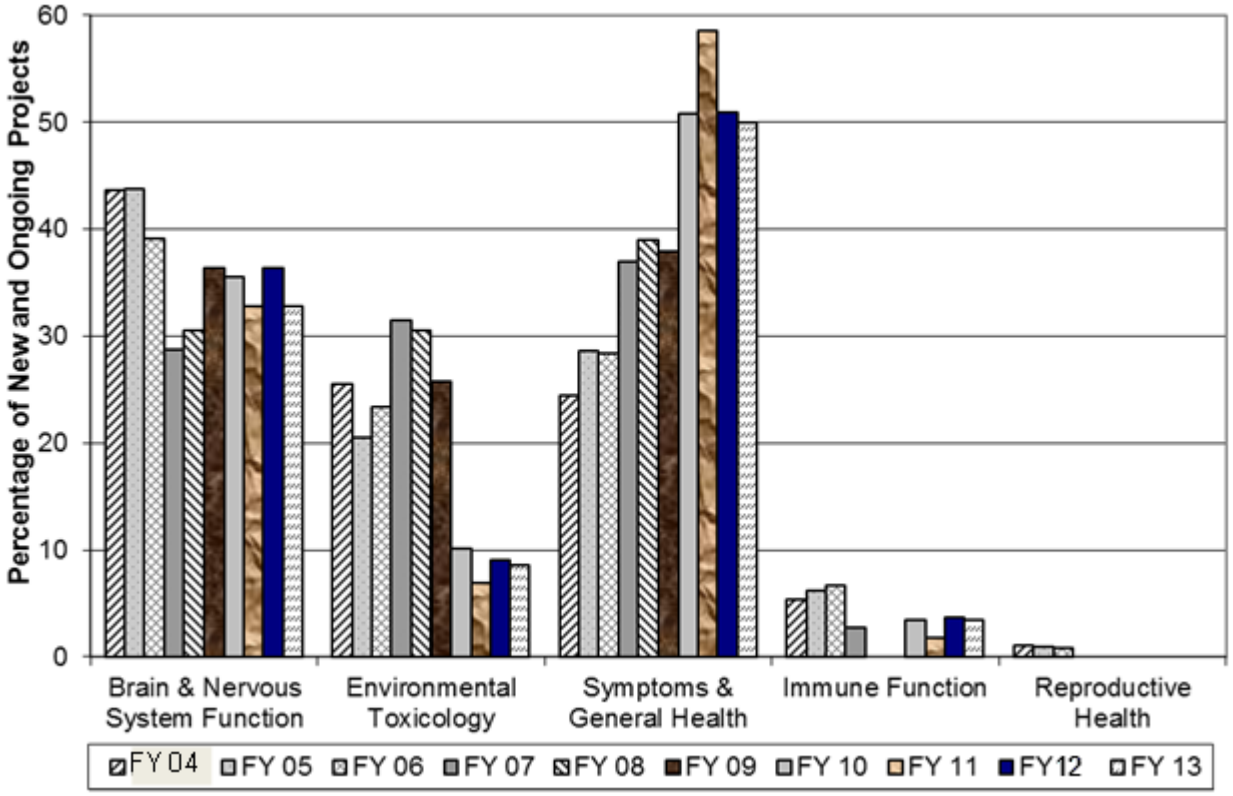



**Figure IV-2. Annual Distribution of Topic Areas for New and Ongoing Projects**



## V. NEW RESEARCH PROJECTS AND INITIATIVES

### A. New Initiatives

Requests for Applications (RFA) were issued by both CDMRP and VA in FY 2013. Proposals received for review in response to these RFAs were reviewed, and projects selected for funding will begin in FY 2014. 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 addition to the regularly-released RFAs, VA is planning special RFAs to address specific questions. An RFA in Health Services Research and Development will ask 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. Other RFAs will focus on the newly-funded DoD Gulf War Research Consortia to induce VA researchers to collaborate more closely with colleagues funded by DoD.

The Institute of Medicine (IOM) is engaged in two studies involving GW Veterans. "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" is expected to be complete in the spring of 2014. These reports should provide recommendations for the GW research programs.

### 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 continue 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 follow-up reviews will be on a regular schedule.

### C. New Projects

This section highlights the new research projects that have been approved since last year's 2012 annual report to Congress. 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 CDMRP-managed projects involve consortia of GW researchers combining their respective abilities to delve deeply into their topic areas. One consortium will study brain-immune interactions to monitor neurotoxic and neuroinflammatory reactions as they 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. 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.

## DoD Projects

Six projects were recommended for funding through the FY 2012 appropriation for the GWIRP managed by CDMRP, but were not finalized and funded until FY 2013. These projects focused on Brain and Nervous System Function (1), Environmental Toxicology (2), and Symptoms and General Health (3).

*DoD-221, "Role of microRNAs in the Pathobiology of Gulf War Illness: Identification of Potential Novel Therapeutic Targets" will use an established rat model of illness in Gulf War Veterans to (1) examine the long-term effects of Gulf War-relevant chemical exposures and stress on neuroinflammation and on miRNA signatures in the central nervous system; and (2) determine the detectability of altered miRNAs in circulation as potential noninvasive biomarkers.

*DoD-222, "Brain Immune Interactions as the Basis of Gulf War Illness: Gulf War Illness Consortium (GWIC)" brings together established Gulf War researchers and leading experts in brain-immune processes associated with neurotoxicology and neuroinflammation, damage to white matter and axonal transport, immunology, and immunogenetics. This team has designed a body of interrelated studies linked together by a cohesive model of brain-immune interactions as the basis for Gulf War Veterans' health problems. The primary objective of the consortium is to provide a cohesive understanding of the pathobiological mechanisms responsible for symptoms in Gulf War Veterans' in order to provide a rational and efficient basis for identifying beneficial treatments and diagnostic markers.

*DoD-223, "Persistent Neural Membrane Protein Misregulation Following Neurotoxicant Exposure" will the test the hypothesis that the chronic and widespread pain reported by Gulf War Veterans arises from altered function of the membrane resistance K2p protein, KCNK9, and/or KDR proteins of the Kv1 family. Prior experiments demonstrated acute interactions of the neurotoxicant permethrin on nociceptor protein Nav1.8, and the interpretation is that these persistent changes are the result of a compensatory response to upregulated Nav activity that was present during the treatment period. Potentially, the persistent increase in KDR activity degraded the fidelity of vascular nociceptor reflex regulation of blood flow with a resultant local ischemic reaction that leads to widespread pain.

*DoD-224, "Understanding Gulf War Illness: An Integrative Modeling Approach" describes a consortium whose goal is to develop a translational model of illness in Gulf War Veterans, integrating both clinical and basic research using a systems biology approach. This approach will enable the consortium to identify signaling mechanisms and outline the most promising biomarkers tied to these signaling pathways for selection and testing of therapeutic interventions to not only improve symptomatology but also reset homeostasis. The studies involved in this consortium will identify pathways and biomarkers tied to regulatory dysfunction in Gulf War Veterans, establish targets for therapy, and perform translational studies.

*DoD-225, “The Role of Protein Radicals in Chronic Neuroimmune Dysfunction and Neuropathology in Response to a Multiple-Hit Model of Gulf War Exposures” will address the complex biological and chemical interaction issues in ill Gulf War Veterans using an in vivo approach with a “Multiple-Hit” model of Gulf War exposures that combines an established model of chronic, self-sustaining neuroinflammation (persisting 10 months after a single lipopolysacharide injection) with a defined, repeated Chlorpyrifos pesticide exposure model that produces delayed and chronic hippocampal damage 3 months later. This study focuses on key molecular targets (NOX2 and NFκB p50) that have been previously identified as critical for chronic, inflammation-mediated central nervous system (CNS) pathology.

*DoD-226, “Gulf War Illness: Assessment of Bioenergetics in Brain and Muscle” will assess whether defects in bioenergics (EN) in brain and muscle are present in ill Gulf War Veterans relative to healthy matched controls, using phosphorus magnetic resonance spectroscopy (31P-MRS). The hypothesis is that illness in Gulf War Veterans involves mechanisms that together conduce to cell bioenergetic (EN) deficits which contribute to symptoms, emphasizing fatigue, cognitive and muscle problems, but extending to manifestations in a range of other organs.

**VA Funded Projects**

VA initiated funding for five new projects during FY 2013. These five projects focused on Brain and Nervous System Function (1) and Symptoms and General Health (4).

VA-178, “rTMS for the Treatment of Chronic Pain in GW1 Veterans” will compare patients receiving repetitive transcranial magnetic stimulation with sham-treated patients. Gulf War Veterans with symptoms of respiratory difficulty, gastrointestinal problems, dermatologic problems, chronic fatigue, depression, and cognitive problems in addition to chronic pain will be selected for the study. Additional examinations will include Positron Emission Tomography (PET) brain imaging and examination of the PON1 gene relationship with GW Veterans’ symptoms.

VA-179, “Vascular and Skeletal Muscle Function in Gulf War Veterans Illness” is a 3-year pilot study designed to determine whether lower extremity (leg) endothelial function, exercise functions, and skeletal muscle mitochondrial gene regulation are different among ill and healthy Gulf War Veterans. These functions are plausible mechanisms for Veterans’ health problems because exposure to anticholinesterase inhibitors during the Gulf War is a possible cause for fatigue and other musculoskeletal symptoms. Cases and controls will have femoral artery microvascular endothelial function assessed invasively in the cardiac catheterization laboratory, an overall functional assessment using cardiopulmonary exercise testing, a skeletal muscle biopsy from the thigh, and RT-PCR to assess nuclear and mitochondrial genes responsible for regulating mitochondrial respiratory function.

VA-180, “Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with GWI” will study independent and complementary markers of mitochondrial damage and

dysfunction (i.e., mtDNA content, respiratory chain enzyme activity) and the response to multiple exercise tests (i.e. breath-by-breath metabolic data, lactate, etc.) as a means of diagnostic testing for ill Gulf War Veterans. Many of the symptoms in ill Gulf War Veterans involve high-energy organ systems (e.g. muscular, central/autonomic nervous, respiratory, and gastrointestinal) and might be related to mitochondrial dysfunction or disease, conditions for which treatments are currently available.

VA-181, “Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI” will investigate if scalp application of non-invasive, LED in red and near-infrared (NIR) wavelengths improves cognition in ill Gulf War Veterans. Pilot data show that scalp application of red/NIR LEDs significantly improves cognition in chronic TBI, and there is improved mitochondrial function with increased production of adenosine tri-phosphate (ATP) in hypoxic/compromised cells treated with red/NIR photons. Mitochondrial dysfunction in ill Gulf War Veterans is reportedly associated with neurotoxicant exposures during deployment. All participants receive a series of sham, followed by a series of real LED treatments.

VA-182, “Consensus Case Definition for Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans” is a project designed to evaluate existing case definitions and determine whether an existing case definition is adequate, an existing case definition needs to be revised, or a new case definition needs to be established. It is also necessary to determine if additional research might be required to more adequately develop a consensus definition. There will be guidelines for the use of the case definition and appropriate terminology for chronic multisymptom illness in 1990-1991 Gulf War Veterans.

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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 |
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| 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 |
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| 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) |
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| 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 |
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| DoD-161 | Glutamate Receptor Aptamers and ALS |
| DoD-162 | Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function |
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| DoD-164 | Efficacy of Adjunct Sleep Interventions for PTSD (EASI-PTSD) |
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| 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 |
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| 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 |
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| DoD-198 | Oxidative Stress |
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| DoD-202 | Brain-Immune Interactions as Basis of Gulf War Illness: Consortium Development |
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| 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 |
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| 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 |

## 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 |

# 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 |
| | 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; 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 |
| 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 |

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| 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 |
| 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 |

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| Symptoms and General Health | Treatment | VA-181 | Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI |
| 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) |
| 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 |
| | Treatment | DoD-189 | Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers |

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| | Treatment | VA-160 | Lipoic Acid Therapy for Experimental Autoimmune Encephalomyelitis |
| 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) |
| 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; 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 |

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| 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 |
| | Symptoms | VA-091 | The Role of Dietary Choline in Neuroprotection |
| | Symptoms | VA-120 | Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis |
| | 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; 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 |

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| 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 |
| 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 |
| 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 |

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| 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 |
| 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 |

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| 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 |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-061 | Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-062 | Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-072 | Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-113 | Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Symptoms | DoD-053 | Long-Term Effects of Subclinical Exposures to Sarin |
| Chemical Weapons; Brain and Nervous System Function | Exposure; Symptoms | DoD-152 | Characterization of Intracellular Signaling Pathways Activated by Nerve Agents |
| Immune Function | Exposure; 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; 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 Pyridostigmine Bromide | Exposure; Interactions | DoD-077 | Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War |
| Immune Function Symptoms and General Health | Exposure; Symptoms | DoD-130 | Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents |
| Pyridostigmine Bromide | Prevention; Exposure | DoD-033 | Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity |
| Pyridostigmine Bromide | Exposure; Interactions | DoD-010 | Pyridostigmine Synergistic Toxicity Study |

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| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Interactions | DoD-002 | Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Interactions | DoD-075 | Toxic Interactions of Prophylactic Drugs and Pesticides |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Interactions | DoD-107 | Stress, Organophosphates and Blood Brain Barrier Integrity |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-078 | Experimental Models of Gulf War Syndrome |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-079 | Time Course of Stress-induced Impairment of Blood Brain Barrier |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Interactions; Symptoms | DoD-139 | Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Interactions; Symptoms | VA-006 C | Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III) |
| Pyridostigmine Bromide; Brain and Nervous System Function | Exposure; Interactions; Symptoms | VA-080 | Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress |
| 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 |

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| 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 Groups |
| | 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 |

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| | | | 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 |
| | 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 | 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 |
|---|---|---|---|
| | Symptoms | VA-053 | Spouses and Children Program |
| Environmental Toxicology; Chemical Weapons | Symptoms | VA-047 | Retrospective Verification of Mustard Gas Exposure |

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| 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 |
| | 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 |
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| 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 |

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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) |

| | | | |
|---|---|---|---|
| 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 |
|---|---|---|---|
| | 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; 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) |
| | Symptoms; Treatment | VA-172 | Understanding Pain of Gastrointestinal Origin in Women that Serve in OEF/OIF |

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|---|---|---|---|
| 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, 2013)**

# NOTES ON REVISED TABLE OF SPENDING FOR GULF WAR VETERANS' ILLNESSES RESEARCH FROM FY 2004-2013

**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 1992-2013 are listed, only the financial data for FY 2004-2013 (a 10-year window) are shown in Appendix C; Totals for FY 2004-2013 do not include funds obligated in FY 1992-2003. Projects that received all of their obligated funds prior to FY 2004 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 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| 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 '04 -'13 do not include funds obligated in FY 1992 -2003

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| 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 | | | | | | | | | | $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 |

*****Totals for FY '04 -'13 do not include funds obligated in FY 1992 -2003

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| 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 |

*****Totals for FY '04 -'13 do not include funds obligated in FY 1992 -2003

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| 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 '04 -'13 do not include funds obligated in FY 1992 -2003

*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| 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 | | | | | | | | | | $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 | | | | | | | | $0 |
| DoD-070 | War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes | C | | | | | | | | | | | $0 |

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*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| 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 | | | | | | | | | | $0 |
| DoD-076 | Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel | C | $0 | | | | | | | | | | $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 | | | | | | | | | | $0 |
| DoD-087 | Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related | C | $0 | | | | | | | | | | $0 |

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## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | 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 | $1,750,000 | $0 | | | | | | | | | $1,750,000 |
| 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 | | | | | $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 | | | | | | | | | | $0 |

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## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | Hospitalizations | | | | | | | | | | | | |
| DoD-100 | Antibodies to Squalene | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| DoD-101 | Mechanisms in Chronic Multisymptom Illnesses | C | $4,781,952 | $2,429,999 | $0 | $0 | $0 | $0 | | | | | $7,211,9518 |
| 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 | $242,424 | $160,000 | $326,570 | $166,570 | $0 | $0 | | | | | $895,5648 |
| 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 | | | | | | | | | | $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 | | | | | | | | | | $0 |
| DoD-108 | Health Status of Current National Guard Members | C | $0 | $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 | | | | | | | | | $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 | | | | | | | | | $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 |

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## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | 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 | | | | | | | | $0 |
| DoD-125 | A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74) | C | $0 | $0 | $0 | | | | | | | | $0 |
| DoD-126 | Blood-Brain Barrier Transport of Uranium | C | $0 | $0 | $0 | $0 | $0 | $0 | | | | | $0 |

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| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-127 | Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man | C | $0 | | | | | | | | | | $0 |
| DoD-128 | Multifactorial Assessment of Depleted Uranium Neurotoxicity | C | $0 | $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 | | | | | $0 |
| DoD-130 | Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents | C | $0 | $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 | | | | | $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 | | | | | | | $0 |
| DoD-133 | Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| DoD-134 | Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| DoD-135 | Biochemical Markers for Exposure to Low Doses of Organophosphorus Exposure | C | $0 | $0 | | | | | | | | | $0 |
| DoD-136 | A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure | C | $0 | $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 | | | | | | | | $0 |
| DoD-138 | Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| DoD-139 | Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses | C | | | | | | | | | | | $0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| DoD-140 | US DOD Surveillance for Neoplasms in Infancy | C | $0 | $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 | | | | | | | | | $0 |
| DoD-143 | Millennium Cohort Study | O | $1,950,000 | $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 | $31,143,000 |
| DoD-144 | Psychological Health Screening: Methods and Metrics for Deployed Forces | C | $0 | $0 | $0 | $0 | $0 | $0 | | | | | $0 |
| DoD-145 | Early Intervention Research Program to Enhance Soldier Resilience | C | $0 | $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 | | | | | | | | $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 | | | | | | | | $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 | | | | | | | | $0 |
| DoD-152 | Characterization of Intracellular Signaling Pathways Activated by Nerve Agents | C | $0 | $0 | $0 | $0 | $0 | $0 | | | | | $0 |
| DoD-153 | Gulf War Illness Research | C | $2,003,000 | $928,000 | $0 | | | | | | | | $2,931,000 |
| DoD-154 | Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study | C | $566,542 | $368,687 | $604,372 | $0 | $0 | $0 | $0 | | | | $1,539,601 |
| DoD-155 | Neuropsychological Functioning in GW Veterans Exposed to Pesticides and Pyridostigmine Bromide | C | $0 | $0 | $0 | $0 | $0 | | | | | | $0 |
| DoD-156 | The Effects of Diesel Exhaust and Stress on the Acute Phase Response | C | $0 | $0 | $0 | $0 | $0 | | | | | | $0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | and Symptoms in the Chemically Intolerant | | | | | | | | | | | | |
| DoD-157 | Novel Leishmania And Malaria Potassium Channels: Candidate Therapeutic Targets | C | $0 | $0 | | | | | | | | | $0 |
| DoD-158 | Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission Of Genetic Damage To Offspring | C | $0 | $0 | | | | | | | | | $0 |
| DoD-159 | Neurotoxicity from Chronic Exposure to Depleted Uranium | C | $0 | $0 | | | | | | | | | $0 |
| DoD-160 | Characterization of the Reproductive Toxicity of Depleted Uranium | C | $0 | $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 | | | | | | $0 |
| DoD-163 | Neuroimmune Effects of Inhaling Low Dose Sarin | C | $0 | $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 Carnosine Therapy in GWI | C | | | $831,200 | $0 | $0 | $0 | | | | | $831,200 |
| DoD-173 | A Randomized, Double-Blind, | C | | | $650,279 | $0 | $0 | $0 | | | | | $650,279 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Placebo-Controlled, Crossover Trial of Mifepristone in GW Veterans with Chronic Multisymptom Illness | | | | | | | | | | | | |
| 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 |
| 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 |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| 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 | O | | | | | | $1,247,995 | $0 | $0 | $0 | | $1,247,995 |
| DoD-192 | Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome | O | | | | | | $742,296 | $0 | $0 | $0 | | $742,296 |
| DoD-193 | Genome Instability: A Common Link in Gulf War Illness Patients | O | | | | | | $904,364 | $0 | $0 | $0 | | $904,364 |
| DoD-194 | Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome | O | | | | | | $705,654 | $0 | $0 | $0 | | $705,654 |
| DoD-195 | Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness | O | | | | | | $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? | O | | | | | | $929,224 | $0 | $0 | $0 | | $929,224 |
| DoD-198 | Oxidative Stress | O | | | | | | $927,000 | $0 | $0 | $0 | | $927,000 |
| DoD-199 | Gulf War Illness: Evaluation of an Innovative Detoxification Program | O | | | | | | $633,677 | $0 | $0 | $0 | | $633,677 |
| DoD-200 | XMRV and GWI: Is There an Association? | O | | | | | | | $565,794 | $0 | $0 | | $565,794 |
| DoD-201 | Synergistic Actions of Pyridostigmine Bromide and Insecticides on Muscle and Vascular Nociceptors | O | | | | | | | $852,157 | $0 | $0 | | $852,157 |
| DoD-202 | Brain-Immune Interactions as Basis of Gulf War Illness: Consortium Development | C | | | | | | | $262,052 | $0 | $0 | | $262,052 |
| DoD-203 | Redefining Gulf War Illness Using Longitudinal Health Data: The | O | | | | | | | $708,169 | $0 | $0 | | $708,169 |

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*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| | Devens Cohort | | | | | | | | | | | | |
| DoD-204 | Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Syndrome | O | | | | | | | $668,072 | $0 | $0 | | $668,072 |
| DoD-205 | The HPA Axis and Metabolic Outcomes in GW Veterans | O | | | | | | | $699,933 | $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 | | $606,496 |
| DoD-207 | Gulf War Illness Research Development Consortium (GWIC) | C | | | | | | | $251,475 | $0 | $0 | | $251,475 |
| DoD-208 | Genome-Wide Association Study of a Validated Case Definition of Gulf War Illness in a Population-Representative Sample | O | | | | | | | $140,357 | $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 | | $925,368 |
| DoD-210 | Assessment of Diverse Biological Indicators in Gulf War Illness: Are They Replicable? Are They Related? | O | | | | | | | $741,013 | $0 | $0 | | $741,013 |
| DoD-211 | Detection of Xenotropic Murine Leukemia Virus-Related Virus (XMRV) in Gulf War Illness: Role in Pathogenesis or Biomarker? | O | | | | | | | $403,050 | $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 | | $254,295 |
| DoD-213 | Effectiveness of Acupressure Treatment for Pain Management and Fatigue Relief in GW Veterans | O | | | | | | | | $677,280 | $0 | | $677,280 |
| DoD-214 | Abnormalities in Human Brain Creatine Metabolism in Gulf War Illness Probed with MRS | O | | | | | | | | $878,051 | $0 | | $878,051 |
| DoD-215 | Identifying Immune Drivers of Gulf War Illness Using a Novel Daily Sampling Approach | O | | | | | | | | $900,642 | $0 | | $900,642 |
| DoD-216 | Intranasal Insulin: A Novel Treatment for Gulf War Multisymptom Illness | O | | | | | | | | $1,492,571 | $0 | | $1,492,571 |
| DoD-217 | Efficacy of Treatments Tried: A Survey of GW Veterans | O | | | | | | | | $527,365 | $0 | | $527,365 |

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*Status: C=Complete; O=Ongoing*

## Department of Defense Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| 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 | | $814,165 |
| DoD-219 | Organophosphate-Related Alterations in Myelin and Axonal Transport in the Living Mammalian Brain | O | | | | | | | | $859,673 | $0 | | $859,673 |
| DoD-220 | Biomarker Discovery in GW Veterans: Development of a War Illness Diagnostic Panel | O | | | | | | | | $784,175 | $0 | | $784,175 |
| DoD-221 | Role of microRNAs in thePathobiology of Gulf War Illness: Identification of Potential Novel Therapeutic Targets | O | | | | | | | | | $339,305 | | $339,305 |
| DoD-222 | Brain Immune Interactions as the Basis of Gulf War Illness: Gulf War Illness Consortium (GWIC) | O | | | | | | | | | $2,642,203 | | $2,642,203 |
| DoD-223 | Persistent Neural Membrane Protein Misregulation Following Neurotoxicant Exposure | O | | | | | | | | | $881,479 | | $881,479 |
| DoD-224 | Understanding Gulf War Illness: An Integrative Modeling Approach | O | | | | | | | | | $2,361,185 | | $2,361,185 |
| 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 | | $884,129 |
| DoD-226 | Gulf War Illness: Assessment of Bioenergetics in Brain and Muscle | O | | | | | | | | | $930,000 | | $930,000 |
| | | | | | | | | | | | | | |
| | | | $11,096,063 | $10,091,848 | $10,128,261 | $3,417,570 | $11,672,967 | $10,380,423 | $10,384,231 | $10,280,922 | $11,714,301 | $3,535,000 | $92,701,586 |

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*Status: C=Complete; O=Ongoing*

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

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY2005 | FY 2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | | | | | | | $0 |
| HHS-010 | Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| HHS-011 | Deployment to the Gulf War and the Subsequent Development of Cancer | C | $0 | $0 | $0 | $0 | | | | | | | $0 |
| HHS-012 | Genetic Epidemiology of ALS in Veterans | C | $466,126 | $466,481 | $455,587 | $441,974 | $433,467 | $0 | $0 | $0 | | | $2,263,635 |
| | | | | | | | | | | | | | |
| | | | $466,126 | $466,481 | $455,587 | $441,974 | $433,467 | $0 | $0 | $0 | $0 | $0 | $2,263,635 |

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## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 2004 | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | | | | | | | | | | $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 2004 | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | $39,375 | | | | | | | | | | $39,375 |
| 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 | $250,000 | | | | | | | $1,000,000 |

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## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | $337,200 | | | | | | | | $1,011,600 |
| 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 | $337,200 | | | | | | | | | | $337,200 |
| 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 2004 | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | $1,912,448 | | | | | | | | | | $1,912,448 |
| VA-075 | ALS and Veterans: Are Veterans at Increased Risk? | C | $78,455 | | | | | | | | | | $78,455 |
| VA-076 | Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD | C | $151,740 | | | | | | | | | | $151,740 |
| VA-077 | HPA Axis Reactivity in Men and Women with Chronic PTSD | C | $113,861 | | | | | | | | | | $113,861 |
| VA-078 | Millenium Cohort Study | C | | | | | | | | | | | $0 |
| VA-080 | Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress | C | $119,818 | $248,458 | $253,277 | $252,602 | | | | | | | $874,155 |
| VA-081 | Stress, Pro-Inflammatory Cytokines and Coping Behavior | C | $186,035 | | | | | | | | | | $186,035 |
| VA-082 | Pituitary Adrenal Function in People with Fatiguing Illness | C | $151,740 | $276,112 | $121,842 | | | | | | | | $549,694 |
| VA-083 | Neuropsychological Assessment of a Population-Based Sample of Persian GW Veterans and Controls | C | $31,012 | | | | | | | | | | $31,012 |
| VA-084 | Neurobiology of Severe Psychological Trauma in Women | C | $151,740 | | | | | | | | | | $151,740 |
| VA-085 | Associative Learning in Veterans with and without Combat Experience | C | $232,458 | | | | | | | | | | $232,458 |
| VA-086 | A Clinical Trial of Magnetic Stimulation in Depression | C | $147,694 | | | | | | | | | | $147,694 |
| VA-087 | Improving Outcomes of Depression in Primary Care | C | $218,280 | | | | | | | | | | $218,280 |
| VA-088 | Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study | C | $47,011 | | | | | | | | | | $47,011 |
| VA-089 | National Registry of Veterans with Amyotrophic Lateral Sclerosis | C | $625,564 | $799,104 | $863,951 | | | | | | | | $2,288,619 |
| VA-090 | Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness | C | $281,000 | $281,000 | $449,990 | $449,990 | $0 | $0 | $0 | $281,000 | $70,250 | | $1,813,230 |

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## Department of Veterans Affairs Gulf War Research Funding

| PROJECT NO | PROJECT TITLE | STATUS | FY 2004 | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | $196,951 | | | | | | | | | | $196,951 |
| VA-092 | Acetylcholinesterase Activity In GW Veterans | C | $49,833 | | | | | | | | | | $49,833 |
| VA-093 | HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans | C | $36,080 | $163,205 | $127,405 | | | | | | | | $326,690 |
| VA-094 | The Immunology of Chronic Cutaneous Leishmaniasis | C | $192,204 | $157,360 | $202,320 | | | | | | | | $551,884 |
| VA-095 | The Role of Signal Regulatory Proteins in Astrocytomas | C | $231,566 | $238,239 | $178,679 | | | | | | | | $648,484 |
| VA-096 | Functional Imaging of Pain in Veterans with Unexplained Muscle Pain | C | $49,035 | $128,698 | $70,302 | $135,127 | $95,382 | | | | | | $478,544 |
| VA-097 | Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas | C | $215,093 | $241,957 | $246,355 | $134,628 | | | | | | | $838,033 |
| VA-098 | Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas | C | $44,420 | $168,600 | $168,600 | | | | | | | | $381,620 |
| VA-099 | Vaccination Against Visceral Leishmaniasis with a multi-epitope vaccine | C | $116,896 | $118,863 | $117,908 | | | | | | | | $353,667 |
| VA-100 | Studies of the Blood-Brain Barrier and its Manipulation | C | $151,740 | $151,740 | $151,740 | | | | | | | | $455,220 |
| VA-101 | Biomarkers Discovery in ALS | C | $50,518 | $227,130 | $151,555 | $112,009 | $299,165 | $274,432 | | | | | $1,114,809 |
| VA-102 | Cholinergic and Monoaminergic Influences on Sleep | C | $134,160 | $175,814 | $134,328 | | | | | | | | $444,302 |
| VA-103 | Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal | C | $296,657 | $307,253 | $317,845 | | | | | | | | $921,755 |
| VA-104 | Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome | C | $168,600 | $168,600 | $84,300 | | | | | | | | $421,500 |
| VA-105 | Expression of the Major Surface Protease of Leishmania Chagasi | C | $298,175 | $119,535 | $92,817 | | | | | | | | $510,527 |
| 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 2004 | FY 2005 | FY2006 | FY 2007 | FY 2008 | FY 2009 | FY 2010 | FY 2011 | FY 2012 | FY 2013 | TOTALS FY 04-13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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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| 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 | O | | | $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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| 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 | | | $3,090,243 |
| VA-152 | Multiple Sclerosis in GW Veterans | C | | | | | $122,010 | $137,791 | $120,866 | | | | $380,687 |
| VA-153 | Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex | O | | | | | | $8,377 | $168,600 | $94,681 | $158,219 | $43,278 | $473,155 |
| 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 | $1,296,069 |
| VA-156 | Gulf War Era Cohort and Biorepository (CSP #585) | O | | | | | | | $28,361 | $5,110 | $2,157,664 | $2,155,789 | $4,346,924 |
| VA-157 | A Clinical Demonstration of an EEG Brain-Computer Interface for ALS Patients (CSP #567) | O | | | | | | | $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 | $93,153 | | $110,746 |
| 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 | O | | | | | | | $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 | $828,543 |
| 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 | $1,112,531 |
| VA-164 | Central Mechanisms Modulating Visceral Sensitivity (renewal of VA-136) | O | | | | | | $255,170 | $267,687 | $119,256 | $90,574 | $112,982 | $845,669 |

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| 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 | $786,701 |
| VA-168 | Sleep Neurobiology and Circuitry | O | | | | | | | | $244,063 | $303,406 | $168,600 | $716,069 |
| VA-169 | Prevention of Hippocampal Neurodegeneration Due to Age and Apnea | O | | | | | | | | $202,742 | $270,322 | $270,322 | $743,386 |
| VA-170 | Epigenetic Mechanisms Relevant to the Pathogenesis of ALS | O | | | | | | | | $182,650 | $168,600 | $168,600 | $519,850 |
| VA-171 | Nanoparticle Coupled Antioxidants for Respiratory Illness in Veterans | O | | | | | | | | $140,500 | $168,600 | $168,600 | $477,700 |
| VA-172 | Understanding Pain of Gastrointestinal Origin in Women that Serve in OEF/OIF | O | | | | | | | | $84,300 | $168,600 | $168,600 | $421,500 |
| VA-173 | Impact of Exercise Training on Pain and Brain Function in GW Veterans | O | | | | | | | | $104,167 | $202,910 | $386,948 | $694,025 |
| VA-174 | GW Veterans' Illnesses Biorepository | O | | | | | | | | | $237,878 | $263,848 | $501,726 |
| VA-175 | Memory and Mood Enhancing Therapies for Gulf War Illness | O | | | | | | | | | $266,950 | $281,000 | $547,950 |
| VA-176 | MEG Synchronous Neural Interactions (SNI) in GW Veterans | O | | | | | | | | | $406,888 | $397,334 | $804,222 |
| VA-177 | Somatic Hypersensitivity in Veterans with IBS (renewal of VA-159) | O | | | | | | | | | $68,970 | $197,998 | $266,968 |
| VA-178 | rTMS for the Treatment of Chronic Pain in GW1 Veterans | O | | | | | | | | | | $309,100 | $309,100 |
| VA-179 | Vascular and Skeletal Muscle Function in Gulf War Veterans Illness | O | | | | | | | | | | $111,330 | $111,330 |
| VA-180 | Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with GWI | O | | | | | | | | | | $92,453 | $92,453 |
| VA-181 | Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI | O | | | | | | | | | | $427,447 | $427,447 |
| VA-182 | Consensus Case Definition for Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans | O | | | | | | | | | | $850,000 | $850,000 |
| | | | | | | | | | | | | | |

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| | | | $7,644,559 | $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 | $124,848,649 |

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