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Federally Sponsored Research on Gulf War Veterans' Illnesses for 2010

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Deployment Health Working Group Research Subcommittee

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Federally Sponsored Research on Gulf War Veterans' Illnesses for 2010

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EXECUTIVE SUMMARY

I. INTRODUCTION

Section 707 of Public Law 102-585, as amended by section 104 of Public Law 105-368 and section 502 of Public Law 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 this *2010 Annual Report to Congress*, which is the seventeenth report on Federal research and research activities. The DHWG tracks all federally funded research projects related to Gulf War Veterans' illnesses (GWVI).

As in previous *Annual Reports to Congress*, the material presented is divided into five sections. 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 ten-year period from FY 2001 through FY 2010; and Section V highlights new research projects and initiatives since the last report.

II. RESEARCH PRIORITIES

The research priorities remain unchanged from last year. The 19 Research Topics (2 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 (VA), the 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 2010

Section III provides brief summaries of research articles on the health problems of GW Veterans published during calendar year 2010 or in 2009 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, Department of Defense (DoD), and Department of Health and Human Services (HHS) funded 378 distinct projects from FY 1992 through FY 2010 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 $255 million for the period from FY 2001 through FY 2010. As of September 30, 2010, 319 projects (84 percent of the 378 projects) were completed, and 59 projects (16 percent) were new or ongoing.

V. NEW RESEARCH PROJECTS AND INITIATIVES

Nine new projects were funded through the FY 2009 appropriation for the Gulf War Illness Research Program (GWIRP) managed by the Congressionally Directed Medical Research Program (CDMRP) at DoD, but did not start until FY 2010. These projects focused on Brain and Nervous System Function (1), Environmental Toxicology (1), and Symptoms and General Health (7). VA funded five new projects in FY 2010 and identified five ongoing projects that were not included in previous *Annual Reports to Congress*. Four of these projects focused on Brain and Nervous System Function and six focused on Symptoms and General Health.

I. INTRODUCTION

The Secretary of VA is required by section 707 of Public Law 102-585, as amended by section 104 of Public Law 105-368 and section 502 of Public Law 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 Gulf War to the Senate and House Committees on Veterans' Affairs. The Research Subcommittee of the interagency Deployment Health Working Group (DHWG) prepared this *2010 Annual Report to Congress*, which is the 17th report on research and research activities (DHWG, 2004; DHWG, 2005; DHWG, 2006a; DHWG, 2006b; DHWG, 2007; DHWG, 2008; DHWG, 2009; DHWG, 2010; 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 five sections. 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 ten-year period from FY 2001 through FY 2010. Section V highlights new research projects and initiatives since the last *Annual Report to Congress*.

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 *2004Annual Report to Congress* (DHWG, 2006a*).*

The original list of 21 questions has been reduced to 19. Based on the Institute of Medicine of the National Academies (IOM) 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 post-traumatic stress disorder (PTSD) that were originally included in the Federal GW research portfolio were closed as of FY2007 (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.

The organization of the remaining 19 Research Topics into five major categories is described in Section B below.

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 agency 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 pyridostigmine bromide, 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) (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.)
- Pyridostigmine bromide and other medical prophylaxes (e.g., vaccines, pyridostigmine bromide, 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 VA, the VA Office of Research and Development (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 chronic multisymptom illnesses (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.) Headaches
    (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) Pyridostigmine bromide
    b) DEET
    c) Permethrin
    d) Oil well fire smoke
    e) Petroleum products (e.g., jet fuels) and combustion products
    f) Multiple vaccinations and other medical prophylaxes

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
    b) Physiological responses to biological stress
    c) Sexual and/or reproductive dysfunction

III. PUBLISHED RESULTS AND STATUS OF THE FIELD IN 2010

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 59 relevant articles published in English in calendar year 2010 or in 2009 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 the1990-1991 Gulf War are presented in this section if they are related to brain and nervous system function. In 2010, most of these studies focused on psychological health and neuroinflammation, with a smaller number of studies investigating the long-term effects of nerve gas exposure primarily on the cholinergic system, learning and memory deficits, general long-term health of GW Veterans, and ALS.

General Brain Function and Exposure Research

There is growing evidence that chronic inflammation from exposure to chemicals or to injury can lead to progressive secondary damage. A recent report indicated that nerve gas exposure results in the chronic reduction in size in certain brain structures related to executive function and memory using functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) methods (Chao et al., 2010). Holzel and coworkers reported a controlled longitudinal study to investigate pre-post changes in brain gray matter concentration attributable to participation in a Mindfulness-based Stress Reduction (MBSR) program. Whole brain analyses of magnetic resonance (MR) images identified increases in the posterior cingulate cortex, the temporoparietal junction, and the cerebellum in the MBSR group compared with the controls. The results suggest that participation in MBSR is associated with changes in gray matter concentration in brain regions involved in learning and memory processes, emotion regulation, self-referential processing, and perspective taking (Holzel et al., 2011). Calley and coworkers used fMRI to examine neuroanatomic correlates of semantic memory processing in 38 GW Veterans in three affected groups and normal-deployed controls. The combination of performance deficits and functional neuroimaging differences between affected GW Veterans and deployed normal controls begins to establish a neurobiological basis for their word-finding deficits (Calley et al., 2010). A study using MRI-based arterial spin labeling (ASL) and phase-contrast techniques confirmed and extended previous findings that patients with GWVI have an abnormal response to an inhibitory cholinergic challenge (physostigmine infusion) compared to age-gender-education matched control Veterans (Liu et al., 2011). In another study, exposure to the nerve gas soman resulted in status epilepticus (epileptic state) and sustained release of pro-inflammatory cytokines. The authors indicated that this increased neuropathology and worsened outcomes (Johnson and Kan, 2010).

Amyotrophic Lateral Sclerosis (ALS)

The understanding of the elucidation of the progression of ALS has been an area of intense study. Recent breakthroughs have been made that reveal the inflammatory cascade that takes place in the spinal cord as motor neurons die. The breakthroughs in the understanding of the toll-like receptors could lead eventually to pharmacological treatments for ALS (Casula et al., 2011).

Non-pharmacological therapies have also been shown to reduce inflammation related to chronic neurological diseases. One such therapy is the use of electroacupuncture in the treatment of ALS (Yang et al., 2010). In this early stage research, the specific placement of the acupuncture at a specific acupoint resulted in a significant reduction in inflammation in the spinal cord of ALS model mice.

Therapeutic development for ALS is being assisted by successes in the early diagnosis of the disease using biomarkers and imaging, as well as the development of an ALS registry (Khishchenko et al., 2010; Metwalli et al., 2010). The

registry will give researchers that ability to follow the progression of the disease in many different people and to delineate all the genotypes associated with ALS. This knowledge will eventually lead to new and improved therapies for the treatment of ALS.

Neuropsychological Functioning and Stress Response

One of the major health issues of the Gulf War was the affect that the war had on the psychological health of our Servicemembers. The major psychological health issue to arise from this war was post-traumatic stress disorder. Stress itself can be the cause of damage to the CNS and impair cognitive function (Apfel et al., 2011; Mauck et al., 2010).

A comparison of combat Veterans who served in Vietnam and the 1990-1991 Gulf War demonstrated that the negative effects of combat on mental health were larger for Veterans of the Gulf War versus Vietnam (Gade and Wenger, 2011). A result of chronic PTSD is decreased social interaction and the lack of social interaction exacerbates the other symptoms of PTSD. Fontana et al., have been developing and testing new psychosocial therapies to treat these psychopathologies to in order to break this cycle that leads to isolation of our Veterans from their communities and families (Fontana and Rosenheck, 2010). In addition, new evidence suggests that females may differ in their aspects of PTSD, suggesting that consideration should be given to program planning and design efforts that address these differences in every program treating female Veterans reporting war zone service (Fontana et al., 2010). McKenzie and coworkers examined the temporal relationships between GW deployment and subsequent psychological disorders in Royal Australian Navy GW Veterans and found that psychological disorder rates peaked in the first two years (1991-1992) following the Gulf War. In Veterans with two or more disorders, anxiety disorders and alcohol disorders tended to appear before affective disorders (McKenzie et al., 2010). Smith-Osborne examined how post-secondary educational attainment among young Veterans of the 1990-1991 Gulf War affected their mental health status. Recent treatment for post-traumatic stress disorder (PTSD) showed an association with use of Veterans' educational benefits (Smith-Osborne, 2009). Tilman and coworkers collected event-related potential (ERP) and behavioral data from 25 GW Veterans who complained of cognitive difficulties and from 23 matched asymptomatic deployed Veterans while they performed a GO-NOGO task that required both a semantic decision and inhibitory processing. A significantly greater false-alarm rate was found among the ill Veterans, which is consistent with previous ERP studies of other patient groups that have shown poor inhibitory response performance. The data support the contention that the ill Veterans' deficit lies more in inhibiting than in detecting task-related differences in the stimuli (Tillman et al., 2010). Yehuda and colleagues administered hydrocortisone (Hcort) to GW Veterans with (PTSD+) and without (PTSD-) chronic PTSD in a randomized, placebo-controlled, double-blind challenge and assessed changes in plasma ACTH, memory, and hippocampal [^{18}F]FDG uptake on positron emission tomography. The PTSD+ group showed greater cortisol and ACTH suppression, reflecting greater peripheral glucocorticoid receptor (GR) responsiveness, and did not show an Hcort-induced decrement in delayed recall or retention. Differences in brain metabolic responses between GW Veterans with and without PTSD may reflect differences in peripheral and central GR responsiveness (Yehuda et al., 2010).

B. Environmental Toxicology

Environmental agents potentially toxic to GW Veterans in theater were the topics of numerous scientific reports in 2010. These agents can be grouped into three areas: (1) depleted uranium, which is used in armor-piercing munitions; (2) chemical and anti-nerve agents (e.g., mustard gas and pyridostigmine bromide); and (3) insecticides (e.g., permethrin, chlorpyrifos).

Depleted Uranium (DU)

In a review of the current state of knowledge concerning the effect of exposure to depleted uranium, Briner differentiated between the effects of large dose exposures on the kidney (tubular necrosis) and low dose exposures which may not produce a clear and defined set of symptoms (Briner, 2010; Young et al., 2010). The renal effects of exposure to depleted uranium were summarized in a review of epidemiologic and experimental data (Arzuaga et al., 2010). The overall conclusion was that DU has a deleterious effect on renal proximal tubule function resulting in elevated concentration of biomarkers in the urine (e.g., β_2-microglobulin, retinol binding protein). Animal studies have routinely shown that DU, oral or implanted exposure, leads to renal toxicity. The most recent follow-up surveillance study of GW Veterans exposed to DU found urinary β_2-microglobulin and retinol binding protein although levels were still within the normal range. It is hypothesized that longer-term studies of GW Veterans exposed to DU could show elevated levels of this biomarker.

Aschner and Jiang reported that DU exhibits low direct neurotoxic potential in primary rat cortical neurons with little change in thiol metabolites, high-energy phosphates, lipid peroxidation products, or cell viability (Aschner and Jiang, 2009). Using isolated human lung epithelial cells, DU was shown to be cytotoxic and, after longer exposure, shown to lead to chromosomal aberrations (LaCerte et al., 2010). Furthermore, isolated human bronchial cells exposed to DU were transformed to a cancerous phenotype associated with significant chromosomal instability consistent with a neoplastic phenotype (Xie et al., 2010). Another study (Bakhmutsky et al., 2010) determined the genotoxic effects (measured as number of micronuclei in peripheral blood lymphocytes) of DU in GW Veterans enrolled in a long-term health surveillance program at the Baltimore VAMC. Urinary uranium (U) levels were used to separate Veterans into low and high exposure groups. There was no measureable difference in genotoxic effect between the two groups.

A study of radiological enhancement associated with embedded particles of DU in the human body was shown to only be on the order of 1-10 times of actual radioactivity and not the previous factor of 500-1000 times (Pattison et al., 2010).

Nerve and Chemical Agents

Sulfur mustard, a potent vesicant employed as a chemical weapon, has been shown (Ebrahimi et al., 2010) to have a genomic effect that results in elevated levels of messenger ribonucleic acid (mRNA) for neutrophil gelatinase-associated lipocalin (NGAL). NGAL participates in the pathway that protects cells against oxidative stress. Stimulation of NGAL production may help protect cells in the pulmonary system from toxicity induced by mustard gas. Soman (pinacolyl methylphosphonofluoridate), a warfare nerve agent, inhibits acetylcholinesterase. This inhibition results in elevated levels of acetylcholine in the nervous system and can cause intense tonic-clonic convulsions, respiratory paralysis and possibly death. Part of the pathological processes after exposure to soman was shown in rodents to result from an increase in neurotoxic cytokines, such as interleukin (IL)-1α, IL-1β, IL-6 and tumor necrosis factor. The exact molecular link between the elevated neurotoxic cytokines and neurological effects seen with soman exposure remains to be elucidated (Johnson and Kan, 2010). Another rodent study (Mauck et al., 2010), demonstrated that brain muscarinic receptor density decreases after exposure to pyridostigmine bromide while stress generally increased muscarinic receptor density. A study of sheep farmers exposed to low level of organophosphate found that such exposure may be linked to impaired behavior (Mackenzie Ross et al., 2010). A study of Japanese survivors of the 1994 and 1995 sarin attacks in Japan revealed continuing neurocognitive effects and PTSD (Loh et al., 2010).

Insecticides and Pesticides

A comprehensive review of the toxic effects organophosphate (OP), organochlorine (OC), and carbamate (CB) compounds concluded that OP and CB impair the enzymatic pathways involved in metabolism of carbohydrates, fats and protein within cytoplasm, mitochondria, and peroxisomes, either through inhibition of acetylcholinesterase (AChE) or by affecting target organs directly. As a shared mechanism, OP, CB and OC compounds induce cellular oxidative stress by affecting mitochondrial function and disrupting neuronal and hormonal status of the body (Karami-Mohajeri and Abdollahi, 2010). Occupational exposure to pesticides was correlated with the incidence of ALS in a population of agricultural workers in a town in Northern Italy (Bonvicini et al., 2010). While the study was small, a significant positive relationship was found between the risk of ALS and exposure to pesticides; a relative risk of 3.6 was reported. A transgenic mouse model of different forms of the human paraoxonase was used to address the role of paraoxonase (PON1) in modulating toxicity associated with exposure to mixtures of organophosphate (e.g., chlorpyrifos oxon, diazoxon) compounds. Overall, expression of PON1 had a major influence on carboxylesterases mediated detoxification of organophosphate compounds (Jansen et al., 2009). Animal and tissue studies of organophosphate neurotoxicity suggested that the toxicity may involve a non-cholinergic mechanism (Proskocil et al., 2010). Rats repeatedly exposed to relatively low levels of the organophosphate, chlorpyrifos, showed protracted impairments of sustained attention and an increase in impulsive behaviors (Middlemore-Risher et al., 2010). Furlong and coworkers developed a new two-substrate assay/analysis protocol that provides PON1 status without use of toxic OP substrates, allowing for use of the protocol in non-specialized laboratories. Immunolocalization studies of PONs 1, 2 and 3 in nearly all mouse tissues suggest that the functions of PONs 1 and 3 extend beyond the plasma and the HDL particle (Furlong et al., 2010).

Oil Well Spills

Sediment samples collected in 2002-2003 from habitats along the shoreline of Saudi Arabia were used to perform an assessment of polycyclic aromatic hydrocarbons (PAHs) from the 1991 Gulf War oil spill. Samples were assigned to one of five environmental risk categories (no risk, low, low-medium, medium, or high). Landscape and geomorphology has played a role in the distribution and persistence in sediments of oil from the Gulf War (Bejarano and Michel, 2010).

C. Immune Dysfunction and Infectious Diseases

Broderick and colleagues examined the patterns of immune markers and their evolution during exercise in ill GW Veterans (Broderick et al., 2011). Cortisol was measured in saliva and other body fluids before and after an exercise test, and immune cell populations were surface-stained for a panel of nine immune cell markers. The results suggested that there may be an autoimmune component in the etiology of GWVI. An examination of the neurological basis of complementary and alternative medical therapies (Oke and Tracey, 2009) indicated that they may play a role in suppressing the innate inflammatory response. Sta and colleagues examined the extent of the immune activation in ALS by measuring the expression and cellular distribution of components of innate and adaptive immunity in spinal cord and motor cortex from patients with rapid and slow sporadic ALS and controls. Their findings demonstrated a persistent and prominent activation of both innate and adaptive immunity in ALS (Sta et al., 2011).

Shoenfeld and Agmon-Levin reviewed the current data on the role of adjuvants in the pathogenesis of immune-mediated diseases with special interest in siliconosis, GWVI, myofasciitis syndrome and post-vaccination phenomena (Shoenfeld and Agmon-Levin, 2010). The term "functional somatic syndromes" has been applied to several syndromes, including GWVI, chronic fatigue syndrome, irritable bowel syndrome, fibromyalgia, multiple chemical sensitivity, and sick building syndrome (SBS). A comparison of the clinical manifestations, symptoms, and signs of the four conditions described by Shoenfeld and Agmon-Levin with those described for SBS showed that nine out of ten main symptoms are present in all 5 conditions (Israeli and Pardo, 2010). Although squalene was proposed as the ingredient in the anthrax vaccine that caused the onset of GWVI in many Veterans, a review of the current scientific evidence about the relationships between squalene, anti-squalene antibodies and vaccination indicates that squalene is poorly immunogenic, that low titers of antibodies to squalene can be also detected in sera from healthy individuals, and that neither the presence of anti-squalene antibodies nor their titer is significantly increased by immunization with vaccines containing squalene (or MF59) as an adjuvant (Lippi et al., 2010).

D. Reproductive Health

Using a transgenic murine (mouse) system Miller and co-workers looked at whether chronic preconceptional paternal DU exposure can lead to transgenerational transmission of genomic instability. The data indicated that there may be a route for transmission of factors leading to genomic instability in progeny from DU-exposed fathers (Miller et al., 2010).

E. Symptoms and General Health

General Health

The U.K. Defence Analytical Services published summary statistics on the causes of deaths that occurred among the UK Veterans of the 1990/91 Gulf Conflict (Defence Analytical Services and Advice, 2010). The mortality rates of 53,409 U.K. GW Veterans were analyzed alongside those of a comparison group, consisting of 53,143 U.K. Armed Forces personnel of similar age, gender, Service, regular/reservist status and rank who were in Service on 1 January 1991 but did not deploy to the 2990-2991 Gulf War.

Bell and coworkers compared Army soldiers who deployed to the Gulf with soldiers who did not. Those who deployed were less likely to have had any prewar hospitalizations or to report experiences of depression/suicidal ideation. They reported greater satisfaction with life and relationships but displayed greater tendencies toward risk taking, such as drunk driving, speeding, and failure to wear safety belts. Postwar excess injury risk may be explained in part by a propensity for greater risk taking, which was evident before and persisted throughout the war (Bell et al., 2010).

Horn and coworkers randomly sampled and surveyed 4,257 non-deployed male participants from a 1997/1998 study of GW Veterans and 4,295 non-deployed participants from a 2004/2006 study of Veterans from the war in Iraq. A comparison of the 2 populations provided clear evidence of an increase in the reporting of non-specific symptoms over a seven-year period in the U.K. Armed Forces, suggesting that the threshold for reporting symptoms has decreased and cannot be explained by psychological distress (Horn et al., 2010).

McCarroll and coworkers studied the relationship between length of soldier deployment and self-reports of moderate and severe spousal violence in a 15 percent random sample of 26,835 deployed and non-deployed married active duty U.S. Army men and women in the 50 United States during the period 1990 to 1994, finding that deployment contributes a significant but small increase to the probability of self-reported spousal aggression during a 1-year period (McCarroll et al., 2010).

Jamil and coworkers studied whether perceived health status of Iraqi immigrants and refugees residing in the United States was related to pre-migration environmental stress, current unemployment, and if they had emigrated before or after the 1991 Gulf War, finding that self-rated health was significantly worse among participants that had left Iraq after the 1991 Gulf War (Jamil et al., 2010).

GWVI, Chronic Fatigue Syndrome, and Fibromyalgia

The U.K. Defence Analytical Services published summary statistics on the causes of deaths that occurred among the U.K. Veterans of the 1990/91 Gulf Conflict (Defence Analytical Services and Advice, 2010). The mortality rates of 53,409 U.K. GW Veterans were analyzed alongside those of a comparison group, consisting of 53,143 U.K. Armed Forces personnel of similar age, gender, Service, regular/reservist status and rank who were in Service on 1 January 1991, but did not deploy to the Gulf.

Horn and coworkers randomly sampled and surveyed 4,257 non-deployed male participants from a 1997/1998 study of GW Veterans and 4,295 non-deployed participants from a 2004/2006 study of Veterans from the war in Iraq. A comparison of the 2 populations provided clear evidence of an increase in the reporting of non-specific symptoms over a seven-year period in the U.K. Armed Forces, suggesting that the threshold for reporting symptoms has decreased and cannot be explained by psychological distress (Horn et al., 2010).

Amin and coworkers found that Veterans with GWI had a significantly increased frequency of arousals related to apneas, hypopneas, and mild inspiratory airflow limitation, suggesting the possibility that treating these sleep disorders might significantly improve their quality of life (Amin et al., 2010a). In a subsequent small pilot study (657) they found that Veterans receiving continuous positive airway pressure (CPAP) treatments experienced improvements in pain (34 percent), fatigue (38 percent), cognitive function (33 percent), sleep quality (41 percent), physical health (34 percent) and mental health (16 percent); larger clinical trials will be required to replicate these findings and establish the utility of this intervention (Amin et al., 2010b).

Cook et al. examined the impact of an acute bout of exercise on pain sensitivity in GW Veterans with chronic musculoskeletal pain (CMP). In response to heat-pain stimuli, GW Veterans with CMP reported higher pain intensity and affect ratings than healthy GW Veterans and exhibited an increase in ratings following exercise. GW Veterans with CMP rated exercise as more painful and effortful, and were generally more sensitive to heat-pain stimuli than healthy GW Veterans (Cook et al., 2010). These results are similar to what has been reported for acute exercise in patients with fibromyalgia.

Fletcher and coworkers measured neuropeptide Y (NPY) in plasma using a radioimmunoassay (RIA) and compared with psychometric measures, available for a subset of chronic fatigue syndrome patients, including: Perceived Stress Scale, Profile of Mood States, Automatic Thoughts Questionnaire (ATQ), Positive and Negative Self-Talk Scores, the Cognitively-Oriented Psychotherapy for Early Psychosis (COPE), the Beck Depression Inventory, Fatigue Symptom Inventory, Cognitive Capacity Screening Examination, Medical Outcomes Survey Short Form-36, and the Quality of Life Scale. Plasma NPY was elevated in CFS subjects, compared to controls and to Gulf War Veterans Illnesses cases (Fletcher et al., 2010).

Johnson and coworkers compared Minnesota Multiphasic Personality Inventory (MMPI-2) profiles of GW Veterans with fibromyalgia (FM) to epileptic seizure (ES) patients, psychogenic non-epileptic seizure (PNES) patients, and GW Veteran healthy controls, finding that GW Veterans with fibromyalgia demonstrate a high level of psychological distress (Johnson et al., 2010).

Younger and coworkers studied the effects of naltrexone on pain sensitivity and mood in fibromyalgia. At baseline, the fibromyalgia group exhibited more somatic complaints, greater sensory sensitivity, more opioid withdrawal somatic symptoms, and lower mechanical and cold pain-tolerance than did the healthy control group. Neither group experienced changes in pain sensitivity due to naltrexone administration nor did naltrexone differentially affect self-reported withdrawal symptoms, or mood (Younger et al., 2009).

Wang and coworkers conducted a small single-blind, randomized trial of classic Yang-style tai chi as compared with a control intervention consisting of wellness education and stretching for the treatment of fibromyalgia (defined by American College of Rheumatology 1990 criteria). Of the 66 randomly assigned patients, the 33 in the tai chi group had clinically important improvements in the fibromyalgia impact quotient score and quality of life, and maintained these improvements for at least 24 weeks (Wang et al., 2010).

Orme proposed that conclusions of the VA's Research Advisory Committee on Gulf War Veterans' Illnesses may be premature because the evidence on which they are based is weak (Orme, 2010) .

Respiratory Illness

Mahmoud and coworkers characterized immunological features of asthma and allergies in 25 long-term residents of Kuwait afflicted with bronchial asthma concurrent with rhinitis, 18 long-term residents not suffering from these conditions and ten newcomers to Kuwait. Significantly elevated frequencies of all activated cell phenotypes were observed in the blood of the asthmatic group, except for CD8+HLA-DR+ cells and a presumed T-regulatory (Treg) subpopulation: $CD4+CD25^{high}$. The asthmatic group was also observed to have larger populations of CD3+ (pan-T cells), CD4+ (T helper cells) and CD8+ (cytotoxic T cells), CD56+CD16+ (natural killer (NK) cells) and CD3+CD56 (NK T-like (NKT) cells) compared to healthy long-term residents. Compared to healthy recent immigrants, the blood of long-term residents contained elevated levels of CD3+CD56+ (NK-like), CD4+CD45RA+/ CD45RO+ (Naive-to-Memory Transitional), but lower $CD4+CD25+^{high}$ (Treg). Elevated representation of NKT cells and memory phenotypes may predispose long-term residents towards enhanced susceptibility for airway disease, while at the same time, reducing representation of Treg cells which are protective against airway disease. This may increase vulnerability to these syndromes (Mahmoud et al., 2010).

Cancer

Young and coworkers used state cancer registry data to determine whether proportional cancer incidence is greater among GW Veterans compared with non-GW Veterans. Only lung cancer showed a small but statistically significant relative excess among GW Veterans compared with non-GW Veterans (adjusted proportional incidence ratios, 1.15; 95% confidence interval, 1.03-1.29). Follow-up studies are required to confirm this finding and to evaluate the role of greater smoking rates among deployed personnel (Young et al., 2010).

F. Abstracts from Published Research

Amin MM, Belisova Z, Hossain S, Gold MS, Broderick JE, Gold AR (2010) Inspiratory airflow dynamics during sleep in veterans with Gulf War illness: a controlled study. Sleep Breath. [Epub ahead of print]
Abstract: PURPOSE: To determine whether veterans with Gulf War Illness (GWI) are distinguished by sleep-disordered breathing, we compared inspiratory airflow dynamics during sleep between veterans with GWI and asymptomatic veterans of the first Gulf War. METHODS: We recruited 18 male veterans with GWI and 11 asymptomatic male veterans of the first Gulf War by advertisement. The two samples were matched for age and body mass index. Each participant underwent a first full-night polysomnogram (PSG) while sleeping supine using standard clinical monitoring of sleep and breathing. A second PSG was performed measuring airflow with a pneumotachograph in series with a nasal mask and respiratory effort with a supraglottic pressure (Psg) catheter to assess the presence of inspiratory airflow limitation during supine N2 sleep. We determined the prevalence of flow-limited breaths by sampling continuous N2 sleep and plotting inspiratory flow against Psg for each breath in the sample. We expressed the prevalence of flow-limited breaths as their percentage in the sample. RESULTS: Compared to controls, veterans with GWI had an increased frequency of arousals related to apneas, hypopneas, and mild inspiratory airflow limitation. During supine N2 sleep, veterans with GWI had 96 +/- 5% (mean +/- SD) of their breaths flow-limited while controls had 36 +/- 25% of their breaths flow limited ($p < 0.0001$). CONCLUSIONS: Veterans with GWI experience sleep-disordered breathing that may distinguish them from asymptomatic veterans of the first Gulf War.

Amin MM, Gold MS, Broderick JE, Gold AR (2010) The effect of nasal continuous positive airway pressure on the symptoms of Gulf War illness. Sleep Breath. [Epub ahead of print]
Abstract: PURPOSE: We performed a pilot study to determine whether nasal continuous positive airway pressure (CPAP) alleviates the symptoms of veterans with Gulf War illness (GWI) and sleep disordered breathing (SDB). METHODS: Eighteen male veterans with GWI and SDB recruited by advertisement, participated in a randomized, single-masked, sham-controlled treatment trial. Participants received 3 weeks of treatment during sleep with either therapeutic nasal CPAP or sham nasal CPAP. Using validated questionnaires, pain, fatigue, cognitive function, sleep disturbance, and general health were assessed by self-report before and after treatment. One of the participants assigned to therapeutic CPAP was excluded from the trial before starting treatment, leaving 17 participants. RESULTS: Compared to the nine sham nasal CPAP recipients, the eight participants receiving therapeutic nasal CPAP experienced improvements in pain (34%; $p = 0.0008$), fatigue (38%; $p = 0.0002$), cognitive function (33%; $p = 0.004$), sleep quality (41%; $p = 0.0003$), physical health (34%; $p = 0.0003$), and mental health (16%; $p = 0.03$). CONCLUSIONS: Our findings in this pilot study suggest that nasal CPAP may greatly improve symptoms in veterans with GWI and SDB.

Apfel BA, Ross J, Hlavin J, Meyerhoff DJ, Metzler TJ, Marmar CR, Weiner MW, Schuff N, Neylan TC (2011) Hippocampal volume differences in Gulf War veterans with current versus lifetime posttraumatic stress disorder symptoms. Biol Psychiatry 69:541-548.
Abstract: BACKGROUND: Decreased hippocampal volume is described in posttraumatic stress disorder (PTSD) and depression. However, it is not known whether it is a risk factor for the development of PTSD or a consequence of PTSD. We sought to determine the effects of PTSD and depressive symptoms on hippocampal volume. METHODS: Clinical and magnetic resonance imaging data were collected in a cross sectional study of 244 Gulf War veterans. Measures included lifetime and current Clinician Administered PTSD Scale, Hamilton Depression Scale, Life Stressor Checklist, and Lifetime Drinking History. Magnetic resonance imaging data were acquired with a 1.5-T scanner and analyzed with automated and semiautomated image processing techniques. RESULTS: Eighty-two veterans had lifetime PTSD, 44 had current PTSD, and 38 had current depression. In the linear regression analysis, current PTSD symptoms (standardized coefficient beta = -.25, p = .03) but neither lifetime PTSD symptoms nor current depression were associated with smaller hippocampal volume. Gender, age, history of early life trauma, education, lifetime and current alcohol use, current marijuana use, and treatment with antidepressants did not have independent effects. Participants with chronic PTSD had, on average, a smaller hippocampus compared with those with remitted PTSD. CONCLUSIONS: The finding that current but not lifetime PTSD symptom severity explains hippocampal size raises two possibilities: either a small hippocampus is a risk factor for lack of recovery from PTSD (trait) or PTSD effects on hippocampal volume are reversible once PTSD symptoms remit and the patient recovers (state).

Arzuaga X, Rieth SH, Bathija A, Cooper GS (2010) Renal effects of exposure to natural and depleted uranium: a review of the epidemiologic and experimental data. J Toxicol Environ Health B Crit Rev 13:527-545.
Abstract: Elevated levels of naturally occurring uranium in groundwater have been found in small geographic areas throughout the world. Relevant research was reviewed pertaining to natural and depleted uranium (DU) exposure and nephrotoxicity, including epidemiologic community-based and occupational studies, studies of Gulf War veterans exposed to DU, and experimental studies in animals. Occupational cohort studies do not provide evidence of an increased risk of kidney-related mortality among uranium-exposed workers. However, occupational and community-based studies of populations chronically exposed to elevated drinking-water concentrations of uranium provide some evidence of adverse renal effects, as assessed by biomarkers of proximal tubule damage such as urinary levels of glucose, calcium, and various low-molecular-weight proteins. Indications of proximal tubule effects, as evidenced by increased urinary β_2-microglobulin and retinol binding protein levels, were also seen in the most recent follow-up surveillance study of Gulf War veterans exposed to DU. The reported β_2-microglobulin levels in these studies were generally considered to be within normal limits, but the long-term implications of the observed variation in these levels are not established. The kidney was observed to be a target of uranium toxicity following oral and implantation exposure routes in several animal species. The interpretation and importance of the observed changes in biomarkers of proximal tubule function are important questions that indicate the need for additional clinical, epidemiological, and experimental research.

Aschner M, Jiang GC (2009) Toxicity studies on depleted uranium in primary rat cortical neurons and in Caenorhabditis elegans: what have we learned? J Toxicol Environ Health B Crit Rev 12:525-539.
Abstract: Depleted uranium (DU) is the major by-product of the uranium enrichment process for its more radioactive isotopes, retaining approximately 60% of its natural radioactivity. Given its properties as a pyrophoric and dense metal, it has been extensively used in armor and ammunitions. Questions have been raised regarding the possible neurotoxic effects of DU in humans based on follow-up studies in Gulf War veterans, where a decrease in neurocognitive behavior in a small population was noted. Additional studies in rodents indicated that DU readily traverses the blood-brain barrier, accumulates in specific brain regions, and results in increased oxidative stress, altered electrophysiological profiles, and sensorimotor deficits. This review summarizes the toxic potential of DU with emphasis on studies on thiol metabolite levels, high-energy phosphate levels, and isoprostane levels in primary rat cortical neurons. Studies in Caenorhabditis elegans detail the role of metallothioneins, small thiol-rich proteins, in protecting against DU exposure. In addition, recent studies also demonstrate that only one of the two forms, metallothionein-1, is important in the accumulation of uranium in worms.

Bakhmutsky MV, Oliver MS, Armid MA, Squibb KS, Tucker JD (2010) Long term depleted uranium exposure in Gulf War I veterans does not cause elevated numbers of micronuclei in peripheral blood lymphocytes. Mutat Res 720:53-57.
Abstract: Depleted uranium (DU) is a high density heavy metal that has been used in military munitions since the 1991 Gulf War. DU is weakly radioactive and chemically toxic. Long term exposure can cause adverse health effects. This study assessed genotoxic effects in DU exposed Gulf War I veterans as a function of uranium (U) body burden. Levels

of urine U were used to categorize the cohort into low and high exposure groups. Exposure to DU occurred during friendly fire incidents in 1991 involving DU munitions resulting in inhalation and ingestion exposure to small particles of DU and soft tissue DU fragments from traumatic injuries. All of these Veterans are enrolled in a long term health surveillance program at the Baltimore Veterans Administration Medical Center. Blood was drawn from 35 exposed male veterans aged 36-59 years, then cultured and evaluated for micronuclei (MN) using the cytokinesis block method. The participants were divided into two exposure groups, low and high, based on their mean urine uranium (uU) concentrations. Poisson regression analyses with mean urine U concentrations, current smoking, X-rays in the past year and donor age as dependent variables revealed no significant relationships with MN frequencies. Our results indicate that on-going systemic exposure to DU occurring in Gulf War I Veterans with DU embedded fragments does not induce significant increases in MN in peripheral blood lymphocytes compared to MN frequencies in Veterans with normal U body burdens.

Bejarano AC, Michel J (2010) Large-scale risk assessment of polycyclic aromatic hydrocarbons in shoreline sediments from Saudi Arabia: environmental legacy after twelve years of the Gulf war oil spill. Environ Pollut 158:1561-1569.
Abstract: A large-scale assessment of polycyclic aromatic hydrocarbons (PAHs) from the 1991 Gulf War oil spill was performed for 2002-2003 sediment samples (n = 1679) collected from habitats along the shoreline of Saudi Arabia. Benthic sediment toxicity was characterized using the Equilibrium Partitioning Sediment Benchmark Toxic Unit approach for 43 PAHs (ESBTU(FCV,43)). Samples were assigned to risk categories according to ESBTU(FCV,43) values: no-risk (< or = 1), low (>1 - < or = 2), low-medium (>2 - < or = 3), medium (>3 - < or = 5) and high-risk (>5). Sixty seven percent of samples had ESBTU(FCV,43) > 1 indicating potential adverse ecological effects. Sediments from the 0-30 cm layer from tidal flats, and the >30 - <60 cm layer from heavily oiled halophytes and mangroves had high frequency of high-risk samples. No-risk samples were characterized by chrysene enrichment and depletion of lighter molecular weight PAHs, while high-risk samples showed little oil weathering and PAH patterns similar to 1993 samples. North of Safaniya sediments were not likely to pose adverse ecological effects contrary to sediments south of Tanaqib. Landscape and geomorphology has played a role on the distribution and persistence in sediments of oil from the Gulf War.

Bell NS, Amoroso PJ, Williams JO, Yore MM, Engel CC, Jr., Senier L, DeMattos AC, Wegman DH (2010) Demographic, physical, and mental health factors associated with deployment of U.S. Army soldiers to the Persian Gulf. Mil Med 175:227-237.
Abstract: A total of 675,626 active duty Army soldiers who were known to be at risk for deployment to the Persian Gulf were followed from 1980 through the Persian Gulf War. Hospitalization histories for the entire cohort and Health Risk Appraisal surveys for a subset of 374 soldiers were used to evaluate prewar distress, health, and behaviors. Deployers were less likely to have had any prewar hospitalizations or hospitalization for a condition commonly reported among Gulf War veterans or to report experiences of depression/suicidal ideation. Deployers reported greater satisfaction with life and relationships but displayed greater tendencies toward risk taking, such as drunk driving, speeding, and failure to wear safety belts. Deployed veterans were more likely to receive hazardous duty pay and to be hospitalized for an injury than nondeployed Gulf War-era veterans. If distress is a predictor of postwar morbidity, it is likely attributable to experiences occurring during or after the war and not related to prewar exposures or health status. Postwar excess injury risk may be explained in part by a propensity for greater risk taking, which was evident before and persisted throughout the war.

Bonvicini F, Marcello N, Mandrioli J, Pietrini V, Vinceti M (2010) Exposure to pesticides and risk of amyotrophic lateral sclerosis: a population-based case-control study. Ann Ist Super Sanita 46:284-287.
Abstract: A few epidemiologic studies have suggested an association of agricultural work and pesticides exposure with a severe degenerative disease of the motor neurons, amyotrophic lateral sclerosis (ALS), though conflicting results have also been provided. We investigated through a population-based case-control study the possible relation between overall occupational exposure to pesticides and ALS risk in the northern Italy municipality of Reggio Emilia. By administering a questionnaire, we investigated occupational history and leisure-time habits of the 41 ALS patients diagnosed in the 1995-2006 period, and of 82 age- and sex-matched randomly sampled population controls. More cases than controls were found to have been exposed to pesticides for at least six months (31.7% vs 13.4%, respectively), in all cases within the occupational environment. In a conditional logistic regression model, we found an excess ALS risk associated with exposure to pesticides, with a relative risk of 3.6 (95% confidence interval 1.2-10.5). Such association persisted after inclusion in the statistical analysis of potential confounders. Despite the limited statistical stability of the risk estimates, these results appear to indicate that occupational exposure to pesticides is a risk factor for ALS, suggesting the need to further investigate this issue.

Briner W (2010) The toxicity of depleted uranium. Int J Environ Res Public Health 7:303-313.
Abstract: Depleted uranium (DU) is an emerging environmental pollutant that is introduced into the environment primarily by military activity. While depleted uranium is less radioactive than natural uranium, it still retains all the chemical toxicity associated with the original element. In large doses the kidney is the target organ for the acute chemical toxicity of this metal, producing potentially lethal tubular necrosis. In contrast, chronic low dose exposure to depleted uranium may not produce a clear and defined set of symptoms. Chronic low-dose, or subacute, exposure to depleted uranium alters the appearance of milestones in developing organisms. Adult animals that were exposed to depleted uranium during development display persistent alterations in behavior, even after cessation of depleted uranium exposure. Adult animals exposed to depleted uranium demonstrate altered behaviors and a variety of alterations to brain chemistry. Despite its reduced level of radioactivity evidence continues to accumulate that depleted uranium, if ingested, may pose a radiologic hazard. The current state of knowledge concerning DU is discussed.

Broderick G, Kreitz A, Fuite J, Fletcher MA, Vernon SD, Klimas N (2011) A pilot study of immune network remodeling under challenge in Gulf War Illness. Brain Behav Immun 25:302-313.
Abstract: Gulf War Illness (GWI) is a complex disorder affecting nervous, endocrine and immune regulation. Accordingly, we propose that GWI presents with a distinct pattern of immune signaling. To explore this we compared interaction patterns linking immune markers and their evolution during exercise. Blood was collected from 9 GWI and 11 control subjects prior to a Graded eXercise Test (GXT) (t_0), at peak effort (t_1) and 4 h post-exercise (t_2). Salivary cortisol and plasma, serum or culture supernatants were analyzed for concentrations of neuropeptide Y (NPY), IL-1α, IL-5, IL-6, IL-10, TNF-α, IFN-γ and soluble CD26 (sCD26). Immune cell populations were surface stained for CD19, CD2, CD3, CD4, CD8, CD26, CD56, CD16, and CD11a. Mutual information (MI) networks linking these immune markers were generated in each group at each time point. Graph theory was used to describe the evolution of each network's structure and identify potential nucleating points. Distinct in topology, GWI networks had more abundant connections but were less organized. NPY, IL-1α, TNF-α and CD2+/CD26+ nodes were better integrated in the GWI network at rest. Under effort (t_1) these differences were replaced by significant restructuring around nodes for CD19+ B cell population, IL-5, IL-6 and soluble CD26 concentrations. This pattern subsided post-exercise. Further analysis indicated that IL-1α and CD2+/CD26+ nodes strongly influenced this characteristic modulation of B and T cell network motifs. This potentially heightened lymphocyte and HPA axis responsiveness to IL-1 stimulation in the context of a mixed Th1:Th2 immune signature supports an autoimmune component in GWI etiology.

Calley CS, Kraut MA, Spence JS, Briggs RW, Haley RW, Hart J, Jr. (2010) The neuroanatomic correlates of semantic memory deficits in patients with Gulf War illnesses: a pilot study. Brain Imaging Behav 4:248-255.
Abstract: We used functional magnetic resonance imaging (fMRI) to study semantic memory processing in 38 Gulf War veterans in 3 affected groups (Syndromes 1, 2, and 3) and normal-deployed controls. Subjects were given the Semantic Object Retrieval Test (SORT), which requires participants to decide whether two features combine and result in the retrieval of a specific object (e.g., "desert" and "humps" --> "camel"). Differences between groups were calculated using a repeated measures analysis of variance (ANOVA). Then, regions of interest were constructed and correlations assessed between the percent signal change (PSC) within these regions, followed by correlations between behavioral measures and PSC. We found affected groups performed less well on the SORT than the controls did, and behavioral differences were correlated to PSC within the caudate and thalamus. The combination of performance deficits and functional neuroimaging differences between affected Gulf War veterans and deployed normal controls begins to establish a neurobiological basis for their word-finding deficits.

Casula M, Iyer AM, Spliet WG, Anink JJ, Steentjes K, Sta M, Troost D, Aronica E (2011) Toll-like receptor signaling in amyotrophic lateral sclerosis spinal cord tissue. Neuroscience 179:233-243.
Abstract: Increasing evidence indicates that inflammatory responses could play a critical role in the pathogenesis of motor neuron injury in amyotrophic lateral sclerosis (ALS). Recent findings have underlined the role of Toll-like receptors (TLRs) and the receptor for advanced glycation endproducts (RAGE) in the regulation of both innate and adaptive immunity in different pathologies associated with neuroinflammation. In the present study we investigated the expression and cellular distribution of TLR2, TLR4, RAGE and their endogenous ligand high mobility group box 1 (HMGB1) in the spinal cord of control (n=6) and sporadic ALS (n=12) patients. The immunohistochemical analysis of TLR2, TLR4 and RAGE showed increased expression in reactive glial cells in both gray (ventral horn) and white matter of ALS spinal cord. TLR2 was predominantly detected in cells of the microglia/macrophage lineage, whereas the TLR4 and RAGE was strongly expressed in astrocytes. Real-time quantitative PCR analysis confirmed the increased expression of both TLR2 and TLR4 and HMGB1 mRNA level in ALS patients. In ALS spinal cord, HMGB1 signal is increased in the cytoplasm of reactive glia, indicating a possible release of this molecule from glial cells. Our findings show increased expression of TLR2, TLR4, RAGE and HMGB1 in reactive glia in human ALS spinal cord, suggesting

activation of the TLR/RAGE signaling pathways. The activation of these pathways may contribute to the progression of inflammation, resulting in motor neuron injury. In this context, future studies, using animal models, will be important to achieve a better understanding of these signaling pathways in ALS in view of the development of new therapeutic strategies.

Chao LL, Rothlind JC, Cardenas VA, Meyerhoff DJ, Weiner MW (2010) Effects of low-level exposure to sarin and cyclosarin during the 1991 Gulf War on brain function and brain structure in US veterans. Neurotoxicology 31:493-501.

Abstract: BACKGROUND: Potentially more than 100,000 US troops may have been exposed to the organophosphate chemical warfare agents sarin (GB) and cyclosarin (GF) when a munitions dump at Khamisiyah, Iraq was destroyed during the Gulf War (GW) in 1991. Although little is known about the long-term neurobehavioral or neurophysiological effects of low-dose exposure to GB/GF in humans, recent studies of GW veterans from the Devens Cohort suggest decrements in certain cognitive domains and atrophy in brain white matter occur individuals with higher estimated levels of presumed GB/GF exposure. The goal of the current study is to determine the generalizability of these findings in another cohort of GW veterans with suspected GB/GF exposure. METHODS: Neurobehavioral and imaging data collected in a study on Gulf War Illness between 2002 and 2007 were used in this study. We focused on the data of 40 GW-deployed veterans categorized as having been exposed to GB/GF at Khamisiyah, Iraq and 40 matched controls. Magnetic resonance images (MRI) of the brain were analyzed using automated and semi-automated image processing techniques that produced volumetric measurements of gray matter (GM), white matter (WM), cerebrospinal fluid (CSF) and hippocampus. RESULTS: GW veterans with suspected GB/GF exposure had reduced total GM and hippocampal volumes compared to their unexposed peers ($p< or =0.01$). Although there were no group differences in measures of cognitive function or total WM volume, there were significant, positive correlations between total WM volume and measures of executive function and visuospatial abilities in veterans with suspected GB/GF exposure. CONCLUSIONS: These findings suggest that low-level exposure to GB/GF can have deleterious effects on brain structure and brain function more than decade later.

Cook DB, Stegner AJ, Ellingson LD (2010) Exercise alters pain sensitivity in Gulf War veterans with chronic musculoskeletal pain. J Pain 11:764-772.

Abstract: Since returning from the Persian Gulf, nearly 100,000 veterans of the first Gulf War (GVs) have reported numerous symptoms with no apparent medical explanation. A primary complaint of these individuals is chronic musculoskeletal pain (CMP). CMP symptoms in GVs are similar to those reported by patients with fibromyalgia (FM), but have not received equivalent scientific attention. Exercise research in CMP patients suggests that acute exercise may exacerbate pain while chronic exercise can reduce pain and improve other symptoms. However, the influence of exercise on GVs with CMP is largely unexplored. This study examined the impact of an acute bout of exercise on pain sensitivity in GVs with CMP. Thirty-two GVs (CMP, n = 15; Control, n = 17) were recruited to complete a series of psychophysical assessments to determine pain sensitivity to heat and pressure stimuli before and after exercise. In response to heat-pain stimuli, GVs with CMP reported higher pain intensity and affect ratings than healthy GVs and exhibited a significant increase in ratings following exercise. GVs with CMP rated exercise as more painful and effortful and were generally more sensitive to heat-pain stimuli than healthy GVs. These results are similar to what has been reported for acute exercise in patients with FM. PERSPECTIVE: Gulf War veterans with CMP perceive exercise as more painful and effortful than healthy GVs and experience increased pain sensitivity following exercise. These results suggest that similar abnormalities in central nervous system processing of nociceptive information documented in FM may also be occurring in GVs with CMP.

Defence Analytical Services and Advice (2010) 1990/1991 Gulf Conflict-UK Veterans Mortality Data: Causes of Death.)

Abstract: The latest UK Gulf Veterans Mortality Data, produced by Defence Analytical Services and Advice (DASA), Ministry of Defence, was released on the 31st March 2010 according to the arrangements approved by the UK Statistics Authority.

This Statistical Notice provides summary statistics on the causes of deaths that occurred among the UK veterans of the 1990/91 Gulf Conflict. The mortality rates of 53,409 UK Gulf veterans were analysed alongside those of a comparison group, the Era cohort. The Era comparison group consists of 53,143 UK Armed Forces personnel of similar age, gender, Service, regular/reservist status and rank who were in Service on 1 January 1991 but did not deploy to the Gulf. The findings include those who died while in Service and those who died after they had left the Services.

Ebrahimi M, Roudkenar MH, Imani Fooladi AA, Halabian R, Ghanei M, Kondo H, Nourani MR (2010) Discrepancy between mRNA and Protein Expression of Neutrophil Gelatinase-Associated Lipocalin in Bronchial Epithelium Induced by Sulfur Mustard. J Biomed Biotechnol 2010:823131.
mustard (SM) is a potent vesicant that has been employed as a chemical weapon in various conflicts during the 20th century. More recently, mustard was used in the Iraq conflict against Iranian troops and civilians. At the present time there are more than 40.000 people suffering from pulmonary lesions special bronchiolitis obliterans (BOs) due to mustard gas. SM increases the endogenous production of reactive oxygen species (ROS). Neutrophil Gelatinase-associated Lipocalin 2 (Lcn2, NGAL) is a member of the lipocalin superfamily for which a variety of functions such as cellular protection against oxidative stress have been reported. Ten normal and Twenty SM-induced COPD patient individuals were studied. Assessment of NGAL expressions in healthy and the patients endobrinchial biopsies were performed by semiquantitative RT-PCR, real-time RT-PCR, and Immunohistochemistry analysis. While Normal control samples expressed same level of mRNA NGAL, expression level of mRNA-NGAL was upregulated about 1.4- to 9.8-folds compared to normal samples. No significant immunoreactivity was revealed in both samples. As we are aware this is the first report of induction of NGAL in patients exposed to SM. NGAL may play an important role in cellular protection against oxidative stress toxicity induced by mustard gas in airway wall of patients.

Fletcher MA, Rosenthal M, Antoni M, Ironson G, Zeng XR, Barnes Z, Harvey JM, Hurwitz B, Levis S, Broderick G, Klimas NG (2010) Plasma neuropeptide Y: a biomarker for symptom severity in chronic fatigue syndrome. Behav Brain Funct 6:76.
Abstract: BACKGROUND: Chronic fatigue syndrome (CFS) is a complex, multi-symptom illness with a multisystem pathogenesis involving alterations in the nervous, endocrine and immune systems. Abnormalities in stress responses have been identified as potential triggers or mediators of CFS symptoms. This study focused on the stress mediator neuropeptide Y (NPY). We hypothesized that NPY would be a useful biomarker for CFS. METHODS: The CFS patients (n = 93) were from the Chronic Fatigue and Related Disorders Clinic at the University of Miami and met the 1994 case definition of Fukuda and colleagues. Healthy sedentary controls (n = 100)) were from NIH or VA funded studies. Another fatiguing, multi-symptom illness, Gulf War Illness (GWI), was also compared to CFS. We measured NPY in plasma using a radioimmunoassay (RIA). Psychometric measures, available for a subset of CFS patients included: Perceived Stress Scale, Profile of Mood States, ATQ Positive & Negative Self-Talk Scores, the COPE, the Beck Depression Inventory, Fatigue Symptom Inventory, Cognitive Capacity Screening Examination, Medical Outcomes Survey Short Form-36, and the Quality of Life Scale. RESULTS: Plasma NPY was elevated in CFS subjects, compared to controls (p = .000) and to GWI cases (p = .000). Receiver operating characteristics (ROC) curve analyses indicated that the predictive ability of plasma NPY to distinguish CFS patients from healthy controls and from GWI was significantly better than chance alone. In 42 patients with CFS, plasma NPY had significant correlations (<0.05) with perceived stress, depression, anger/hostility, confusion, negative thoughts, positive thoughts, general health, and cognitive status. In each case the correlation (+ or -) was in the anticipated direction. CONCLUSIONS: This study is the first in the CFS literature to report that plasma NPY is elevated compared to healthy controls and to a fatigued comparison group, GWI patients. The significant correlations of NPY with stress, negative mood, general health, depression and cognitive function strongly suggest that this peptide be considered as a biomarker to distinguish subsets of CFS.

Fontana A, Rosenheck R (2010) War zone veterans returning to treatment: effects of social functioning and psychopathology. J Nerv Ment Dis 198:699-707.
Abstract: Patients with mental illness often return for further treatment after an initial episode of care. Two processes that may contribute to the return for further treatment are the severity of patients' initial social and clinical status; and/or deterioration in their status over time, regardless of their initial status. This study examined these processes in an administrative database of war zone veterans who had received outpatient treatment from a Veterans Affairs specialized posttraumatic stress disorder program. The results suggest that both initial severity and deterioration of status contribute to return to treatment and involve changes in both social functioning and psychopathology. Determination of the direction of effects between social functioning and psychopathology showed that psychopathology in the form of PTSD, other Axis I disorder or violent behavior generally affected subsequent social functioning, but not vice versa. Psychopathology in the form of alcohol or drug abuse/dependence, however, showed reciprocal effects with social functioning. These results point to the importance of emphasizing interventions that address social dysfunction and that address psychopathology, from the beginning of treatment as a way of maximizing the benefits and minimizing the need for recurrent care.

Fontana A, Rosenheck R, Desai R (2010) Female Veterans of Iraq and Afghanistan seeking care from VA specialized PTSD Programs: comparison with male veterans and female war zone veterans of previous eras. J Womens Health (Larchmt) 19:751-757.

Abstract: BACKGROUND: Differences in the characteristics and mental health needs of female veterans of the Iraq/Afghanistan war compared with those of veterans of other wars may have useful implications for VA program and treatment planning. METHODS: Female veterans reporting service in the Iraq/Afghanistan war were compared with women reporting service in the Persian Gulf and Vietnam wars and to men reporting service in the Iraq/Afghanistan war. Subjects were drawn from VA administrative data on veterans who sought outpatient treatment from specialized posttraumatic stress disorder (PTSD) treatment programs. A series of analyses of covariance (ANCOVA) was used to control for program site and age. RESULTS: In general, Iraq/Afghanistan and Persian Gulf women had less severe psychopathology and more social supports than did Vietnam women. In turn, Iraq/Afghanistan women had less severe psychopathology than Persian Gulf women and were exposed to less sexual and noncombat nonsexual trauma than their Persian Gulf counterparts. Notable differences were also found between female and male veterans of the Iraq/Afghanistan war. Women had fewer interpersonal and economic supports, had greater exposure to different types of trauma, and had different levels of diverse types of pathology than their male counterparts. CONCLUSIONS: There appear to be sufficient differences within women reporting service in different war eras and between women and men receiving treatment in VA specialized treatment programs for PTSD that consideration should be given to program planning and design efforts that address these differences in every program treating female veterans reporting war zone service.

Furlong CE, Suzuki SM, Stevens RC, Marsillach J, Richter RJ, Jarvik GP, Checkoway H, Samii A, Costa LG, Griffith A, Roberts JW, Yearout D, Zabetian CP (2010) Human PON1, a biomarker of risk of disease and exposure. Chem Biol Interact 187:355-361.

Abstract: Human paraoxonase 1 (PON1) is a high-density lipoprotein (HDL)-associated serum enzyme that exhibits a broad substrate specificity. In addition to protecting against exposure to some organophosphorus (OP) pesticides by hydrolyzing their toxic oxon metabolites, PON1 is important in protecting against vascular disease by metabolizing oxidized lipids. Recently, PON1 has also been shown to play a role in inactivating the quorum sensing factor N-(3-oxododecanoyl)-l-homoserine lactone (3OC12-HSL) of Pseudomonas aeruginosa. Native, untagged engineered recombinant human PON1 (rHuPON1) expressed in Escherichia coli and purified by conventional column chromatographic purification is stable, active, and capable of protecting PON1 knockout mice ($PON1^{-/-}$) from exposure to high levels of the OP compound diazoxon. The bacterially derived rHuPON1 can be produced in large quantities and lacks the glycosylation of eukaryotic systems that can produce immunogenic complications when inappropriately glycosylated recombinant proteins are used as therapeutics. Previous studies have shown that the determination of PON1 status, which reveals both $PON1_{192}$ functional genotype and serum enzyme activity level, is required for a meaningful evaluation of PON1's role in risk of disease or exposure. We have developed a new two-substrate assay/analysis protocol that provides PON1 status without use of toxic OP substrates, allowing for use of this protocol in non-specialized laboratories. Factors were also determined for inter-converting rates of hydrolysis of different substrates. PON1 status also plays an important role in revealing changes in HDL-associated PON1 activities in male patients with Parkinson disease (PD). Immunolocalization studies of PONs 1, 2 and 3 in nearly all mouse tissues suggest that the functions of PONs 1 and 3 extend beyond the plasma and the HDL particle.

Gade DM, Wenger JB (2011) Combat exposure and mental health: the long-term effects among US Vietnam and Gulf war veterans. Health Econ 20:401-416.

Abstract: Using a random sample of more than 4000 veterans, we test the effects of combat exposure on mental health. We focus on two cohorts of veterans: those who served in Vietnam (1964-1975) and the Gulf War (1990-1991). Combat exposure differed between these groups in intensity, duration and elapsed time since exposure. We find that combat exposure generally, and exposure to dead, dying, or wounded people, specifically, is a significant predictor of mental health declines as measured by an individual's Mental Component Summary score. Under our general specifications, the negative effects of combat on mental health were larger for Gulf war veterans than for Vietnam veterans as of 2001. These effects persist after controlling for demographic characteristics, insurance coverage, income and assets. Using discrete factor, nonparametric maximum likelihood (DFML) estimation we controlled for unobserved heterogeneity as well as the factors above. In the DFML specifications we find a negative impact of exposure to dead, wounded or dying people for both Gulf and Vietnam veterans, but find no statistically significant effect for combat exposure overall for Vietnam veterans as of 2001. Based on our Gulf war parameters, we estimate that the costs of mental health declines to be between $87 and $318 per year for each soldier with combat service and exposure to dead, dying and wounded people.

Holzel BK, Carmody J, Vangel M, Congleton C, Yerramsetti SM, Gard T, Lazar SW (2011) Mindfulness practice leads to increases in regional brain gray matter density. Psychiatry Res 191:36-43.
Abstract: Therapeutic interventions that incorporate training in mindfulness meditation have become increasingly popular, but to date little is known about neural mechanisms associated with these interventions. Mindfulness-Based Stress Reduction (MBSR), one of the most widely used mindfulness training programs, has been reported to produce positive effects on psychological well-being and to ameliorate symptoms of a number of disorders. Here, we report a controlled longitudinal study to investigate pre-post changes in brain gray matter concentration attributable to participation in an MBSR program. Anatomical magnetic resonance (MR) images from 16 healthy, meditation-naive participants were obtained before and after they underwent the 8-week program. Changes in gray matter concentration were investigated using voxel-based morphometry, and compared with a waiting list control group of 17 individuals. Analyses in a priori regions of interest confirmed increases in gray matter concentration within the left hippocampus. Whole brain analyses identified increases in the posterior cingulate cortex, the temporo-parietal junction, and the cerebellum in the MBSR group compared with the controls. The results suggest that participation in MBSR is associated with changes in gray matter concentration in brain regions involved in learning and memory processes, emotion regulation, self-referential processing, and perspective taking.

Horn O, Sloggett A, Ploubidis GB, Hull L, Hotopf M, Wessely S, Rona RJ (2010) Upward trends in symptom reporting in the UK Armed Forces. Eur J Epidemiol 25:87-94.
Abstract: Several reports have shown increases in the prevalence of non-specific symptoms in the general population. Research in the military tends to focus on comparisons between deployed and non-deployed personnel and does not examine trends over time. 4,257 and 4,295 male participants of the Gulf war and Iraq war studies not deployed to either of these wars were randomly sampled and surveyed in 1997/1998 and 2004/2006 in two independent cross-sectional studies. Information was collected on 50 symptoms and the General Health Questionnaire (GHQ-12). Factor analysis was performed to identify an underlying pattern of symptom dimensions, and multivariate regressions were carried out to examine changes in symptom dimensions between the two surveys and the possible role of psychological morbidity. Factor analysis identified a robust pattern of eight symptom dimensions. An increase in the prevalence of symptoms was evident across all symptom dimensions. Adjustment for demographic and service characteristics revealed increases in the odds of scoring highly on symptom dimensions, varying from odds ratios 1.57, 95% CI 1.36-1.81 (cardio-respiratory dimension) to 2.24, 95% CI 1.93-2.60 (fatigue dimension). Unexpectedly, increases were even greater when adjusting for psychological morbidity. There is clear evidence of an increase in the reporting of non-specific symptoms over a 7 year period in the UK Armed Forces. It suggests that the threshold for reporting symptoms has decreased and cannot be explained by psychological distress. The possible implication of this trend for medical practice in the wider population deserves close scrutiny.

Israeli E, Pardo A (2010) The sick building syndrome as a part of the autoimmune (auto-inflammatory) syndrome induced by adjuvants. Mod Rheumatol. [Epub ahead of print]
Abstract: Sick building syndrome (SBS) is a term coined for a set of clinically recognizable symptoms and ailments without a clear cause reported by occupants of a building. In the 1990s the term "functional somatic syndromes" was applied to several syndromes, including SBS, multiple chemical sensitivity, repetition stress injury, the side effects of silicone breast implants, the Gulf War syndrome (GWS), chronic fatigue syndrome, the irritable bowel syndrome, and fibromyalgia. Recently, Shoenfeld and Agmon-Levin suggested that four conditions-siliconosis, macrophagic myofascitis, the GWS, and post-vaccination phenomena-which share clinical and pathogenic resemblances, may be included under a common syndrome entitled the "autoimmune (auto-inflammatory) syndrome induced by adjuvants". Comparison of the clinical manifestations, symptoms, and signs of the four conditions described by Shoenfeld and Agmon-Levin with those described for SBS shows that nine out of ten main symptoms are present in all 5 conditions. Shoenfeld and Agmon-Levin further propose several major and minor criteria, which, although requiring further validation, may aid in the diagnosis of this newly defined syndrome. We propose here that SBS may also be included as a part of "Shoenfeld's syndrome"
Notes: Immune Function

Jamil H, Nassar-McMillanb S, Lambert R, Wangd Y, Ager J, Arnetz B (2010) Pre- and post-displacement stressors and time of migration as related to self-rated health among Iraqi immigrants and refugees in Southeast Michigan. Med Confl Surviv 26:207-222.
Abstract: The objective of this study was to determine whether perceived health status of Iraqi immigrants and refugees residing in the United States was related to pre-migration environmental stress, current unemployment, and if they had emigrated before or after the 1991 Gulf War. A random sample of Iraqis residing in Southeast Michigan, US, was interviewed using an Arab language structured survey. The main outcome measure was self-rated health (SRH). Major

predictors included socioeconomics, employment status, pre-migration environmental stress, and health disorders. Path analysis was used to look at mediating effects between predictors and SRH. We found that SRH was significantly worse among participants that had left Iraq after the 1991 Gulf War. Unemployment and environmental stress exposure were inversely related to SRH. There was a direct path between Gulf War exposure and poor health. In addition, there were indirect paths mediated through psychosomatic and psychiatric disorders to SRH. Another path went from Gulf War exposure, via environmental stress and somatic health to poor health. Unemployment had a direct path, as well as indirect paths mediated through psychiatric and psychosomatic disorders, to poor self-rated health. In conclusion, these results suggest that pre- as well as post-migration factors, and period of migration, affect health.

Jansen KL, Cole TB, Park SS, Furlong CE, Costa LG (2009) Paraoxonase 1 (PON1) modulates the toxicity of mixed organophosphorus compounds. Toxicol Appl Pharmacol 236:142-153.
Abstract: A transgenic mouse model of the human $hPON1_{Q192R}$ polymorphism was used to address the role of paraoxonase (PON1) in modulating toxicity associated with exposure to mixtures of organophosphorus (OP) compounds. Chlorpyrifos oxon (CPO), diazoxon (DZO), and paraoxon (PO) are potent inhibitors of carboxylesterases (CaE). We hypothesized that a prior exposure to these OPs would increase sensitivity to malaoxon (MO), a CaE substrate, and the degree of the effect would vary among PON1 genotypes if the OP was a physiologically significant PON1 substrate in vivo. CPO and DZO are detoxified by PON1. For CPO hydrolysis, $hPON1_{R192}$ has a higher catalytic efficiency than $hPON1_{Q192}$. For DZO hydrolysis, the two alloforms have nearly equal catalytic efficiencies. For PO hydrolysis, the catalytic efficiency of PON1 is too low to be physiologically relevant. When wild-type mice were exposed dermally to CPO, DZO, or PO followed 4-h later by increasing doses of MO, toxicity was increased compared to mice receiving MO alone, presumably due to CaE inhibition. Potentiation of MO toxicity by CPO and DZO was greater in $PON1^{-/-}$ mice, which have greatly reduced capacity to detoxify CPO or DZO. Potentiation by CPO was more pronounced in $hPON1_{Q192}$ mice than in $hPON1_{R192}$ mice due to the decreased efficiency of $hPON1_{Q192}$ for detoxifying CPO. Potentiation by DZO was similar in $hPON1_{Q192}$ and $hPON1_{R192}$ mice, which are equally efficient at hydrolyzing DZO. Potentiation by PO was equivalent among all four genotypes. These results indicate that PON1 status can have a major influence on CaE-mediated detoxication of OP compounds.

Johnson AL, Storzbach D, Binder LM, Barkhuizen A, Kent AW, Salinsky MC, Tun SM, Rohlman DS (2010) MMPI-2 profiles: fibromyalgia patients compared to epileptic and non-epileptic seizure patients. Clin Neuropsychol 24:220-234.
Abstract: We compared MMPI-2 profiles of Gulf War veterans with fibromyalgia (FM) to epileptic seizure (ES) patients, psychogenic non-epileptic seizure (PNES) patients, and Gulf War veteran healthy controls. Both PNES and FM are medically unexplained conditions. In previous MMPI-2 research PNES patients were shown to have significantly higher Hs and Hy clinical scales than ES patients. In the present research the FM group had significantly higher Hs and Hy scale scores than both the ES group and the healthy control group. There was no significant difference between the FM and PNES Hs scale scores; however, the FM Hy scale score was significantly lower than the PNES Hy scale score. Present findings indicate a high level of psychological distress in the FM group.

Johnson EA, Kan RK (2010) The acute phase response and soman-induced status epilepticus: temporal, regional and cellular changes in rat brain cytokine concentrations. J Neuroinflammation 7:40.
Abstract: BACKGROUND: Neuroinflammation occurs following brain injury, including soman (GD) induced status epilepticus (SE), and may contribute to loss of neural tissue and declined behavioral function. However, little is known about this important pathological process following GD exposure. Limited transcriptional information on a small number of brain-expressed inflammatory mediators has been shown following GD-induced SE and even less information on protein upregulation has been elucidated. The purpose of this study is to further characterize the regional and temporal progression of the neuroinflammatory process following acute GD-induced SE. METHODS: The protein levels of 10 cytokines was quantified using bead multiplex immunoassays in damaged brain regions (i.e., piriform cortex, hippocampus and thalamus) up to 72 hours following seizure onset. Those factors showing significant changes were then localized to neural cells using fluorescent IHC. RESULTS: A significant concentration increase was observed in all injured brain regions for four acute phase response (APR) induction cytokines: interleukin (IL)-1α, IL-1β, IL-6, and tumor necrosis factor (TNF)-α. Increases in these APR cytokines corresponded both temporally and regionally to areas of known seizure damage and neuronal death. Neurotoxic cytokines IL-1α and IL-1β were primarily expressed by activated microglia whereas the potentially neuroprotective cytokine IL-6 was expressed by neurons and hypertrophic astrocytes. CONCLUSIONS: Increases in neurotoxic cytokines likely play an active role in the progression of GD-induced SE neuropathology though the exact role that these and other cytokines play in this process require further study.

Karami-Mohajeri S, Abdollahi M (2010) Toxic effects of organophosphate, carbamate, and organochlorine pesticides on cellular metabolism of lipids, proteins, and carbohydrates: A comprehensive review. Hum Exp Toxicol. [Epub ahead of print]

Abstract: Pesticides, including organophosphate (OP), organochlorine (OC), and carbamate (CB) compounds, are widely used in agricultural and indoor purposes. OP and CB act as acetyl cholinesterase (AChE) inhibitors that affect lots of organs such as peripheral and central nervous systems, muscles, liver, pancreas, and brain, whereas OC are neurotoxic involved in alteration of ion channels. There are several reports about metabolic disorders, hyperglycemia, and also oxidative stress in acute and chronic exposures to pesticides that are linked with diabetes and other metabolic disorders. In this respect, there are several in vitro and in vivo but few clinical studies about mechanism underlying these effects. Bibliographic databases were searched for the years 1963-2010 and resulted in 1652 articles. After elimination of duplicates or irrelevant papers, 204 papers were included and reviewed. Results indicated that OP and CB impair the enzymatic pathways involved in metabolism of carbohydrates, fats and protein within cytoplasm, mitochondria, and proxisomes. It is believed that OP and CB show this effect through inhibition of AChE or affecting target organs directly. OC mostly affect lipid metabolism in the adipose tissues and change glucose pathway in other cells. As a shared mechanism, all OP, CB and OC induce cellular oxidative stress via affecting mitochondrial function and therefore disrupt neuronal and hormonal status of the body. Establishing proper epidemiological studies to explore exact relationships between exposure levels to these pesticides and rate of resulted metabolic disorders in human will be helpful.

Khishchenko N, Allen KD, Coffman CJ, Kasarskis EJ, Lindquist JH, Morgenlander JC, Norman BB, Oddone EZ, Rozear MP, Sabet A, Sams L, Bedlack RS (2010) Time to diagnosis in the National Registry of Veterans with Amyotrophic Lateral Sclerosis. Amyotroph Lateral Scler 11:125-132.

Abstract: Our objective was to determine the interval from symptom onset to diagnosis, and to evaluate associated factors in a cohort of U.S. Veterans with motor neuron diseases. We retrospectively evaluated 1359 patients enrolled in the National Registry of Veterans with Amyotrophic Lateral Sclerosis (ALS). The main outcome measures were time from symptom onset to first diagnosis and to second opinion. Predictor variables included age at symptom onset, year of symptom onset, race, onset site, final diagnosis, number of diagnostic tests performed and clinical sites visited. Median time to first diagnosis was 11 months; median time to second opinion was two months. In a multivariable model, more recent calendar year of symptom onset, younger age, bulbar onset and a diagnosis of ALS versus non-ALS motor neuron disease were all significantly associated with a shorter time to first diagnosis. Later year of symptom onset and white race were significantly associated with a shorter time to second opinion. While the interval from symptom onset to diagnosis, and many of the associated factors are similar between our large cohort of U.S. Veterans with ALS and other smaller published cohorts, we found that the diagnostic interval among U.S. Veterans has significantly decreased over time.

LaCerte C, Xie H, Aboueissa AM, Wise JP, Sr. (2010) Particulate depleted uranium is cytotoxic and clastogenic to human lung epithelial cells. Mutat Res 697:33-37.

Abstract: Depleted uranium (DU) is commonly used in military applications and consequently exposure to soldiers and non-combatants is potentially frequent and widespread. DU is suspected to be a carcinogen, potentially affecting the bronchial cells of the lung. Few studies have considered DU in human bronchial cells. Accordingly, we determined the cytotoxicity and clastogenicity of particulate DU in human bronchial epithelial cells (BEP2D cells). DU-induced concentration-dependent cytotoxicity in human bronchial epithelial cells, and was not clastogenic after 24h but induced chromosomal aberrations after 48h. These data indicate that if DU is a human bronchial carcinogen, it is likely acting through a mechanism that involves DNA breaks after longer exposures.

Lippi G, Targher G, Franchini M (2010) Vaccination, squalene and anti-squalene antibodies: facts or fiction? Eur J Intern Med 21:70-73.

Abstract: Squalene, a hydrocarbon obtained for commercial purposes primarily from shark liver oil and other botanic sources, is increasingly used as an immunologic adjuvant in several vaccines, including seasonal and the novel influenza A (H1N1) 2009 pandemic flu vaccines. Nearly a decade ago, squalene was supposed to be the experimental anthrax vaccine ingredient that caused the onset of Persian Gulf War syndrome in many veterans, since antibodies to squalene were detected in the blood of most patients affected by this syndrome. This evidence has raised a widespread concern about the safety of squalene containing adjuvants (especially MF59) of influenza vaccines. Nevertheless, further clinical evidence clearly suggested that squalene is poorly immunogenic, that low titres of antibodies to squalene can be also detected in sera from healthy individuals, and that neither the presence of anti-squalene antibodies nor their titre is significantly increased by immunization with vaccines containing squalene (or MF59) as an adjuvant. This

review summarizes the current scientific evidence about the relationship between squalene, anti-squalene antibodies and vaccination.

Liu P, Aslan S, Li X, Buhner DM, Spence JS, Briggs RW, Haley RW, Lu H (2011) Perfusion deficit to cholinergic challenge in veterans with Gulf War Illness. Neurotoxicology 32:242-246.
Abstract: A highly plausible etiology for Gulf War Illness (GWI) is that the neural damage and cognitive deficits are associated with excessive exposure to cholinesterase-inhibiting cholinergic stimulants. Our previous SPECT study provided strong indication that cerebral blood flow (CBF) in veterans with GWI may be different from those of unaffected control veterans. The present study confirmed and extended previous findings that patients with GWI have abnormal response to an inhibitory cholinergic challenge, physostigmine infusion, when compared to age-gender-education matched control veterans. The MRI-based arterial spin labeling (ASL) and phase-contrast techniques have several key advantages over SPECT, including shorter experiment duration, complete non-invasiveness, and higher spatial and temporal resolutions, and therefore may provide a cost-effective biomarker for characterization of GWI.

Loh Y, Swanberg MM, Ingram MV, Newmark J (2010) Case report: Long-term cognitive sequelae of sarin exposure. Neurotoxicology 31:244-246.
Abstract: The long-term sequelae of acute sarin exposure are not well understood. The largest clinical cohort resulted from the 1994 and 1995 attacks in Japan. Observers noted mostly psychiatric sequelae, with a high prevalence of post-traumatic stress disorder (PTSD). We describe neurocognitive findings that may represent sequelae of low-level sarin exposure in Iraq.

Mackenzie Ross SJ, Brewin CR, Curran HV, Furlong CE, Abraham-Smith KM, Harrison V (2010) Neuropsychological and psychiatric functioning in sheep farmers exposed to low levels of organophosphate pesticides. Neurotoxicol Teratol 32:452-459.
Abstract: The study aim was to determine whether low level exposure to organophosphate pesticides (OPs) causes neuropsychological or psychiatric impairment. Methodological weaknesses of earlier studies were addressed by: recruiting participants who had retired on ill health grounds; excluding participants with a history of acute poisoning, medical or psychiatric conditions that might account for ill health; and exploring factors which may render some individuals more vulnerable to the effects of OPs than others. Performance on tests of cognition and mood of 127 exposed sheep farmers (67 working, 60 retired) was compared with 78 unexposed controls (38 working, 40 retired) and published test norms derived from a cross section of several thousand adults in the general population. Over 40% of the exposed cohort reported clinically significant levels of anxiety and depression compared to less than 23% of controls. Exposed subjects performed significantly worse than controls and standardisation samples on tests of memory, response speed, fine motor control, mental flexibility and strategy making, even after controlling for the effects of mood. The pattern was similar for both working and retired groups. The cognitive deficits identified cannot be attributed to mood disorder, malingering, a history of acute exposure or genetic vulnerability in terms of PON1(192) polymorphisms. Results suggest a relationship may exist between low level exposure to organophosphates and impaired neurobehavioural functioning and these findings have implications for working practice and for other occupational groups exposed to OPs such as aviation workers and Gulf War veterans.

Mahmoud F, Habeeb F, Arifhodzic N, Haines D, Novotny L (2010) T lymphocyte activation profiles in peripheral blood of long- versus short-term residents of Kuwait: comparison with asthmatics. Ann Acad Med Singapore 39:854-860.
Abstract: INTRODUCTION: During the Arabian Gulf Wars of 1991 and 2003, the resident population of Kuwait sustained heavy exposure to environmental toxicants introduced by military activities. No comprehensive studies have been conducted to assess how exposure to the wartime and postwar environment may have altered the fundamental patterns of immune reactivity among Kuwaitis in ways that affect pathogenesis of disease. This present study addresses this issue by characterising immunological features of asthma and allergies in a Kuwaiti population that is unique and possibly correlates with toxicant exposures. MATERIALS AND METHODS: Twenty-five long-term residents of Kuwait afflicted with bronchial asthma concurrent with rhinitis; and 2 healthy control groups: 18 long-term residents and 10 newcomers to Kuwait were evaluated by 2- and 3-colour flow cytometry for peripheral blood T cell subpopulation frequencies. RESULTS: Relative to healthy, long-term residents, significantly elevated frequencies of all activated cell phenotypes were observed in the blood of the asthmatic group ($P < 0.05$ to $P < 0.001$), except for CD8+HLA-DR+ cells and a presumed T-regulatory (Treg) subpopulation: $CD4+CD25^{high}$. The asthmatic group was also observed to have larger populations of CD3+ (pan-T cells), CD4+ (T helper cells) and CD8+ (cytotoxic T cells), CD3+CD56 (NKT-like cells) and CD56+CD16+ (NK cells) compared to healthy long-term residents. Compared to healthy recent immigrants, the blood of long-term residents contained elevated levels of CD3+CD56+ (NK-like), CD4+CD45RA+/ CD45RO+ (Naive-to-Memory Transitional), but lower $CD4+CD25+^{high}$ (Treg) ($P < 0.05$).

CONCLUSIONS: Elevated representation of natural killer (NKT)-like and memory phenotypes may predispose long-term residents towards enhanced susceptibility for airway disease; while at the same time, reducing representation of Treg cells which are protective against airway disease, and this may increase vulnerability to these syndromes among the residents of Kuwait. These results may provide insight into the features of immunopathogenesis of asthma and allergies in Kuwait that arise as a result of the special environment of the country.

Mauck B, Lucot JB, Paton S, Grubbs RD (2010) Cholinesterase inhibitors and stress: effects on brain muscarinic receptor density in mice. Neurotoxicology 31:461-467.
Abstract: Exposure to the reversible cholinesterase inhibitor, pyridostigmine bromide (PB), in conjunction with stress, has been suggested as a possible cause of Gulf War Syndrome. This work explores the hypothesis that PB exposure coupled with stress will alter cholinergic receptor density based on the rationale that prolonged exposure to PB and stress will lead to increased stimulation of cholinergic receptors due to the reduced capacity to degrade acetylcholine, leading to changes in receptor levels. Male C57Bl6 mice were exposed to PB (3 or 10 mg/kg/day) or physostigmine (2.88 mg/kg/day) for 7 days via ALZET mini-osmotic pumps implanted subcutaneously. The mice were stressed by shaking at random intervals (avg of 2 min/30 min) for 1 week, which was sufficient to increase blood cortisol levels. Brain tissue for autoradiographic analysis was collected on day 7 of treatment. While we examined many brain regions, analysis revealed that most of the significant changes ($p<0.05$) were seen in cholinergic nuclei. Stress typically increased muscarinic receptor density, while PB and PHY generally decreased muscarinic receptor density.

McCarroll JE, Ursano RJ, Liu X, Thayer LE, Newby JH, Norwood AE, Fullerton CS (2010) Deployment and the probability of spousal aggression by U.S. Army soldiers. Mil Med 175:352-356.
Abstract: OBJECTIVE: To determine the relationship between length of soldier deployment and self-reports of moderate and severe spousal violence. METHODS: The Conflict Tactics Scale was used to measure self-reports of behaviors exhibited in marital conflict. Surveys were administered to a 15% random sample of 26,835 deployed and nondeployed married active duty U.S. Army men and women in the 50 United States during the period 1990 to 1994. Multinomial logistic regression and ordered probit analysis were used to estimate the probabilities of moderate and severe violence by length of deployment. RESULTS: After controlling for demographic variables, the probability of severe aggression was significantly greater for soldiers who had deployed in the past year compared with soldiers who had not deployed. CONCLUSIONS: Deployment contributes a significant but small increase to the probability of self-reported spousal aggression during a 1-year period. Although deployment is a military operation, similar effects may be observed in certain civilian occupations.

McKenzie DP, Creamer M, Kelsall HL, Forbes AB, Ikin JF, Sim MR, McFarlane AC (2010) Temporal relationships between Gulf War deployment and subsequent psychological disorders in Royal Australian Navy Gulf War veterans. Soc Psychiatry Psychiatr Epidemiol 45:843-852.
Abstract: BACKGROUND: Although much has been published on the effects of the 1990/1991 Gulf War on the psychological health of veterans, few studies have addressed the pattern and timing of post-war development of psychological disorders. Our study aims to identify the most common psychological disorders that first appeared post-Gulf War, the period of peak prevalence and the sequence of multiple psychological disorders. METHODS: The temporal progression of psychological disorders in male Australian naval Gulf War veterans with no prior psychological disorders was calculated across each year of the post-Gulf War period. DSM-IV diagnoses were obtained using the Composite International Diagnostic Interview. RESULTS: Psychological disorder rates peaked in the first 2 years (1991-1992) following the Gulf War. Alcohol use disorders were the most likely to appear first. Classification and regression tree analysis found that risk of disorder was exacerbated if veterans had been exposed to a high number of potential psychological stressors during their military service. Lower military rank was associated with increased risk of alcohol disorders, particularly during the first 2 years post-Gulf War. In veterans with two or more disorders, anxiety disorders and alcohol disorders tended to appear before affective disorders. CONCLUSIONS: Our study found that psychological disorders occur in sequence following Gulf War deployment. Our findings may help clinicians to anticipate, and better manage, multiple symptomatology. The findings may also assist veteran and defence organisations in planning effective mental health screening, management and prevention policy.

Metwalli NS, Benatar M, Nair G, Usher S, Hu X, Carew JD (2010) Utility of axial and radial diffusivity from diffusion tensor MRI as markers of neurodegeneration in amyotrophic lateral sclerosis. Brain Res 1348:156-164.
Abstract: Objective: To investigate changes in the diffusion tensor imaging measures, axial diffusivity and radial diffusivity, in addition to the more commonly used fractional anisotropy and mean diffusivity, in patients with amyotrophic lateral sclerosis (ALS) using the voxel-based statistical analysis tool, tract based spatial statistics. Methods: We studied 12 patients with ALS and 19 normal controls using diffusion tensor imaging; tract based spatial statistics was applied to study changes in fractional anisotropy, mean diffusivity, axial diffusivity and radial diffusivity values in

brain white matter tracts. ALS patients were evaluated using clinical examination, administration of the revised ALS functional rating scale and measurement of the forced vital capacity. Results: In ALS patients, we found significant increases in axial diffusivity, radial diffusivity, and mean diffusivity and significant decreases in fractional anisotropy. Increases in axial diffusivity and radial diffusivity were more widespread and more prominent in the corticospinal tract than the decreases in fractional anisotropy. The decreases in fractional anisotropy were evident only in the corona radiata and genu of the corpus callosum. Conclusion: In ALS, axial diffusivity and radial diffusivity may be useful diffusion tensor imaging-derived indices to consider in addition to fractional anisotropy and mean diffusivity to aid in demonstrating neurodegenerative changes.

Middlemore-Risher ML, Buccafusco JJ, Terry AV, Jr. (2010) Repeated exposures to low-level chlorpyrifos results in impairments in sustained attention and increased impulsivity in rats. Neurotoxicol Teratol 32:415-424.
Abstract: Organophosphates such as chlorpyrifos (CPF) are among the most commonly used pesticides in the world. Therefore, it is not surprising that measurable levels of organophosphates (including CPF) are found in over 50% of fresh fruits, vegetables and grains that we consume and that approximately 80% of adults in the US have detectable levels of CPF metabolites in their urine. It is well known that acute exposure to organophosphates can cause cognitive deficits; however, the effects of daily or intermittent contact with low levels of organophosphates (often reflective of environmental exposures) are not well understood. The objective of this study was to determine if repeated low-level exposures to CPF impaired the performance of the 5-Choice Serial Reaction Time Task (5C-SRTT), an animal model of sustained attention. Adult rats were trained to stably perform the 5C-SRTT, then treated with vehicle or CPF 18.0 mg/kg daily for 14 consecutive days or every other day for 30 days. Behavioral testing occurred daily during the CPF-exposure period and throughout a 30 day washout period to assess recovery. All CPF-treated animals exhibited deficits in percent correct, an increase in omissions and premature responses without signs of impaired motivation or overt toxicity. Deficits in 5C-SRTT accuracy were apparent well into the 30 day washout period despite significant recovery of cholinesterase activity. These results indicate that repeated exposures to relatively low levels of chlorpyrifos lead to protracted impairments of sustained attention and an increase in impulsive behaviors in rats.

Miller AC, Stewart M, Rivas R (2010) Preconceptional paternal exposure to depleted uranium: transmission of genetic damage to offspring. Health Phys 99:371-379.
Abstract: Depleted uranium (DU) is an alpha particle emitter and radioactive heavy metal used in military applications. Due to internalization of DU during military operations and the ensuing chronic internal exposure to DU, there are concerns regarding its potential health effects. Preconceptional paternal irradiation has been implicated as a causal factor in childhood cancer and it has been suggested that this paternal exposure to radiation may play a role in the occurrence of leukemia and other cancers to offspring. Similarly, in vivo heavy metal studies have demonstrated that carcinogenic effects can occur in unexposed offspring. Using a transgenic mouse system employing a λ shuttle vector allowing mutations (in the *lacI* gene) to be analyzed in vitro, we have investigated the possibility that chronic preconceptional paternal DU exposure can lead to transgenerational transmission of genomic instability. The mutation frequencies in vector recovered from the bone marrow cells of the F1 offspring of male parents exposed to low, medium, and high doses of internalized DU for 7 mo were evaluated and compared to control, tantalum, nickel, and gamma radiation F1 samples. Results demonstrate that as paternal DU-dose increased there was a trend towards higher mutation frequency in vector recovered from the DNA obtained from bone marrow of F1 progeny; medium and high dose DU exposure to P1 fathers resulted in a significant increase in mutation frequency in F1 offspring (3.57 ± 0.37 and $4.81 \pm 0.43 \times 10^{-5}$; $p < 0.001$) in comparison to control ($2.28 \pm 0.31 \times 10^{-5}$). The mutation frequencies from F1 offspring of low dose DU, Ta- or Ni-implanted fathers (2.71 ± 0.35, 2.38 ± 0.35, and $2.93 \pm 0.39 \times 10^{-5}$, respectively) were not significantly different than control levels ($2.28 \pm 0.31 \times 10^{-5}$). Offspring from ^{60}Co (4 Gy) irradiated fathers did demonstrate an increased *lacI* mutation frequency ($4.69 \pm 0.48 \times 10^{-5}$) as had been shown previously. To evaluate the role of radiation involved in the observed DU effects, males were exposed to equal concentrations (50 mg U L^{-1}) of either enriched uranium or DU in their drinking water for 2 mo prior to breeding. A comparison of these offspring indicated that there was a specific-activity dependent increase in offspring bone marrow mutation frequency. Taken together these uranyl nitrate data support earlier results in other model systems showing that radiation can play a role in DU-induced biological effects in vitro. However, since the *lacI* mutation model measures point mutations and cannot measure large deletions that are characteristic of radiation damage, the role of DU chemical effects in the observed offspring mutation frequency increase may also be significant. Regardless of the question of DU-radiation vs. DU-chemical effects, the data indicate that there exists a route for transgenerational transmission of factor(s) leading to genomic instability in F1 progeny from DU-exposed fathers.

Oke SL, Tracey KJ (2009) The inflammatory reflex and the role of complementary and alternative medical therapies. Ann N Y Acad Sci 1172:172-180.
Abstract: The body's first defense against invading pathogens or tissue injury is the innate immune system. Since excessive immune responses can be damaging, anti-inflammatory mechanisms function to control the pro-inflammatory response and prevent injury. The cholinergic anti-inflammatory pathway is a neural mechanism that suppresses the innate inflammatory response. Knowledge concerning innervation of the immune system offers a unique opportunity to explore previously unrecognized techniques to treat disease. It also enables consideration of the neurological basis of complementary and alternative medical therapies, such as meditation and acupuncture. This evolving area of research has implications for the pathogenesis of chronic inflammatory conditions including inflammatory bowel disease, rheumatoid arthritis, type 2 diabetes, and other conditions of excessive cytokine release.

Orme D (2010) Is Gulf War Illness "Real"? The Jury is Still Out. Federal Practitioner 27:13-20
Abstract: This author proposes that conclusions of the Research Advisory Committee on Gulf War Veterans' Illnesses are premature because the evidence on which they are based is weak.

Pattison JE, Hugtenburg RP, Green S (2010) Enhancement of natural background gamma-radiation dose around uranium microparticles in the human body. J R Soc Interface 7:603-611.
Abstract: Ongoing controversy surrounds the adverse health effects of the use of depleted uranium (DU) munitions. The biological effects of gamma-radiation arise from the direct or indirect interaction between secondary electrons and the DNA of living cells. The probability of the absorption of X-rays and gamma-rays with energies below about 200 keV by particles of high atomic number is proportional to the third to fourth power of the atomic number. In such a case, the more heavily ionizing low-energy recoil electrons are preferentially produced; these cause dose enhancement in the immediate vicinity of the particles. It has been claimed that upon exposure to naturally occurring background gamma-radiation, particles of DU in the human body would produce dose enhancement by a factor of 500-1000, thereby contributing a significant radiation dose in addition to the dose received from the inherent radioactivity of the DU. In this study, we used the Monte Carlo code EGSnrc to accurately estimate the likely maximum dose enhancement arising from the presence of micrometre-sized uranium particles in the body. We found that although the dose enhancement is significant, of the order of 1-10, it is considerably smaller than that suggested previously.

Proskocil BJ, Bruun DA, Thompson CM, Fryer AD, Lein PJ (2010) Organophosphorus pesticides decrease M2 muscarinic receptor function in guinea pig airway nerves via indirect mechanisms. PLoS One 5:e10562.
Abstract: BACKGROUND: Epidemiological studies link organophosphorus pesticide (OP) exposures to asthma, and we have shown that the OPs chlorpyrifos, diazinon and parathion cause airway hyperreactivity in guinea pigs 24 hr after a single subcutaneous injection. OP-induced airway hyperreactivity involves M2 muscarinic receptor dysfunction on airway nerves independent of acetylcholinesterase (AChE) inhibition, but how OPs inhibit neuronal M2 receptors in airways is not known. In the central nervous system, OPs interact directly with neurons to alter muscarinic receptor function or expression; therefore, in this study we tested whether the OP parathion or its oxon metabolite, paraoxon, might decrease M2 receptor function on peripheral neurons via similar direct mechanisms.
METHODOLOGY/PRINCIPAL FINDINGS: Intravenous administration of paraoxon, but not parathion, caused acute frequency-dependent potentiation of vagally-induced bronchoconstriction and increased electrical field stimulation (EFS)-induced contractions in isolated trachea independent of AChE inhibition. However, paraoxon had no effect on vagally-induced bradycardia in intact guinea pigs or EFS-induced contractions in isolated ileum, suggesting mechanisms other than pharmacologic antagonism of M2 receptors. Paraoxon did not alter M2 receptor expression in cultured cells at the mRNA or protein level as determined by quantitative RT-PCR and radio-ligand binding assays, respectively. Additionally, a biotin-labeled fluorophosphonate, which was used as a probe to identify molecular targets phosphorylated by OPs, did not phosphorylate proteins in guinea pig cardiac membranes that were recognized by M2 receptor antibodies. CONCLUSIONS/SIGNIFICANCE: These data indicate that neither direct pharmacologic antagonism nor downregulated expression of M2 receptors contributes to OP inhibition of M2 function in airway nerves, adding to the growing evidence of non-cholinergic mechanisms of OP neurotoxicity.

Shoenfeld Y, Agmon-Levin N (2010) 'ASIA' - autoimmune/inflammatory syndrome induced by adjuvants. J Autoimmun 36:4-8.
Abstract: The role of various environmental factors in the pathogenesis of immune mediated diseases is well established. Of which, factors entailing an immune adjuvant activity such as infectious agents, silicone, aluminium salts and others were associated with defined and non-defined immune mediated diseases both in animal models and in humans. In recent years, four conditions: siliconosis, the Gulf war syndrome (GWS), the macrophagic myofasciitis syndrome (MMF) and post-vaccination phenomena were linked with previous exposure to an adjuvant. Furthermore, these four diseases share a similar complex of signs and symptoms which further support a common denominator.Thus,

we review herein the current data regarding the role of adjuvants in the pathogenesis of immune mediated diseases as well as the amassed data regarding each of these four conditions. Relating to the current knowledge we would like to suggest to include these comparable conditions under a common syndrome entitled ASIA, "Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants".

Smith-Osborne A (2009) Mental health risk and social ecological variables associated with educational attainment for gulf war veterans: implications for veterans returning to civilian life. Am J Community Psychol 44:327-337.
Abstract: This study examines how post-secondary educational attainment among young veterans of the first gulf war affects their mental health status. The all-volunteer military attracts recruits by offering them veterans' educational benefits. Education should help veterans adjust to civilian life. Few studies have shown whether education following military service helps improve veterans' mental health, however. Viewing resiliency, life span and life course, and social geography theories through the lens of social ecology, it is hypothesized that selected contextual factors in the personal, interpersonal, and organizational domains could mediate or moderate the relationship between education and veterans' mental health. Informational social networks showed an association with obtaining mental illness treatment. Recent treatment for post-traumatic stress disorder (PTSD) showed an association with use of veterans' educational benefits. Residing with a small nuclear family in conjunction with having higher levels of health and educational benefits and a higher family income was associated with higher educational attainment.

Sta M, Sylva-Steenland RM, Casula M, de Jong JM, Troost D, Aronica E, Baas F (2011) Innate and adaptive immunity in amyotrophic lateral sclerosis: Evidence of complement activation. Neurobiol Dis 42:211-220.
Abstract: Increasing evidence suggests a role for the immune system in amyotrophic lateral sclerosis (ALS). To determine the extent of the immune activation in ALS we analyzed the expression and cellular distribution of components of innate and adaptive immunity in spinal cord (SC) and motor cortex (MCx) from patients with rapid and slow sporadic ALS and controls. High levels of mRNA and protein of classical complement pathway, C1q and C4, as well as the downstream complement components C3 and C5b-9 were found in all ALS samples. Furthermore, we found higher numbers of activated microglia, reactive astrocytes, dendritic cells (DCs) and $CD8^+$ T-cells in ALS than in control tissue. Rapid ALS cases had more dendritic cells than slow ALS cases, whereas slow ALS cases had more activated microglia than rapid cases. Our findings demonstrate a persistent and prominent activation of both innate and adaptive immunity in ALS. We propose a complement-driven immune response which may contribute to the progression of the inflammation and ultimately lead to even more motor neuron injury.

Tillman GD, Green TA, Ferree TC, Calley CS, Maguire MJ, Briggs R, Hart J, Jr., Haley RW, Kraut MA (2010) Impaired response inhibition in ill Gulf War veterans. J Neurol Sci 297:1-5.
Ref ID: 664
Abstract: Poor performance on tasks requiring response inhibition has been observed among chronically ill veterans of the 1991 Persian Gulf War. Semantic difficulties have also been reported. We collected event-related potential (ERP) and behavioral data from 25 Gulf War veterans who complained of cognitive difficulties and from 23 matched controls, who were deployed but not symptomatic, while they performed a GO-NOGO task that required both a semantic decision and inhibitory processing. A significantly greater false-alarm rate among the ill veterans was accompanied in the ERP data by significantly reduced amplitude in the NOGO P3, consistent with previous ERP studies of other patient groups that have shown poor inhibitory response performance. This supports the contention that the ill veterans' deficit lies more in inhibiting than in detecting task-related differences in the stimuli.

Wang C, Schmid CH, Rones R, Kalish R, Yinh J, Goldenberg DL, Lee Y, McAlindon T (2010) A randomized trial of tai chi for fibromyalgia. N Engl J Med 363:743-754.
Abstract: BACKGROUND: Previous research has suggested that tai chi offers a therapeutic benefit in patients with fibromyalgia. METHODS: We conducted a single-blind, randomized trial of classic Yang-style tai chi as compared with a control intervention consisting of wellness education and stretching for the treatment of fibromyalgia (defined by American College of Rheumatology 1990 criteria). Sessions lasted 60 minutes each and took place twice a week for 12 weeks for each of the study groups. The primary end point was a change in the Fibromyalgia Impact Questionnaire (FIQ) score (ranging from 0 to 100, with higher scores indicating more severe symptoms) at the end of 12 weeks. Secondary end points included summary scores on the physical and mental components of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). All assessments were repeated at 24 weeks to test the durability of the response. RESULTS: Of the 66 randomly assigned patients, the 33 in the tai chi group had clinically important improvements in the FIQ total score and quality of life. Mean (+/-SD) baseline and 12-week FIQ scores for the tai chi group were 62.9+/-15.5 and 35.1+/-18.8, respectively, versus 68.0+/-11 and 58.6+/-17.6, respectively, for the control group (change from baseline in the tai chi group vs. change from baseline in the control group, -18.4 points; $P<0.001$).

The corresponding SF-36 physical-component scores were 28.5+/-8.4 and 37.0+/-10.5 for the tai chi group versus 28.0+/-7.8 and 29.4+/-7.4 for the control group (between-group difference, 7.1 points; P=0.001), and the mental-component scores were 42.6+/-12.2 and 50.3+/-10.2 for the tai chi group versus 37.8+/-10.5 and 39.4+/-11.9 for the control group (between-group difference, 6.1 points; P=0.03). Improvements were maintained at 24 weeks (between-group difference in the FIQ score, -18.3 points; P<0.001). No adverse events were observed. CONCLUSIONS: Tai chi may be a useful treatment for fibromyalgia and merits long-term study in larger study populations. (Funded by the National Center for Complementary and Alternative Medicine and others; ClinicalTrials.gov number, NCT00515008.).

Xie H, LaCerte C, Thompson WD, Wise JP, Sr. (2010) Depleted uranium induces neoplastic transformation in human lung epithelial cells. Chem Res Toxicol 23:373-378.
Abstract: Depleted uranium (DU) is commonly used in military armor and munitions, and thus, exposure of soldiers and noncombatants is frequent and widespread. Previous studies have shown that DU has both chemical and radiological toxicity and that the primary route of exposure of DU to humans is through inhalation and ingestion. However, there is limited research information on the potential carcinogenicity of DU in human bronchial cells. Accordingly, we determined the neoplastic transforming ability of particulate DU to human bronchial epithelial cells (BEP2D). We observed the loss of contact inhibition and anchorage independent growth in cells exposed to DU after 24 h. We also characterized these DU-induced transformed cell lines and found that 40% of the cell lines exhibit alterations in plating efficiency and no significant changes in the cytotoxic response to DU. Cytogenetic analyses showed that 53% of the DU-transformed cell lines possess a hypodiploid phenotype. These data indicate that human bronchial cells are transformed by DU and exhibit significant chromosome instability consistent with a neoplastic phenotype.

Yang EJ, Jiang JH, Lee SM, Hwang HS, Lee MS, Choi SM (2010) Electroacupuncture reduces neuroinflammatory responses in symptomatic amyotrophic lateral sclerosis model. J Neuroimmunol 223:84-91.
Abstract: Amyotrophic lateral sclerosis (ALS) is a paralyzing disorder that is characterized by the progressive degeneration and death of motor neurons. Acupuncture or electroacupuncture (EA) has been used for the treatment of various conditions including osteoarthritis, asthma, and other types of chronic pain conditions. It has been hypothesized that acupuncture exerts anti-inflammatory and anti-nociceptive effects on inflammatory reactions processes. The purpose of this study was to determine whether acupuncture at a specific acupoint could produce anti-inflammatory responses and suppress motor neuron loss in the hG93ASOD1 mouse, commonly used as a model for inherited ALS. We delivered EA at the Zusanli (ST36) acupuncture point in the symptomatic hSOD1G93A animal model. The EA-treated mutant hSOD1 transgenic mice showed decreases in microglial cell activity and TNF-alpha expression in the spinal cord and brain stem. Furthermore, EA significantly improved motor activity compared to the control group and reduced neuronal cell loss in hSOD1G93A mice. Our research suggests a potential functional link between EA therapy and anti-neuroinflammatory response in an ALS animal model

Yehuda R, Golier JA, Bierer LM, Mikhno A, Pratchett LC, Burton CL, Makotkine I, Devanand DP, Pradhaban G, Harvey PD, Mann JJ (2010) Hydrocortisone responsiveness in Gulf War veterans with PTSD: effects on ACTH, declarative memory hippocampal [(18)F]FDG uptake on PET. Psychiatry Res 184:117-127.
Abstract: Neuroendocrine, cognitive and hippocampal alterations have been described in Gulf War (GW) veterans, but their inter-relationships and significance for posttraumatic stress disorder (PTSD) have not been described. Hydrocortisone (Hcort) was administered to GW veterans with (PTSD+ n=12) and without (PTSD- n=8) chronic PTSD in a randomized, placebo-controlled, double-blind challenge. Changes in plasma ACTH, memory, and hippocampal [^{18}F]FDG uptake on positron emission tomography were assessed. The low-dose dexamethasone suppression test was also administered. The PTSD+ group showed greater cortisol and ACTH suppression, reflecting greater peripheral glucocorticoid receptor (GR) responsiveness, and did not show an Hcort-induced decrement in delayed recall or retention. The groups had comparable relative regional hippocampal [^{18}F]FDG uptake at baseline, but only the PTSD- group had an Hcort-associated decrease in hippocampal [^{18}F]FDG uptake. Asymmetry in hippocampal hemispheric volumes differed between PTSD+ and PTSD- groups. This asymmetry was associated with cortisol, ACTH, retention and functional hippocampal asymmetry before, but not after, Hcort administration. Differences in brain metabolic responses between GW veterans with and without PTSD may reflect differences in peripheral and central GR responsiveness.

Young HA, Maillard JD, Levine PH, Simmens SJ, Mahan CM, Kang HK (2010) Investigating the risk of cancer in 1990-1991 US Gulf War veterans with the use of state cancer registry data. Ann Epidemiol 20:265-272.
Abstract: PURPOSE: The purpose of this study was to determine whether proportional cancer incidence is greater among Gulf War veterans compared with non-Gulf War veterans. METHODS: Files obtained from the Defense Manpower Data Center included data for 621,902 veterans who were deployed to the Persian Gulf during the 1990 to 1991 Gulf War (August 2, 1990, to March 1, 1991) and 746,248 non-Gulf War veteran controls. Identification of

veterans who received a cancer diagnosis between 1991 and 2006 was accomplished through record linkage of the Defense Manpower Data Center dataset with files from 28 state cancer registries and the Department of Veterans Affairs Central Cancer Registry. By the use of logistic regression, proportional incidence ratios adjusted for demographic and military characteristics were calculated by comparing the proportion of a specific cancer among all cancers in the Gulf War veterans to the proportion of that specific cancer among all cancers in the non-Gulf War veterans. RESULTS: Only lung cancer showed a statistically significant relative excess among Gulf War veterans compared with non-Gulf War veterans (adjusted proportional incidence ratios, 1.15; 95% confidence interval, 1.03-1.29). When adjusted for race, age, and sex, the overall proportion of cancers among Gulf War and non-Gulf War veterans was similar (odds ratio, 0.99; 95% CI, 0.96-1.02). CONCLUSIONS: With the exception of lung cancer, there is little evidence of excess risk of cancer associated with Gulf War deployment. A follow-up study is warranted to confirm this finding and to evaluate the role of greater smoking rates among deployed personnel.

Younger JW, Zautra AJ, Cummins ET (2009) Effects of naltrexone on pain sensitivity and mood in fibromyalgia: no evidence for endogenous opioid pathophysiology. PLoS One 4:e5180.
Abstract: The pathophysiological mechanisms underlying fibromyalgia are still unknown, although some evidence points to endogenous opioid dysfunction. We examined how endogenous opioid antagonism affects pain and mood for women with and without fibromyalgia. Ten women with fibromyalgia and ten age- and gender-matched, healthy controls each attended two laboratory sessions. Each participant received naltrexone (50mg) at one session, and placebo at the other session, in a randomized and double-blind fashion. Participants were tested for changes in sensitivity to heat, cold, and mechanical pain. Additionally, we collected measures of mood and opioid withdrawal symptoms during the laboratory sessions and at home the night following each session. At baseline, the fibromyalgia group exhibited more somatic complaints, greater sensory sensitivity, more opioid withdrawal somatic symptoms, and lower mechanical and cold pain-tolerance than did the healthy control group. Neither group experienced changes in pain sensitivity due to naltrexone administration. Naltrexone did not differentially affect self-reported withdrawal symptoms, or mood, in the fibromyalgia and control groups. Consistent with prior research, there was no evidence found for abnormal endogenous opioid activity in women with fibromyalgia.

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 2001-2010, and the number of research projects in which the Federal Government has invested.

The appropriated funds for FY 2001 through 2010, centrally obligated to each project, are shown in Appendix C and summarized in Table IV-1. Federal funding for GW research totaled approximately $242 million during this period. Funds obligated for these projects prior to FY 2001 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 2001are 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 2001-2010) Funding Trends for GW Research in Millions of Dollars

Department	FY '01	FY '02	FY '03	FY '04	FY '05	FY '06	FY '07	FY '08	FY '09	FY '10	Total Costs FY '01-'10
DoD	$ 31.6	$ 18.8	$ 16.4	$ 11.1	$ 10.1	$ 10.1	$ 3.4	$ 11.7	$ 10.4	$ 3.2	**$ 126.80**
HHS	$ 1.0	$ 0.8	$ 1.0	$ 0.5	$ 0.5	$ 0.4	$ 0.4	$ 0.4	$ 0	$ 0	**$ 5.00**
VA	$ 8.6	$ 4.5	$ 5.7	$ 7.6	$ 9.5	$13.0	$ 22.1	$ 21.9	$ 16.6	$ 13.9	**$ 123.40**
Total	**$ 41.2**	**$ 24.1**	**$ 23.1**	**$ 19.2**	**$ 20.1**	**$ 23.5**	**$ 25.9**	**$ 34.0**	**$ 27.0**	**$ 17.1**	**$ 255.20**

Funding levels for FY 2008 and 2009 in the table above differ from the values reported in the *2008 and 2009 Annual Reports to Congress* due to identification of funded projects that were not identified in the previous reports and the delayed start of nine projects funded through the FY09 appropriation for the Gulf War Illness Research (GWIRP) managed by the Congressionally Directed Medical Research Program (CDMRP) at DoD.
VA, DoD, and HHS sponsored a total of 378 distinct research projects on GWVI during the period of FY 1992 through FY 2010. 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 (DoD, HHS, and VA). 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 2001 - FY 2010 are shown in Figure IV-1. As of September 30, 2010, 319 projects (84 percent of the 378 projects) were completed, and 59 projects (16 percent) were new or ongoing; the numbers of new, ongoing, and completed projects for each fiscal year are shown in Figure IV-1.

The annual distribution of new and ongoing projects within the five major Research Focus Areas is shown in Figure IV-2. From FY 2001 through 2010 new and ongoing research assigned to the Brain and Nervous System Function, Environmental Toxicology and General Health and Symptoms categories has represented 95.7 ± 1.1 percent of all new and ongoing projects.

Figure IV-1. Cumulative Number of Funded Projects (FY 2001 – FY 2010)

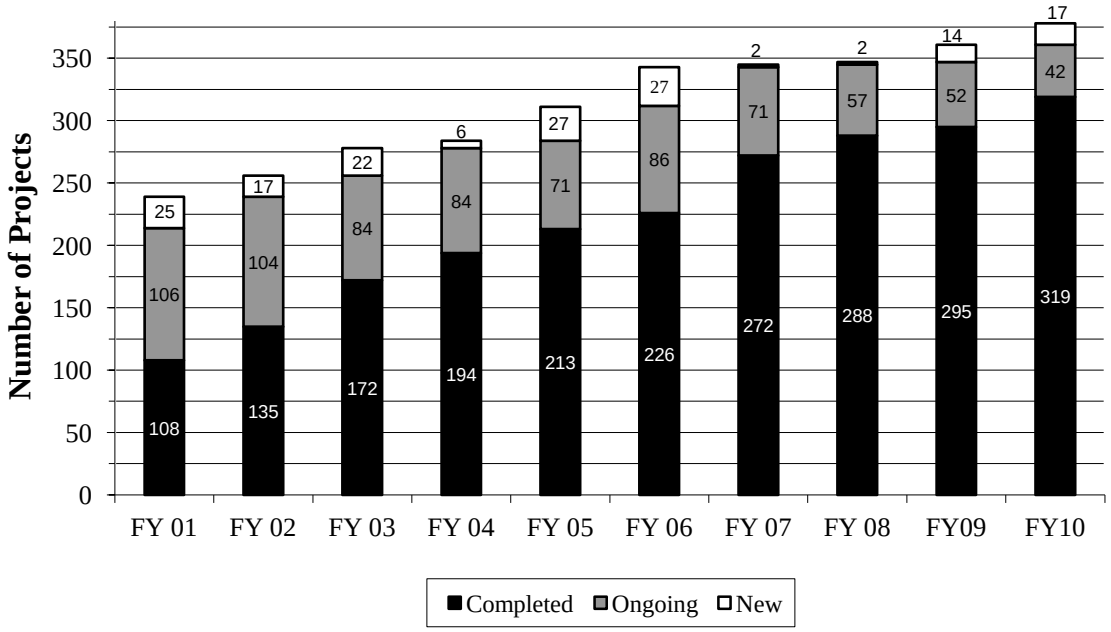
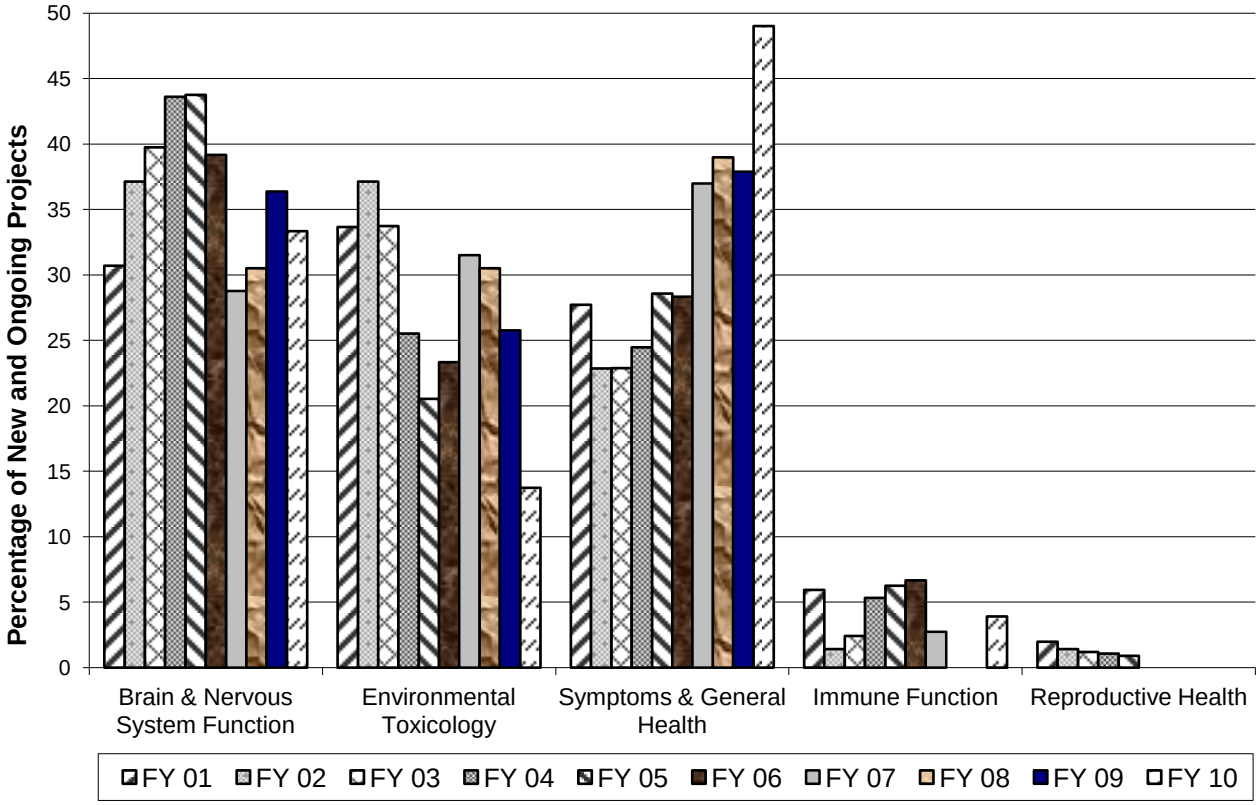


Figure IV-2. Annual Distribution of Topic Areas for New and Ongoing Projects



V. NEW RESEARCH PROJECTS AND INITIATIVES

A. New Initiatives

Requests for Applications (RFAs) were issued by both CDMRP and VA in FY 2010. Proposals received for review in response to these RFAs will be reviewed, and projects selected for funding will begin in FY 2011.

B. Portfolio Review

The Federal Gulf War 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.

C. New Projects

This section highlights the new research projects that have been approved since last year's *2009 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.

Department of Defense (DoD)

Nine projects were funded through the FY 20009 appropriation for the Gulf War Illness Research Program (GWIRP) managed by the CDMRP, but did not start until FY 2010. These projects focused on Brain and Nervous System Function (1), Environmental Toxicology (1), and Symptoms and General Health (7).

*DoD-191, "Neuroimmune Interactions, Low-Dose Sarin Inhalation, and Gulf War Syndrome" is designed to (1) determine the type of cholinergic receptors involved in sarin-induced T cell dysfunction and changes in ACTH/CORT production, (2) ascertain whether sarin-induced immunosuppression increases susceptibility and inflammatory response to bacterial infection and increases susceptibility to dextran-induced colitis, and (3) determine the efficacy of some anti-inflammatory and anticholinergic therapies in attenuating sarin-induced immunosuppression and changes in the HPA axis.

*DoD-192, "Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome" will use a powerful new technology that allows multiple molecules to be measured non-invasively, simultaneously, sequentially, repeatedly, accurately, and with great sensitivity (in parts per billion) on small samples of exhaled breath gas to develop distinguishing biomarkers for GWVI.

*DoD-193, "Genome Instability: A Common Link in Gulf War Illness Patients" is based on the complex system theory that states that various factors trigger the genetic system (genome) to become unstable in ill GW Veterans (possibly only to those with a genetic predisposition to becoming unstable) and that an unstable genome causes the many varying symptoms associated with GWVI. Both in vitro and in vivo systems will be used to link identified causative diverse factors to genome instability and GWVI status.

*DoD-194, "Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome" is designed to assess two parts of the sleep/alert system that help a person sleep at night and stay awake in the day for differences in Veterans of the 1990-1991 Gulf War who have persistent fatigue compared to those who do not have fatigue.

*DoD-195, "Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness" will examine how poorly tuned the fight-or-flight survival response may have become in ill Gulf War Veterans using a computer mock-up of the human body's fight-or-flight response to improve our understanding of GWVI. Using such simulations, we hope to map the new characteristics of this altered survival response in sick veterans and find safe ways of bringing it back into its normal performance envelope.

*DoD-196, "Probiotic (Bifidobacterium Infantis) for Gulf War Illness" is a double blind, placebo-controlled trial of a novel probiotic, Bifidobacterium infantis 35624 (Align®) (BI), for treatment of intestinal and non-intestinal symptoms of IBS (fatigue, joint pains, general stiffness, and headache) in GW Veterans.

*DoD-197, "Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness?" will develop better tests for screening GW Veterans for a neurological illness, small-fiber polyneuropathy (SFPN), that may be one cause of the puzzling symptoms seen in GWVI.

*DoD-198, "Oxidative Stress" will examine a spectrum of markers related to oxidative stress to see which markers, individually or as part of a pattern, discriminate ill GW Veterans from controls; and relate to severity of illness within affected GW Veterans.

*DoD-199, "Gulf War Illness: Evaluation of an Innovative Detoxification Program" will examine the ability of this therapy to reduce symptoms and improve functional status in GW Veterans with chronic health problems. The detoxification regimen includes exercise, low heat sauna, and vitamin and mineral supplements and is thought to repair and rebuild the body and to encourage the release of stored toxins through sweat and increased metabolism.

Department of Veterans Affairs (VA)

VA initiated funding for five new projects during FY 2010 and identified five ongoing projects that had not been included in previous *Annual Reports to Congres*s. These ten projects focused on Brain and Nervous System Function (4), and Symptoms and General Health (6).

*VA-155, "Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis" is a project initiated in FY 2007 that was not identified as Gulf War research until the portfolio review for the current report. This project examines the

effects of oil well fire smoke on carcinogenesis. The long term goal of these studies is to identify individuals at risk for polyaromatic hydrocarbon carcinogenesis and to evaluate the role of CD4+ and CD8+ T-cells in carcinogenesis. This may form the basis for novel immunopreventive strategies for individuals at high risk for development of tumors that may result from exposure to oil well fire smoke.

VA-156, "Gulf War Era Cohort and Biorepository (CSP 585)" is a service-directed project to develop a large cohort and biorepository (blood samples) of Gulf War Era Veterans and to obtain health information, survey data, and blood specimens. The data and specimens collected will be used for future research on a range of areas including genomics and genetics, biologics and immunologic studies, and epidemiology, and health care utilization and needs.

VA-157, "A Clinical Demonstration of an EEG Brain-Computer Interface for ALS Patients (CSP 567)" is a service-directed project to demonstrate that the BCI system can be successfully installed in the homes of VA patients with ALS and that the BCI system will be used, as well as to quantify and describe the impact of the BCI system on the patient and care-givers.

VA-158, "Testing the Feasibility of MC CBT for Veterans with IBS" will test the feasibility of delivering minimal contact cognitive behavioral therapy (MC-CBT) for IBS in a VA sample in terms of 1) establishing the interest level of Veterans in MC-CBT for IBS, 2) documenting rates of subject participation and drop-out, 3) measuring Veterans' satisfaction with the treatment, 4) measuring changes in gastrointestinal symptoms and quality of life, and 5) collecting data on co-morbidities and health care utilization amongst Veterans with a diagnosis of IBS. A target sample size of approximately 30 participants will be recruited.

*VA-159, "Somatic hypersensitivity in Veterans with IBS" will test the novel, mechanistic hypothesis that Veterans with IBS have a generalized but graded hypersensitivity to both somatic and visceral nociceptive stimuli. The results will increase our understanding of the pathophysiology of IBS and allow the development more effective treatments for Veterans suffering from IBS.

VA-160, "Lipoic Acid Therapy for Experimental Autoimmune Encephalomyelitis" will assess the effects and identify the mechanism of action of the antioxidant couple lipoic acid (LA) and dihydrolipoic acid (DHLA) on T cell immunomodulation and trafficking, determine its pharmacokinetics, and relate its peak serum levels to therapeutic benefit. The results of this research will provide further insights into the mechanism of action of lipoic acid in an animal model of MS and provide additional pre-clinical data needed for guiding the development of lipoic acid as a treatment for MS in Veterans.

VA-161, "Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease" is designed to evaluate the influence of specific multiple antigenic peptides (MAPs) on the development and expression of an experimental autoimmune disease in an animal model of MS. Candidate targets of the immunopathologic response have been identified for some autoimmune diseases, and MAPs may offer a significant improvement in antigen-specific therapy for diseases such as Multiple Sclerosis.

*VA-162, "Transcription factors regulating sensory gene expression and pain pathways" is focused on gene regulation in sensory neurons of the trigeminal and dorsal root ganglia, which are the gatekeepers for the reception of position, touch, and pain signals throughout the body, conveyed by proprioceptors, mechanoreceptors, and nociceptors, respectively.

*VA-163, "Immunoregulation of Myelin Specific T Lymphocytes" is an animal study aimed at development of new treatments for GW Veterans with multiple sclerosis (MS). The investigator has designed and developed a novel family of molecules, called RTLs (Recombinant T cell receptor Ligands, RTL), that can selectively block the inflammatory effects of these damaging white blood cells.

*VA-164, Central Mechanisms Modulating Visceral Sensitivity" is a renewal of VA-136 which aims to provide new pathophysiological information about disordered brain-gut communication that may lead to the development of novel therapies for Veterans with abnormalities of the gastrointestinal tract including IBS, characterized by abdominal pain and altered bowel patterns.

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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 Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees
DoD-001B	Epidemiologic Studies of Morbidity Among Gulf War 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 Gulf War 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
DoD-001D	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in Gulf War Veterans
DoD-001E	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study
DoD-001F	Epidemiologic Studies of Morbidity Among Gulf War 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 Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian Gulf War 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

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 Gulf War Veterans

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 Gulf War 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 Gulf War Veterans
DoD-058	Illness Among Persian Gulf War 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 Gulf War Veterans
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 Gulf War Veterans
DoD-075	Toxic Interactions of Prophylactic Drugs and Pesticides
DoD-076	Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel
DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War
DoD-078	Experimental Models of Gulf War Syndrome
DoD-079	Time Course of Stress-induced Impairment of Blood Brain Barrier
DoD-080	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells
DoD-081	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress
DoD-082	Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs
DoD-083	Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism
DoD-084	Psychobiologic Alterations in Persian Gulf War Veterans with and without PTSD
DoD-085	CNS Cytokines and CRH in Gulf War 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. Gulf War 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 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 Gulf War 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 Gulf War 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 Gulf War Veterans (See also VA-61)

DoD-119	Antibiotic Treatment of Gulf War 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 Department of Defense Surveillance for Neoplasms in Infancy
DoD-141	Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans
DoD-142	Illnesses Among Persian Gulf War Veterans: Case Validation Studies (Iowa / Great Britain)

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 Gulf War Veterans
DoD-150	Validation Study of Gulf War Deployment Files
DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in Gulf War Veterans
DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents
DoD-153	Gulf War Illness Research
DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-88)
DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide
DoD-156	The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant
DoD-157	Novel Leishmania and Malaria Potassium Channels: Candidate Therapeutic Targets
DoD-158	Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission of Genetic Damage to Offspring
DoD-159	Neurotoxicity from Chronic Exposure to Depleted Uranium
DoD-160	Characterization of the Reproductive Toxicity of Depleted Uranium
DoD-161	Glutamate Receptor Aptamers and ALS
DoD-162	Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function
DoD-163	Neuroimmune Effects of Inhaling Low Dose Sarin
DoD-164	Efficacy of Adjunct Sleep Interventions for PTSD (EASI-PTSD)
DoD-165	Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military – BALSAM
DoD-166	A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance

DoD-167	Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure
DoD-168	Developing Biomarkers for Fibromyalgia
DoD-169	Development of Novel Therapy for Chronic Neuropathic Pain
DoD-170	Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I
DoD-171	Q10 for Gulf War Veterans
DoD-172	CNDP1 Polymorphisms and Carnosine Therapy in GWI
DoD-173	A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in Gulf War Veterans with Chronic Multisymptom Illness
DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness
DoD-175	Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium
DoD-176	Studies on Axonal Transport in an Animal Model for Gulf War Syndrome
DoD-177	Randomized Trial of an Environmental Medicine Approach to Gulf War Veterans' Illness
DoD-178	Analysis of Paraoxonase Status among US Navy Gulf War 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 Gulf War Veterans' Illness
DoD-183	Biomarkers of Gulf War Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation
DoD-184	Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the Gulf War 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

DoD-191	Neuroimmune Interactions, Low-Dose Sarin Inhalation, and Gulf War Syndrome
DoD-192	Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome
DoD-193	Genome Instability: A Common Link in Gulf War Illness Patients
DoD-194	Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome
DoD-195	Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness
DoD-196	Probiotic (Bifidobacterium Infantis) for Gulf War Illness
DoD-197	Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness?
DoD-198	Oxidative Stress
DoD-199	Gulf War Illness: Evaluation of an Innovative Detoxification Program

DEPARTMENT OF HEALTH AND HUMAN SERVICES PROJECTS

HHS-001	Health Assessment of Persian Gulf War 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 Gulf War 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

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 Gulf War 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 Gulf War Veterans Over Time

VA-009	Evaluation of Cognitive Functioning in Persian Gulf War 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 Gulf War Veterans' Illnesses (ABT) (See also DoD-119)
VA-056	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13)
VA-057	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13)
VA-058	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13)
VA-059	Demonstration Treatment Program for Gulf War Veterans with Unexplained Physical Symptoms (13)
VA-060	Identification and Management of Sleep Disorders in Gulf War Veterans

VA-061	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War 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 Gulf War Veterans
VA-068	Family Study of Fibromyalgia
VA-069	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans
VA-070	A Clinical Evaluation of the Health Status of Persian Gulf War 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 Gulf War 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

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 Gulf War 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 Gulf War 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

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 Gulf War 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 Gulf War 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 Gulf War 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

VA-129	Glucocorticoid Responsivity in Gulf War 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 Gulf War Veterans with Unexplained Illnesses
VA-135	Motor Neuron Function of Gulf War 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	Gulf War Veterans Illnesses' Research IDIQ Contract with UTSW
VA-151	Genetic Epidemiology of ALS
VA-152	Multiple Sclerosis in Gulf War Veterans
VA-153	Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex
VA-154	Imaging Pain Modulation in Gulf War Veterans with Chronic Muscle Pain
VA-155	Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis

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)

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 Gulf War 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	Symptoms	HHS-005	Cognitive Function and Symptom Patterns in Persian Gulf Veterans
Symptoms and General Health	Symptoms	VA-004	Boston Environmental Hazards Research Center Program
Symptoms and General Health	Symptoms	VA-004 A	Evaluation of Cognitive Functioning of Persian Gulf Veterans
Symptoms and General Health	Symptoms	VA-004 B	Evaluation of Neurological Functioning in Persian Gulf Veterans
Symptoms and General Health	Diagnosis	VA-004 F	Validity of Computerized Tests

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
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 Gulf War 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

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Treatment	VA-112	National VA Amyotrophic Lateral Sclerosis Research Consortium
Symptoms and General Health	Diagnosis	VA-125	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla
Symptoms and General Health	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 Gulf War 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 Gulf War 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; Symptoms;	VA-087	Improving Outcomes of Depression in Primary Care
Symptoms and General Health	Treatment; Symptoms;	VA-138	Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP
Symptoms and General Health; Environmental Toxicology	Symptoms;	VA-008	Psychological Test Data of Gulf War Veterans Over Time
Symptoms and General Health;	Symptoms; Diagnosis;	DoD-197	Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness?

Brain and Nervous System Function

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
	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 Gulf War 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 Gulf War Veterans
Symptoms and General Health	Symptoms	DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War 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 Gulf War 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 Gulf War Veterans: Secondary Analysis of CSP#458 Data
Symptoms and General Health	Symptoms	VA-150	Gulf War Veterans Illnesses' Research IDIQ Contract

Brain and Nervous System Function

Epidemiology

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Diagnosis	VA-151	Genetic Epidemiology of ALS Veterans
Symptoms and General Health	Symptoms	VA-152	Multiple Sclerosis in Gulf War 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 Gulf War Veterans
Symptoms and General Health	Diagnosis; Symptoms;	DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-088)
Symptoms and General Health	Diagnosis; Symptoms;	HHS-002	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18
Symptoms and General Health	Diagnosis; Symptoms;	VA-088	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also DoD-154)

Mechanistic

Research Focus	Project Focus	Project	Project Title
	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	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

Brain and Nervous System Function

Mechanistic

Research Focus	Project Focus	Project	Project Title
Environmental Toxicology;	Treatment; Exposure; Immune Function	DoD-185	Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model
Environmental Toxicology; Symptoms and General Health	Symptoms; Exposure;	DoD-170	Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I
Environmental Toxicology; Symptoms and General Health	Symptoms; Exposure;	DoD-198	Oxidative Stress
Symptoms and General Health	Symptoms	DoD-080	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells
Symptoms and General Health	Symptoms	DoD-091	Neurological and Circadian Substrates of PTSD-like Behaviors
Symptoms and General Health	Symptoms	DoD-092	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder
Symptoms and General Health	Symptoms	DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala
Symptoms and General Health	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 Gulf War 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 Gulf War Veterans
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

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	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 Gulf War 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 Gulf War 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

Environmental Toxicology

Development

Research Focus	Project Focus	Project	Project Title
Chemical Weapons	Diagnosis; Exposure;	DoD-050	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways
Chemical Weapons	Diagnosis; Exposure;	DoD-137	Low Level Exposure to Sulfur Mustard: Development of an SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin
Chemical Weapons	Diagnosis; Exposure;	DoD-167	Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure
Symptoms and General Health	Diagnosis; Exposure;	DoD-018	Kuwait Oil Fires Troop Exposure Assessment Model (TEAM)
Symptoms and General Health	Diagnosis; Exposure;	DoD-019	Persian Gulf Veterans Health Tracking System
Symptoms and General Health	Diagnosis; Exposure;	DoD-100	Antibodies to Squalene
Symptoms and General Health	Diagnosis; Exposure; Symptoms	DoD-016	Kuwait Oil Fire Health Risk Assessment

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. Gulf War Veterans

Environmental Toxicology

Epidemiology

Research Focus	Project Focus	Project	Project Title
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
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 Gulf War 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

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
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; 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
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

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
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
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

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Exposure	VA-065	San Antonio Environmental Hazards Research Center
Symptoms and General Health	Exposure	VA-065 A	Does a variant of the human SOD2 gene increase sensitivity to hazards?
Symptoms and General Health	Exposure	VA-065 B	The contribution of FEN-1 to genetic integrity subsequent to oxidative stress
Symptoms and General Health	Exposure	VA-065 C	The importance of hydrogen peroxide detoxification in cellular protection
Symptoms and General Health	Exposure	VA-065 D	Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental hazards?
Symptoms and General Health	Symptoms	VA-155	Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis
Symptoms and General Health	Exposure; Symptoms	DoD-160	Characterization of the Reproductive Toxicity of Depleted Uranium
Symptoms and General Health	Exposure; Symptoms	DoD-192	Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome
Symptoms and General Health;	Exposure	DoD-007 B	Carcinogenicity of Depleted Uranium Fragments
Symptoms and General Health;	Exposure; Symptoms	DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys
Symptoms and General Health;	Exposure; Symptoms	DoD-127	Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man

Immune Function and Infectious Diseases

Clinical

Research Focus	Project Focus	Project	Project Title
	Diagnosis	DoD-047	Study of Mycoplasmal Infections in Gulf War 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

Immune Function and Infectious Diseases

Clinical

Research Focus	Project Focus	Project	Project Title
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 Gulf War Veterans' Illnesses (ABT) (See also VA-55)
Symptoms and General Health	Treatment; Symptoms;	VA-055	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also DoD-119)

Development

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

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Treatment	DoD-009	Identification of the Genetic Factors Which Control Tropism in Leishmania
	Treatment	DoD-157	Novel Leishmania and Malaria Potassium Channels: Candidate Therapeutic Targets
	Prevention	VA-015	Vaccine-Mediated Immunity Against Leishmaniasis
	Prevention	VA-016	Protective Immunity in Experimental Visceral Leishmaniasis
	Symptoms	VA-127	Interactions of the Leishmania sp. with Mammalian Cells
	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

Immune Function and Infectious Diseases

Mechanistic

Research Focus	Project Focus	Project	Project Title
Environmental Toxicology	Exposure	DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in Gulf War 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
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 Gulf War 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 Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in Gulf War Veterans
	Symptoms	DoD-001 G	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian Gulf War 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 Gulf War Veterans in Mississippi

Reproductive Health

Mechanistic

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

Symptoms and General Health

Clinical

Research Focus	Project Focus	Project	Project Title
	Symptoms	DoD-001 A	Epidemiologic Studies of Morbidity Among Gulf War 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 Gulf War 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; Symptoms	VA-056	Birmingham's Gulf War Veterans' Illness Demonstration Clinic
	Treatment; Symptoms;	VA-058	Implementation and Evaluation of Gulf War 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
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 Gulf War Veterans: Case Validation Studies
Brain and Nervous System Function	Symptoms	DoD-085	CNS Cytokines and CRH in Gulf War 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

Symptoms and General Health

Clinical

Research Focus	Project Focus	Project	Project Title
Brain and Nervous System Function	Symptoms	VA-073	Pain Sensitivity in Gulf War 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 Gulf War Veterans with CMI
Brain and Nervous System Function	Symptoms	VA-134	Autonomic Functions of Gulf War Veterans with Unexplained Illnesses
Brain and Nervous System Function	Symptoms	VA-135	Motor Neuron Function of Gulf War Veterans with Excessive Fatigue
Brain and Nervous System Function	Symptoms	VA-154	Imaging Pain Modulation in Gulf War 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 Gulf War 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 Gulf War Veterans with Chronic Multisymptom Illness
Brain and Nervous System Function	Treatment; Symptoms;	DoD-182	Trial of Naltrexone and Dextromethorphan for Gulf War 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 Gulf War 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;	Diagnosis; Symptoms	DoD-031	Dysregulation of the Stress Response in the Persian Gulf Syndrome
Brain and Nervous System Function	Treatment; Symptoms;	D0D-199	Gulf War Illness: Evaluation of an Innovative Detoxification Program
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

Symptoms and General Health

Development

Research Focus	Project Focus	Project	Project Title
	Treatment; Symptoms	DoD-169	Development of Novel Therapy for Chronic Neuropathic Pain
Brain and Nervous System Function	Diagnosis; Symptoms	DoD-168	Developing Biomarkers for Fibromyalgia
Immune Function	Symptoms; Diagnosis;	DoD-183	Biomarkers of Gulf War 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 Gulf War 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 Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study
	Symptoms	DoD-001 F	Epidemiologic Studies of Morbidity Among Gulf War 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 Gulf War 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 Department of Defense Surveillance for Neoplasms in Infancy
	Symptoms	DoD-148	Predicting Operational Readiness for Deployed Army National Guard and Army Reserve Soldiers and Families

Symptoms and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Symptoms	DoD-150	Validation Study of Gulf War Deployment Files
	Symptoms	HHS-001	Health Assessment of Persian Gulf War 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
	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; Exposure;	DoD-073	Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes
	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
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 Gulf War Veterans: Case Validation Studies (Iowa / Great Britain)

Symptoms and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Symptoms	VA-148	Profile of GW Veterans Who Applied for Undiagnosed Illness Compensation
Brain and Nervous System Function	Symptoms	DoD-143	Millennium Cohort Study
Brain and Nervous System Function	Symptoms	DoD-149	Longitudinal Health Study of Gulf War 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
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 Gulf War 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
	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 and General Health

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Symptoms; Treatment;	VA-164	Central Mechanisms Modulating Visceral Sensitivity (renewal of VA-136)
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
Environmental Toxicology	Exposure; Symptoms	DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness
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, 2010)

NOTES ON REVISED TABLE OF SPENDING FOR GULF WAR VETERANS' ILLNESSES RESEARCH FROM FY 2001-2010

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 1992-2010 are listed, only the financial data for FY 2001-2010 (a 10-year window) are shown in Appendix C; Totals for FY '01-'10 do not include funds obligated in FY 1992-2000. Projects that received all of their obligated funds prior to FY 2001 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 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
DoD-001	Naval Health Study Program	C											$0
DoD-001 A	Epidemiologic Studies of Morbidity Among Gulf War 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 Gulf War 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 Gulf War 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	C											$0
DoD-001 D	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in Gulf War Veterans	C											$0
DoD-001 E	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study	C											$0
DoD-001 F	Epidemiologic Studies of Morbidity Among Gulf War 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 Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian Gulf War Veterans	C											$0

*****Totals for FY '01 -'10 do not include funds obligated in FY 1992 -2000

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
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	$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	$306,000	$195,000	$225,000								$726,000
DoD-019	Persian Gulf Veterans Health Tracking System	C	$0	$100,000	$50,000								$150,000

*****Totals for FY '01 -'10 do not include funds obligated in FY 1992 -2000

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
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										$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										$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										$0
DoD-040	Psychological and Neurobiological Consequences of the Gulf War Experience	C	$0										$0
DoD-041	Evaluation of Muscle Function in Persian Gulf Veterans	C											$0

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
DoD-042	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment	C	$0										$0
DoD-044	Investigation of Seminal Plasma Hypersensitivity Reactions	C											$0
DoD-045	Air Force Women's Health Surveillance Study	C	$99,628	$0									$99,628
DoD-046	Exploratory Data Analysis with the CCEP Database	C											$0
DoD-047	Study of Mycoplasmal Infections in Gulf War 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 Gulf War Veterans	C											$0
DoD-053	Long-Term Effects of Subclinical Exposures to Sarin	C	$0										$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										$0

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DoD-056	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine	C	$0										$0
DoD-057	Physiologic Effects of Stress in Gulf War Veterans	C	$0	$0									$0
DoD-058	Illness Among Persian Gulf War Veterans: Case Validation Studies	C	$267,337	$0	$0	$0							$267,337
DoD-059	Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis	C	$0										$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										$0
DoD-065	Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment	C	$0										$0
DoD-066	Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction	C	$0										$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	$245,910	$0	$0	$0	$0					$245,910
DoD-070	War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes	C	$0										$0

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DoD-071	A Comparison of Post Deployment Hospitalization Between Vietnam and Gulf War Veterans	C											$0
DoD-072	Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals	C	$0	$0									$0
DoD-073	Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes	C	$0										$0
DoD-074	Relationship of Stress Exposures to Health in Gulf War Veterans	C	$0	$0									$0
DoD-075	Toxic Interactions of Prophylactic Drugs and Pesticides	C	$0	$0	$0								$0
DoD-076	Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel	C	$0	$0	$0								$0
DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War	C	$0	$0									$0
DoD-078	Experimental Models of Gulf War Syndrome	C	$0	$0									$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	$0									$0
DoD-081	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress	C	$0	$0									$0
DoD-082	Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs	C	$0	$0									$0
DoD-083	Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism	C	$0	$0									$0
DoD-084	Psychobiologic Alterations in Persian Gulf War Veterans with and without PTSD	C	$0	$0									$0
DoD-085	CNS Cytokines and CRH in Gulf War Veterans with Multiple Unexplained Symptoms	C	$0	$0									$0
DoD-086	Effects of Combat Stress on Structure and Function of the Hippocampus	C	$0	$0	$0								$0

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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	C	$68,044	$0	$0								$68,044
DoD-088	Clinical Relevance of Novel Immunological Markers in PTSD	C	$0	$0									$0
DoD-089	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder	C	$0	$0									$0
DoD-090	SPECT Benzodiazepine Receptor and MR Imaging in PTSD	C	$0	$0									$0
DoD-091	Neurological and Circadian Substrates of PTSD-like Behaviors	C	$0										$0
DoD-092	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder	C	$0	$0									$0
DoD-093	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up	C	$0										$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. Gulf War Veterans	C	$0	$0									$0
DoD-095	Development of Diagnostic tools and alternative treatment drugs for Leishmania	C	$1,500,000	$1,500,000									$3,000,000
DoD-096	Deployment Health Center	C	$2,250,000	$1,750,000	$1,750,000	$1,750,000	$0						$7,500,000
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	$151,202	$151,000									$302,202
DoD-098	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans	O	$364,182	$0	$0	$0	$0	$0	$0	$0	$0		$364,182

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DoD-099	DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1: Hospitalizations	C	$224,265	$0	$0								$224,265
DoD-100	Antibodies to Squalene	C	$50,000	$487,333	$0	$0	$0	$0	$0	$0	$0		$537,333
DoD-101	Mechanisms in Chronic Multisymptom Illnesses	C	$0	$4,786,192	$644,870	$4,781,952	$2,429,999	$0	$0	$0	$0		$12,643,013
DoD-102	Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans	C	$253,793	$0	$281,950								$535,743
DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals	C	$0	$0	$349,994	$242,424	$160,000	$326,570	$166,570	$0	$0		$1,245,558
DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome	C	$0	$0	$40,844								$40,844
DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala	C	$0	$0	$0	$0							$0
DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War-related illness	C	$0	$0									$0
DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity	C	$0	$0	$0	$0							$0
DoD-108	Health Status of Current National Guard Members	C	$264,375	$174,651	$0	$0	$0						$439,026
DoD-109	Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms	C	$397,243	$0	$0								$397,243
DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy	C	$0	$0									$0
DoD-111	Autonomic Dysfunction in Gulf War Veterans	C	$0	$0	$189,609	$0	$0						$189,609
DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?	C	$0	$0									$0
DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects	C	$0	$0	$0	$0							$0
DoD-114	A Re-examination of Neuropsychological Functioning in Persian Gulf War Veterans	C	$0	$0									$0

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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)	C	$0	$0									$0
DoD-116	VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V)	C	$250,000	$250,000	$250,000								$750,000
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	$0									$0
DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also VA-61)	C	$832,272	$0									$832,272
DoD-119	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also VA-55)	C	$0	$0									$0
DoD-120	Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents	C	$0	$0									$0
DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development	C	$15,000										$15,000
DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys	C	$35,000										$35,000
DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys	C	$15,000										$15,000
DoD-124	Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin	C	$0	$0	$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	$0						$0

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DoD-126	Blood-Brain Barrier Transport of Uranium	O	$0	$0	$0	$0	$0	$0	$0	$0	$0		$0
DoD-127	Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man	C	$399,582	$0	$0								$399,582
DoD-128	Multifactorial Assessment of Depleted Uranium Neurotoxicity	C	$0	$0	$328,734	$0	$89,055	$0	$0	$0	$0		$417,789
DoD-129	Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness	C	$1,276,220	$0	$0	$0	$0	$0	$0	$0	$0		$1,276,220
DoD-130	Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents	C	$983,164	$0	$0	$0	$0	$0	$0	$0	$0		$983,164
DoD-131	Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses	C	$5,377,526	$0	$500,000	$0	$0	$0	$0	$0	$0		$5,877,526
DoD-132	Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness	C	$792,198	$0	$0	$0	$0	$0					$792,198
DoD-133	Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome	C	$884,087	$0	$0	$0	$0	$0					$884,087
DoD-134	Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin	C	$0	$0	$0	$0	$0	$0	$0	$0	$0		$0
DoD-135	Biochemical Markers for Exposure to Low Doses of Organophosphorus Exposure	C	$0	$0	$0	$0	$0						$0
DoD-136	A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure	C	$748,858	$0	$0	$0	$0						$748,858
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	$600,111	$0	$0	$0	$0	$0					$600,111
DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents	C	$434,795	$0	$0	$0	$0	$0	$0	$0	$0		$434,795

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DoD-139	Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses	C	$500,885	$0	$0								$500,885
DoD-140	US Department of Defense Surveillance for Neoplasms in Infancy	C	$764,879	$0	$0	$0	$0	$0					$764,879
DoD-141	Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans	C	$149,993	$0	$0								$149,993
DoD-142	Illnesses Among Persian Gulf War Veterans: Case Validation Studies (Iowa / Great Britain)	C			$168,962	$0		$0					$168,962
DoD-143	Millennium Cohort Study	O	$1,000,000	$1,250,000	$2,000,000	$1,950,000	$2,880,000	$2,893,000	$3,251,000	$3,160,000	$3,145,000	$3,145,000	$24,674,000
DoD-144	Psychological Health Screening: Methods and Metrics for Deployed Forces	C	$250,000	$300,000		$0	$0	$0	$0	$0	$0		$550,000
DoD-145	Early Intervention Research Program to Enhance Soldier Resilience	C	$250,000	$275,000	$275,000	$0	$0	$0	$0	$0	$0		$800,000
DoD-146	Assessment of Toxicology Assay Methods and Chemical Exposures Among a Cohort of US Marines Deployed in the Gulf War	C	$100,000										$100,000
DoD-147	Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications	C	$412,000	$696,111	$292,530	$0	$0	$0					$1,400,641
DoD-148	Predicting Operational Readiness for Deployed Army National Guard and Army Reserve Soldiers and Families	C	$100,000										$100,000
DoD-149	Longitudinal Health Study of Gulf War Veterans	C	$1,689,945	$0	$0	$0	$0	$0					$1,689,945
DoD-150	Validation Study of Gulf War Deployment Files	C		$134,348	$0								$134,348
DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in Gulf War Veterans	C		$482,274	$0	$0	$0	$0					$482,274
DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents	C		$1,000,000	$1,019,440	$0	$0	$0	$0	$0	$0		$2,019,440
DoD-153	Gulf War Illness Research	C	$4,694,500	$4,950,000	$920,838	$2,003,000	$928,000	$0					$13,496,338
DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study	C		$100,000	$566,542	$368,687	$604,372	$0	$0	$0	$0		$1,639,601

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DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide	C			$1,021,862	$0	$0	$0	$0	$0			$1,021,862
DoD-156	The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant	C			$1,519,951	$0	$0	$0	$0	$0	$0		$1,519,951
DoD-157	Novel Leishmania And Malaria Potassium Channels: Candidate Therapeutic Targets	C	$789,805	$0	$0	$0	$0						$789,805
DoD-158	Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission Of Genetic Damage To Offspring	C	$382,829	$0	$0	$0	$0	$0					$382,829
DoD-159	Neurotoxicity from Chronic Exposure to Depleted Uranium	C	$965,931	$0	$0	$0	$0	$0					$965,931
DoD-160	Characterization of the Reproductive Toxicity of Depleted Uranium	C	$696,357	$0	$0	$0	$0						$696,357
DoD-161	Glutamate Receptor Aptamers and ALS	O			$1,152,744	$0	$0	$0	$0	$0	$0	$0	$1,152,744
DoD-162	Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function	C			$1,041,751	$0	$0	$0	$0	$0			$1,041,751
DoD-163	Neuroimmune Effects of Inhaling Low Dose Sarin	C			$1,828,876	$0	$0	$0	$0	$0			$1,828,876
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	O						$840,574	$0	$0	$0	$0	$840,574

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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 Gulf War Veterans	C						$718,261	$0	$0	$0		$718,261
DoD-172	CNDP1 Polymorphisms and Carnosine Therapy in GWI	O						$831,200	$0	$0	$0	$0	$831,200
DoD-173	A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in Gulf War Veterans with Chronic Multisymptom Illness	O						$650,279	$0	$0	$0	$0	$650,279
DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness	O						$687,530	$0	$0	$0	$0	$687,530
DoD-175	Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium	O						$767,061	$0	$0	$0	$0	$767,061
DoD-176	Studies on Axonal Transport in an Animal Model for Gulf War Syndrome	C						$112,500	$0	$0			$112,500
DoD-177	Randomized Trial of an Environmental Medicine Approach to Gulf War Veterans' Illness	C						$445,865	$0	$0	$0		$445,865
DoD-178	Analysis of Paraoxonase Status among US Navy Gulf War Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions	C						$73,153	$0	$0			$73,153
DoD-179	Mechanisms of Mitochondrial Defects in Gulf War Syndrome	O					$0	$0	$0	$440,674	$0	$0	$440,674
DoD-180	Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of Fatigue	O					$0	$0	$0	$921,000	$0	$0	$921,000
DoD-181	Effectiveness of Acupuncture in the Treatment of Gulf War Illness	O					$0	$0	$0	$1,015,733	$0	$0	$1,015,733
DoD-182	Trial of Naltrexone and Dextromethorphan for Gulf War Veterans' Illness	O					$0	$0	$0	$1,063,641	$0	$0	$1,063,641
DoD-183	Biomarkers of Gulf War Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation	O					$0	$0	$0	$653,460	$0	$0	$653,460
DoD-184	Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the Gulf War Veterans' Illnesses	O					$0	$0	$0	$311,135	$0	$0	$311,135

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
DoD-185	Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model	O					$0	$0	$0	$718,326	$0	$0	$718,326
DoD-186	Small Intestinal Microbial Community in Gulf War Illness	O					$0	$0	$0	$634,142	$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	O					$0	$0	$0	$715,456	$0	$0	$715,456
DoD-188	Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War Illness	O					$0	$0	$0	$842,400	$0	$0	$842,400
DoD-189	Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers	O					$0	$0	$0	$303,000	$0	$0	$303,000
DoD-190	Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness	O					$0	$0	$0	$894,000	$0	$0	$894,000
DoD-191	Neuroimmune Interactions, Low-Dose Sarin Inhalation, and Gulf War Syndrome	O									$1,247,995	$0	$1,247,995
DoD-192	Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome	O									$742,296	$0	$742,296
DoD-193	Genome Instability: A Common Link in Gulf War Illness Patients	O									$904,364	$0	$904,364
DoD-194	Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome	O									$705,654	$0	$705,654
DoD-195	Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness	O									$678,953	$0	$678,953
DoD-196	Probiotic (Bifidobacterium Infantis) for Gulf War Illness	O									$466,260	$0	$466,260
DoD-197	Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness?	O									$929,224	$0	$929,224
DoD-198	Oxidative Stress	O									$927,000	$0	$927,000
DoD-199	Gulf War Illness: Evaluation of an Innovative Detoxification Program	O									$633,677	$0	$633,677
			$31,587,006	$18,827,819	$16,419,497	$11,096,063	$10,091,848	$10,128,261	$3,417,570	$11,672,967	$10,380,423	$3,145,000	$126,766,454

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Department of Health and Human Services Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
HHS-001	Health Assessment of Persian Gulf War Veterans from Iowa	C	$0										$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 Gulf War Veterans In Mississippi	C											$0
HHS-005	Cognitive Function and Symptom Patterns in Persian Gulf Veterans	C	$0	$0									$0
HHS-006	Defining Gulf War Illness	C	$200,000	$0									$200,000
HHS-007	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid	C	$0										$0
HHS-008	Strategy to Identify Non-Additive Response to Chemical Mixtures	C	$0										$0
HHS-009	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments	C	$337,693	$339,814	$339,814	$0	$0	$0	$0				$1,017,321
HHS-010	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline	C	$461,177	$460,000	$460,000	$0	$0	$0	$0				$1,381,177
HHS-011	Deployment to the Gulf War and the Subsequent Development of Cancer	C			$164,291	$0	$0	$0	$0				$164,291
HHS-012	Genetic Epidemiology of ALS in Veterans	O				$466,126	$466,481	$455,587	$441,974	$433,467	$0	$0	$2,263,635
			$998,870	$799,814	$964,105	$466,126	$466,481	$455,587	$441,974	$433,467	$0	$0	$5,026,424

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
VA-001	Mortality Follow-up Study of Persian Gulf Veterans	C	$171,154	$128,496	$0								$299,650
VA-002	National Health Survey of Persian Gulf Veterans	C	$0	$0									$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	$2,344,427	$30,000									$2,374,427
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 Gulf War 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

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
VA-006 A	Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I)	C											$0
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 Gulf War Veterans Over Time	C	$0	$0									$0
VA-009	Evaluation of Cognitive Functioning in Persian Gulf War 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	$114,336	$119,600	$59,800								$293,736
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

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VA-040	Musculoskeletal Symptoms in Gulf War Syndrome	C											$0
VA-046	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder	C											$0
VA-047	Retrospective Verification of Mustard Gas Exposure	C											$0
VA-048	Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance	C	$45,000										$45,000
VA-049	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction	C	$144,024	$125,862									$269,886
VA-050	Neuropsychological findings in a sample of Operation Desert Storm veterans	C											$0
VA-051	Psychobiological Assessment of Desert Storm Veterans	C	$0										$0
VA-053	Spouses and Children Program	C	$12,934	$25,000									$37,934
VA-054	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress	C	$86,895	$86,350	$72,700	$39,375							$285,320
VA-055	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also DoD-119)	C	$1,981,963	$254,000									$2,235,963
VA-056	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13)	C											$0
VA-057	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13)	C											$0
VA-058	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13)	C											$0
VA-059	Demonstration Treatment Program for Gulf War Veterans With Unexplained Physical Symptoms (13)	C											$0
VA-060	Identification and Management of Sleep Disorders in Gulf War Veterans	C											$0
VA-061	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also DoD-118)	C	$0	$110,600									$110,600
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	$1,971,233	$44,250									$2,015,483

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
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	$250,000	$250,000	$250,000				$1,750,000
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	$299,700	$300,000	$297,000	$337,200	$337,200	$337,200					$1,908,300
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	$350,000	$300,000	$300,000	$337,200							$1,287,200
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										$0
VA-067	Olfactory Functioning in Gulf War Veterans	C	$7,500										$7,500
VA-068	Family Study of Fibromyalgia	C	$50,000	$50,000									$100,000
VA-069	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans	C	$135,487	$141,815	$48,947								$326,249

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
VA-070	A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8	C	$4,884	$4,900									$9,784
VA-071	Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome	C	$181,692	$186,524	$47,975								$416,191
VA-072	Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses	C		$50,000	$50,000								$100,000
VA-073	Pain Sensitivity in Gulf War Veterans with Medically Unexplained Musculoskeletal Pain	C		$50,000	$50,000								$100,000
VA-074	A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125)	C	$291,804	$896,550	$1,346,863	$1,912,448							$4,447,665
VA-075	ALS and Veterans: Are Veterans at Increased Risk?	C	$73,000	$139,600	$139,600	$78,455							$430,655
VA-076	Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD	C		$145,100	$135,000	$151,740							$431,840
VA-077	HPA Axis Reactivity in Men and Women with Chronic PTSD	C		$101,400	$101,300	$113,861							$316,561
VA-078	Millenium Cohort Study	C											$0
VA-080	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress	C			$203,400	$119,818	$248,458	$253,277	$252,602				$1,077,555
VA-081	Stress, Pro-Inflammatory Cytokines and Coping Behavior	C			$193,800	$186,035							$379,835
VA-082	Pituitary Adrenal Function in People with Fatiguing Illness	C		$88,000	$135,000	$151,740	$276,112	$121,842					$772,694
VA-083	Neuropsychological Assessment of a Population-Based Sample of Persian Gulf War Veterans and Controls	C		$18,988	$50,000	$31,012							$100,000
VA-084	Neurobiology of Severe Psychological Trauma in Women	C		$135,000	$135,000	$151,740							$421,740
VA-085	Associative Learning in Veterans with and without Combat Experience	C		$60,400	$74,000	$232,458							$366,858
VA-086	A Clinical Trial of Magnetic Stimulation in Depression	C		$131,400	$131,400	$147,694							$410,494
VA-087	Improving Outcomes of Depression in Primary Care	C		$152,065	$201,926	$218,280							$572,271
VA-088	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study	C			$24,057	$47,011							$71,068

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Department of Veterans Affairs Gulf War Research Funding

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VA-089	National Registry of Veterans with Amyotrophic Lateral Sclerosis	C			$319,229	$625,564	$799,104	$863,951					$2,607,848
VA-090	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness	O			$250,000	$281,000	$281,000	$449,990	$449,990	$0	$0	$0	$1,711,980
VA-090A	Neuronal Hyperexcitability and Motor Neuron Regeneration	O											$0
VA-090B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders	O											$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 Gulf War Veterans	C			$89,920	$49,833							$139,753
VA-093	HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans	C			$56,750	$36,080	$163,205	$127,405					$383,440
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			$54,158	$231,566	$238,239	$178,679					$702,642
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			$99,563	$215,093	$241,957	$246,355	$134,628				$937,596
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		$65,700	$123,413	$116,896	$118,863	$117,908					$542,780
VA-100	Studies of the Blood-Brain Barrier and its Manipulation	C		$151,875	$151,875	$151,740	$151,740	$151,740					$758,970
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	$60,642	$92,588	$92,588	$134,160	$175,814	$134,328					$690,120
VA-103	Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal	C			$210,600	$296,657	$307,253	$317,845					$1,132,355

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
VA-104	Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome	C			$114,975	$168,600	$168,600	$84,300					$536,475
VA-105	Expression of the Major Surface Protease of Leishmania Chagasi	C		$76,613	$135,628	$298,175	$119,535	$92,817					$722,768
VA-106	Interoceptive Stressor Conditioning: A Model for Gulf War Illness	C					$193,440	$198,161					$391,601
VA-107	Evaluation of Stress Response Systems in Gulf War Veterans with CMI	O					$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 Gulf War 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 Gulf War 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

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
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	O					$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
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 Gulf War Veterans	C					$168,600	$167,164	$168,600				$504,364
VA-130	Tissue Factor and Gulf War-Associated Chronic Coagulopathies	O						$194,826	$217,055	$248,741	$273,861	$158,089	$1,092,572
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	O						$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 Gulf War Veterans with Unexplained Illnesses	O						$8,880	$0	$0	$25,880	$101,863	$136,623
VA-135	Motor Neuron Function of Gulf War Veterans with Excessive Fatigue	O						$6,744	$0	$0	$79,242	$103,549	$189,535
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	O						$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

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PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
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	$9,494,485
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	O						$129,260	$224,800	$224,800	$112,400	$67,752	$759,012
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	O							$129,861	$268,901	$273,801	$136,900	$809,463
VA-150	Gulf War Veterans Illnesses' Research IDIQ Contract with UTSW	O							$15,000,000	$15,000,000	$6,972,481	$2,288,755	$39,261,236
VA-151	Genetic Epidemiology of ALS Veterans	O								$2,116,602	$377,557	$353,309	$2,847,468
VA-152	Multiple Sclerosis in Gulf War Veterans	O								$122,010	$137,791	$120,866	$380,667
VA-153	Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex	O									$8,377	$168,600	$176,977
VA-154	Imaging Pain Modulation in Gulf War Veterans with Chronic Muscle Pain (renewal of VA-096)	O									$300,782	$258,076	$558,858
VA-155	Bacterial Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis	O							$156,461	$140,500	$165,790	$165,790	$628,541
VA-156	Gulf War Era Cohort and Biorepository (CSP 585)	O										$28,361	$28,361
VA-157	A Clinical Demonstration of an EEG Brain-Computer Interface for ALS Patients (CSP #567)	O										$2,368,460	$2,368,460
VA-158	Testing the Feasibility of MC CBT for Veterans with IBS	O										$17,953	$17,953
VA-159	Somatic hypersensitivity in Veterans with IBS	O									$56,200	$112,400	$168,600

*****Totals for FY '01 -'10 do not include funds obligated in FY 1992 -2000

Status: C=Complete; O=Ongoing

Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	TOTALS FY 01-10
VA-160	Lipoic Acid Therapy for Experimental Autoimmune Encephalomyelitis	O										$224,126	$224,126
VA-161	Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease	O										$332,743	$332,743
VA-162	Transcription factors regulating sensory gene expression and pain pathways	O									$94,416	$168,600	$263,016
VA-163	Immunoregulation of Myelin Specific T Lymphocytes	O									$371,209	$361,972	$733,181
VA-164	Central Mechanisms Modulating Visceral Sensitivity (renewal of VA-136)	O									$255,170	$267,687,	$768,940
		O	$8,576,675	$4,512,676	$5,746,467	$7,644,559	$9,484,679	$13,013,552	$22,059,061	$21,934,214	$16,600,799	$13,856,752	$123,429,434

*****Totals for FY '01 -'10 do not include funds obligated in FY 1992 -2000

Status: C=Complete; O=Ongoing