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Federally Sponsored Research on Gulf War Veterans' Illnesses for 2005

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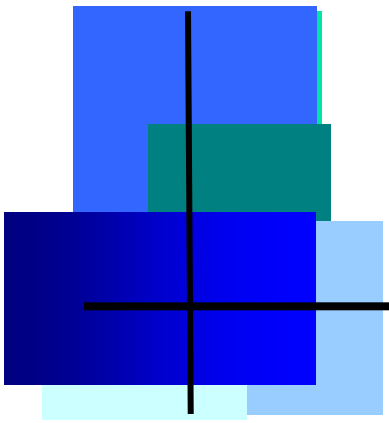
Deployment Health Working Group Research Subcommittee



Annual Report to Congress – 2005

Federally Sponsored Research on Gulf War Veterans' Illnesses for 2005

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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, 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 (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 *2005 Annual Report to Congress*, which is the twelfth report on research and research activities. The DHWG tracks all federally funded research projects related to Gulf War veterans' illnesses.

As in previous Annual Reports to Congress, the material presented is divided into 5 sections. Section I is an introduction; Section II summarizes the research priorities and organization of the federal Gulf War research portfolio; Section III highlights and summarizes research progress published since the last Annual Report; Section IV summarizes federal funding trends for Gulf War research during the 10-year period from fiscal year (FY) 1996 through FY 2005; and Section V highlights new research projects and initiatives.

II. RESEARCH PRIORITIES

The research priorities remain unchanged from previous years. The 21 Research Topics are grouped into five major Research Focus Areas. These 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 Gulf War 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 and the results of the review are presented in Section V.

III. RESEARCH RESULTS IN 2005

Section III provides brief summaries of research on the health problems of Gulf War veterans which was published in English during calendar year 2005. Research results are grouped according to the 5 Research Focus Areas used to organize the 21 Research Topics (see Section II): Brain and Nervous System Function, Environmental Toxicology, Immune Function and Infectious Diseases, 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

The Departments of Veterans Affairs (VA), Defense (DoD), and Health and Human Services (HHS) sponsored 300 distinct projects related to health problems affecting Gulf War veterans from FY 1992 through FY 2005. 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 Gulf War veterans' illnesses totaled $260.6 million for the period from FY 1996 through FY 2005. As of September 30, 2005, 210 projects were completed (70% of the 300 projects), and 90 projects (30%) were new or ongoing.

V. NEW RESEARCH PROJECTS AND INITIATIVES

VA funded 24 new projects in FY 2005. The primary research foci of these projects included Brain and Nervous System Function (13), Environmental Toxicology (3), Immune Function and Infectious Diseases (2), and Symptoms and General Health (6). Special solicitations accounted for 15 of the new projects; the remaining 9 were identified during a review of all VA-funded research projects. An additional 7 ongoing projects were added to the VA Gulf War research portfolio as a result of this review. The details of this portfolio review are fully described in Sections II and V.

I. INTRODUCTION

The Secretary of Veterans Affairs (VA) is required by Section 707 of Public Law 102-585 as amended by Section 104 of Public Law 105-368, 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 2005 Annual Report to Congress, which is the twelfth report on research and research activities (DHWG, 2004; DHWG, 2005; DHWG, 2006; MVHCB, 2001; MVHCB, 2002; PGVCB, 1995; PGVCB, 1996; PGVCB, 1997; PGVCB, 1998; PGVCB, 1999; PGVCB, 2001). The DHWG tracks all federally funded research projects related to Gulf War veterans' illnesses.

As in previous Annual Reports to Congress, the material presented is divided into five sections. For this report, however, the sequence of the sections has been rearranged to present a more logical flow. Section I is an introduction. Section II summarizes the research priorities and organization of the federal Gulf War research portfolio. Section III highlights and summarizes published research progress since the last Annual Report. Section IV summarizes federal funding trends for Gulf War research during the 10-year period from FY 1996 through FY 2005. Section V highlights new research projects and initiatives since the last Annual Report.

II. RESEARCH PRIORITIES

A. Twenty-One Research Topics

VA, DoD, and HHS created the Persian Gulf Veterans Coordinating Board (PGVCB) to coordinate research on Gulf War veterans' illnesses. In 1995, the PGVCB decided to provide 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, 1996b) The comprehensive Gulf War research portfolio has addressed each of these 21 questions, and relevant results have been published on each one. The Medical 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 *Annual Report to Congress for 2000* (MVHCB, 2001a). 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 *Annual Report to Congress for 2004* (DHWG, 2006). The organization of the Research Topics into five major categories is presented below:

Brain & Nervous System Function

- Organic neuropsychological and neurological deficits (Question 16)
- Psychological symptoms and/or diagnoses (Question 18)

Environmental Toxicology

- Petroleum products and combustion products (Question 3)
- Occupational/environmental hazards (Question 4)
- Organophosphorus nerve agent and/or sulfur mustard from bombing at Muhammadiyat or weapons bunker at Khamisiyah (Question 5)
- Chemical agents, other than at Khamisiyah (Question 6)
- Pyridostigmine bromide and other medical prophylaxes (e.g. vaccines and anti-malarials) (Question 7)
- Psychophysiological stressors (Question 8)
- Short term, low level exposures to pyridostigmine bromide, DEET, or permethrin, alone or in combination as a cause of short-term and/or long-term neurological effects (Question 17)

Immune Function and Infectious Diseases

Leishmania tropica (Question 2)

Altered immune function or host defense (Question 10)

Other infectious diseases (Question 19)

Reproductive Health

Birth defects in offspring (Question 11)

Lower reproductive success (Question 12)

Sexual dysfunction (Question 13)

Symptoms and General Health Status

Increased prevalence or severity of symptoms and/or illnesses (Question 1)

Nonspecific symptoms and symptom complexes (e.g., chronic multisymptom illnesses) (Question 9)

Changes in lung function or airway reactivity (Question 14)

Smaller baseline lung function or greater degree of nonspecific airway reactivity (Question 15)

Development of cancers of any type (Question 20)

Mortality rates (Question 21)

B. Research Portfolio Descriptors

VA maintains a research database of federally sponsored research on Gulf War veterans' illnesses. 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 Gulf War veterans' illnesses. 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 is a listing of the projects that VA, DoD, and HHS have funded to date. Research projects are grouped according to the department that is responsible for their funding. Dual-funded projects are listed under both departments.

Appendix B is a categorized listing of all federally funded Gulf War 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** of the project. The five Research Focus Areas are also used to organize the 21 Research Topics (see Section A, above).

- Brain and Nervous System Function (e.g., studies on neurological or psychological deficits and/or alterations)
- Environmental Toxicology (e.g., studies focused on specific environmental exposures such as pesticides, oil well fires, jet fuel, vaccines, medical prophylactic agents, etc.)
- Immune Function and Infectious Diseases (e.g. studies on alterations in immune function, host defenses, or detection and treatment of infectious diseases)
- Reproductive Health (e.g. studies on sexual and/or reproductive dysfunction)
- Symptoms and General Health (e.g., studies on mortality, pulmonary disease, cancer, chronic multisymptom illnesses, etc.)

Secondary and/or tertiary Research Focus Areas from the above list may also be assigned. Two additional 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 (i.e., studies that will improve the ability to diagnose previously unexplained conditions, or to better refine diagnoses with new tools)
- Exposure
- Interactions of exposures (chemical, biological, pharmacological, physiological, etc.)
- Prevention of diseases (i.e., studies that will produce knowledge that could lead to disease prevention strategies)
- Prevalence and risk factors for symptoms and alterations in general health status
- Treatment

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 Gulf War veterans' illnesses uses a method of approach to test a specific research hypothesis. Approaches range in type from mechanistic research, addressing potential biological mechanisms of causation, to clinical and epidemiological research that attempt to determine illness prevalence and risk factors. 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: Research into underlying mechanisms of diseases and illnesses using in vitro and in vivo models.

CLINICAL RESEARCH: 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 RESEARCH: 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.

In addition to the research on Gulf War veterans' illnesses, the Deployment Health Working Group (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 Gulf War veterans' illnesses, the DHWG categorizes activities as development as follows:

DEVELOPMENT: 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 Gulf War veterans' illnesses catalogs only research and development activities that either directly involve Gulf War veterans or have been initiated to 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 biomedical research over the past 50 years.

B. FY 2005 Portfolio Review

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 Gulf War research portfolio and then evaluated the entire VA research portfolio for projects meeting those criteria. The results of the review are presented in Section V. The criteria and references used as the basis for the review are presented below:

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 Gulf War 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)
e) Multiple chemical sensitivity
   (Fiedler et al., 2004; Gray et al., 2002)

Conditions and/or symptoms occurring with higher prevalence in Gulf War 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 et al., 2002; 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.)
   (CDC, 1995; Coker et al., 1999; Eisen et al., 2005; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997b; Kang et al., 2000; Proctor et al., 1998)
d) Cognitive dysfunction (memory, attention, etc.)[3]
   (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; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997b; Kang et al., 2000; Knoke et al., 2000; Pierce, 1997; Proctor et al., 1998; Unwin et al., 1999; Wolfe et al., 2002)
f) Central Nervous System disorders (ALS, glioblastoma, imaging studies, etc.)
   (Bullman et al., 2005; Haley, 2003; Horner et al., 2003; Weisskopf et al., 2005)
g) Headaches
   (CDC, 1995; Coker et al., 1999; Fukuda et al., 1998; Gray et al., 1999; Haley et al., 1997b; Kang et al., 2000; Knoke et al., 2000; Proctor et al., 1998; Unwin et al., 1999; Wolfe et al., 2002)
h) Dermatologic conditions
   (CDC, 1995; Coker et al., 1999; Eisen et al., 2005; Fukuda et al., 1998; Gray et al., 1999; Kang et al., 2000; Knoke et al., 2000; Pierce, 1997; Proctor et al., 1998; Wolfe et al., 2002)

Long-term health effects of potentially hazardous substances, alone and in combination, to which Gulf War 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

Other topics from the 21 Topics forming the framework for the Annual Report to Congress on Federally Sponsored Research on Gulf War Veterans' Illnesses*:*

a) Altered immune function and/or host defense
b) Exposure to, and prevalence of, leishmania tropica
c) Physiological responses to biological stress
d) Sexual and/or reproductive dysfunction

III. RESEARCH RESULTS AND STATUS OF THE FIELD IN 2005

In 2005, numerous research studies provided new and detailed information on the health problems of Gulf War veterans. A PubMed search retrieved 82 relevant articles published in English in calendar year 2005. These articles include federally and non-federally funded research, as well as international research. This section provides brief highlights of published research in 2005, followed by PubMed abstracts. Where possible, the source of funding or relevant federally funded project is included with each abstract.

This report presents published research based on the 5 Research Focus Areas used to organize the 21 Research Topics: Brain and Nervous System Function; Environmental Toxicology; Immune Function and Infectious Diseases; Reproductive Health; and Symptoms and General Health Status.

A. Brain and Nervous System Function

Seventeen reports related to Gulf War research on the brain and nervous system were published in 2005. The majority of these were related to physical and psychological effects of combat exposure. Several large epidemiology studies were completed and are briefly summarized here. Kelsall and co-workers reported that while Australian Gulf War veterans had higher rates of self-reported symptoms, the rates of diagnosable neurologic impairments were not higher on physical examination (Kelsall et al., 2005). From a prior report of higher incidence of amyotrophic lateral sclerosis (ALS) in Gulf War veterans, data were re-examined and did reveal some under-counting of ALS in the non-deployed comparison sample. After correcting for under-ascertainment the risk of ALS remained elevated among deployed veterans (Coffman et al., 2005). A study examining ALS mortality reported a higher risk for men born between 1915 and 1939 who served in the military in general (across branches of service and over the time period 1989-1998) versus those who did not serve (Weisskopf et al., 2005). A review of the literature on environmental influences on the incidence of ALS did not find a consistent link between exposure to pesticides/insecticides or chemical solvents, or increased rates of deaths from ALS in Gulf War veterans (Wicklund, 2005). A study of the Iowa Gulf War cohort determined that one-third of Gulf War veterans with a mental disorder also suffered with at least one other mental illness; further, the quality of life in those suffering with co-morbid conditions was poorer (Forman-Hoffman et al., 2005). A study of Gulf War veterans with PTSD in the United Kingdom found that early diagnosis and treatment by psychiatrists knowledgeable regarding military culture and the impact of conflict resulted in successful psychotherapeutic outcomes at 1-year follow-up times (Lee et al., 2005b). Iversen and co-workers found that depression was more common than PTSD in UK veterans; only about half of those who have a diagnosis are seeking help and few see specialists (Iversen et al., 2005a). Two studies examined issues in

the design and conduction of clinical trials. Dobscha and co-workers examined the use of videoconferencing on participant enrollment, research measurement administration and responses, study retention, and satisfaction in a clinical trial of care management intervention for depression (Dobscha et al., 2005). Videoconferencing allowed patients in rural and remote locations to participate and expanded the sources of recruitment for the project. Schnurr and co-workers examined issues encountered in performing a multi-site clinical trial of psychotherapy for treating PTSD (Schnurr et al., 2005). Two reports indicated finding a smaller hippocampus by magnetic resonance imaging in veterans with PTSD (Kitayama et al., 2005; Vythilingam et al., 2005). Another study reported a smaller volume of the anterior cingulate cortex in Gulf War and Vietnam veterans with PTSD (Woodward et al., 2005). Functional neuroimaging experiments in PTSD and trauma-exposed controlled subjects identified trauma-specific patterns that may represent compensatory changes to traumatic reminders and other patterns in PTSD patients that may reflect neural substrates specific to PTSD pathophysiology (Britton et al., 2005). Hilsenroth and co-workers used the Hand Test (a projective psychological instrument) to distinguish between subclinical and clinical cases of PTSD among Gulf War veterans (Hilsenroth et al., 2005). Studies on the psychological consequences of Gulf War deployment primarily examined risk factors important to consider in this population, including gender (Vogt et al., 2005), personality characteristics (Axelrod et al., 2005), and history of prior trauma (Kang et al., 2005; Stein et al., 2005). Studies also emphasized the importance of documenting experiences as close to the exposure as possible (Ikin et al., 2005). One study measured substance abuse in Gulf War veterans over time (Shipherd et al., 2005).

B. Environmental Toxicology

The 2005 reports on exposures of Gulf War veterans to potentially toxic agents focused on depleted uranium (DU), which was used in tank armor and armor-piercing munitions, and sarin, an organophosphate nerve agent that was released during the March 1991 weapons demolitions at Khamisiyah, Iraq.

Work on DU in 2005 included development of a new method to measure uranium in urine (Ejnik et al., 2005) and a new model of urinary excretion of inhaled uranium (Leggett et al., 2005). Gulf War veterans with embedded DU shrapnel continued to have significantly elevated urine levels of uranium (McDiarmid et al., 2006; Squibb et al., 2005), indicative of a continued systemic exposure to uranium even after more than 12 years. No clinically significant uranium-related health effects were observed in these veterans. In animal studies, systemic DU rapidly entered the brain and was concentrated in select brain regions (Barber et al., 2005; Briner and Murray, 2005); clearance from the brain was relatively slow. Physical stress was found to increase the clearance of uranium from the brain without affecting the initial tissue levels (Barber et al., 2005). DU exposures of 6 – 9 months resulted in changes in locomotor and grooming behaviors in rats (Briner and Murray, 2005; Monleau et al., 2005), alterations in neurotransmitter (dopamine and serotonin) systems in the brain (Bussy et al., 2006), and altered REM sleep and sleep-wake cycles (Lestaevel et al., 2005b; Lestaevel et al., 2005a). DU was also found to be increase the likelihood of developing leukemia in mice injected with special white blood cells selected for their tendency to cause leukemia in mice (Miller et al., 2005). Exposure to DU by inhalation resulted in DNA strand breaks in broncho-alveolar lavage (BAL) cells and an increase of inflammatory cytokine expression and production of hydroperoxides in lung tissue suggesting that the DNA damage was in part a consequence of the inflammatory processes and oxidative stress (Monleau et al., 2006).

Exposure of animals to low (non-lethal) doses of sarin, with or without pyridostigmine bromide, produced transient, but not permanent, alterations in blood flow and metabolic activity in the brain (Scremin et al., 2005), as well as dose-related changes in body weight and blood acetylcholinesterase activity (Langston et al., 2005). Repeated exposure to sarin (or cyclosarin) resulted in desensitization (inactivation) of certain neurotransmitter receptors in the pupil of the eye (Dabisch et al., 2005b; Dabisch et al., 2005a). Sarin was also found to alter gene expression profiles for proteins in the brain involved in neurotransmission (Bloch-Shilderman et al., 2005; Damodaran et al., 2006). Cyclosarin was found to have a prolonged effect on behavior (Krejcova-Kunesova et al., 2005). Animals exposed to sarin also had a long-lasting susceptibility to developing cardiac arrhythmia following epinephrine challenge (Allon et al., 2005). Bide and co-workers described a new method for estimating acute human toxicity of sarin from animal inhalation toxicity data (Bide et al., 2005). Studies on Tokyo subway passengers who were exposed to sarin on

March 20, 1995 revealed sleep disturbances (Kawada et al., 2005) and memory and psychomotor dysfunction (Miyaki et al., 2005). Li and co-workers published results that highlight a potential pitfall in the use of animal models for neurotoxicology studies (Li et al., 2005). They demonstrated that mice, unlike humans, have substantial amounts of soluble acetylcholinesterase as well as butyrylcholinesterase (BChE) in their blood plasma. Thus the metabolism of systemically administered drugs and toxicants may differ.

Additional studies reported the effects of compounds in widespread use during the 1990-1991 Gulf War such as organophosphate pesticides, JP-8 jet fuel (Bell et al., 2005), and multiple vaccinations. During the 1990-1991 Gulf War military personnel were exposed to multiple stressors, one or more vaccines, pyridostigmine bromide (PB), and other chemicals. Two studies examined how pesticides, vaccines and stress interact with a variety of enzyme systems. Stress, vaccination and PB were found to act synergistically on multiple stress-activated enzymes in the brains of mice (Wang et al., 2005). Combined exposure to PB and stress was also found to produce prolonged functional changes in brain metabolism (Taysse et al., 2005). PB exposure in rats affected learning and responses to environmental stimuli (Servatius and Beck, 2005). Hodgson and co-workers have begun to examine the metabolism of deployment-related chemicals (pyridostigmine bromide, permethrin, DEET, chlorpyrifos, JP-8 jet fuel, etc.) in human cell fractions (microsomes, cytosol, etc.), isolated cells (e.g., primary hepatocytes) rather than in surrogate animal models (Edwards et al., 2005; Hodgson and Rose, 2005; Rose et al., 2005; Rose and Hodgson, 2005). They found that pesticides interacted with each other to alter the enzymes responsible for metabolizing (inactivating) them and that JP-8 fuel inhibited the metabolism of DEET by some cytochrome P450 isozymes, indicating that they may share a common metabolic pathway. These experiments are the first steps in better defining the risks (and underlying mechanisms) represented by multiple exposures. To further these efforts, a new blood marker for exposure to some organophosphate pesticides and chemical warfare agents was identified (Quistad et al., 2005). A recent review of the literature concluded that while there is probably a causal link between deployment to the Persian Gulf theater of operation and the development of multisymptom illness, there is insufficient evidence to determine if exposure to toxins encountered during the Persian Gulf war are the cause (Gronseth, 2005).

C. Immune Dysfunction and Infectious Diseases

A study by Rijpkema and co-workers examined the toxicity and immunogenicity of anthrax and pertussis vaccine combinations in a mouse model (Rijpkema et al., 2005). They found that while the pertussis vaccine enhances the immune response to the anthrax vaccine, it also contributes to most of the toxicity of the combination vaccine. In another study, Skowera and co-workers examined the reason for requiring repeated doses of the anti-biowarfare vaccine against anthrax and plague using immune cell cultures (Skowera et al., 2005). They found that anthrax was a poor inducer of one type of immune cells called dendritic cells (DCs), which may explain in part why repeated doses of the vaccine are needed. They suggested complementing the vaccine with substances that can boost the maturation of DCs.

Griffiths and coworkers (Griffiths et al., 2005) tested the effects of the current US and UK nerve agent pre-treatment, pyridostigmine (PB) as well as the related anti-acetylcholinesterase compounds physostigmine and BW284c51,on spleen cell and immune T cell functions in a murine model. Their results indicated that neither was remarkably affected by the administration of PB at pre-treatment doses.

D. Reproductive Health

Four studies on reproductive health related to Gulf War research were published in 2005. None of the studies detected an adverse impact of Gulf War related service on reproduction. The anthrax vaccine did not adversely affect males undergoing assisted reproduction (Catherino et al., 2005)**.** The incidence of infants born with Goldenhar syndrome, a variant of the malformation hemifacial microsomia, was not higher than expected in the children born to U.S. Gulf War veterans (Werler et al., 2005)**.** Two animal studies showed no adverse effects from implanted depleted uranium pellets on male reproductivity or on offspring (Arfsten et al., 2005b; Arfsten et al., 2005a)**.**

E. Symptoms and General Health

A large multi-site study to evaluate medical health determined that deployed and nondeployed Gulf War era veterans showed similar physical health, with the exceptions of increased risk in the deployed veterans for fibromyalgia, CFS, skin conditions and dyspepsia (Eisen et al., 2005). A small study conducted to determine the cause of GW veteran's gastrointestinal symptoms found endoscopic and histopathologic evidence for a variety of conditions including esophagitis and gastritis, with or without H. pylori infection (Koch and Emory, 2005). Lucas and co-workers reported that many Gulf War veterans with chronic fatigue syndrome also have neurally mediated abnormalities in heart function (Lucas et al., 2005). Baraniuk and co-workers found an identical set of proteins in cerebrospinal fluid from two independent cohorts of subjects with overlapping chronic fatigue syndrome, Persian Gulf War illness, and fibromyalgia; these proteins may indicate common pathological mechanisms (Baraniuk et al., 2005). Another study found elevated levels of markers for oxidative stress in the blood of patients with chronic fatigue syndrome(Kennedy et al., 2005). Blanchard and co-workers (Blanchard et al., 2006) reported on the ten-year persistence of Chronic Multisymptom Illness in a subset of veterans deployed to the Gulf War, although the symptomology did not differ from that in the non-deployed comparison group. A literature review of chronic fatigue syndrome (CFS) found that, while fatigue is a commonly reported symptom, CFS is relatively rare (Ranjith, 2005). In a study aimed at examining the relationship between personality dimensions and hypochondriacal concerns and somatic symptoms in Gulf War veterans, Noyes and co-workers found few significant correlations between personality measures and hypochondriacal concerns or somatic symptoms. Negative temperament or neuroticism was found to be strongly associated with hypochondriacal concerns (Noyes, Jr. et al., 2005). Proctor and co-workers used geographic information system (GIS) techniques to identify spatial patterns of 1991 Gulf War troop locations in relationship to postwar diagnosis of chronic multisymptom illness (CMI). Spatial clusters (primarily in the coastal Dammam/Dharhan and the central inland areas of Saudi Arabia) were identified for several time periods studied (Proctor et al., 2005). A study of Air Force women deployed to the Gulf War theater found that significant health problems have persisted for an extended period of time and that the prevalence of symptoms remains statistically different from that among women deployed elsewhere during the same period of time (Pierce, 2005). Two recent studies on health outcomes in Saudi Arabian National Guard (SANG) soldiers following the 1991 Gulf War (Gackstetter et al., 2005; Hooper et al., 2005b) may provide an appropriate comparison group for future studies on US Gulf War veterans. Hooper et al (Hooper et al., 2005a) examined non-disease mortality in a study of fatal motor vehicle crashes and found a disproportionate rate of death in the younger, less educated, unmarried, deployed group.

A series of studies examined morbidity and mortality related to exposures at Khamisiyah. Page and co-workers found no differences in self-reported health effects (Page et al., 2005a; Page et al., 2005b). One report suggested an increased risk of brain cancer deaths, with other diseased-based mortality and total mortality rates similar between Khamisiyah exposed and non-exposed GW veterans (Bullman et al., 2005). Another study suggested a temporal effect in the incidence of testicular cancer between 2-5 years post-Gulf War, and further suggested this may bear relationship to military deployment not specific to Gulf War (Levine et al., 2005). Schumm and co-workers analyzed self-reported data from Reserve Component Persian Gulf War veterans and non-deployed veterans to assess associations between symptoms of Gulf War illnesses and a variety of potential risk factors. The most significant risk factors included perceived exposure to nerve agents, pyridostigmine bromide (PB), insect repellant, anthrax vaccination, use of personal insecticide, reported reactions to vaccines, and botulinum toxoid vaccine (Schumm et al., 2005).

An in-depth physical examination of Gulf War veterans identified a subset of ill veterans, all of whom had diagnosable disease conditions (ICD-10). There was no evidence of medically unexplained conditions or of a unique Gulf War syndrome (Bale and Lee, 2005). Similarly, a study at the UK Gulf Veterans' Medical Assessment Programme found that echocardiogram and ultrasound abnormalities were seen only in patients with known clinical diagnoses and almost all blood tests proved normal (Lee et al., 2005a). A study of a large cohort of Gulf War veterans suggested no overall difference in mortality between deployed and non-deployed military personnel (Macfarlane et al., 2005). In a recent review, Hotopf and co-workers discuss some of the methodological issues that have adversely affected epidemiological studies aimed at identifying the nature and causes of Gulf War illnesses. These include low-response rates, ascertainment

bias, recall bias, problems identifying suitable control groups, and problems defining outcomes (Hotopf and Wessely, 2005).

A study of British GW veterans showed that a clear majority were full-time employed and doing well. Those with poor mental health during service were more likely to leave and had a greater chance of becoming unemployed after leaving (Iversen et al., 2005b). Black and co-workers found that while GW deployment did not increase the incidence of incarceration, a history of incarceration may be a behavioral marker for substance abuse, antisocial behavior, and mental illness (Black et al., 2005). A model of predicting health care costs for ill GW veterans was presented (McFall et al., 2005).

F. Abstracts from Published Research

Allon N, Rabinovitz I, Manistersky E, Weissman BA, Grauer E (2005) Acute and long-lasting cardiac changes following a single whole-body exposure to sarin vapor in rats. Toxicol Sci 87:385-390. (Israeli Government)
Abstract: Epinephrine-induced arrhythmias (EPIA) are known to be associated with local cardiac cholinergic activation. The present study examined the development of QT prolongation and the effect on EPIA of whole-body exposure of animals to a potent acetylcholine esterase inhibitor. Freely moving rats were exposed to sarin vapor (34.2 +/- 0.8 μg/liter) for 10 min. The electrocardiograms (ECG) of exposed and control animals were monitored every 2 weeks for 6 months. One and six months post exposure, rats were challenged with epinephrine under anesthesia, and the threshold for arrhythmias was determined. Approximately 35% of the intoxicated rats died within 24 h of sarin exposure. Additional occasional deaths were recorded for up to 6 months (final mortality rate of 48%). Surviving rats showed, agitation, aggression, and weight loss compared to non-exposed rats, and about 20% of them experienced sporadic convulsions. Sarin-challenged rats with severe symptoms demonstrated QT segment prolongation during the first 2-3 weeks after exposure. The EPIA that appeared at a significantly lower blood pressure in the treated group in the first month after intoxication lasted for up to 6 months. This decrease in EPIA threshold was blocked by atropine and methyl-atropine. Three months post exposure no significant changes were detected in either k_D or B_{max} values of ^{3}H-N-methyl scopolamine binding to heart homogenates, or in the affinity of carbamylcholine to cardiac muscarinic receptors. The increase in the vulnerability to develop arrhythmias long after accidental or terror-related organophosphate (OP) intoxication, especially under challenging conditions such as stress or intensive physical exercise, may explain the delayed mortality observed following OP exposure.

Arfsten DP, Bekkedal M, Wilfong ER, Rossi J, III, Grasman KA, Healey LB, Rutkiewicz JM, Johnson EW, Thitoff AR, Jung AE, Lohrke SR, Schaeffer DJ, Still KR (2005a) Study of the reproductive effects in rats surgically implanted with depleted uranium for up to 90 days. J Toxicol Environ Health A 68:967-997. (Department of Defense)
Abstract: In 2001, the Naval Health Research Center Toxicology Detachment was funded by the U.S. Army Medical Research Acquisition Activity (USAMRAA) to conduct a study of the effects of surgically implanted depleted uranium (DU) pellets on adult rat reproductive success and development across two successive generations. This article presents some of the findings for the group of offspring from adult rats mated at 30 d post surgical implantation of DU pellets. Adult male and female Sprague-Dawley rats (P1 generation) were surgically implanted with 0, 4, 8, or 12 DU pellets (1 x 2 mm). The P1 generation was then cross-mated at 30 d post surgical implantation. Urine collected from P1 animals at 27 d post surgical implantation showed that DU was excreted in the urine of DU-implanted animals in a dose-dependent manner. DU surgical implantation did not have a negative impact on P1 reproductive success, survival, or body weight gain through post surgical implantation d 90. There were no statistically significant differences in F1 birth weight, survival, and litter size at postnatal day (PND) 0, 5, and 20. No gross physical abnormalities identified in the offspring were attributable to neonatal DU exposure. A series of neurodevelopment and immune function assessments were also conducted on F1 offspring. No group differences were observed that were related to parental DU exposure. Studies are ongoing on the impact of leaving DU embedded in soft tissue for 120 d on rat reproduction and subsequent offspring survival and development.

Arfsten DP, Schaeffer DJ, Johnson EW, Robert CJ, Still KR, Wilfong ER (2005b) Evaluation of the effect of implanted depleted uranium on male reproductive success, sperm concentration, and sperm velocity. Environ Res 100:205-215. (Department of Defense)

Abstract: Depleted uranium (DU) projectiles have been used in battle in Iraq and the Balkans and will continue to be a significant armor-penetrating munition for the US military. As demonstrated in the Persian Gulf War, battle injury from DU projectiles and shrapnel is a possibility, and removal of embedded DU fragments from the body is not always practical because of their location in the body or their small size. Previous studies in rodents have demonstrated that implanted DU mobilizes and translocates to the gonads, and natural uranium may be toxic to spermatozoa and the male reproductive tract. In this study, the effects of implanted DU pellets on sperm concentration, motility, and male reproductive success were evaluated in adult (P1) Sprague-Dawley rats implanted with 0, 12, or 20, DU pellets of 1x2 mm or 12 or 20 tantalum (Ta) steel pellets of 1x2mm. Twenty DU pellets of 1x2mm (760mg) implanted in a 500-g rat are equal to approximately 0.2 pound of DU in a 154-lb (70-kg) person. Urinary analysis found that male rats implanted with DU were excreting uranium at postimplantation days 27 and 117 with the amount dependent on dose. No deaths or evidence of toxicity occurred in P1 males over the 150-day postimplantation study period. When assessed at postimplantation day 150, the concentration, motion, and velocity of sperm isolated from DU-implanted animals were not significantly different from those of sham surgery controls. Velocity and motion of sperm isolated from rats treated with the positive control compound alpha-chlorohydrin were significantly reduced compared with sham surgery controls. There was no evidence of a detrimental effect of DU implantation on mating success at 30-45 days and 120-145 days postimplantation. The results of this study suggest that implantation of up to 20 DU pellets of 1x2mm in rats for approximately 21% of their adult lifespan does not have an adverse impact on male reproductive success, sperm concentration, or sperm velocity**.**

Axelrod SR, Morgan CA, III, Southwick SM (2005) Symptoms of posttraumatic stress disorder and borderline personality disorder in veterans of Operation Desert Storm. Am J Psychiatry 162:270-275. (DoD-040)

Abstract: OBJECTIVE: The present report is part of a follow-along investigation focusing on the evolution of trauma-related symptoms in veterans of Operation Desert Storm. The goal of the current report was to examine three hypotheses on the relationship between severity of war-related trauma, symptoms of posttraumatic stress disorder (PTSD), and symptoms of borderline personality disorder with a mixed retrospective/prospective design. METHOD: Ninety-four National Guard reservists completed self-administered measures of combat-related trauma, PTSD symptoms, and borderline personality disorder features after their Gulf War duty. RESULTS: Consistent with study hypotheses, prewar features of borderline personality disorder predicted variability in postwar PTSD symptoms beyond that predicted by combat exposure, combat exposure predicted variability in postwar features of borderline personality disorder, and PTSD severity assessed shortly after combat exposure accounted for additional variability in subsequent features of borderline personality disorder. CONCLUSIONS: Taken together, the present findings suggest that trauma, symptoms of PTSD, and features of borderline personality disorder are related to one another in a complex fashion that may exceed simple linear models. Clinical and research implications for the relationships among trauma, PTSD, and borderline personality disorder are discussed.

Bale AJ, Lee HA (2005) An observational study on diagnoses of 3,233 Gulf Veterans (Op Granby 1990-91) who attended the Ministry of Defence's Medical Assessment Programme 1993-2004. J R Nav Med Serv 91:99-111. (UK Ministry of Defence)

Abstract: BACKGROUND: This is the result of an observational study on 3,233 Gulf veterans who have attended our medical assessment program. We wanted to determine as a result of in-depth interviews, full medical examination and appropriate investigations, whether there was any unique Gulf war related medical condition. METHODS: Over a period of 10 years, 3,233 veterans have been assessed. All diagnoses have been made according to ICD-10 classifications. All psychiatric diagnoses have been confirmed by consultant psychiatrists. FINDINGS: 75% of veterans were well. Of the 25% unwell, 83% of ill health was accounted for by a psychiatric disorder. 3% of veterans had organic conditions which could be linked to Gulf deployment. The most common of these were respiratory disorders, followed by digestive disorders, injuries and skin disorders. Only 11 of these cases could be linked to the use of medical countermeasures. A further, 51 cases (41 respiratory disorders, 6 infections, 2 skin disorders and 2 eye conditions) could be linked to environmental conditions. INTERPRETATION: All veterans seen with

health problems could be identified as per ICD-10 classification of disease. We did not find any medically unexplained conditions. We found no evidence of a unique 'Gulf War Syndrome'.

Baraniuk JN, Casado B, Maibach H, Clauw DJ, Pannell LK, Hess SS (2005) A chronic fatigue syndrome - related proteome in human cerebrospinal fluid. BMC Neurol 5:22.
Abstract: BACKGROUND: Chronic Fatigue Syndrome (CFS), Persian Gulf War Illness (PGI), and fibromyalgia are overlapping symptom complexes without objective markers or known pathophysiology. Neurological dysfunction is common. We assessed cerebrospinal fluid to find proteins that were differentially expressed in this CFS-spectrum of illnesses compared to control subjects. METHODS: Cerebrospinal fluid specimens from 10 CFS, 10 PGI, and 10 control subjects (50 mul/subject) were pooled into one sample per group (cohort 1). Cohort 2 of 12 control and 9 CFS subjects had their fluids (200 mul/subject) assessed individually. After trypsin digestion, peptides were analyzed by capillary chromatography, quadrupole-time-of-flight mass spectrometry, peptide sequencing, bioinformatic protein identification, and statistical analysis. RESULTS: Pooled CFS and PGI samples shared 20 proteins that were not detectable in the pooled control sample (cohort 1 CFS-related proteome). Multilogistic regression analysis (GLM) of cohort 2 detected 10 proteins that were shared by CFS individuals and the cohort 1 CFS-related proteome, but were not detected in control samples. Detection of >/=1 of a select set of 5 CFS-related proteins predicted CFS status with 80% concordance (logistic model). The proteins were alpha-1-macroglobulin, amyloid precursor-like protein 1, keratin 16, orosomucoid 2 and pigment epithelium-derived factor. Overall, 62 of 115 proteins were newly described. CONCLUSION: This pilot study detected an identical set of central nervous system, innate immune and amyloidogenic proteins in cerebrospinal fluids from two independent cohorts of subjects with overlapping CFS, PGI and fibromyalgia. Although syndrome names and definitions were different, the proteome and presumed pathological mechanism(s) may be shared.

Barber DS, Ehrich MF, Jortner BS (2005) The effect of stress on the temporal and regional distribution of uranium in rat brain after acute uranyl acetate exposure. J Toxicol Environ Health A 68:99-111. (DoD-128)
Abstract: Long-term exposure to depleted uranium (DU) has been shown to increase brain uranium and alter hippocampal function; however, little is known about the short-term kinetics of DU in the brain. To address this issue, temporal and regional distribution of brain uranium was investigated in male Sprague-Dawley rats treated with a single intraperitoneal injection of 1 mg uranium/kg as uranyl acetate. Due to the inherent stress of combat and the potential for stress to alter blood-brain barrier permeability, the impact of forced swim stress on brain uranium distribution was also examined in this model. Uranium in serum, hippocampus, striatum, cerebellum, and frontal cortex was quantified by inductively coupled plasma-mass spectrometry (ICP-MS) at 8 h, 24 h, 7 d, and 30 d after exposure. Uranium entered the brain rapidly and was initially concentrated in hippocampus and striatum. While multiple phases of uranium clearance were observed, overall clearance was relatively slow and the uranium content of hippocampus, cerebellum, and cortex remained elevated for more than 7 d after a single exposure. Prior exposure to stress significantly reduced hippocampal and cerebellar uranium 24 h post-exposure and tended to reduce uranium in all brain regions 7 d after exposure. The application of stress appeared to increase brain uranium clearance, as initial tissue levels were similar in stressed and unstressed rats.

Bell IR, Brooks AJ, Baldwin CM, Fernandez M, Figueredo AJ, Witten ML (2005) JP-8 jet fuel exposure and divided attention test performance in 1991 Gulf War veterans. Aviat Space Environ Med 76:1136-1144. (VA-048)
Abstract: INTRODUCTION: Previous research indicates that a large cohort of veterans from the 1991 Gulf War report polysymptomatic conditions. These syndromes often involve neurocognitive complaints, fatigue, and musculoskeletal symptoms, thus overlapping with civilian illnesses from low levels of environmental chemicals, chronic fatigue syndrome, and fibromyalgia. METHODS: To test for time-dependent changes over repeated intermittent exposures, we evaluated objective performance on a computerized visual divided attention test in chronically unhealthy Gulf War veterans (n = 22 ill with low-level chemical intolerance (CI); n = 24 ill without CI), healthy Gulf War veterans (n = 23), and healthy Gulf War era veterans (n = 20). Testing was done before and after each of three weekly, double blind, low-level JP-8 jet fuel or clean air sham exposure laboratory sessions, including acoustic startle stimuli. RESULTS: Unhealthy veterans receiving jet fuel had faster mean peripheral reaction times over sessions

compared with unhealthy veterans receiving sham clean air exposures. Unhealthy Gulf veterans with CI exhibited faster post- vs. pre-session mean central reaction times compared with unhealthy Gulf veterans without CI. Findings were controlled for psychological distress variables. DISCUSSION: These data on unhealthy Gulf veterans show an acceleration of divided attention task performance over the course of repeated low-level JP-8 exposures. The present faster reaction times are consistent with rat neurobehavioral studies on environmental toxicant cross-sensitization and nonlinear dose-response patterns with stimulant drugs, as well as some previous civilian studies using other exposure agents. Together with previous research findings, the data suggest involvement of central nervous system dopaminergic pathways in affected Gulf veterans.

Bide RW, Armour SJ, Yee E (2005) GB toxicity reassessed using newer techniques for estimation of human toxicity from animal inhalation toxicity data: new method for estimating acute human toxicity (GB). J Appl Toxicol 25:393-409. (Defence Research & Development Canada)
Abstract: Estimated human inhalation toxicity values for Sarin (GB) were calculated using a new two independent (concentration, exposure time), one dependent (toxic response), nonlinear dose response (toxicity) model combined with re-evaluated allometric equations relating to animal and human respiration. Historical animal studies of GB toxicity containing both exposure and fractional animal response data were used to test the new process. The final data set contained 6621 animals, 762 groups, 37 studies and 7 species. The toxicity of GB for each species was empirically related to exposure concentration (C; mg m^{-3}) and exposure time (T; min) through the surface function $Y = b0 + b1\ Log_{10}C + b2\ Log_{10}T$ or $Y = b0 + b2\ Log_{10}C(n)T$ where Y is the Normit, b0, b1 and b2 are constants and n is the 'toxic load exponent' (Normit is PROPROBIT - 5). Between exposure times of 0.17 and 30 min, the average value for n in seven species was 1.35 +/- 0.15. The near parallel toxic load equations for each species and the linear relationship between minute volume/body weight ratio and the inhalation toxicity (LC_{t50}) for GB were used to create a pseudo-human data set and then an exposure time/toxicity surface for the human. The calculated n for the human was 1.40. The pseudo-human data had much more variability at low exposure times. Raising the lower exposure limit to 1 min, did not change the LCt50 but did result in lower variability. Raising the lower value to 2 min was counterproductive. Based on the toxic load model for 1-30 min exposures, the human GB toxicities (LC_{t01}, LC_{t05}, LC_{t50} and LC_{t95}) for 70 kg humans breathing 15 l min^{-1} were estimated to be 11, 16, 36 and 83; 18, 25, 57 and 132 and 24, 34, 79 and 182 mg x min m^{-3} for 2, 10 and 30 min exposures, respectively. These values are recommended for general use for the total human population. The empirical relationships employed in the calculations may not be valid for exposure times >30 min.

Black DW, Carney CP, Peloso PM, Woolson RF, Letuchy E, Doebbeling BN (2005) Incarceration and veterans of the first Gulf War. Mil Med 170:612-618.
Abstract: OBJECTIVE: This study investigated the prevalence of incarceration and the association with deployment among veterans of the first Persian Gulf War (GW). METHODS: A structured telephone interview of military personnel from Iowa deployed to the Persian Gulf and a comparison sample of nondeployed military personnel was conducted. The interview consisted of validated questions, validated instruments, and investigator-derived questions to assess relevant medical and psychiatric conditions. A total of 4,886 subjects were randomly drawn from one of four study domains, i.e., GW regular military, GW National Guard/Reserve, non-GW regular military, or non-GW National Guard/Reserve. Symptoms of medical conditions, psychiatric disorders, and health care utilization were the main outcome measures. RESULTS: Nearly one-quarter (845 of 3,695 subjects, 22.9%) had been incarcerated at some point before the interview ("ever incarcerated"). Ever incarcerated veterans had a higher frequency of psychiatric and medical comorbidity and higher rates of health care utilization. Ever incarcerated status was associated with male gender, enlisted rank, lower educational levels, low levels of military preparedness, discharge from service, cigarette smoking, antisocial traits, court martial and/or other military discipline, having seen a mental health professional, and having used illegal drugs. GW veterans who participated in combat had a modestly higher risk for incarceration after the GW than did noncombatants (odds ratio, 1.6; 95% confidence interval, 1.0-2.5). CONCLUSIONS: Military recruits with a history of incarceration more often displayed problematic behaviors, more often developed psychiatric/medical conditions, and had high rates of health care utilization. A history of incarceration may be a behavioral marker for substance abuse, antisocial behavior, and mental illness. Importantly, GW deployment carried no increased risk of subsequent incarceration overall.

Blanchard MS, Eisen SA, Alpern R, Karlinsky J, Toomey R, Reda DJ, Murphy FM, Jackson LW, Kang HK (2006) Chronic Multisymptom Illness Complex in Gulf War I Veterans 10 Years Later. Am J Epidemiol. 163:66-75 (EPub ahead of print, November 2005)

Abstract: Prior research has demonstrated that shortly after the 1991 Gulf War (Gulf War I), chronic multisymptom illness (CMI) was more common among deployed veterans than among nondeployed veterans. The aims of the current study were to determine the prevalence of CMI among deployed and nondeployed veterans 10 years after Gulf War I, compare the distribution of comorbid conditions, and identify prewar factors associated with CMI. Cross-sectional data collected from 1,061 deployed veterans and 1,128 nondeployed veterans examined between 1999 and 2001 were analyzed. CMI prevalence was 28.9% among deployed veterans and 15.8% among nondeployed veterans (odds ratio = 2.16, 95% confidence interval: 1.61, 2.90). Deployed and nondeployed veterans with CMI had similarly poorer quality-of-life measures and higher prevalences of symptom-based medical conditions, metabolic syndrome, and psychiatric disorders. Diagnoses of prewar anxiety disorders (not related to post-traumatic stress disorder) and depression were associated with CMI among both deployed and nondeployed veterans. Nicotine dependence and veteran-reported physician-diagnosed infectious mononucleosis were associated with CMI among deployed veterans, and migraine headaches and gastritis were associated with CMI among nondeployed veterans. CMI continues to be substantially more prevalent among deployed veterans than among nondeployed veterans 10 years after Gulf War I, but it manifests similarly in both groups. It is likely to be a common, persistent problem among veterans returning from the current Gulf War.

Bloch-Shilderman E, Kadar T, Levy A, Sahar R, Rabinovitz I, Gilat E (2005) Subcellular alterations of protein kinase C isozymes in the rat brain after organophosphate poisoning. J Pharmacol Exp Ther 313:1082-1089.

Abstract: The protein kinase C (PKC) signaling pathway has been associated with modulation of N-metyl-D-aspartate receptor activity, motor behavior, learning, and memory, all of which are severely impaired in organophosphate (OP) intoxication. Nevertheless, the role of PKC in OP intoxication is largely unknown. The present study attempted to characterize alterations in the immunoreactivity levels of PKC isozymes expressed in different brain areas in the rat following exposure to the nerve agent sarin (1x LD_{50}). Furthermore, possible neuroprotective effect of selective PKC regulating peptide after such insult was evaluated. The results indicated that a significant reduction in the immunoreactivity level of the conventional beta-II-PKC and the atypical zeta-PKC was observed in frontal cortex up to 24 h post-sarin and in the striatum up to 5 days post-sarin exposure. This reduction was in contrast to the increase in the immunoreactivity level of both isozymes seen in the hippocampus or thalamus. Treatment with the anticonvulsant midazolam (0.5 mg/kg) 10 min post-sarin exposure markedly reduced zeta-PKC immunoreactivity level and beta-II-PKC in the membrane fractions in the hippocampus. Beta-II-PKC peptide (380 ng/kg), known to inhibit PKC translocation and activation, attenuated sarin-induced neuropathology. These observations suggest a role for both conventional and atypical PKC isozymes in OP-induced neuropathy in the rat and further support their involvement in cell death.

Briner W, Murray J (2005) Effects of short-term and long-term depleted uranium exposure on open-field behavior and brain lipid oxidation in rats. Neurotoxicol Teratol 27:135-144. (University of Nebraska)

Abstract: Male and female rats were exposed to depleted uranium acetate (DU) in drinking water at doses of 0, 75, or 150 mg/L for either 2 weeks or 6 months. After exposure, the animals were tested for behaviors in the open-field. After testing in the open-field, the brains were examined for levels of lipid oxidation using the thiobarbituric acid (TBA) assay. Behavioral differences (line crossing and rearing) were seen in male rats after 2 weeks exposure to DU in drinking water for the highest dose group. Increased brain lipid oxidation was seen for the highest dose group for both genders. Lipid oxidation levels correlated significantly with line crossing and rearing in the open-field. After 6 months exposure, behavioral differences for male rats in the open-field remained and expanded to include other behaviors (grooming, defecation, and urination). Female rats also demonstrated some behavioral changes after 6 months exposure. Lipid oxidation in the brain continued to be seen; however, these levels no longer correlated with open-field behaviors. These data suggest that DU is a toxin that crosses the blood-brain barrier, producing behavioral changes in male rats and lipid oxidation regardless of gender in as little as 2 weeks in the rat. Longer exposures to DU may produce greater behavioral changes but compensatory mechanisms may reduce the effects of lipid oxidation. Males appear to be more sensitive to the behavioral effects of DU.

Britton JC, Phan KL, Taylor SF, Fig LM, Liberzon I (2005) Corticolimbic blood flow in posttraumatic stress disorder during script-driven imagery. Biol Psychiatry 57:832-840. (DoD-089)
BACKGROUND: Functional neuroimaging experiments targeting personal recall of emotional events may help elucidate neural substrates underlying posttraumatic stress disorder (PTSD). Studies suggest that limbic and paralimbic function might be altered in PTSD, as compared with trauma-exposed control subjects; however, little is known about functional changes resulting from traumatic experience itself. The present study examined both PTSD-specific and trauma-specific regional cerebral blood flow (rCBF) patterns during script-driven imagery. METHODS: Sixteen combat veterans with PTSD (PP); 15 combat veterans without PTSD (CC); and 14 healthy, aged-matched non-combat control subjects (NC) underwent [15O] H20 positron emission tomography (PET) scanning during script-driven imagery of emotionally evocative and neutral autobiographic events. RESULTS: Differential patterns of activation were detected in amygdala and medial frontal cortex. Past trauma experience was associated with decreased amygdala activity (i.e., less activity than healthy control subjects); however, combat control subjects deactivated this region (i.e., greater activity to neutral scripts). All subjects deactivated medial frontal cortex; PTSD patients had greater rostral anterior cingulate (rACC) deactivation compared with control groups, who deactivated ventromedial prefrontal cortex (vmPFC). CONCLUSIONS: Trauma-specific patterns may represent potential compensatory changes to traumatic reminders, while patterns observed only in the PTSD group may reflect neural substrates specific to PTSD pathophysiology.

Bullman TA, Mahan CM, Kang HK, Page WF (2005) Mortality in US Army Gulf War veterans exposed to 1991 Khamisiyah chemical munitions destruction. Am J Public Health 95:1382-1388.
Abstract: OBJECTIVES: We investigated whether US Army Gulf War veterans who were potentially exposed to nerve agents during the March 1991 weapons demolitions at Khamisiyah, Iraq, are at increased risk of cause-specific mortality. METHODS: The cause-specific mortality of 100487 exposed US Army Gulf War veterans was compared with that of 224980 unexposed US Army Gulf War veterans. Exposure was determined with the Department of Defense 2000 plume model. Relative risk estimates were derived from Cox proportional hazards models. RESULTS: The risks of most disease-related mortality were similar for exposed and unexposed veterans. However, exposed veterans had an increased risk of brain cancer deaths (relative risk [RR]=1.94; 95% confidence interval [CI]=1.12, 3.34). The risk of brain cancer death was larger among those exposed 2 or more days than those exposed 1 day when both were compared separately to all unexposed veterans (RR=3.26; 95% CI=1.33, 7.96; RR=1.72; 95% CI=0.95,3.10, respectively). CONCLUSIONS: Exposure to chemical munitions at Khamisiyah may be associated with an increased risk of brain cancer death. Additional research is required to confirm this finding.

Bussy C, Lestaevel P, Dhieux B, Amourette C, Paquet F, Gourmelon P, Houpert P (2005) Chronic ingestion of uranyl nitrate perturbs acetylcholinesterase activity and monoamine metabolism in male rat brain. Neurotoxicology 27:252 (EPub ahead of print, Dec 2005).
Abstract: Recent animal studies have shown that uranium can reach the brain after chronic exposure. However, little information is available on the neurological effects of chronic long-term exposure to uranium. In the present study, the effects during 1.5, 6 and 9-month periods of chronic ingestion of uranyl nitrate (UN) in drinking water (40mg of uranium per liter) on cholinergic acetylcholinesterase (AChE) activity and on dopaminergic and serotoninergic metabolisms were investigated in several areas of male Sprague Dawley rat brains. Uranium brain accumulation and distribution was also investigated after 1.5 and 9 months. Both after 1.5, 6 and 9 months of exposure, AChE activity was unaffected in the striatum, hippocampus and frontal cortex. Nevertheless, AChE activity was transitionally perturbed in the cerebellum after 6 months of exposure. After 1.5 months of exposure, dopamine levels increased in hypothalamus. After 6 months of exposure, a tiny but significant modification of the dopaminergic turnover ratio was detected in the frontal cortex. And after 9 months, UN produced a significant decrease in the 5HIAA level and the serotoninergic turn-over ratio in the frontal cortex and also a decrease in the DOPAC level and dopaminergic turn-over ratio in the striatum. Uranium brain accumulation was statistically significant in striatum after 1.5 months and in striatum, hippocampus and frontal cortex after 9 months of exposure. Although neurochemical changes did not always correlated with increased accumulation of uranium in specific areas, these results suggest that chronic ingestion of UN can cause chronic and progressive perturbations of physiological level of neurotransmitter systems. Considering previous reports on behavioral uranium-induced effects and the involvement of neurotransmitters in various behavioral

processes, it would be crucial to determine whether these neurochemical disorders were accompanied by neurobehavioral deficits even at 40mg of uranium per liter exposure.

Catherino WH, Levi A, Kao TC, Leondires MP, McKeeby J, Segars JH (2005) Anthrax vaccine does not affect semen parameters, embryo quality, or pregnancy outcome in couples with a vaccinated male military service member. Fertil Steril 83:480-483. (Department of Defense)
Abstract: Anthrax vaccination has been used in an effort to prevent infection should anthrax be used as a biological weapon, and widespread use has been considered in the event of another anthrax attack on American soil, but the long-term impact of anthrax vaccination on reproductive outcome is unknown. We found that exposure to the anthrax vaccine by males who were undergoing assisted reproduction did not negatively impact semen parameters, fertilization rate, embryo quality, or clinical pregnancy rates.

Coffman CJ, Horner RD, Grambow SC, Lindquist J (2005) Estimating the occurrence of amyotrophic lateral sclerosis among Gulf War (1990-1991) veterans using capture-recapture methods. Neuroepidemiology 24:141-150. (VA-061 and DoD-118)
Abstract: OBJECTIVE: Using data from a recent report that indicated a 2-fold higher risk of amyotrophic lateral sclerosis (ALS) among veterans of the 1991 Gulf War, we applied capture-recapture methodology to estimate possible under-ascertainment of ALS cases among deployed and non-deployed military personnel who were on active duty during that war. STUDY DESIGN AND SETTING: One of the most serious concerns facing field epidemiological investigations is that of case ascertainment bias, particularly when it is differential among the study groups. Capture-recapture methods, however, have promise as an approach to assessing the impact of case ascertainment bias in such studies. To overcome potential limitations of any one approach, three different estimation methods were used: log-linear models, sample coverage, and ecological models, to obtain a comprehensive view of under-ascertainment bias in these populations. RESULTS: All three approaches indicated differential undercount of ALS cases with modest under-ascertainment likely to have occurred among non-deployed military personnel, but little under-ascertainment among the deployed. After correcting the rates for under-ascertainment, the age-adjusted risk of ALS remained elevated among military personnel who had been deployed to S.W. Asia during the 1991 Gulf War, confirming the earlier report. CONCLUSIONS: Capture-recapture methods are a useful approach to assessing the magnitude of case ascertainment bias in epidemiological studies from which ascertainment-adjusted estimates of rates and relative risks can be calculated.

Dabisch PA, Burnett DC, Miller DB, Jakubowski EM, Muse WT, Forster JS, Scotto JA, Jarvis JR, Davis EA, Hulet SW, Reutter SA, Mioduszewski RJ, Thomson SA (2005a) Tolerance to the miotic effect of sarin vapor in rats after multiple low-level exposures. J Ocul Pharmacol Ther 21:182-195. (Department of Defense)
Abstract: Inhibition of acetylcholinesterase (AChE) by the organophosphorous compound sarin (GB) results in the accumulation of acetylcholine and excessive cholinergic stimulation. There are few data in the literature regarding the effects of multiple low-level exposures to GB and other organophosphorous compounds via relevant routes of exposure. Therefore, the present study was undertaken, and is the first, to investigate the effect of low-level repeated whole-body inhalation exposures to GB vapor on pupil size and cholinesterase activity in the eyes and blood. Male Sprague-Dawley rats were exposed to 4.0 mg/m3 of GB vapor for 1 h on each of 3 consecutive days. Pupil size and cholinesterase activities were determined at various points throughout the exposure sequence. The results demonstrate that multiple inhalation exposures to GB vapor produce a decrease in the miotic potency of GB in rats. This tolerance developed at a dose of GB that produced no overt signs of intoxication other than miosis. AChE and butyrylcholinesterase activity did not increase throughout the exposure sequence, suggesting that the tolerance cannot be attributed to a reduced inhibitory effect of GB. A decrease in the amount of GB present in the eye occurred after the third exposure. However, this change is insufficient to explain the tolerance, as there was no corresponding increase in AChE activity. Thus, the mechanism mediating the miotic tolerance observed after multiple inhalation exposures to the nerve agent GB remains uncertain, although several possibilities can be excluded based on the results of the present study.

Dabisch PA, Miller DB, Reutter SA, Mioduszewski RJ, Thomson SA (2005b) Miotic tolerance to sarin vapor exposure: role of the sympathetic and parasympathetic nervous systems. Toxicol Sci 85:1041-1047. (Department of Defense)

Abstract: O-isopropyl methylphosphonofluoridate, also known as sarin or GB, is a highly toxic organophosphorous compound that exerts its effect by inhibiting the enzyme acetylcholinesterase. While the effects of a single exposure to GB vapor are well characterized, the effects of multiple exposures to GB vapor are less clear. Previous studies in the rat and guinea pig have demonstrated that multiple exposures result in tolerance to the miotic effect of nerve agents. The aim of the present study was to examine potential mechanisms responsible for tolerance to the miotic effect of GB vapor that has been observed in the rat after multiple exposures. Multiple whole-body inhalation exposures to GB vapor were conducted in a dynamic airflow chamber. Exposures lasted 60 min and each of the three exposures occurred at 24-h intervals. The results of the present study demonstrate that the alpha-adrenergic antagonist phentolamine and the beta-adrenergic receptor antagonist propranolol did not affect the development of tolerance to the miotic effect of GB vapor, suggesting that enhanced sympathetic tone to the eye is not responsible for the observed tolerance. Administration of atropine before the first exposure prevented the tolerance to the miotic effect of GB vapor after the third exposure, suggesting that the tolerance is the result of muscarinic receptor desensitization secondary to receptor stimulation. The present study extends the findings of previous studies to strengthen the hypothesis that the miotic tolerance observed in the rat upon repeated exposure to nerve agents is due to desensitization of muscarinic acetylcholine receptors located on the pupillary sphincter.

Damodaran TV, Patel AG, Greenfield ST, Dressman HK, Lin SM, bou-Donia MB (2006) Gene expression profiles of the rat brain both immediately and 3 months following acute sarin exposure. Biochem Pharmacol 71:497-520 (EPub ahead of print, December 2005).

Abstract: We have studied sarin-induced global gene expression patterns at an early time point (15min; $0.5xLD_{50}$) and a later time point (3 months; $1xLD_{50}$) using Affymetrix: Rat Neurobiology U34 chips in male, Sprague-Dawley rats and have identified a total of 65 (early) and 38 (late) genes showing statistically significant alterations from control levels at 15min and 3 months, respectively. At the early time point, those that are classified as ion channel, cytoskeletal and cell adhesion molecules, in addition to neuropeptides and their receptors predominated over all other groups. The other groups included: cholinergic signaling, calcium channel and binding proteins, transporters, chemokines, GABAnergic, glutamatergic, aspartate, catecholaminergic, nitric oxide synthase, purinergic, and serotonergic signaling molecules. At the late time point, genes that are classified as calcium channel and binding proteins, cytoskeletal and cell adhesion molecules and GABAnergic signaling molecules were most prominent. Seven molecules (Ania-9, Arrb-1, CX-3C, Gabab-1d, Nos-2a, Nrxn-1b, PDE2) were identified that showed altered persistent expression in both time points. Selected genes from each of these time points were further validated using semi quantitative RT-PCR approaches. Some of the genes that were identified in the present study have been shown to be involved in organophosphate-induced neurotoxicity by both other groups as well as ours. Principal component analysis (PCA) of the expression data from both time points was used for comparative analysis of the gene expression, which indicated that the changes in gene expression were a function of dose and time of euthanasia after the treatment. Our model also predicts that besides dose and duration of post-treatment period, age and possibly other factors may be playing important roles in the regulation of pathways, leading to the neurotoxicity.

Dobscha SK, Corson K, Solodky J, Gerrity MS (2005) Use of videoconferencing for depression research: enrollment, retention, and patient satisfaction. Telemed J E Health 11:84-89. (VA-087)

The goal of this study was to describe the effects of using videoconferencing on participant enrollment, research measure administration and responses, study retention, and satisfaction. We recruited 400 patients from the Portland Veterans Affairs Primary Care Clinics for a randomized clinical trial of a care management intervention for depression. Patients recruited from distant clinic sites had the option of traveling to Portland, Oregon, for initial interviews or being interviewed using videoconferencing. Interviews included obtaining informed consent and administration of research measures. Remote participants were subsequently asked to complete a 12-item mail survey regarding the interview. There were no significant problems with the process of interviewing and obtaining informed consent by videoconferencing, as reported by patients and clinic staff. Twenty of the 31 participants interviewed by videoconferencing returned the satisfaction questionnaire. Participants indicated a high degree of

satisfaction with these interviews, and expressed willingness to recommend videoconferencing to others. No differences were observed between the Patient Health Questionnaire depression scores of videoconferencing and in-person participants, and there was no significant difference in the 6-month rate of loss to follow-up in the randomized trial. Videoconferencing allows patients in rural and remote locations to participate in psychiatric research and expands sources of recruitment for research projects.

Edwards JE, Rose RL, Hodgson E (2005) The metabolism of nonane, a JP-8 jet fuel component, by human liver microsomes, P450 isoforms and alcohol dehydrogenase and inhibition of human P450 isoforms by JP-8. Chem Biol Interact 151:203-211. (DoD-103)

Abstract: Nonane, a component of jet-propulsion fuel 8 (JP-8), is metabolized to 2-nonanol and 2-nonanone by pooled human liver microsomes (pHLM). Cytochrome P450 (CYP) isoforms 1A2, 2B6 and 2E1 metabolize nonane to 2-nonanol, whereas alcohol dehydrogenase, CYPs 2B6 and 2E1 metabolize 2-nonanol to 2-nonanone. Nonane and 2-nonanol showed no significant effect on the metabolism of testosterone, estradiol or N,N-diethyl-m-toluamide (DEET), but did inhibit carbaryl metabolism. JP-8 showed modest inhibition of testosterone, estradiol and carbaryl metabolism, but had a more significant effect on the metabolism of DEET. JP-8 was shown to inhibit CYPs 1A2 and 2B6 mediated metabolism of DEET, suggesting that at least some of the components of JP-8 might be metabolized by CYPs 1A2and/or 2B6.

Eisen SA, Kang HK, Murphy FM, Blanchard MS, Reda DJ, Henderson WG, Toomey R, Jackson LW, Alpern R, Parks BJ, Klimas N, Hall C, Pak HS, Hunter J, Karlinsky J, Battistone MJ, Lyons MJ (2005) Gulf War veterans' health: medical evaluation of a U.S. cohort. Ann Intern Med 142:881-890. (VA-002C)

Abstract: BACKGROUND: United States military personnel reported various symptoms after deployment to the Persian Gulf during the 1991 Gulf War. However, the symptoms' long-term prevalence and association with deployment remain controversial. OBJECTIVE: To assess and compare the prevalence of selected medical conditions in a national cohort of deployed and nondeployed Gulf War veterans who were evaluated by direct medical and teledermatologic examinations. DESIGN: A cross-sectional prevalence study performed 10 years after the 1991 Gulf War. SETTING: Veterans were examined at 1 of 16 Veterans Affairs medical centers. PARTICIPANTS: Deployed (n = 1061) and nondeployed (n = 1128) veterans of the 1991 Gulf War. MEASUREMENTS: Primary outcome measures included fibromyalgia, the chronic fatigue syndrome, dermatologic conditions, dyspepsia, physical health-related quality of life (Short Form-36 [SF-36]), hypertension, obstructive lung disease, arthralgias, and peripheral neuropathy. RESULTS: Of 12 conditions, only 4 conditions were more prevalent among deployed than nondeployed veterans: fibromyalgia (deployed, 2.0%; nondeployed, 1.2%; odds ratio, 2.32 [95% CI, 1.02 to 5.27]); the chronic fatigue syndrome (deployed, 1.6%; nondeployed 0.1%; odds ratio, 40.6 [CI, 10.2 to 161]); dermatologic conditions (deployed, 34.6%; nondeployed, 26.8%; odds ratio, 1.38 [CI, 1.06 to 1.80]), and dyspepsia (deployed, 9.1%; nondeployed, 6.0%; odds ratio, 1.87 [CI, 1.16 to 2.99]). The mean physical component summary score of the SF-36 for deployed and nondeployed veterans was 49.3 and 50.8, respectively. LIMITATIONS: Relatively low participation rates introduce potential participation bias, and deployment-related illnesses that resolved before the research examination could not, by design, be detected. CONCLUSIONS: Ten years after the Gulf War, the physical health of deployed and nondeployed veterans is similar. However, Gulf War deployment is associated with an increased risk for fibromyalgia, the chronic fatigue syndrome, skin conditions, dyspepsia, and a clinically insignificant decrease in the SF-36 physical component score.

Ejnik JW, Todorov TI, Mullick FG, Squibb K, McDiarmid MA, Centeno JA (2005) Uranium analysis in urine by inductively coupled plasma dynamic reaction cell mass spectrometry. Anal Bioanal Chem 382:73-79. (Department of Defense)

Abstract: Urine uranium concentrations are the best biological indicator for identifying exposure to depleted uranium (DU). Internal exposure to DU causes an increased amount of urine uranium and a decreased ratio of $^{235}U/^{238}U$ in urine samples, resulting in measurements that vary between 0.00725 and 0.002 (i.e., natural and depleted uranium's $^{235}U/^{238}U$ ratios, respectively). A method based on inductively coupled plasma dynamic reaction cell mass spectrometry (ICP-DRC-MS) was utilized to identify DU in urine by measuring the quantity of total U and the $^{235}U/^{238}U$ ratio. The quantitative analysis was achieved using ^{233}U as an internal standard. The analysis was performed both with and without the reaction gas

oxygen. The reaction gas converted ionized $^{235}U^{+}$ and $^{238}U^{+}$ into $^{235}UO^{2+}$ (m/z = 267) and $^{238}UO^{2+}$ (m/z = 270). This conversion was determined to be over 90% efficient. A polyatomic interference at m/z 234.8 was successfully removed from the 235U signal under either DRC operating conditions (with or without oxygen as a reaction gas). The method was validated with 15 urine samples of known uranium compositions. The method detection limit for quantification was determined to be 0.1 pg U mL^{-1} urine and an average coefficient of variation (CV) of 1-2% within the sample measurements. The method detection limit for determining $^{235}U/^{238}U$ ratio was 3.0 pg U mL^{-1} urine. An additional 21 patient samples were analyzed with no information about medical history. The measured 235U/238U ratio within the urine samples correctly identified the presence or absence of internal DU exposure in all 21 patients.

Forman-Hoffman VL, Carney CP, Sampson TR, Peloso PM, Woolson RF, Black DW, Doebbeling BN (2005) Mental health comorbidity patterns and impact on quality of life among veterans serving during the first gulf war. Qual Life Res 14:2303-2314. (D0D-058 and HHS-001)
Abstract: Purpose: To examine the patterns of coexisting (comorbid) mental disorders and whether comorbidity influences quality of life ratings in a sample of U.S. veterans. Patients and Methods: The Iowa Gulf War Study Case Validation study evaluated 602 military personnel, two-thirds of whom had symptoms of depression, cognitive dysfunction, or chronic widespread pain, who were activated or on active duty sometime during the first Gulf War (GW). Mental health disorders were defined using the SCID-IV, and the Health Utilities Index Mark 3 (HUI3) was used to measure health-related quality of life (HRQoL). Comorbidity was defined as having two or more mental disorders that spanned across at least two separate categories (e.g., depressive disorders and anxiety disorders). Results: Over 35% of veterans with a current mental disorder had at least one other comorbid mental disorder. Those with mental disorder comorbidity had lower HUI scores than veterans with only one or less mental disorders (mean 0.41 +/- 0.30 vs. 0.72 +/- 0.25, $p < 0.0001$). Conclusion: The co-occurrence of mental disorders that span at least two mental disorder categories is associated with impaired HRQoL in this veteran population. Early identification of mental health comorbidity may lead to interventions to enhance HRQoL among military personnel.

Gackstetter GD, Hooper TI, Al Qahtani MS, Smith TC, Memish ZA, Schlangen KM, Cruess DF, Barrett DH, Ryan MA, Gray GC (2005) Assessing the potential health impact of the 1991 Gulf War on Saudi Arabian National Guard soldiers. Int J Epidemiol 34:801-808. (DoD-120)
BACKGROUND: There has been considerable publicity that the 1991 Gulf War may have caused a wide array of health problems in military personnel. Although post-war health outcomes have been studied in US, British, Canadian, Danish, and other deployed troops, this issue has not been previously evaluated in coalition forces native to the Gulf region. METHODS: A collaborative team of US and Saudi health researchers was assembled, data sources evaluated, and hospitalizations among Saudi Arabian National Guard (SANG) soldiers between 1991 and 1999 analysed. Multivariate modelling was used to evaluate differences between 8342 soldiers exposed to combat at Al Khafji and a comparison group of 7270 soldiers in the Riyadh area. RESULTS: Among 15 612 SANG soldiers, we identified 148 with at least one hospitalization over the 9 years following the war. The adjusted rate of hospitalization was higher in the combat-exposed group (risk ratio (RR) = 1.80, 95% confidence interval (CI) 1.25-2.59). No unusual patterns of diagnoses were found and, because the overall number of hospitalizations was low, the absolute difference in risk was found to be very small. CONCLUSIONS: This is the first reported epidemiological investigation of post-war hospitalizations among coalition forces native to the Gulf region that participated in the 1991 Gulf War. A very small increase in hospitalizations was identified in SANG soldiers exposed to combat at Al Khafji. However, because of data limitations, the clinical relevance of this finding should be interpreted with caution. Future collaborative studies to better understand the health effects of deployment should be encouraged.

Griffiths GD, Telford G, Hooi DS, Cook DL, Wilkinson LJ, Green CA, Pritchard DI (2005) A T-cell-dependent humoral immune response is preserved during the administration of the nerve agent pre-treatment pyridostigmine bromide in a murine model. Int Immunopharmacol 5:525-540.
Abstract: Immune regulation, either via the autonomic nervous system or by a proposed "non-neuronal" cholinergic system, suggests that the immune system may be susceptible to perturbation by compounds affecting cholinergic function. Here, the current UK and US nerve agent pre-treatment, pyridostigmine bromide (PB) and the related anti-acetylcholinesterase (AChE) compounds physostigmine (PHY) and

BW284c51 were tested for their ability to affect mouse splenocyte function in vitro. In addition, PB, at a dose equivalent to that received during pre-treatment for nerve agent poisoning, was tested for its effect on a T-cell-dependent humoral response to antigen in vivo in the mouse. None of the anti-AChEs tested affected concanavalin A (Con A)-, anti-CD3- or lipopolysaccharide LPS-driven splenocyte proliferation, in vitro, at concentrations expected to give effective nerve agent pre-treatment. However, higher concentrations (>100 μM) particularly of PHY caused some inhibition of the proliferative responses. In vivo, PB or saline was administered via 28-day mini-osmotic pumps to give a 25-40% inhibition of whole blood AChE in the PB-treated animals. During PB or saline administration, primary and secondary doses (i.p.) of sheep red blood cells (SRBC) were given and the humoral response determined by monitoring anti-SRBC IgM and IgG levels. Splenocytes isolated from the experimental animals were also examined for their proliferative and cytokine responses to stimulation. No remarkable effects of PB were seen during the period of AChE inhibition on the humoral immune response. However, a modest elevation in IL-2 and IFNγ in Con A-stimulated lymphocytes was seen in PB-treated animals following pump removal. Overall these data suggest that, in vivo, the SRBC stimulated T-cell-dependent immune response is unaffected by the administration of PB at pre-treatment doses.

Gronseth GS (2005) Gulf war syndrome: a toxic exposure? A systematic review. Neurol Clin 23:523-540.

Abstract: Using the strength-of-conclusion scheme enumerated in Box 2, based on two class II studies, there is probably a causal link between deployment to the Persian Gulf theater of operation and the development of the poorly defined multisymptom illness known as Gulf War syndrome (GWS; level B). Based on class IV studies, there is insufficient evidence to determine if exposure to toxins encountered during the Persian Gulf War caused GWS (level U). A major limitation of the literature regarding GWS is the reliance on self-reporting to measure exposure to putative causal toxins. Although objective measures of toxin exposure in Gulf War veterans (GWV) generally is unavailable, modeling techniques to estimate exposure levels to low-level nerve agents and smoke from oil well fires have been developed. It would be useful to determine if exposure levels determined by these techniques are associated with GWS. The lack of a clear case definition GWS also hampers research. Some go even further, claiming that the absence of such a definition renders the condition illegitimate. Although an objective marker to GWS would be useful for studies, the absence of such a marker does not make the syndrome any less legitimate. In essence, GWS merely is a convenient descriptive term that describes a phenomenon: GWV reporting suffering from medically unexplained health-related symptoms. In this sense, it shares much with the other medically unexplained syndromes encountered in practice. The real debate surrounding medically unexplained conditions is not whether or not they exist, but defining their cause. In this regard, investigators fall into two camps. One camp insists that the conditions are caused by a yet-to-be-discovered medical problem, rejecting out of hand the possibility of a psychologic origin. The other camp insists the conditions are fundamentally psychogenic, rejecting the possibility of an undiscovered medical condition. The evidence shows, however, that the conditions exist, the suffering is real, and the causes are unknown.

Hilsenroth M, Arsenault L, Sloan P (2005) Assessment of combat-related stress and physical symptoms of Gulf War veterans: criterion validity of selected hand test variables. J Pers Assess 84:155-162. (VA-008)

Abstract: We examined the utility of selected Hand Test (Wagner, 1983) variables in relation to posttraumatic stress and physical symptoms in Gulf War (GW) veterans. In this study, we sought to replicate and expand on prior empirical findings that have demonstrated efficacy of the Hand Test in the assessment of posttraumatic stress disorder (PTSD; Walter, Hilsenroth, Arsenault, Sloan, & Harvill, 1998). Based on this previous research, Hand Test variables were selected a priori and examined across three groups of veterans: (a) a control group of participants who were in a reserve unit not deployed to the GW theater of operations, (b) a subclinical group of deployed GW veterans who reported 1 to 5 Diagnostic and Statistical Manual of Mental Disorders (4th ed. [DSM-IV]; American Psychiatric Association, 1994) criteria for PTSD, and (c) a group of deployed GW veterans who met DSM-IV criteria for PTSD. Analyses demonstrated significant differences across the three groups and significant relationships among selected Hand Test variables with the number of DSM-IV symptoms of PTSD reported in the interviews as well as with the number of physical problems reported by these veterans. We discuss these findings in relation to the assessment and treatment of posttraumatic stress symptomatology.

Hodgson E, Rose RL (2005) Human metabolism and metabolic interactions of deployment-related chemicals. Drug Metab Rev 37:1-39. (DoD-103)
Abstract: It has been suggested that chemicals and, more specifically, chemical interactions, are involved as causative agents in deployment-related illnesses. Unfortunately, this hypothesis has proven difficult to test, because toxicological investigations of deployment-related chemicals are usually carried out on surrogate animals and are difficult to extrapolate to humans. Other parts of the problem, such as the definition of variation within human populations and the development of methods for designating groups or individuals at significantly greater risk, cannot be carried out on surrogate animals, and the data must be derived from humans. The relatively recent availability of human cell.fractions, such as microsomes, cytosol, etc., human cells such as primary hepatocytes, recombinant human enzymes, and their isoforms and polymorphic variants has enabled a significant start to be made in developing the human data needed. These initial studies have examined the human metabolism by cytochrome P450, other phase I enzymes, and their isoforms and, in some cases, their polymorphic variants of compounds such as chlorpyrifos, carbaryl, DEET, permethrin, and pyridostigmine bromide, and, to a lesser extent, other chemicals from the same chemical and use classes, including solvents, jet fuel components, and sulfur mustard metabolites. A number of interactions at the metabolic level have been described both with respect to other xenobiotics and to endogenous metabolites. Probably the most dramatic have been seen in the ability of chlorpyrifos to inhibit not only the metabolism of other xenobiotics such as carbaryl and DEET but also to inhibit the metabolism of steroid hormones.

Hooper TI, DeBakey SF, Lincoln A, Kang HK, Cowan DN, Gackstetter GD (2005a) Leveraging existing databases to study vehicle crashes in a combat occupational cohort: epidemiologic methods. Am J Ind Med 48:118-127. (DoD-102)
Abstract: BACKGROUND: The US military is a large, well-defined occupational cohort offering tremendous opportunities to study risk factors for important health outcomes. This article describes our nested case-control methods to evaluate risk factors for fatal motor vehicle crashes (MVC) within all Service branches in a 1991 Gulf War era cohort. METHODS: We identified 1,343 cases of fatal MVC between 1991 and 1995 that were also included in the Department of Transportation's Fatality Analysis Reporting System database and, using risk set sampling, selected 13,430 controls. Our final analytic dataset consisted of 980 male driver cases and 12,807 controls linked to multiple databases. RESULTS: Cases were disproportionately younger, less educated, not married, enlisted, and deployed to the Gulf War, compared to controls. CONCLUSIONS: The ability to leverage multiple databases to study risk factors for fatal MVC is clearly advantageous and could eventually lead to the reduction of fatalities in similar occupational cohorts.

Hooper TI, Smith TC, Gray GC, Al Qahtani MS, Memish ZA, Barrett DH, Schlangen KM, Cruess DF, Ryan MA, Gackstetter GD (2005b) Saudi Arabia-United States collaboration in health research: a formula for success. Am J Infect Control 33:192-196. (DoD-120)
Abstract: The aim of this article is to share our experiences from an international collaborative effort to study health outcomes among Saudi Arabian National Guard (SANG) soldiers following the 1991 Gulf War. By paying particular attention to distinct social and religious customs, geopolitical differences, and unique aspects of the health care system, we achieved a successful international collaboration in health research.

Hotopf M, Wessely S (2005) Can epidemiology clear the fog of war? Lessons from the 1990-91 Gulf War. Int J Epidemiol 34:791-800.
Abstract: Despite over US $200 million having been spent researching illnesses following the 1990-91 Persian Gulf War, the nature and cause of such illnesses remains controversial. In this narrative review, we discuss some of the methodological issues that have affected epidemiological studies on this topic. These include low-response rates, ascertainment bias, recall bias, problems identifying suitable control groups, and problems defining the outcomes to study. From this we argue that difficulties have arisen partly owing to the significant delay between the point at which illnesses were first identified by veterans and the reporting of epidemiological studies and that health surveillance should be routine following future deployments.

Ikin JF, McKenzie DP, Creamer MC, McFarlane AC, Kelsall HL, Glass DC, Forbes AB, Horsley KW, Harrex WK, Sim MR (2005) War zone stress without direct combat: The Australian naval experience of the Gulf War. J Trauma Stress 18:193-204. (Australian Government, Department of Veterans' Affairs)
Abstract: This study examines psychological stressors reported by Australian Navy Gulf War veterans in relation to the 1991 Gulf War and other military service. Using a 44-item questionnaire, veterans reported few direct-combat encounters during the Gulf War; however, they reported many other stressful experiences, including fear of death and perceived threat of attack, more frequently in relation to the Gulf War than other military service. Reporting of stressful experiences was associated with younger age, lower rank, and deployment at the height of the conflict. These experiences may partly explain increased rates of psychological disorders previously demonstrated in this Navy veteran population. Findings highlight the importance of documenting war experiences in close proximity to deployment, and developing war exposure instruments which include naval activities and which reflect stressors other than those related to direct combat.

Iversen A, Dyson C, Smith N, Greenberg N, Walwyn R, Unwin C, Hull L, Hotopf M, Dandeker C, Ross J, Wessely S (2005a) 'Goodbye and good luck': the mental health needs and treatment experiences of British ex-service personnel. Br J Psychiatry 186:480-486. (DoD-039 / UK Medical Research Council)
BACKGROUND: Little is known about the psychological health or treatment experiences of those who have left the British armed forces. AIMS: To describe the frequency and associations of common mental disorders and help-seeking behaviors in a representative sample of UK veterans at high risk of mental health problems. METHOD: A cross-sectional telephone survey of 496 'vulnerable' ex-service personnel selected from an existing epidemiological military cohort. RESULTS: The response rate was 64%; 44% of these had a psychiatric diagnosis, most commonly depression. Those with a diagnosis were more likely to be of lower rank and divorced or separated. Just over half of those with self-reported mental health problems were currently seeking help, most from their general practitioners. Most help-seekers received treatment, usually medication; 28% were in touch with a service charity and 4% were receiving cognitive-behavioral therapy. CONCLUSIONS: Depression is more common than post-traumatic stress disorder in UK ex-service personnel. Only about half of those who have a diagnosis are seeking help currently, and few see specialists.

Iversen A, Nikolaou V, Greenberg N, Unwin C, Hull L, Hotopf M, Dandeker C, Ross J, Wessely S (2005b) What happens to British veterans when they leave the armed forces? Eur J Public Health 15:175-184. (DoD-039 and UK Medical Research Council)
Abstract: BACKGROUND: Little is known about the factors associated with leaving the armed forces, or what predicts subsequent employment success for veterans. It is likely that there is a complex interaction of adverse social outcomes and mental health status in this group. METHOD: Analysis of existing data from the King's Military Cohort, a large, randomly selected, longitudinal cohort of service personnel, many of whom have now left the armed forces. The sample consisted of 8195 service personnel who served in the armed forces in 1991; a third deployed to the Gulf (1990-91), a third deployed to Bosnia (1992-97) and the final third an 'Era' control group in the Armed Forces in 1991 but not deployed. RESULTS: The majority of service leavers do well after leaving and are in full-time employment. Those with poor mental health during service were more likely to leave and had a greater chance of becoming unemployed after leaving. Mental health problems appear to remain static for veterans after leaving. Veterans of the Gulf War enjoyed more favorable employment outcomes, provided that they came home well. CONCLUSIONS: Only a minority of veterans fare badly after service, even amongst those with active tours of duty behind them. Veterans with mental health problems during service seem to be at higher risk of social exclusion after leaving and therefore these individuals represent an especially vulnerable group of the veteran population.

Kang H, Dalager N, Mahan C, Ishii E (2005) The role of sexual assault on the risk of PTSD among Gulf War veterans. Ann Epidemiol 15:191-195. (VA-002A and VA-002B)
Abstract: PURPOSE: The 1991 Gulf War was the first major military deployment where female troops were integrated into almost every military unit, except for combat ground units. We evaluated the impact of reported sexual trauma during this deployment on the risk of post-traumatic stress disorder (PTSD) after the war. METHODS: A nested case-control analysis was conducted using the data collected in a population-

based health survey of 30,000 Gulf War era veterans. A total of 1381 Gulf War veterans with current PTSD were compared with 10,060 Gulf veteran controls without PTSD for self-reported in-theater experiences of sexual harassment/assault and combat exposure. RESULTS: The adjusted odds ratio (aOR) for PTSD associated with a report of sexual assault was 5.41 (95% confidence interval [CI], 3.19-9.17) in female veterans and 6.21 (95% CI, 2.26-17.04) in male veterans. The aOR for PTSD associated with "high" combat exposure was also statistically significant (aOR, 4.03 [95% CI, 1.97-8.23] for females; aOR, 4.45 [95% CI, 3.54-5.60] for males). CONCLUSION: Notwithstanding a possibility of recall bias, sexual trauma and combat exposure appear to be strong risk factors for PTSD for both men and women.

Kawada T, Katsumata M, Suzuki H, Li Q, Inagaki H, Nakadai A, Shimizu T, Hirata K, Hirata Y (2005) Insomnia as a sequela of sarin toxicity several years after exposure in Tokyo subway trains. Percept Mot Skills 100:1121-1126.
Abstract: More than 5,000 passengers on Tokyo subway trains were injured with toxic chemicals including the nerve gas "sarin" on March 20, 1995. The purpose of this study was to identify the effect of sarin exposure on insomnia in a cross-sectional study. A self-administered questionnaire concerning sleep-related items was distributed to victims of sarin exposure in October and November, 2003. Questionnaires were completed by 161 of the 163 participants (98.8%), who were selected from 1,500 subjects. Among them, the authors selected 75 women 30 to 69 years of age. Control participants were collected from inhabitants living in Maebachi City, Gunma Prefecture, Japan. For the younger exposed group (under 50 yr. of age), percentages of poor sleep, difficulty falling asleep, intermittent awakening, early morning awakening, a feeling of light overnight sleep, and insomnia were significantly higher than those for the control group. In contrast, the older exposed group (ages 50 to 69 years) had significantly higher prevalence of poor sleep, a feeling of light overnight sleep, and early morning awakening for the exposed group when compared with the control group. The high prevalence of insomnia and insomnia-related factors for victims especially under 50 years of age suggests a need for research on sleep quality after sarin exposure. Although posttraumatic stress disorder is assumed to be a psychological effect of exposure to a toxic substance, a cause-and-effect relationship has not been established.

Kelsall H, Macdonell R, Sim M, Forbes A, McKenzie D, Glass D, Ikin J, Ittak P (2005) Neurological status of Australian veterans of the 1991 Gulf War and the effect of medical and chemical exposures. Int J Epidemiol 34:810-819. (Australian Government, Department of Veterans' Affairs)
Abstract: BACKGROUND: Since the 1991 Gulf War, concerns have been voiced about the effects on the health of veterans of Gulf War related medical and chemical exposures. METHODS: Our cross-sectional study compared 1424 male Australian Gulf War veterans and a randomly sampled military comparison group (n = 1548). A postal questionnaire asked about the presence of current neurological type symptoms, medically diagnosed neurological conditions, and medical and chemical exposures. A neurological examination was performed as part of a physical assessment. RESULTS: Veterans have a higher prevalence of neurological type symptoms (ratio of means 1.4, 95% confidence interval (CI) 1.2-1.5). Although the odds ratio (OR) of lower limb neurological type symptoms and signs in veterans compared with the comparison group was increased (OR = 1.6, 95% CI 1.0-2.7), it was of borderline significance, and there was no difference between groups according to a Neuropathy Score based on neurological signs alone (ratio of means 1.1, 95% CI 0.9-1.3). The increased OR of neurological type symptoms and signs suggestive of a central nervous system disorder (OR = 1.8, 95% CI 1.0-3.1) was also of borderline significance. Veterans were not more likely to have self-reported medically diagnosed neurological conditions, or to have neurological type symptoms and signs suggestive of an anterior horn cell disorder (OR = 0.9, 95% CI 0.5-1.6). The total number of neurological type symptoms reported by veterans, but not the Neuropathy Score, was associated with Gulf War related exposures including immunizations and pyridostigmine bromide in dose-response relationships, anti-biological warfare tablets, solvents, pesticides, and insect repellents. CONCLUSIONS: This study shows increased reporting of neurological type symptoms in Gulf War veterans, but no evidence for increased neurological effects based on objective physical signs. There may be a number of factors, including information bias, relating to increased neurological type symptom reporting in veterans.

Kennedy G, Spence VA, McLaren M, Hill A, Underwood C, Belch JJ (2005) Oxidative stress levels are raised in chronic fatigue syndrome and are associated with clinical symptoms. Free Radic Biol Med 39:584-589.

Abstract: The aetiology of chronic fatigue syndrome (CFS) is unknown; however, recent evidence suggests excessive free radical (FR) generation may be involved. This study investigated for the first time levels of 8-iso-prostaglandin-F(2 alpha)-isoprostanes alongside other plasma markers of oxidative stress in CFS patients and control subjects. Forty-seven patients (18 males, 29 females, mean age 48 [19--63] years) who fulfilled the Centres for Disease Control classification for CFS and 34 healthy volunteers (13 males, 21 females, 46 [19--63] years) were enrolled in the study. The CFS patients were divided into two groups; one group had previously defined cardiovascular (CV) risk factors of obesity and hypertension (group 1) and the second were normotensive and non-obese (group 2). Patients had significantly increased levels of isoprostanes (group 1, P=0.007; group 2, P=0.03, unpaired t test compared to controls) and oxidized low-density lipoproteins (group 2, P=0.02) indicative of a FR attack on lipids. CFS patients also had significantly lower high-density lipoproteins (group 1, P=0.011; group 2, P=0.005). CFS symptoms correlated with isoprostane levels, but only in group 2 low CV risk CFS patients (isoprostanes correlated with total symptom score P=0.005; joint pain P=0.002; post-exertional malaise P=0.027, Pearson). This is the first time that raised levels of the gold standard measure of in vivo oxidative stress (isoprostanes) and their association with CFS symptoms has been reported.

Kitayama N, Vaccarino V, Kutner M, Weiss P, Bremner JD (2005) Magnetic resonance imaging (MRI) measurement of hippocampal volume in posttraumatic stress disorder: a meta-analysis. J Affect Disord 88:79-86.

Abstract: BACKGROUND: Studies in animals showed that the hippocampus, a brain area involved in learning and memory, is sensitive to stress. Although several MRI studies showed smaller hippocampal volume in adults with chronic PTSD, others did not show significant differences from controls. These studies are typified by small sample sizes which may limit the ability to show significant differences. We therefore performed a meta-analytic study of all of these studies to clarify the role of hippocampal structural changes in subjects with PTSD. METHODS: Nine studies with a total of 133 adult subjects with chronic PTSD, 148 healthy controls, and 53 traumatized controls were included in the meta-analysis. RESULTS: There was significantly smaller volume in both right and left hippocampi in adult subjects with chronic PTSD in comparison with both healthy controls and traumatized controls. CONCLUSION: These findings are consistent with smaller hippocampal volume in adult subjects with chronic PTSD.

Koch TR, Emory TS (2005) Evaluation of chronic gastrointestinal symptoms following Persian Gulf War exposure. Mil Med 170:696-700. (VA)

Abstract: This was a prospective study performed in a Department of Veterans Affairs Medical Center. The aim of this study was to use endoscopic and histological examinations to determine the potential diagnostic origins of chronic gastrointestinal symptoms among patients who were part of the deployment of troops to the Persian Gulf after August 1990. Twenty-four (8%) male patients (mean age, 42 years) of 308 patients in the Persian Gulf War Registry agreed to undergo endoscopic examination of chronic symptoms, including heartburn (29%), dyspepsia (33%), dysphagia (8%), diarrhea (63%), Hemoccult-positive stool (21%), and rectal bleeding (17%). There were 17 upper endoscopies, 18 colonoscopies, and 4 flexible sigmoidoscopies performed, all with biopsies. Five (33%) of 15 patients had positive serological findings for Helicobacter pylori. With upper endoscopy, major findings included esophagitis (12%), Schatzki's ring (12%), hiatal hernia (47%), antral erythema (59%), and duodenal erythema (29%). With lower endoscopy, major findings included ileitis (5%), lymphoid hyperplasia (9%), polyps (27%), diverticulosis (23%), and hemorrhoids (23%). Major histopathological findings included microscopic esophagitis (24%), gastritis with H. pylori (35%), gastritis without H. pylori (18%), Crohn's disease (5%), tubular adenoma (5%), hyperplastic polyps (18%), and melanosis coli (5%). Most patients with chronic heartburn or dyspepsia have evidence of esophagitis or H. pylori. Individuals with these chronic symptoms should undergo evaluation.

Krejcova-Kunesova G, Bartosova L, Kuca K (2005) Signs of cyclosarin-induced neurotoxicity and its pharmacological treatment with quaternary pyridinium-oximes reactivators. Toxicology 216:32-40.
Abstract: Cyclosarin (GF-agent; O-cyclohexylmethylfluorophosphonate) belongs to highly toxic organophosphorus compounds. Potential for exposure to chemical warfare organophosphorus nerve agents, such as cyclosarin exists on the battlefield or in the civilian sector as a threat by a terrorist group, as well as an accident as part of current demilitarization efforts. Cyclosarin was not in the forefront of scientific interest for long time. The research interest was increased after Operation Desert Shield and Desert Storm with the possibility (later confirmed by the UN special commission) that cyclosarin constituted the Iraqi chemical agent inventory. In this study, the neurotoxicity of cyclosarin and therapeutic efficacy of three oximes [HI-6(1-(2-hydroxyiminomethylpyridinium)-3-(4-carbamoylpyridinium)-2-oxa-p ropane dichloride), BI-6(2-hydroxyiminomethylpyridinium)-4-(4-carbamoylpyridinium)-but-2-ene dibromide), HS-6(2-hydroxyiminomethylpyridinium)-3-(3-carbamoylpyridinium)-2-oxa-propa ne dichloride)] as acetylcholinesterase reactivators in combination with atropine was studied in rats. The therapy was administered intramuscularly (i.m.) 1 min after i.m. GF-agent challenge (1 LD_{50}). Testing of cyclosarin-induced neurotoxicity progress was carried out using the method of Functional observational battery (FOB). The experimental animals were observed at 24 h and 7 days following cyclosarin administration. The results were compared to the condition of control rats that received physiological solution instead of cyclosarin and treatment. All tested antidotal compounds induced neuroprotective efficacy, because decrease of neurotoxicity signs was recorded. There was no poisoned experimental group treated with atropine only, because our preliminary study showed no therapeutic effect of atropine alone. Cyclosarin caused a marked statistically significant change in most of the neurobehavioral parameters (FOB) at 24 h and 7 days after exposure, compared to the saline control group. Survival was 7/10 at 24 h and 5/10 at 7 days. Oxime (BI-6, HS-6 or HI-6) + atropine treatment caused a progressing recovery of the neurobehavioral disturbances caused by cyclosarin at 24 h and 7 days after exposure.

Langston JL, Adkins AL, Moran AV, Rockwood GA, Deford MS (2005) Effects of sarin on the operant behavior of guinea pigs. Neurotoxicol Teratol 27:841-853. (Department of Defense)
Abstract: The present study evaluated the dose-response effects of subacute exposure to sublethal doses of the organophosphorus (OP) chemical warfare nerve agent (CWNA) sarin (GB) on the operant behavior of guinea pigs. Dietary restricted guinea pigs, trained to respond for food under a progressive ratio (PR) schedule of reinforcement, were injected five times per week (Monday-Friday) for 2 weeks with fractions (0.1, 0.2, and 0.4) of the established LD_{50} of GB (42 μg/kg). Changes in body weight, whole blood (WB) acetylcholinesterase (AChE) levels, and operant performances were monitored over the 2 weeks of GB exposure and for an additional 2 weeks following the termination of exposures. There were dose-related changes in body weight and WB AChE levels throughout the exposure and post-exposure periods. Several parameters of PR performance were disrupted during exposure to 0.4 LD_{50} GB, however, concurrent weight loss indicated the presence of overt toxicity. PR performance recovered following the termination of exposures. Lower doses (0.1 and 0.2 LD_{50}) of GB failed to produce reliable effects on operant performance during the exposure period. Overall responding decreased during exposure to 0.4 LD_{50} GB, resulting in reduced response rates and break points. The decrease in overall response rates was attributed to an increase in pausing since there was no decrease in running rate. Motor effects of 0.4 LD_{50} GB were evident as an increase in the proportion of lever press durations ≥1.0 s. In the present study, doses of GB lower than 0.4 LD_{50} produced no marked alteration of operant performance in guinea pigs, although WB AChE levels were maximally inhibited to 20% of control.

Lee HA, Bale AJ, Gabriel R (2005a) Results of investigations on Gulf War veterans. Clin Med 5:166-172. (UK Ministry of Defence)
Abstract: Investigations were undertaken on veterans of the Gulf conflict of 1990/91 at the Gulf Veterans' Medical Assessment Programme (GVMAP), to determine whether routine investigations should be carried out on these veterans. Blood investigations were analyzed of a 10% random sample of veterans and also of two veteran groups--one group was well (asymptomatic) and the other unwell (post-traumatic stress disorder). Neurological investigations were carried out as well as 1,000 ultrasound studies and 3,000 ECGs. Almost all blood tests proved normal. The only significant differences found between the two groups were for the alanine/aspartate transaminase and gamma glutamyl transaminase values, where there were more abnormal findings in the unwell group. Abnormal, but expected, neurological investigations were found in those referred for these tests. Ultrasound abnormalities were related to known established clinical

diagnoses, apart from three cases. ECG abnormalities were only present in those with known clinical diagnoses. It was concluded that reducing the number of investigations would not only be cost effective but should help to lessen veterans' anxieties.

Lee HA, Gabriel R, Bale AJ (2005b) Clinical outcomes of Gulf veterans' medical assessment programme referrals to specialized centers for Gulf veterans with post-traumatic stress disorder. Mil Med 170:400-405. (UK Ministry of Defence)
Abstract: The study sought to ascertain whether referring veterans of the 1990-1991 Persian Gulf conflict with chronic post-traumatic stress disorder (PTSD) to specialized centers with knowledge of military culture and the impact of conflict resulted in successful psychotherapeutic outcomes at 1-year follow-up times. A total of 120 referrals to specialist centers were made by general physicians. Of these, 19 were non-PTSD referrals, and 80 patients were confirmed by a psychiatrist as having PTSD. A degree of success in psychotherapeutic interventions for PTSD at 1 year, determined from general practitioner follow-up correspondence, was obtained for 95% of referrals. There were no distinguishing features between successful and unsuccessful outcomes. This study shows that early attention, i.e., diagnosis and treatment by psychiatrists knowledgeable regarding the service environment, can be beneficial for this group.

Leggett RW, Eckerman KF, Boice Jr JD (2005) A respiratory model for uranium aluminide based on occupational data. J Radiol Prot 25:405-416. (Department of Energy)
Abstract: As part of an epidemiological study, doses from intake of radionuclides were estimated for workers employed during a 52-year period at the Rocketdyne/Atomics International facility in California. The facility was involved in a variety of research programs, including nuclear fuel fabrication, spent nuclear fuel decladding, and reactor operation and disassembly. Most of the documented intakes involved inhalation of enriched uranium (U), fission products, or plutonium (Pu). Highest doses were estimated for a group of workers exposed to airborne uranium aluminide (UAl_x) during the fabrication of reactor fuel plates. Much of the exposure to UAl_x occurred early in the fuel fabrication program, before it was recognized that intake and lung retention were being underestimated from urinary data due to an unexpected delayed dissolution of the inhaled material. In workers who had been removed from exposure, the rate of urinary excretion of U increased for a few months, peaked, and then declined at a rate consistent with moderately soluble material. This pattern differs markedly from the monotonically decreasing absorption rates represented by the default absorption types in the Human Respiratory Tract Model (HRTM) of the International Commission on Radiological Protection (ICRP). This paper summarizes the findings on the behavior of UAl_x in these workers and describes material-specific parameter values of the HRTM based on this information.

Lestaevel P, Bussy C, Paquet F, Dhieux B, Clarencon D, Houpert P, Gourmelon P (2005a) Changes in sleep-wake cycle after chronic exposure to uranium in rats. Neurotoxicol Teratol 27:835-840.
Abstract: Uranium is a heavy metal known to induce toxicity in kidneys. It is also known to enter the central nervous system, thus inducing neurophysiological effects, after exposure to relatively high concentrations. The effect of chronic uranium exposure (40 mg l^{-1} in drinking water, for 90 days) on electroencephalographic architecture has been studied on freely moving rats using a telemetry technique. The main effects of uranium on the sleep-wake cycle were an increase in rapid eye movement sleep (REM-sleep) and theta band power during the light period, as early as Day 30 after exposure commenced. The most probable explanation for these effects is that uranium directly affects the brain. This increase in REM-sleep was previously described in human depression or models of chronically stressed rats and it may be assimilated with some protective or compensatory mechanisms.

Lestaevel P, Houpert P, Bussy C, Dhieux B, Gourmelon P, Paquet F (2005b) The brain is a target organ after acute exposure to depleted uranium. Toxicology 212:219-226.
Abstract: The health effects of depleted uranium (DU) are mainly caused by its chemical toxicity. Although the kidneys are the main target organs for uranium toxicity, uranium can also reach the brain. In this paper, the central effects of acute exposure to DU were studied in relation to health parameters and the sleep-wake cycle of adult rats. Animals were injected intraperitoneally with 144+/-10 µg DU kg-1 as nitrate. Three days after injection, the amounts of uranium in the kidneys represented 2.6 µg of DU g^{-1} of tissue, considered as a sub-nephrotoxic dosage. The central effect of uranium could be seen through a decrease in food intake as early as the first day after exposure and shorter paradoxical sleep 3 days after acute DU

exposure (-18% of controls). With a lower dosage of DU (70+/-8 μg DU kg^{-1}), no significant effect was observed on the sleep-wake cycle. The present study intends to illustrate the fact that the brain is a target organ, as are the kidneys, after acute exposure to a moderate dosage of DU. The mechanisms by which uranium causes these early neurophysiological perturbations shall be discussed.

Levine PH, Young HA, Simmens SJ, Rentz D, Kofie VE, Mahan CM, Kang HK (2005) Is testicular cancer related to Gulf War deployment? Evidence from a pilot population-based study of Gulf War era veterans and cancer registries. Mil Med 170:149-153. (HHS-011)
Abstract: The possible relationship between military deployment and the subsequent increase in cancer rates has been prominent since the Vietnam War. The objective of this study was to investigate whether any form of cancer was increased among veterans deployed to the Persian Gulf in the 1991 conflict. This study matched data from central cancer registries in the District of Columbia and New Jersey with the records for 1.4 million Gulf War era veterans, i.e., 621,902 veterans who arrived in the Persian Gulf before March 1, 1991, and 746,248 non-Gulf veterans. Using a proportional incidence ratio, testicular cancer was found to be the only significantly increased malignancy among deployed Persian Gulf War veterans. The increase became apparent 2 to 3 years after the Persian Gulf War and peaked 4 to 5 years afterward. Our data and those of investigators studying Vietnam veterans suggest that testicular cancer may be related to military deployment.

Li B, Sedlacek M, Manoharan I, Boopathy R, Duysen EG, Masson P, Lockridge O (2005) Butyrylcholinesterase, paraoxonase, and albumin esterase, but not carboxylesterase, are present in human plasma. Biochem Pharmacol 70:1673-1684. (DoD-135)
The goal of this work was to identify the esterases in human plasma and to clarify common misconceptions. The method for identifying esterases was non-denaturing gradient gel electrophoresis stained for esterase activity. We report that human plasma contains four esterases: butyrylcholinesterase (EC 3.1.1.8), paraoxonase (EC 3.1.8.1), acetylcholinesterase (EC 3.1.1.7), and albumin. Butyrylcholinesterase (BChE), paraoxonase (PON1), and albumin are in high enough concentrations to contribute significantly to ester hydrolysis. However, only trace amounts of acetylcholinesterase (AChE) are present. Monomeric AChE is seen in wild-type as well as in silent BChE plasma. Albumin has esterase activity with alpha- and beta-naphthylacetate as well as with p-nitrophenyl acetate. Misconception #1 is that human plasma contains carboxylesterase. We demonstrate that human plasma contains no carboxylesterase (EC 3.1.1.1), in contrast to mouse, rat, rabbit, horse, cat, and tiger that have high amounts of plasma carboxylesterase. Misconception #2 is that lab animals have BChE but no AChE in their plasma. We demonstrate that mice, unlike humans, have substantial amounts of soluble AChE as well as BChE in their plasma. Plasma from AChE and BChE knockout mice allowed identification of AChE and BChE bands without the use of inhibitors. Human BChE is irreversibly inhibited by diisopropylfluorophosphate, echothiophate, and paraoxon, but mouse BChE spontaneously reactivates. Since human plasma contains no carboxylesterase, only BChE, PON1, and albumin esterases need to be considered when evaluating hydrolysis of an ester drug in human plasma.

Lucas KE, Armenian HK, Debusk K, Calkins HG, Rowe PC (2005) Characterizing Gulf War Illnesses: neurally mediated hypotension and postural tachycardia syndrome. Am J Med 118:1421-1427. (DoD-109)
A high proportion of 1991 Gulf War veterans report nonspecific symptoms, which have been termed Gulf War Illnesses. Symptom complaints overlap with those of another medically unexplained illness, chronic fatigue syndrome. Many with chronic fatigue syndrome also have neurally mediated hypotension and postural tachycardia syndrome. We hypothesized that those with Gulf War Illnesses have a greater prevalence of neurally mediated hypotension or postural tachycardia syndrome than healthy controls.

Macfarlane GJ, Hotopf M, Maconochie N, Blatchley N, Richards A, Lunt M (2005) Long-term mortality amongst Gulf War Veterans: is there a relationship with experiences during deployment and subsequent morbidity? Int J Epidemiol 34:1403-1408. (UK Ministry of Defence)
Abstract: BACKGROUND: Gulf War Veterans have previously been shown to have, in the short-term, an excess risk of death from 'external' (i.e. non-disease) causes of death. This study aims to determine whether there remains an excess of non-disease-related deaths in Gulf Veterans, 13 years after deployment, and, for the first time, to determine whether there is a relationship between experiences reported in the Gulf, post-

war symptoms, and subsequent mortality experience. METHODS: We conducted a cohort study with follow-up from April 1, 1991 (the end of the Gulf War) to June 30, 2004. Participants were 53 462 Gulf War Veterans and a cohort of military personnel, matched for age-group, sex, rank, service and level of fitness, who were not deployed to the Gulf. The outcome measure used was mortality as recorded on the NHS central register. RESULTS: There is no difference, 13 years after the end of the Gulf War, in the overall mortality experience of Gulf War Veterans. The excess in non-disease-related deaths previously reported is confined to the initial 7 years of follow-up [mortality rate ratio (MRR) 1.31, 95% confidence interval (CI) 1.06-1.63] rather than the more recent period (MRR 1.05, 95% CI 0.83-1.33). Overall experiences reported during Gulf deployment did not influence subsequent risk of dying, but there was non-significant increased risk of dying from a disease-related death (MRR 1.99, 95% CI 0.98-4.04) associated with reported exposure to depleted uranium and of a non-disease-related death associated with reporting handling of pesticides (MRR 2.05, 95% CI 0.91-4.61). Reporting of morbidity in the health surveys conducted was not related to future risk of death. CONCLUSION: The higher rates of non-disease-related deaths in Gulf War Veterans are not evident in the period of follow-up since 1997. Neither the excess morbidity reported in health surveys nor the experiences during deployment significantly influenced future mortality. The two non-significant associations found (reported depleted uranium exposure and disease death, reporting handling pesticides and non-disease deaths) need to be considered in the context of the number of possible associations examined and potential biases-although they are biologically plausible.

McDiarmid MA, Engelhardt SM, Oliver M, Gucer P, Wilson PD, Kane R, Kabat M, Kaup B, Anderson L, Hoover D, Brown L, Albertini RJ, Gudi R, Jacobson-Kram D, Thorne CD, Squibb KS (2006) Biological monitoring and surveillance results of Gulf War I veterans exposed to depleted uranium. Int Arch Occup Environ Health 79:11-21(EPub ahead of print, August 2005). (VA)
Abstract: Objective: To relate medical surveillance outcomes to uranium biomonitoring results in a group of depleted uranium (DU)-exposed, Gulf War I veterans. Methods: Thirty-two veterans of Gulf War I who were victims of 'friendly fire' involving DU weapons, in whom exposure assessment can accurately be measured, had urine uranium concentrations determined using inductively coupled plasma-mass spectrometry (ICP-MS) technology. Clinical laboratory parameters were measured and related to urine uranium concentrations. Data were examined by stratifying the cohort into a low U group, <0.10 mug/g creatinine versus a high U group, >/=0.10 mug/g creatinine and assessing differences between groups. Results: Over a decade after first exposure, soldiers possessing embedded DU fragments continue to excrete elevated concentrations of uranium in urine. No clinically significant uranium related health effects were observed in blood count, blood chemistries including renal markers, neuropsychological measures, and semen quality or genotoxicity measures. Markers of early changes in renal glomerular and tubular function were not statistically different between groups; however, genotoxicity measures continue to show subtle, mixed results. Conclusion: Persistent urine uranium elevations continue to be observed more than 12 years since first exposure. Despite this, renal and other clinical abnormalities were not observed, likely due to the 'relatively' low uranium burden in this cohort compared to historical uranium-exposed occupational groups. Continuing surveillance is indicated, however, due to the on-going nature of the exposure. These results are an important finding in light of the on-going controversy regarding health effects observed in soldiers of the Gulf War and other conflicts, whose uranium exposure assessment is unable to be accurately determined.

McFall M, Tackett J, Maciejewski ML, Richardson RD, Hunt SC, Roberts L (2005) Predicting costs of Veterans Affairs health care in Gulf War veterans with medically unexplained physical symptoms. Mil Med 170:70-75. (VA-058)
Abstract: Measures of post-traumatic stress disorder (PTSD) and depression were used to predict Veterans Affairs outpatient treatment costs among Persian Gulf War veterans with medically unexplained physical symptoms. Patients (N = 206) enrolled in a Veterans Affairs primary care clinic for Persian Gulf War veterans completed study assessments at the initial appointment or at a proximal follow-up visit. Costs of care for mental health, medical, and pharmacy services for these veterans were computed for the subsequent 6-month period. Depression and PTSD symptoms explained a significant share of variance in costs of mental health care and pharmacy services, after adjustment for covariates. None of the mental status measures was significantly related to costs of medical care. Models using global measures of mental health status were as robust as models using disorder-specific measures of PTSD and depression in

predicting mental health care and pharmacy costs. The implications of these findings for anticipating costs of care for Persian Gulf War veterans are discussed.

Miller AC, Bonait-Pellie C, Merlot RF, Michel J, Stewart M, Lison PD (2005) Leukemic transformation of hematopoietic cells in mice internally exposed to depleted uranium. Mol Cell Biochem 279:97-104. (Department of Defense)
Abstract: Depleted uranium (DU) is a dense heavy metal used in military applications. During military conflicts, US military personnel have been wounded by DU shrapnel. The health effects of embedded DU are unknown. Published data from our laboratory demonstrated that DU exposure in vitro can transform immortalized human osteoblast cells (HOS) to the tumorigenic phenotype. Results from our laboratory have also shown that DU is genotoxic and mutagenic in cultured human cells. Internalized DU could be a carcinogenic risk and concurrent alpha particle and heavy metal toxic effects complicate this potential risk. Anecdotal reports have suggested that DU can cause leukemia. To better assess this risk, we have developed an in vivo leukemogenesis model. This model involves using murine hematopoietic cells (FDC-P1) that are dependent on stimulation by granulocyte-macrophage colony stimulating factor (GM-CSF) or interleukin 3 (IL-3) and injected into mice to produce myeloid leukemia. Although immortalized, these cells are not tumorigenic on subcutaneous inoculation in mice. Intravenous injection of FDC-P1 cells into DU-implanted DBA/2 mice was followed by the development of leukemias in 76% of all mice implanted with DU pellets. In contrast, only 12% of control mice developed leukemia. Karyotypic analysis confirmed that the leukemias originated from FDC-P1 cells. The growth properties of leukemic cells from bone marrow, spleen, and lymph node were assessed and indicate that the FDC-P1 cells had become transformed in vivo. The kidney, spleen, bone marrow, muscle, and urine showed significant elevations in tissue uranium levels prior to induction of leukemia. These results demonstrated that a DU altered in vivo environment may be involved in the pathogenesis of DU induced leukemia in an animal model.

Miyaki K, Nishiwaki Y, Maekawa K, Ogawa Y, Asukai N, Yoshimura K, Etoh N, Matsumoto Y, Kikuchi Y, Kumagai N, Omae K (2005) Effects of sarin on the nervous system of subway workers seven years after the Tokyo subway sarin attack. J Occup Health 47:299-304.
Abstract: This study was designed to assess the after effects of sarin exposure on the nervous system in victims of the Tokyo Subway Sarin Attack, which occurred on 20 March, 1995. We performed a similar study 3 yr after the disaster. This time, we newly enrolled 36 staff of the Teito Rapid Transit Authority (Tokyo Eidan subway) to assess the 7 yr after effects on the nervous system, and merged previous data including unpublished data to enhance statistical power. New subjects consisted of 23 male exposed subjects and 13 referent subjects matched for age and working types. Neurobehavioral tests for psychomotor function and memory, stabilometry, and Benton visual retention test were performed. As reported previously, the exposed group performed significantly less well in the psychomotor function test (tapping) than the referent group (117.8 +/- 1.2 vs. 105.6 +/- 1.2 msec). Using merged data, this phenomenon was also observed in a dose-dependent manner and the exposed group performed significantly less well in the backward digit span test (4.47 +/- 1.17 vs. 5.11 +/- 1.65 digits). These results indicate that chronic decline of psychomotor function and memory function still exist 7 yr after the sarin exposure.

Monleau M, Bussy C, Lestaevel P, Houpert P, Paquet F, Chazel V (2005) Bioaccumulation and behavioural effects of depleted uranium in rats exposed to repeated inhalations. Neurosci Lett 390:31-36. (French Government, Institute of Radioprotection and Nuclear Safety)
Abstract: Depleted uranium has numerous industrial and military uses. Contamination by inhalation of airborne compounds is probably the most important route of exposure. In humans, there are no data clearly demonstrating neurotoxicity of uranium, yet some experimental studies suggest a link between neurological toxicity and uranium exposure. In this work, the bioaccumulation of uranium in male rats after exposure to repeated depleted uranium dioxide inhalation (30 min inhalation at 197 mgm^{-3}, 4 days a week for 3 weeks) has been studied, together with the behavioral effects. The uranium concentrations in the brain 1 day after the end of the exposure period varied as follows: olfactory bulb>hippocampus>frontal cortex>cerebellum, subsequently decreasing rapidly. The spontaneous locomotion activity of exposed rats was increased 1 day post exposure and the spatial working memory was less efficient 6 days post exposure, compared with control rats. These data suggest that depleted uranium is able to enter the brain after exposure to repeated inhalation, producing behavioral changes.

Monleau M, De MM, Paquet F, Chazel V, Dumenil G, Donnadieu-Claraz M (2006) Genotoxic and inflammatory effects of depleted uranium particles inhaled by rats. Toxicol Sci 89:287-295 (EPub ahead of print, October 2005). (French Government, Institute of Radioprotection and Nuclear Safety)

Depleted uranium (DU) is a radioactive heavy metal coming from the nuclear industry and used in numerous military applications. Uranium inhalation can lead to the development of fibrosis and neoplasia in the lungs. As little is known concerning the molecular processes leading to these pathological effects, some of the events in terms of genotoxicity and inflammation were investigated in rats exposed to DU by inhalation. Our results show that exposure to DU by inhalation resulted in DNA strand breaks in broncho-alveolar lavage (BAL) cells and in increase of inflammatory cytokine expression and production of hydroperoxides in lung tissue suggesting that the DNA damage was in part a consequence of the inflammatory processes and oxidative stress. The effects seemed to be linked to the doses, were independent of the solubility of uranium compounds and correlating with the type of inhalation. Repeated inhalations seemed to induce an effect of potentiation in BAL cells and also in kidney cells. Comet assay in neutral conditions revealed that DNA damage in BAL cells was composed partly by double strands breaks suggesting that radiation could contribute to DU genotoxic effects in vivo. All these in vivo results contribute to a better understanding of the pathological effect of DU inhalation.

Noyes R, Jr., Watson DB, Letuchy EM, Longley SL, Black DW, Carney CP, Doebbeling BN (2005) Relationship between hypochondriacal concerns and personality dimensions and traits in a military population. J Nerv Ment Dis 193:110-118. (DoD-058 and HHS-001)

Abstract: Our aim was to examine the relationship between personality dimensions and hypochondriacal concerns and somatic symptoms in a military population. The Schedule of Nonadaptive and Adaptive Personality along with measures of hypochondriacal concerns and somatic symptoms were administered to 602 military veterans who had been on active duty during the 1991 Gulf War. Factor analyses identified six separable dimensions-two of hypochondriacal concerns, two of somatic symptoms, and two of possible mechanisms of symptom generation-for study. Multiple regression models determined the proportion of variation in these measures of somatic distress explained by personality scales. Personality measures explained between 26% and 38% of the variance in hypochondriacal concerns and somatic symptoms, and Negative Temperament accounted for most of this. Moderately strong positive correlations were observed between trait scales Mistrust, Low Self-Esteem, and Eccentric Perceptions and the various measures of somatic distress. Thus, when Negative Temperament was taken into account, few significant correlations between personality measures and hypochondriacal concerns or somatic symptoms remained. Negative temperament or neuroticism is strongly associated with hypochondriacal concerns. Important features of hypochondriasis and somatic distress appear to lie within the domain of personality. It remains for future research to show whether negative temperament is a vulnerability factor for hypochondriasis or hypochondriasis is itself a personality disorder.

Page WF, Mahan CM, Bullman TA, Kang HK (2005a) Health Effects in Army Gulf War Veterans Possibly Exposed to Chemical Munitions Destruction at Khamisiyah, Iraq: Part I. Morbidity Associated with Potential Exposure. Mil Med 170:935-944. (DoD-069)

Abstract: In March 1991, U.S. troops detonated the Khamisiyah, Iraq, ammunition depot, possibly releasing two chemical warfare agents, sarin and cyclosarin. The long-term health effects associated with possible exposure to these chemical warfare agents are unknown. This study was undertaken to investigate whether possible exposure was associated with morbidity among Army Gulf War veterans using morbidity data for 5,555 Army veterans who were deployed to the Gulf region. Responses to 86 self-assessed health measures, as reported in the 1995 Department of Veterans Affairs National Health Survey of Gulf War Era Veterans, were evaluated. We found little association between potential exposure and health, after adjustment for demographic variables, and conclude that potential exposure to sarin or cyclosarin at Khamisiyah does not seem to have adversely affected self-perceived health status, as evidenced by a wide range of health measures.

Page WF, Mahan CM, Kang HK, Bullman TA (2005b) Health Effects in Army Gulf War Veterans Possibly Exposed to Chemical Munitions Destruction at Khamisiyah, Iraq: Part II. Morbidity Associated with Notification of Potential Exposure. Mil Med 170:945-951. (DoD-069)
Abstract: The purpose of this study was to examine the association of notification of potential exposure to chemical warfare agents in the 1991 Gulf War with subsequent self-reported morbidity. The study sample included 1,056 deployed Army Gulf War veterans who responded to the 1995 National Health Survey of Gulf War Era Veterans and who were resurveyed in 2000. One-half of the subjects had been notified of potential exposure to chemical warfare agents and one-half had not. Comparing notified and non-notified subjects, there were no statistically significant differences with respect to bed days, activity limitations, clinic visits, or hospital visits. Among 71 self-reported medical conditions and symptoms, there were 5 statistically significant differences, 4 of which were for lower rates of illness among notified subjects. Our findings contradict the prevailing notion that perceived exposure to chemical warfare agents should be considered an important cause of morbidity among Gulf War veterans.

Pierce PF (2005) Monitoring the health of Persian Gulf War veteran women. Federal Nursing Service Award. Mil Med 170:349-354. (DoD-045)
The Persian Gulf War imposed unique threats and stressors on our military forces. Mobilization included an unprecedented number of women, with more than 33,000 U.S. military women serving in key combat positions throughout the region. Despite their increasing numbers, little is known about the general health effects of combat exposure on women's long-term health. Objective: The aim of the study was to assess whether the prevalence of health problems remained elevated among women deployed to th4 Gulf at 6 years after deployment. Methods: This comprehensive self-report survey compared the prevalence of physical health problems among 900 Air Force women deployed to the Gulf and 900 Air Force women deployed elsewhere. Results: Findings indicate that significant health problems among women deployed to the theater have persisted for an extended period and the prevalence remains statistically different from that among women deployed elsewhere during the same period of time. Conclusions: Long-term health surveillance is critical for monitoring the health and well-being of our nation's military members. Ultimately, through this program of research, we hope to be able to determine whether there are preventable risks to women that are associated with specific military duties, deployment, occupational exposures, or combinations of these factors.

Proctor S, Gopal S, Imai A, Wolfe J, Ozonoff D, White R (2005) Spatial Analysis of 1991 Gulf War Troop Locations in Relationship with Postwar Health Symptom Reports Using GIS Techniques. Transactions in GIS 9:381-396. (VA-004)
Abstract: Spatial autocorrelation analysis was used to identify spatial patterns of 1991 Gulf War (GW) troop locations in relationship to subsequent postwar diagnosis of chronic multisymptom illness (CMI). Criteria for the diagnosis of CMI include reporting from at least two of three symptom clusters: fatigue, musculoskeletal pain, and mood and cognition. A GIS-based methodology was used to examine associations between potential hazardous exposures or deployment situations and postwar health outcomes using troop location data as a surrogate. GW veterans from the Devens Cohort Study were queried about specific symptoms approximately four years after the 1991 deployment to the Persian Gulf. Global and local statistics were calculated using the Moran's *I* and G statistics for six selected date periods chosen *a priori* to mark important GW-service events or exposure scenarios among 173 members of the cohort. Global Moran's *I* statistics did not detect global spatial patterns at any of the six specified data periods, thus, indicating there is no significant spatial autocorrelation of locations over the entire Gulf region for veterans meeting criteria for severe postwar CMI. However, when applying local G* and local Moran's *I* statistics, significant spatial clusters (primarily in the coastal Dammam/Dharhan and the central inland areas of Saudi Arabia) were identified for several of the selected time periods. Further study using GIS techniques, coupled with epidemiological methods, to examine spatial and temporal patterns with larger sample sizes of GW veterans is warranted to ascertain if the observed spatial patterns can be confirmed.

Quistad GB, Klintenberg R, Casida JE (2005) Blood acylpeptide hydrolase activity is a sensitive marker for exposure to some organophosphate toxicants. Toxicol Sci 86:291-299.
Abstract: Acylpeptide hydrolase (APH) unblocks N-acetyl peptides. It is a major serine hydrolase in rat blood, brain, and liver detected by derivatization with ^{3}H-diisopropyl fluorophosphate (DFP) or a biotinylated fluorophosphonate. Although APH does not appear to be a primary target of acute poisoning

by organophosphorus (OP) compounds, the inhibitor specificity of this secondary target is largely unknown. This study fills the gap and emphasizes blood APH as a potential marker of OP exposure. The most potent in vitro inhibitors for human erythrocyte and mouse brain APH are DFP (IC_{50} 11-17 nM), chlorpyrifos oxon (IC_{50} 21-71 nM), dichlorvos (IC_{50} 230-560 nM), naled (IC_{50} 370-870 nM), and their analogs with modified alkyl substituents. ^{3}H-diisopropyl fluorophosphate is a potent inhibitor of mouse blood and brain APH in vivo (ED_{50} 0.09-0.2 mg/kg and 0.02-0.03 mg/l for ip and vapor exposure, respectively). Mouse blood and brain APH and blood butyrylcholinesterase (BChE) are of similar sensitivity to DFP in vitro and in vivo (ip and vapor exposure), but APH inhibition is much more persistent in vivo (still >80% inhibition after 4 days). The inhibitory potency of OP pesticides in vivo in mice varies from APH selective (dichlorvos, naled, and trichlorfon), to APH and BChE selective (profenofos and tribufos), to ChE selective or nonselective (many commercial insecticides). Sarin administered ip at a lethal dose to guinea pigs inhibits blood acetylcholinesterase and BChE completely but erythrocyte APH only partially. Blood APH activity is therefore a sensitive marker for exposure to some but not all OP pesticides and chemical warfare agents.

Ranjith G (2005) Epidemiology of chronic fatigue syndrome. Occup Med (Lond) 55:13-19.
Abstract: BACKGROUND: Chronic fatigue syndrome (CFS) is a controversial disorder with different case definitions, aetiological models and proposed treatments. An epidemiological approach is likely to bring some clarity to the field. AIM: The aim of this article is to review the literature on the epidemiology of fatigue, chronic fatigue and CFS. METHOD: A literature search was conducted using the databases Medline and PubMed as well as the reference lists of recent reviews to identify the relevant studies. The aim was not to do a systematic review but to review the key studies in the area to highlight the methodological issues. RESULTS: The review is organized according to the following areas: the prevalence of fatigue and chronic fatigue, the prevalence and incidence of CFS, epidemiological associations such as gender, social class and psychiatric co-morbidity and CFS in special groups such as those recovering from a viral infection, specific occupational groups and Gulf War veterans. CONCLUSION: While fatigue as a symptom is very common, CFS is relatively rare. Many of the epidemiological associations seen in specialist clinics are not found in community samples. It is unlikely that one specific causal factor can explain CFS. Future studies should go beyond estimating the prevalence to testing more complex etiological models.

Rijpkema SG, Adams T, Rigsby P, Xing DK, Corbel MJ (2005) Investigation in a Model System of the Effects of Combinations of Anthrax and Pertussis Vaccines Administered to Service Personnel in the 1991Gulf War. Human vaccines 1:165-169. (UK Ministry of Defence)
Abstract: The toxicity and immunogenicity of the anthrax and pertussis vaccine combinations used in the 1991 Gulf War was assessed in NIH, A/J and Balb/c mice. Inoculation of pertussis vaccines, vaccine combinations, or aluminium salt caused illness, splenomegaly and significant weight loss. Although some animals recovered eventually, a lethal form of ascites developed in some NIH mice and body weights of A/J and Balb/c mice remained below normal levels. Inoculation of anthrax vaccine produced little effect. Exposure to diluted vaccine combinations produced less serious side effects of shorter duration. Single vaccinations induced specific IgG1 antibodies whereas a mixture of IgG1 and IgG2a was produced after multiple injections. Antigen stimulation of spleen cells from mice exposed to pertussis vaccines induced high levels of NO and IL-6, whereas stimulated spleen cells from mice exposed to anthrax vaccine produced only low levels of IL-6. In mice, pertussis vaccines act as an adjuvant for anthrax vaccine, but these vaccines are also the major cause of toxicity of the vaccine combination. The relatively high vaccine dose used, together with the low sensitivity of mice to anthrax toxin, emphasizes that caution should be exercised in applying these results to human recipients of these vaccines.

Rose RL, Hodgson E (2005) Pesticide metabolism and potential for metabolic interactions. J Biochem Mol Toxicol 19:276-277. (DoD-103)
Organophosphate insecticides are one of the predominant pesticide classes that have seen decades of use. Most organophosphates are like chlorpyrifos, in that they require metabolic activation for their toxic effects. Similarly, metabolism is responsible for the degradation and subsequent elimination from the body. Humans are less efficient than rats and mice in the production of both the active metabolite as well as the primary detoxification product. The mechanisms and pathways of chlorpyrifos activation and

degradation were examined using human liver microsomes. Metabolism of chlorpyrifos involves specific isoforms of cytochrome P450 and this metabolism was found to inhibit the metabolism of testosterone.

Rose RL, Tang J, Choi J, Cao Y, Usmani A, Cherrington N, Hodgson E (2005) Pesticide metabolism in humans, including polymorphisms. Scand J Work Environ Health 31 Suppl 1:156-163. (DoD-103)
Abstract: Recent epidemiologic studies involving Gulf War veterans or agricultural workers suggest that pesticide-pesticide or pesticide-drug interactions may be related to Gulf-War-related illnesses or elevated cancer risks, respectively. Metabolic interactions are one of many potential mechanisms requiring exploration in humans. The goal of the studies is to characterize important metabolic profiles of selected pesticides and examine potential interactions to characterize human risks associated with exposure. Pesticides examined using human liver microsomes and cytosolic fractions included chlorpyrifos, carbaryl and permethrin. The metabolic pathways involved include cytochrome P450 monooxygenases (CYP), esterases, and alcohol and aldehyde dehydrogenases. Specific isoforms and some polymorphic enzymes were characterized. Pesticide-pesticide interactions with metabolizing enzymes were demonstrated. Exposure of human hepatocytes to chlorpyrifos and permethrin demonstrated their potential to induce CYP isoforms using the branched deoxyribonucleic acid assay normally used to monitor messenger ribonucleic acid levels. These studies suggest that knowledge of human metabolic pathways will provide information that can aid the risk assessment process.

Schnurr PP, Friedman MJ, Engel CC, Foa EB, Shea MT, Resick PM, James KE, Chow BK (2005) Issues in the design of multisite clinical trials of psychotherapy: VA Cooperative Study No. 494 as an example. Contemp Clin Trials 26:626-636. (DoD-125 / VA-074)
This article describes issues in the design of an ongoing multisite randomized clinical trial of psychotherapy for treating posttraumatic stress disorder (PTSD) in female veterans and active duty personnel. Research aimed at testing treatments for PTSD in women who have served in the military is especially important due to the high prevalence of PTSD in this population. VA Cooperative Study 494 was designed to enroll 384 participants across 12 sites. Participants are randomly assigned to receive 10 weekly sessions of individual psychotherapy: Prolonged Exposure, a specific cognitive-behavioral therapy protocol for PTSD, or present-centered therapy, a comparison treatment that addresses current interpersonal problems but avoids a trauma focus. PTSD is the primary outcome. Additional outcomes are comorbid problems such as depression and anxiety; psychosocial function and quality of life; physical health status; satisfaction with treatment; and service utilization. Follow-up assessments are conducted at the end of treatment and then 3 and 6 months after treatment. Both treatments are delivered according to a manual. Videotapes of therapy sessions are viewed by experts who provide feedback to therapists throughout the trial to ensure adherence to the treatment manual. Discussion includes issues encountered in multisite psychotherapy trials along with the rationale for our decisions about how we addressed these issues in CSP #494.

Schumm WR, Jurich AP, Bollman SR (2005) The long term safety of anthrax vaccine, pyridostigmine bromide (PB) tablets, and other risk factors among Reserve Component Veterans of the First Persian Gulf War. Medical Vertas 2:348-362.
Abstract: Data from several hundred Reserve Component Persian Gulf War veterans were analyzed to assess associations between the symptoms of Gulf War illness, as defined by both the CDC and Kansas classifications, and a variety of potential risk factors. The most significant risk factors, in order of importance for their possible contributions to Gulf War illness were perceived exposure to nerve agent, ciprofloxacin pills, gum problems, insect repellant, anthrax vaccination, use of personal insecticide, reported reactions to vaccines, and botulim toxoid vaccine. Of those, PB tablets, gum problems, insect repellants, insecticide use, and anthrax vaccination were more significant statistically when veterans reported that they had experienced reactions to vaccines. Insect repellant and insecticide remained significantly related to Gulf War illness among veterans who remained in the United States during the war; among those non-deployed veterans, anthrax vaccine was associated with Gulf War illness (10% versus 4% for those with or without anthrax vaccine), but the relationship was not statistically significant if those who were "not sure" about their vaccination were removed from the analysis. For anthrax vaccine, Gulf War veterans needed only to report a "mild reaction" to maintain a significant relationship with Gulf War illness under the reaction condition. Anthrax vaccine seemed to be more reactive than other vaccines, especially for female veterans. A dose-response relationship was observed for PB tablets. Recall bias was reduced in

several ways but may not have been eliminated. It is recommended that PB tablets, ciprofloxacin pills, as well as insect repellants and insecticides be used with caution, especially not exceeding recommended daily amounts. Anthrax vaccine should be administered on a voluntary basis only, given the long-term safety risks observed here, especially for those who experience even mild reactions.

Scremin OU, Shih TM, Huynh L, Roch M, Sun W, Chialvo DR, Jenden DJ (2005) Low-dose cholinesterase inhibitors do not induce delayed effects on cerebral blood flow and metabolism. Pharmacol Biochem Behav 80:529-540. (DoD-113)

Abstract: The acetylcholinesterase (AChE) inhibitors sarin and pyridostigmine bromide (PB) have been proposed as causes of neurobehavioral dysfunction in Persian Gulf War veterans. To test possible delayed effects of these agents, we exposed rats to low (subsymptomatic) levels of sarin (0.5 LD50 s.c. 3 times weekly) and/or PB (80 mg/L in drinking water) for 3 weeks. Controls received saline s.c. and tap water. At 2, 4 and 16 weeks after exposure, regional cerebral blood flow (rCBF) and glucose utilization (rCGU) were measured in conscious animals with the Iodo-14C-antipyrine and 14C-2 deoxyglucose methods, respectively. Two weeks after exposure, PB+sarin caused significant rCBF elevations, but no changes in rCGU, in neocortex, with lesser effects on allocortex. Four weeks after exposure, the same general pattern was found with sarin. Only a few changes were found at 16 weeks post-treatment. The predominant effects of sarin or PB+sarin on rCBF at earlier times after treatment are consistent with the well known direct cerebral vascular effect of cholinergic agonists. The lack of changes in rCBF and rCGU observed at 16 weeks after treatment does not support the hypothesis that repeat exposure to low-dose cholinesterase inhibitors can generate permanent alterations in cerebral activity.

Servatius RJ, Beck KD (2005) Mild interoceptive stressors affect learning and reactivity to contextual cues: toward understanding the development of unexplained illnesses. Neuropsychopharmacology 30:1483-1491. (VA-106)

Abstract: Contextual learning is evident with repeated experiences with agents and treatments that induce frank illness and interoceptive stress. Here, we examined whether acute treatment with mild interoceptive stressors (low doses of pyridostigmine bromide (PB), neostigmine bromide (NB), and interleukin (IL-1β) may serve as unconditional stimuli supporting contextual learning. Rats were exposed to interoceptive and exteroceptive stressors in contexts distinguished by visual or olfactory cues. Acoustic startle responses (ASRs) were measured the day following exposure and 2 weeks thereafter, without delivery of the unconditional stimuli. The appearance, form, and duration of startle potentiation depended on the distinguishing features of the context and the nature of the interoceptive stressor. Rats given cholinesterase inhibitors (PB and NB), but not IL-1beta or exposed to an exteroceptive stressor, exhibited exaggerated ASRs in a novel context distinguished by visual cues. Treatment with either PB or IL-1β led to potentiated ASRs in the presence of odors congruent with those experiences during exposure to the stressor. Startle potentiation by odor was still apparent 2 weeks after treatment. For contexts differentiated by visual stimuli, cholinomimetics transiently alter reactivity within novel contexts. In the case of contexts differentiated by odors, learning is apparent at least 2 weeks after acute treatment of cholinomimetics and IL-1β. Contextual learning and changes in reactivity consequent to mild interoceptive stressors such as PB may play a role in the development of nonspecific symptoms typical of unexplained illnesses, such as Gulf War Illness.

Shipherd JC, Stafford J, Tanner LR (2005) Predicting alcohol and drug abuse in Persian Gulf War veterans: what role do PTSD symptoms play? Addict Behav 30:595-599. (DoD-052 and VA National Center for PTSD)

Abstract: This study is a prospective longitudinal examination of symptoms of drug and alcohol use (SUD) and PTSD symptoms in 1006 veterans in the 6 years (T3) following return from the Persian Gulf War (PGW). Both alcohol and drug use at T3 were significantly correlated with demographic variables and all three types of PTSD symptoms (re-experiencing, avoidance, and arousal) as measured at T2. Hierarchical regressions were conducted to examine the self-medication hypothesis, which was supported for drug use but not for alcohol use at T3.

Skowera A, de Jong EC, Schuitemaker JH, Allen JS, Wessely SC, Griffiths G, Kapsenberg M, Peakman M (2005) Analysis of anthrax and plague biowarfare vaccine interactions with human monocyte-derived dendritic cells. J Immunol 175:7235-7243. (DoD-151)

Abstract: The anti-biowarfare anthrax and plague vaccines require repeated dosing to achieve adequate protection. To test the hypothesis that this limited immunogenicity results from the nature of vaccine interactions with the host innate immune system, we investigated molecular and cellular interactions between vaccines, dendritic cells (DCs), and T cells and explored the potential for adjuvants (pertussis) to boost induction of host immunity. Human monocyte-derived DCs were matured in the presence of vaccines and analyzed for their ability to induce Th1/Th2 development from naive T cells, expression of cell surface maturation/co-stimulation molecules, and cytokine production. The vaccines showed different behavior patterns. Although the plague vaccine is equivalent to control maturation factors in maturation and stimulation of DCs and induces strong MLR and Th outgrowth, the anthrax vaccine is a poor inducer of DC maturation, as indicated by low levels of HLA-DR, CD86, and CD83 induction and minimal proinflammatory cytokine production. Interestingly, however, anthrax vaccine-treated DCs stimulate Th1 and Th2 outgrowth and a limited MLR response. There were no sustained negative modulatory effects of the anthrax vaccine on DCs, and its limited stimulatory effects could be overridden by coculture with pertussis. These results were supported by analysis of anthrax vaccine recall responses in subjects vaccinated using pertussis as an adjuvant and who demonstrate anthrax-specific effector T cell responses. These data show that the anthrax vaccine is a suboptimal DC stimulus that may in part explain the observation that it requires repeated administration in vivo and offer a rational basis for the use of complementary DC-maturing adjuvants in combined immunotherapy.

Squibb KS, Leggett RW, McDiarmid MA (2005) Prediction of renal concentrations of depleted uranium and radiation dose in Gulf War veterans with embedded shrapnel. Health Phys 89:267-273. (VA)

Abstract: Mobilization of uranium (U) from embedded depleted uranium (DU) metal fragments in Gulf War veterans presents a unique exposure scenario for this radioactive and nephrotoxic metal. In a cohort of exposed veterans, urine U concentrations measured every two years since 1993 persistently range from 10 to over 500 times normal levels, indicating that embedded DU fragments give rise to chronic, systemic exposure to U. Health effects of this exposure are not fully known, but clinical surveillance of these soldiers continues in light of animal studies showing that U released from implanted DU pellets results in tissue accumulation of U. The biokinetic model for uranium recommended by the International Commission on Radiological Protection was used to predict kidney U concentrations and tissue radiation doses in veterans with DU shrapnel based on their urine U excretion. Results suggest that kidney U concentrations in some individuals reached their peak within six years after the war; in others, concentrations continue to increase and are approaching 1 ppm after 10 y. These results are consistent with urine biomarker tests of renal proximal tubular cell function and cytotoxicity which have shown elevated mean urinary protein excretion indicative of functional effects in veterans with high urine U concentrations (> or =0.10 $\mu g\ g^{-1}$ creatinine). Predicted lifetime effective radiation dose from DU released to the blood for the highest exposed individual in this cohort was substantially less than the National Council on Radiation Protection (NCRP) limit for occupational exposure. These results provide further support for current health protection guidelines for DU, which are based on the metal's chemical rather than its radiological toxicity. In light of the potential for continued accumulation of U in the kidney to concentrations approaching the traditional guidance level of 3 ppm U, these results indicate the need for continued surveillance of this population for evidence of developing renal dysfunction.

Stein AL, Tran GQ, Lund LM, Haji U, Dashevsky BA, Baker DG (2005) Correlates for posttraumatic stress disorder in Gulf War veterans: a retrospective study of main and moderating effects. J Anxiety Disord 19:861-876. (VA-059)

Abstract: With a sample of 120 Gulf War veterans, the present study investigated the main effects of childhood and lifetime trauma, combat exposure, and coping strategies on posttraumatic stress disorder (PTSD), as well as combat exposure's moderating effects on the other variables' relationships with PTSD. Logistic regression results indicated correct classification of PTSD diagnosis for 88% of the participants, with combat exposure and avoidant coping making significant contributions to this classification. Multiple regression results indicated that lifetime trauma, combat exposure, and avoidant coping were strongly related to PTSD symptoms. Multiple regression results also revealed that combat exposure moderated the

strength and direction of PTSD's relationships with childhood trauma and avoidant coping. Study findings have implications for longitudinal investigation of PTSD development and preventive interventions.

Taysse L, Christin D, Delamanche S, Bellier B, Breton P (2005) Peripheral ChE inhibition modulates brain monoamines levels and c-fos oncogene in mice subjected to a stress situation. Neurochem Res 30:391-402.
Abstract: The present study examined, in mice, whether regional patterns of brain dopamine (DA) and serotonin (5-HT) concentrations (and their metabolites) and expression of c-Fos protein, that may represent a prolonged functional change in neurons, could be changed after a combined exposure to stress and the peripheral cholinesterase reversible inhibitor pyridostigmine (PYR). Animals were subjected every day to a random combination of mild inescapable electric foot shocks and immobilization over a 12-day period, resulting in a significant increase of glucocorticoids levels and an activation of c-fos in hippocampus, thalamus and piriform cortex. This stress protocol induced a significant increase of 5-HT levels in striatum, hippocampus and ponto mesencephalic area (PMA) but failed to induce any DA activation. When PYR (0.2 mg/kg s.c. inducing 19-35% inhibition of the plasmatic ChE activity) was administered twice a day during the last 5 days of the stress session, 5-HIAA levels and expression of c-fos oncogene were significantly increased in the most of the brain areas studied. DA levels were also enhanced in striatum/hippocampus as a result of a possible activation of mesolimbic and nigrostriatal dopamine systems. Taken together, these results suggest that a combined exposure to certain stress conditions and PYR leads, in mice, to functional changes in neurons and may affect centrally controlled functions. The mechanisms underlying these modifications and their behavioral implications remain to be further investigated.

Vogt DS, Pless AP, King LA, King DW (2005) Deployment stressors, gender, and mental health outcomes among Gulf War I veterans. J Trauma Stress 18:115-127. (DoD-087)
Abstract: Findings indicate that war-zone exposure has negative implications for the postdeployment adjustment of veterans; however, most studies have relied on limited conceptualizations of war-zone exposure and focused on male samples. In this study, an array of deployment stressors that were content valid for both female and male Gulf War I military personnel was examined to elucidate gender differences in war-zone exposure and identify gender-based differential associations between stressors and mental health outcomes. While women and men were exposed to both mission-related and interpersonal stressors and both stressor categories were associated with mental health outcomes, women reported more interpersonal stressors and these stressors generally had a stronger impact on women's than on men's mental health. Exceptions are described, and implications are discussed.

Vythilingam M, Luckenbaugh DA, Lam T, Morgan CA, III, Lipschitz D, Charney DS, Bremner JD, Southwick SM (2005) Smaller head of the hippocampus in Gulf War-related posttraumatic stress disorder. Psychiatry Res 139:89-99. (DoD-040)
Abstract: Reductions in hippocampal volume and impairment in short-term verbal memory have been reported in Vietnam combat veterans with posttraumatic stress disorder (PTSD) and in women with abuse-related PTSD. The present investigation evaluated hippocampal volume and memory in Gulf War veterans. This research is timely given the ongoing war in Iraq and the anticipated high rates of PTSD among returning combat soldiers. Fourteen veterans with PTSD related to traumatic experiences during the Gulf War (1990-1991), 23 deployed veterans without PTSD, 22 non-deployed reservists and 29 healthy civilians were studied. Volumes of the hippocampus, temporal lobe, and whole brain were measured on coronal MRI scans, and hippocampal mediated memory function was evaluated. The head of the hippocampus was the only subregion that was significantly smaller in Gulf War veterans with PTSD than in healthy civilians. Deployed veterans with PTSD, deployed veterans without PTSD, and non-deployed reservists had significantly smaller whole hippocampal volume and lower scores on immediate and delayed verbal and visual retrieval compared with healthy civilians.

Wang D, Perides G, Liu YF (2005) Vaccination alone or in combination with pyridostigmine promotes and prolongs activation of stress-activated kinases induced by stress in the mouse brain. J Neurochem 93:1010-1020. (DoD-139)
Abstract: Gulf war illnesses (GWI) are currently affecting thousands of veterans. To date, the molecular mechanisms underlying the pathogenesis of these illnesses remain unknown. During Gulf war I, military personnel were exposed to multiple stressors, one or more vaccines, pyridostigmine (PY), and other

chemicals. In our previous studies, we found that stress induces activation of mitogen activated protein-kinase kinase 4 (MKK4) and c-Jun-N-terminal kinase (JNK) in the mouse brain (Liu et al. 2004). Our working hypothesis is that stress, vaccination, and PY may synergistically induce activation of MKK4 and JNK in the brain, leading to over-activation of these kinases and neurological injuries. To test our hypothesis, we examined the effect of keyhole limpet hemocyanin (KLH) immunization alone or in combination with PY on activation of MKK4 and JNK induced by stress. We found that KLH immunization alone had a small effect on MKK4 or JNK activity but it significantly enhanced and prolonged activation of these kinases induced by stress, from a few hours to several days. Additionally, KLH immunization caused activation of p38MAPK. PY treatment further enhanced and prolonged activation of these kinases induced by stress in combination with KLH immunization and triggered activation of caspase-3. Our current studies suggest that stress, vaccination, and PY may synergistically act on multiple stress-activated kinases in the brain to cause neurological impairments in GWI.

Weisskopf MG, O'Reilly EJ, McCullough ML, Calle EE, Thun MJ, Cudkowicz M, Ascherio A (2005) Prospective study of military service and mortality from ALS. Neurology 64:32-37. (American Cancer Society)
Abstract: BACKGROUND: Two recent studies suggest that the risk of ALS is increased among Gulf War veterans. It is not known whether military service outside of the Gulf War is associated with increased risk of ALS. METHODS: The authors prospectively assessed the relationship between service in the military and ALS mortality among participants in the Cancer Prevention Study II cohort of the American Cancer Society, a cohort that includes over 500,000 men from the 50 states, Washington, DC, and Puerto Rico. Participant follow-up was conducted from 1989 through 1998 for ALS mortality. There were a total of 280 deaths from ALS among 126,414 men who did not serve in the military and 281,874 who did. Adjusted relative risks (RRs) were calculated using Mantel-Haenszel weights and Cox proportional hazards. RESULTS: Men who served in the military had an increased death rate from ALS (RR = 1.53; 95% CI: 1.12 to 2.09; p = 0.007) compared with those who did not serve. The increase in ALS mortality was observed among men who served in the Army or National Guard (RR = 1.54), Navy (RR = 1.87), Air Force (RR = 1.54), and Coast Guard (RR = 2.24); no increase in risk was found in men who served in the Marine Corps, although there were only 13,670 men in this group. The risk of ALS among men who served was elevated in every 5-year birth cohort from 1915 through 1939. CONCLUSIONS: Military personnel have an increased risk of ALS. This increase appeared to be largely independent of the branch of service and the time period served.

Werler MM, Sheehan JE, Mitchell AA (2005) Gulf War veterans and hemifacial microsomia. Birth Defects Res A Clin Mol Teratol 73:50-52. (National Institute of Dental and Craniofacial Research)
Abstract: BACKGROUND: Concerns have been raised that more infants with Goldenhar syndrome were born to U.S. Gulf War veterans than expected. Goldenhar syndrome is considered a variant of the malformation hemifacial microsomia (HFM). We used data collected from a case-control study of HFM to estimate risk in relation to parental military service and, in particular, Gulf War service. METHODS: Cases with HFM who were three years old or younger were identified at craniofacial clinics in 24 U.S. cities and matched to controls by age and pediatrician. The mothers of 232 cases and 832 controls were interviewed between April 1996 and November 2002 about pregnancy events and exposures, including military service before the child was born and Gulf War deployment five to 11 years before the child was born. Odds ratios were adjusted for family income, race, and body mass index in early pregnancy. RESULTS: Four (1.7%) case mothers and 10 (1.2%) control mothers served in the military. Among fathers, 30 (12.9%) cases and 100 (12.0%) controls served in the military. The parents of four (1.7%) cases and 23 (2.8%) controls served in the Gulf War (multivariate adjusted odds ratio [MVOR], 0.8; 95% confidence interval [CI], 0.3-2.3). All four case parents with Gulf War service were in the Army compared to 9 of 23 control parents. The MVOR for parental Gulf War service in the Army was 2.8 (95% CI, 0.8-9.6). The corresponding MVOR for any parental service in the Army was 2.4 (95% CI, 1.4-4.2), based on 22 cases and 45 controls. CONCLUSIONS: The risk of HFM in offspring was not associated with parental service in the Gulf War five to 11 years before birth. The odds ratio for service in the Army was independent of Gulf War service and was associated with a modest increase in risk. Our findings for service in the Army may be confounded by unmeasured lifestyle factors.

Wicklund MP (2005) Amyotrophic lateral sclerosis: possible role of environmental influences. Neurol Clin 23:461-484.
Abstract: This treatise briefly discusses the genetic features of ALS and reviews environmental exposures in sporadic ALS. At least 10 genetic foci are responsible for cases of familial motor neuron disease and more are yet to be discovered. Research into sporadic ALS suggests that abundant factors apparently participate in the disease process. A singular cause and unifying disease and nerve dysfunction in polyneuropathies, a multitude of genetic, toxic, autoimmune, infectious, and systematic processes seem to be at play. The ALS syndrome likely will not be dissimilar.

Woodward SH, Kaloupek DG, Streeter CC, Martinez C, Schaer M, Eliez S (2005) Decreased Anterior Cingulate Volume in Combat-Related PTSD. Biol Psychiatry. (DoD-086)
Abstract: BACKGROUND: Neuroanatomical data point to functional relationships between the anterior cingulate cortex (ACC) and subcortical centers regulating fear, in particular, the amygdala. Functional brain imaging has disclosed divergent patterns of ACC activation in persons with posttraumatic stress disorder (PTSD). In addition, two preliminary structural imaging studies have found evidence of smaller ACC volume in PTSD. We explored associations between PTSD and ACC volumes in a relatively large sample of adult combat veterans in which PTSD, lifetime alcohol abuse/dependence, and Vietnam versus Gulf War service were crossed. METHODS: Subjects were US military combat veterans of the Vietnam and Gulf Wars recruited from two metropolitan areas served by allied Department of Veterans Affairs PTSD treatment/research centers. Anterior cingulate cortex volume was analyzed as a function of grouping factors with and without adjustment for body size. RESULTS: Posttraumatic stress disorder was associated with smaller anterior cingulate cortex volume. This effect persisted in subjects without histories of alcoholism, did not interact with cohort effects, and was not modified by adjustment for body size. CONCLUSIONS: Anterior cingulate cortex volume is substantially smaller in association with combat-related PTSD, a finding broadly consistent with cingulate hypofunctionality in that disorder.

IV. RESEARCH FUNDING TRENDS

The following section provides a quantitative overview of the current research portfolio on Gulf War veterans' illnesses and the evolution of the portfolio since 1996. Topics that are covered include research expenditures by VA, DoD, and HHS from FY 1996-2005, and the number of research projects in which the Federal Government has invested.

VA, DoD, and HHS sponsored a total of 300 distinct research projects on Gulf War veterans' illnesses during the period of FY 1992 through FY 2005. 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, the total number of funded projects was corrected for the number of dual funded projects. 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 was, therefore, treated as 2 distinct projects.

The numbers of new, ongoing and completed projects for FY 2000 - FY 2005 are shown in Figure IV-1. This data was compiled by reevaluation of previous Annual Reports and correcting for any projects that were listed as new when they were approved for funding but before actual funding began. The number of new and completed projects in FY2005 includes 7 ongoing VA projects identified in the 2005 VA Portfolio review and 8 VA projects closed for not meeting VA's new inclusion criteria (see Sections II and V). As of September 30, 2005, 210 projects (70% of the 300 projects) were completed, and 90 projects (30%) were new or ongoing.

The appropriated funds for FY 1996 through 2005, centrally obligated to each project, are shown in Appendix C and summarized in Table IV-1. Federal funding for Gulf War research totaled $260.6 million during this period. Funds obligated for these projects prior to FY 1996 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 1996 are listed with no associated obligation ($0) in Appendix C. Federal funds for these earlier projects were reported in prior Annual Reports to Congress.

Figure IV-1. Cumulative Number of Funded Projects (FY 2000 – FY2005)

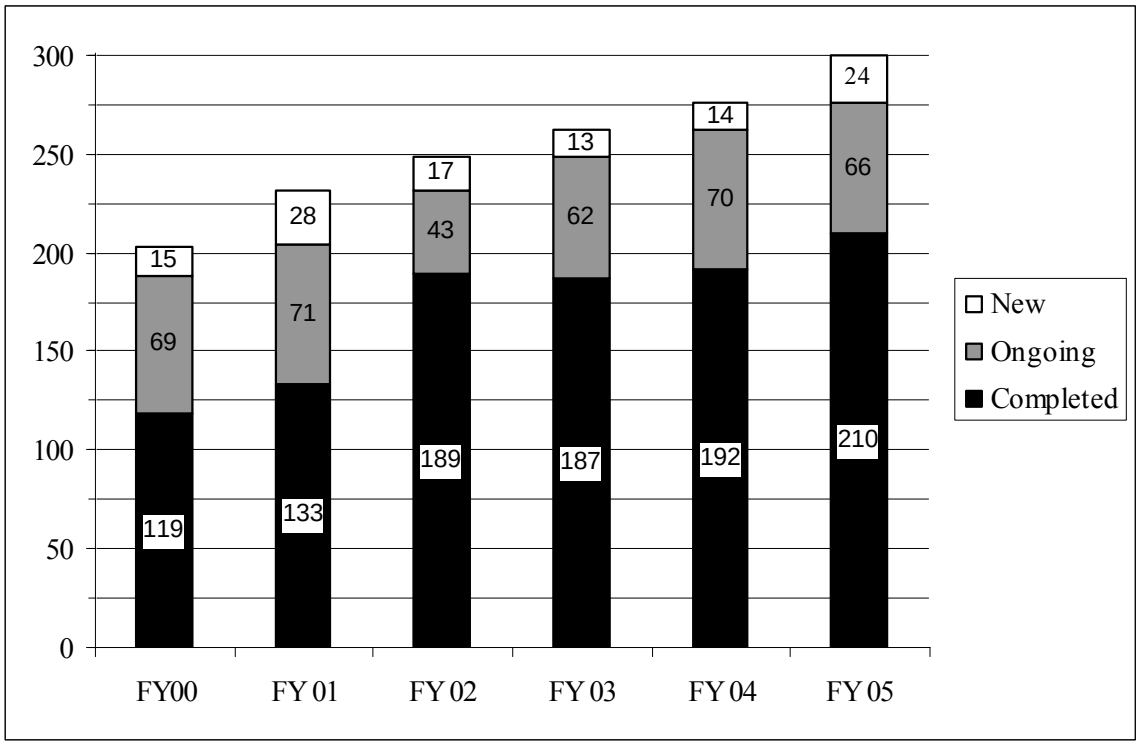

Table IV-1. 10-Year (FY'1996-2005) Funding Trends for Gulf War Research in Millions of Dollars

Department	FY'96	FY'97	FY'98	FY'99	FY'00	FY'01	FY'02	FY'03	FY'04	FY'05	Total Costs FY'96-05
DoD	$11.9	$28.9	$13.2	$22.7	$23.8	$28.8	$18.8	$12.4	$15.3	$ 6.2	**$ 182.0**
HHS	$ 1.6	$ 0.0	$ 1.6	$ 1.6	$ 1.6	$ 1.00	$ 0.8	$ 1.0	$ 0.5	$ 0.5	**$ 10.2**
VA	$ 3.9	$ 2.8	$ 4.7	$ 9.0	$12.0	$ 8.6	$ 4.5	$ 5.7	$ 7.7	$ 9.5	**$ 68.4**
Total	**$ 17.4**	**$ 31.7**	**$ 19.5**	**$ 33.3**	**$ 37.4**	**$ 38.4**	**$24.1**	**$ 19.1**	**$ 23.5**	**$16.2**	**$ 260.6**

V. NEW RESEARCH PROJECTS AND INITIATIVES

A. New Initiatives

VA Request for Applications on Gulf War Veterans Research

In April 2004, the VA Office of Research and Development issued a Request for Applications (RFA) on Gulf War Veterans Research. Forty-five proposals were received by the application deadline of June 25, 2004. These proposals were reviewed on September 14-15, 2004. Thirteen proposals (VA-106, VA-107, VA-108, VA-111, VA-115, VA-117, VA-118, VA-119, VA-124, VA-125, VA-126, VA-128, and VA-129) were selected for funding in FY 2005.

Research Enhancement Award Program (REAP) Solicitation

In March 2004 a "Solicitation for Applications for the Biomedical Laboratory Research and Development Service/Clinical Science Research and Development Service (BLRD/CSRD) Research Enhancement Award Program (REAP)" was issued. These awards are intended to support groups of VA investigators in programs of exceptional quality that address specific medical problems of veterans through fundamental, translational, and/or clinical research. Each REAP needs to focus on a medical problem of importance to the veteran population. A total of 46 proposals were submitted for review and 11 were selected for funding. Of these, two (VA-114 and VA-121) met the inclusion criteria for the VA Gulf War research portfolio; VA-121 was formerly funded as VA-065, The San Antonio Environmental Hazards Center.

B. Portfolio Review (see Section II for criteria)

As a result of an ORD-wide review of all new and ongoing funded projects, nine new proposals (VA-109, VA-110, VA-112, VA-113, VA-116, VA-120, VA-122, VA-123, and VA-127) that had been submitted through ongoing solicitations (Merit Review, Career Development, etc.) were identified as meeting the inclusion criteria and were added to the VA Gulf War research portfolio for this Report. Seven ongoing projects (VA-095, VA-097, VA-099, VA-100, VA-102, VA-103, and VA-105) that were submitted through ongoing solicitations also met the inclusion criteria; these projects were included in the FY 2004 Annual Report to Congress (DHWG, 2006). In addition, eight projects (VA-074, VA-076, VA-081, VA-084, VA-085, VA-086, VA-088, and VA-091) that were currently in the portfolio failed to meet inclusion criteria and funding for these projects will no longer be included in the Annual Reports to Congress. Ten projects (VA-065, VA-065A, VA-065B, VA-065C, VA-065D, VA-075, VA-077, VA-083, VA-087, and VA-092) were completed by the end of FY 2004 and were considered to be closed for FY 2005 in Appendix C.

C. New Projects

This section highlights the new research projects that have been approved since last year's *Annual Report to Congress*.

VA initiated funding for 24 new projects during FY05 focused on Brain and Nervous System Function (13), Environmental Toxicology (3), Immune Function and Infectious Diseases (2), and Symptoms and General Health (6).

VA-106, "Interoceptive Stressor Conditioning: A Model for Gulf War Illness," will determine if stress from pyridostigmine bromide administration occurs through muscarinic or nicotinic receptors and if signaling through the vagus nerve to the brain is necessary for the development of conditioned responses. Several physiological parameters will be measured to delineate the scope of the conditional responses (nausea, sympathetic/parasympathetic tone, and algesia/analgesia). **(Gulf War RFA**)

VA-107, "Evaluation of Stress Response Systems in Gulf War Veterans with CMI," will establish whether there are measurable physiologic abnormalities in Gulf War Veterans with Chronic Multisymptom Illness and whether these measures differentiate affected (cases) from unaffected (noncases) deployed veterans. **(Gulf War RFA**)

VA-108, "Telemedicine Treatment for Veterans with Gulf War Illness," will test a cost-effective and innovative strategy for delivering cognitive behavioral therapy (CBT), a treatment that has been developed to lessen symptom-related distress and reduce unnecessary healthcare utilization, over the telephone. The long term goal is to make specialized Telephone CBT services widely available to veterans regardless of their geographic location. **(Gulf War RFA**)

VA-109, "Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics," will provide important new information on how stress disturbs memory, drug sensitivity, electrophysiological plasticity and behavior. These experiments will provide insight into the endocrine basis of stress effects on memory and physiological plasticity. **(Portfolio Review)**

VA-110, "Pain Among Gulf War Veterans: Secondary Analysis of CSP#458 Data," will a evaluate the nature of pain with the following aims: (1) assess and compare the prevalence, anatomic distribution, and character of acute and chronic pain among deployed (DV) and non-deployed veterans (NDV); (2) examine the prevalence, distribution, character, and specificity of pain among DV and NDV; (3) assess and compare current physical functioning and quality of life of DV with pain to NDV with pain; and (4) characterize and compare current cognitive functioning of DV with pain to NDV with pain. **(Portfolio Review)**

VA-111, "T Cell Responses to Multiple Immunizations and Stress," will use a well-characterized murine system in order to step back from the clinical studies which have produced conflicting results, and ask whether the timing of multiple immunizations and/or the juxtaposition of immunization to stress result in any measurable immunologic alterations. **(Gulf War RFA**)

VA-112, "National VA Amyotrophic Lateral Sclerosis Research Consortium," proposes to build upon exciting and novel findings in the ALS mice generated at the Bedford VA and to translate these into human studies. The outcomes of the proposed aims will contribute greatly to the planning of future clinical trials using phenylbutyrate alone or in combination with uncontrolled compounds, such as riluzole, in ALS patients. **(Portfolio Review)**

VA-113, "Novel Cause of Motor Neuron Disease," will study the link between mutation in the gene for neuropathy target esterase, exposure to organophosphate compounds, and development of motor neuron disease (ALS) in animals. **(Portfolio Review)**

VA-114, "Strategies in Therapeutic Development of Neurodegenerative Diseases," is an interdisciplinary and integrated program to foster new strategies for development of treatments of neurodegenerative diseases with a focus in amyotrophic lateral sclerosis (ALS). Five pilot projects will explore the development of new model systems for evaluation of potential neuroprotectants; novel imaging methods to guide delivery of therapeutics and initial trials of cellular, anti-excitotoxic and anti-inflammatory neuroprotectants. **(REAP Solicitation)**

VA-115, "Autonomic System Changes Cause Intestinal Symptoms in Gulf War Veterans," will test the hypothesis that acute stress leading to anxiety associated with Gulf War Service produces long-term changes in the central nervous system mechanisms that regulate visceral perception. These studies will offer new insights into the mechanisms of brain-gut dysfunction that likely lead to chronic abdominal pain and may identify novel targets for new therapies directed at the brain and spinal cord to improve the treatment or even reduce the risk for the development of visceral pain in Gulf War Veterans. **(Gulf War RFA**)

VA-116, “Quantitative Trait Genes Controlling Circadian and Sleep Behaviors,” will look for genes responsible for the normal differences in circadian and sleep behaviors and then find the particular gene responsible for altering behavior. Once identified, such genes offer new insights into the molecular basis of sleep disorders. **(Portfolio Review)**

VA-117, “Estimates of Cancer Prevalence in Gulf Veterans Using State Registries,” will assess and compare the prevalence, distribution, and characteristics of cancer among 621,902 Gulf War veterans to 746,248 non-Gulf War veterans and assess demographic, military, and in-theater exposure characteristics associated with the cancer. **(Gulf War RFA**)

VA-118, “Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004,” will evaluate whether Gulf War veterans are at increased risk of overall deaths or any cause-specific death, especially deaths such as amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) or brain cancer. Study subjects will be 621,902 Gulf War veterans, who arrived in the Gulf theater prior to March 1, 1991. Comparison group veterans will consist of 746,248 veterans randomly selected from all veterans who served in the military during the period of Gulf War but did not serve in-theater. **(Gulf War RFA**)

VA-119, “Patterns of Microarray Gene Expression in Gulf War Illness,” will use exercise stress testing, and compare gene expression before and after the challenge in ill deployed Gulf War veterans, chronic fatigue syndrome ill controls, and healthy controls. Findings from this study will suggest future studies needed to identify the underlying pathophysiology of Gulf War Illness. **(Gulf War RFA**)

VA-120, “Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis,” will examine the role of nitric oxide (NO), a free radical that can be synthesized by NO synthase (NOS) from arginine, in the pathogenesis of ALS. Competition between NOS and arginase for their common substrate, arginine, may therefore directly impact the production of NO. These studies will test the hypothesis that mutant superoxide dismutase 1 (SOD1) activates caspases that cleave arginase, leading to increased NOS expression anc NO-mediated oxidative injury. **(Portfolio Review)**

VA-121, “Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders,” will use novel transgenic/knockout mouse models to identify environmental hazards, genetic deficiencies, and therapies that play a role in the etiology of neurodegenerative diseases of importance to Veterans and to use the data obtained with animal models to study potential mechanisms of neurodegeneration in human subjects. Core facilities will include an Animal Core, a Transgenic Core, a Proteomics/Oxidative Stress Core, and a Neuropathology Core. **(REAP Solicitation)**

VA-122, “Role of Mitochondrial Oxidative Stress in ALS,” will investigate the role of mitochondrial generated oxidative stress in the etiology of Amyotrophic Lateral Sclerosis (ALS) using transgenic mice expressing a mutation in the Cu-Zn-superoxide dismutase (SOD 1) gene. These experiments will determine if an increase in mitochondrial reactive oxygen species (free radicals) production and mitochondrial dysfunction precedes disease onset and whether mitochondrial oxidative stress modulates changes in oxidative damage, cell death and disease initiation/progression. **(Portfolio Review)**

VA-123, “Interactions Between Maternal Care, Stress and Pyridostigmine Bromide,” will determine the relative importance of stress reactivity and/or cholinergic responses to PB in producing the vulnerability to PB detected in rats separated from their mothers, a procedure that leads to dampened hypothalamic-pituitary-adrenal (HPA) responses to stressors in adult offspring. These experiments are aimed at determining how early life experiences can lead to vulnerabilities to mass treatment regimens in adults. Accounting for such vulnerabilities will lead to better mass treatment regimens, ultimately reducing the number of veterans developing unexplained illness after wartime service. **(Portfolio Review)**

VA-124, “Early Life Determinants of Vulnerability to Pyridostigmine Bromide,” will determine how the environmental context of pyridostigmine bromide (PB) exposure can impact developmentally determined vulnerability to persistent effects of PB. Postnatally determined vulnerability to PB can be considered a "state" which can be manipulated by environmental cues whereas postnatally determined immunity to PB can be considered a "trait" which is not altered by environmental cues. **(Gulf War RFA**)

VA-125, "Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla," will test the hypothesis that subjects with Gulf War Illness (GWI) have metabolic, structural, or functional changes in the basal ganglia (a site of proposed brain injury in GWI) and other regions of the brain, which are not accounted for by confounds such as post traumatic stress disorder (PTSD), depression, and/or alcoholism. **(Gulf War RFA**)

VA-126, "Structural Magnetic Resonance Imaging in Gulf War-Era Veterans," will examine structural brain characteristics, cognition and mood as they relate to health symptom complaints among Gulf War (GW) veterans. The proposed studies will determine whether these findings are related to deployment status or to some kind of vulnerability to physical stress, and whether cognitive and affective symptoms in GW veterans and pain patients are related to morphologic measures on MRI of white matter volume. **(Gulf War RFA**)

VA-127, "Interactions of the Leishmania sp. with Mammalian Cells," will test the hypothesis that the initial route of entry into the mammalian cell, and reactions that this entry pathway stimulates, influence the downstream survival or immune killing of the Leishmania sp. parasite and consequently the course of disease. **(Portfolio Review)**

VA-128, "MR Tracking of Stem Cells for Replacement Therapy in ALS," will investigate how transplanted stem cells can be used to restore function in a rat model of Amyotrophic Lateral Sclerosis (ALS) and how their migration and integration in vivo can be monitored. **(Gulf War RFA**)

VA-129, "Glucocorticoid Responsivity in Gulf War Veterans," is a multidimensional study, combining FDG-PET (fluorodeoxyglucose and Positron Emission Tomography) neuroimaging, neuropsychiatric evaluation and glucocorticoid challenge tests to examine the glucocorticoid responsiveness in Gulf War Veterans (GWV). In GWV, neuroendocrine alterations appear to be associated with symptoms of Gulf War Illness (GWI) independent from, and in a different direction than, their associations with PTSD, raising the possibility that GWI and PTSD act synergistically (either by enhancing each other's effects or inhibiting them). **(Gulf War RFA**)

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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 Organophosphorous 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

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	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

Appendix B

Project List by Research Focus Areas

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
Environmental Toxicology	Symptoms; Exposure;	VA-064A	Functional Neuroimaging in Lead Exposed Adults
Environmental Toxicology; Chemical Weapons	Symptoms	DoD-063	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity
Immune Function and Infectious Diseases; Symptoms and General Health	Symptoms	VA-005B	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-004A	Evaluation of Cognitive Functioning of Persian Gulf Veterans
Symptoms and General Health	Symptoms	VA-004B	Evaluation of Neurological Functioning in Persian Gulf Veterans
Symptoms and General Health	Diagnosis	VA-004F	Validity of Computerized Tests
Symptoms and General Health	Symptoms	VA-004	Boston Environmental Hazards Research Center Program
Symptoms and General Health	Symptoms	VA-005	East Orange Environmental Hazards Research Center Program

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Symptoms	VA-006A	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

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Symptoms	VA-085	Associative Learning in Veterans with and without Combat Experience
Symptoms and General Health	Treatment	VA-089	National Registry of Veterans with Amyotrophic Lateral Sclerosis
Symptoms and General Health	Symptoms	VA-093	HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans
Symptoms and General Health	Treatment	VA-112	National VA Amyotrophic Lateral Sclerosis Research Consortium
Symptoms and General Health	Diagnosis	VA-125	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla
Symptoms and General Health	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;	VA-060	Identification and Management of Sleep Disorders in Gulf War Veterans
Symptoms and General Health	Diagnosis; Symptoms;	VA-064B	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

Brain and Nervous System Function

Clinical

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Treatment; Symptoms;	VA-087	Improving Outcomes of Depression in Primary Care
Symptoms and General Health; Environmental Toxicology	Symptoms; Exposure;	VA-008	Psychological Test Data of Gulf War Veterans Over Time

Brain and Nervous System Function

Development

Research Focus	Project Focus	Project	Project Title
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	Diagnosis	VA-113	Novel Cause of Motor Neuron Disease
Symptoms and General Health	Treatment; Symptoms;	VA-128	MR Tracking of Stem Cells for Replacement Therapy in ALS

Brain and Nervous System Function

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Symptoms	VA-061	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also DoD-118)
	Treatment; Prevention;	DoD-145	Early Intervention Research Program to Enhance Soldier Resilience
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
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)

Brain and Nervous System Function

Epidemiology

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Symptoms	HHS-006	Defining Gulf War Illness
Symptoms and General Health	Symptoms	HHS-012	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-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; Diagnosis;	DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome
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
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

Brain and Nervous System Function

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
Environmental Toxicology	Symptoms	VA-126	Structural Magnetic Resonance Imaging in Gulf War-Era Veterans
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

Brain and Nervous System Function

Mechanistic

Research Focus	Project Focus	Project	Project Title
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
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 Psychiatric Disorders
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	Treatment; Symptoms;	VA-100	Studies of the Blood-Brain Barrier and its Manipulation
Symptoms and General Health	Prevention; Symptoms;	VA-102	Cholinergic and Monoaminergic Influences on Sleep
Symptoms and General Health	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

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-005C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans
Chemical Weapons	Symptoms	DoD-060	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness
Chemical Weapons	Exposure	DoD-146	Assessment of Toxicology Assay Methods and Chemical Exposures Among a Cohort of US Marines Deployed in the Gulf War
Pyridostigmine Bromide	Exposure; Prevention;	DoD-011	Male/Female Differential Tolerances to Pyridostigmine Bromide
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions;	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
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

Environmental Toxicology

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

Environmental Toxicology

Development

Research Focus	Project Focus	Project	Project Title
Brain and Nervous System Function; Symptoms and General Health	Diagnosis; Exposure; Symptoms	VA-064C	Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in veteran populations
Chemical Weapons	Diagnosis	DoD-049	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts
Chemical Weapons	Exposure; Diagnosis;	DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents
Chemical Weapons	Diagnosis; Exposure;	DoD-050	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways
Chemical Weapons	Diagnosis; Exposure;	DoD-137	Low Level Exposure to Sulfur Mustard: Development of a SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin
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

Environmental Toxicology

Epidemiology

Research Focus	Project Focus	Project	Project Title
Chemical Weapons	Exposure; Symptoms;	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)
Chemical Weapons	Exposure; Symptoms;	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)
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

Environmental Toxicology

Epidemiology

Research Focus	Project Focus	Project	Project Title
Pyridostigmine Bromide	Exposure	DoD-017	Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning
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
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

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Exposure; Interactions;	DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals
	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-004E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility
Brain and Nervous System Function; Chemical Weapons	Exposure; Symptoms;	DoD-022	Chronic Organophosphorus Exposure and Cognition
Brain and Nervous System Function; Immune Function and Infectious	Exposure; Interactions;	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

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
Brain and Nervous System Function;	Exposure; Symptoms;	DoD-128	Multifactorial Assessment of Depleted Uranium Neurotoxicity
Brain and Nervous System Function;	Exposure; Symptoms;	DoD-129	Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness
Brain and Nervous System Function; Symptoms and General Health	Exposure; Symptoms;	DoD-007A	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-006D	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 Organophosphorous 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;	DoD-054	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions;	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;	DoD-056	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions;	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;	DoD-062	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions;	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;	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

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
Immune Function and Infectious Diseases	Exposure; Interactions;	HHS-007	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid
Immune Function and Infectious Diseases	Exposure	DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys
Immune Function and Infectious Diseases; Pyridostigmine Bromide	Exposure; Interactions;	DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War
Immune Function and Infectious Diseases; 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;	DoD-078	Experimental Models of Gulf War Syndrome
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions;	DoD-079	Time Course of Stress-induced Impairment of Blood Brain Barrier
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions;	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;	VA-006C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III)
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions;	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

Environmental Toxicology

Mechanistic

Research Focus	Project Focus	Project	Project Title
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;	VA-005D	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
Symptoms and General Health	Exposure	VA-065	San Antonio Environmental Hazards Research Center
Symptoms and General Health	Exposure	VA-065A	Does a Variant of the Human SOD2 Gene Increase Sensitivity to Hazards?
Symptoms and General Health	Exposure	VA-065B	The Contribution of FEN-1 to Genetic Integrity Subsequent to Oxidative Stress
Symptoms and General Health	Exposure	VA-065C	The Importance of Hydrogen Peroxide Detoxification in Cellular Protection
Symptoms and General Health	Exposure	VA-065D	Do Defective Gpx1 and ALDH2 Genes Increase Sensitivity to Environmental Hazards?
Symptoms and General Health;	Exposure	DoD-007B	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; Treatment;	VA-006E	Clinical and Epidemiology Leishmania Research

Immune Function and Infectious Diseases

Clinical

Research Focus	Project Focus	Project	Project Title
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;	DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War-related illness
Symptoms and General Health	Treatment; Diagnosis;	DoD-067	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria
Symptoms and General Health	Symptoms; Exposure;	VA-006B	Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II)
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)

Immune Function and Infectious Diseases

Development

Research Focus	Project Focus	Project	Project Title
	Diagnosis	DoD-008A	Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL)
	Diagnosis	DoD-008B	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

Immune Function and Infectious Diseases

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Treatment	DoD-009	Identification of the Genetic Factors Which Control Tropism in Leishmania
	Prevention	VA-015	Vaccine-Mediated Immunity Against Leishmaniasis
	Prevention	VA-016	Protective Immunity in Experimental Visceral Leishmaniasis
	Prevention; Treatment;	VA-094	The Immunology of Chronic Cutaneous Leishmaniasis
	Symptoms	VA-127	Interactions of the Leishmania sp. with Mammalian Cells
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;	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 and Infectious Diseases	Symptoms	DoD-044	Investigation of Seminal Plasma Hypersensitivity Reactions

Reproductive Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Prevention	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
	Prevention	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
	Symptoms	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
	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

Symptoms and General Health

Clinical

Research Focus	Project Focus	Project	Project Title
	Symptoms	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
	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; Symptoms;	VA-056	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13)
	Treatment; Symptoms;	VA-058	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13)
	Diagnosis; Symptoms;	VA-104	Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome
Brain and Nervous System Function	Symptoms	DoD-036	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms

Symptoms and General Health

Clinical

Research Focus	Project Focus	Project	Project Title
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
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	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-Model Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D)
Brain and Nervous System Function	Treatment; Symptoms;	VA-057	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13)
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-Model 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

Symptoms and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Symptoms	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.
	Symptoms	DoD-001E	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study
	Symptoms	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
	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-116B	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	DoD-150	Validation Study of Gulf War Deployment Files
	Symptoms	HHS-001	Health Assessment of Persian Gulf War Veterans from Iowa

Symptoms and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
	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-002A	VA National Survey of Persian Gulf Veterans - Phase I
	Symptoms	VA-002B	VA National Survey of Persian Gulf Veterans - Phase II
	Symptoms	VA-004C	Gulf War And Vietnam Veterans Cancer Incidence Surveillance
	Symptoms	VA-046	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder
	Symptoms	VA-063B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-
	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

Symptoms and General Health

Epidemiology

Research Focus	Project Focus	Project	Project Title
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)
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-002C	VA National Survey of Persian Gulf Veterans - Phase III
Brain and Nervous System Function	Symptoms	VA-005A	Health and Exposure Survey of Persian Gulf Veterans
Brain and Nervous System Function	Symptoms	VA-078	Millennium 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; Reproductive Health	Symptoms	DoD-045	Air Force Women's Health Surveillance Study
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

Symptoms and General Health

Mechanistic

Research Focus	Project Focus	Project	Project Title
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

Appendix C
Project Funding

(As of September 30, 2005)

NOTES ON REVISED TABLE OF SPENDING FOR GULF WAR VETERANS' ILLNESSES RESEARCH

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 1992-2005 are listed, only the financial data for FY 1996-2005 (a 10-year window) are shown in Appendix C; Totals for FY '96-'05 do not include funds obligated in FY 1992-1995. Projects that received all of their obligated funds prior to FY 1996 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 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS* FY '96-'05
DoD-001	Naval Health Study Program	C	$2,250,000	$2,000,000	$2,654,000								$6,904,000
DoD-001 A	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors; Study 1: 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

*****Totals for FY '96-'05 do not include funds obligated in FY 1992-1995

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS* FY '96-'05
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: PGW vs. EV.	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
DoD-002	Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET.	C	$0	$0									$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				$121,400	$0						$121,400
DoD-008	Program DoD-8.	C	$652,000	$695,000	$694,000	$0							$2,041,000
DoD-008 A	Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL).	C	$0										$0

*****Totals for FY '96-'05 do not include funds obligated in FY 1992-1995

Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS* FY '96-'05
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	$0	$0								$0
DoD-010	Pyridostigmine Synergistic Toxicity Study.	C											
DoD-011	Male/Female Differential Tolerances to Pyridostigmine Bromide.	C	$0	$0	$0								$0
DoD-013	Effects of Persian Gulf War Service on Military Working Dogs.	C	$97,000	$200,000	$120,000	$200,000	$0	$0	$0	$0			$617,000
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	$50,000	$127,000									$177,000
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	$770,000	$193,000	$290,000	$295,000	$295,000	$306,000	$195,000	$225,000			$2,569,000
DoD-019	Persian Gulf Veterans Health Tracking System.	C	$0	$0	$450,000	$450,000	$0	$0	$100,000	$50,000			$1,050,000

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Department of Defense Gulf War Research Funding

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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	$0									$0
DoD-022	Chronic Organophosphorus Exposure and Cognition.	C		$0	$0	$0	$0						$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	$764,000	$985,000									$1,749,000
DoD-030	Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study.	C	$0	$0	$0	$0	$0	$0					$0
DoD-031	Dysregulation of the Stress Response in the Persian Gulf Syndrome.	C	$0	$0	$0	$0	$0						$0
DoD-032	Neuropsychological Functioning in Persian Gulf Era Veterans.	C	$0	$0	$0	$0							$0
DoD-033	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity.	C	$0	$0	$0	$0							$0
DoD-034	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents.	C	$0	$0	$0	$0							$0
DoD-035	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War.	C	$10,000	$63,000	$0	$10,500	$0	$0					$83,500
DoD-036	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms.	C	$138,000	$0	$0	$0							$138,000

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DoD-037	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats.	C	$5,000	$0	$0	$0							$5,000
DoD-038	Diagnostic Antigens of Leishmania tropica.	C	$0	$0	$0								$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	$28,400	$155,000	$0	$124,868	$0					$308,268
DoD-040	Psychological and Neurobiological Consequences of the Gulf War Experience.	C	$0	$0	$0	$0	$0	$0					$0
DoD-041	Evaluation of Muscle Function in Persian Gulf Veterans.	C	$0	$0	$0	$0	$0						$0
DoD-042	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment.	C	$700,000	$0	$0	$0	$0	$0					$700,000
DoD-044	Investigation of Seminal Plasma Hypersensitivity Reactions.	C	$634,000	$0	$5,000	$14,200							$653,200
DoD-045	Physical and Emotional Health of Gulf War Veterans Women.	C	$299,274	$0	$456,732	$20,505	$0	$99,628	$0				$876,139
DoD-046	Exploratory Data Analysis with the CCEP Database.	C	$60,000	$100,000									$160,000
DoD-047	Study of Mycoplasmal Infections in Gulf War Veterans.	C	$112,000	$0	$0								$112,000
DoD-048	Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf War Syndrome Cohort vs. Selected Control Groups.	C	$74,000	$0	$0								$74,000

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DoD-049	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts.	C	$927,000	$0	$0	$0	$0						$927,000
DoD-050	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways.	C	$699,000	$0	$0	$0							$699,000
DoD-051	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses.	C	$864,000	$0	$0	$0	$0						$864,000
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	$1,000,000	$400,000	$0	$0	$217,137	$0					$1,617,137
DoD-054	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure.	C	$315,000	$100,000	$0	$0	$0						$415,000
DoD-055	Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects.	C	$500,000	$136,000	$0	$0	$0	$0					$636,000
DoD-056	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine.	C	$685,000	$100,000	$0	$0	$0	$0					$785,000

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DoD-057	Physiologic Effects of Stress in Gulf War Veterans.	C		$909,000	$0	$0	$0	$0	$0				$909,000
DoD-058	Illness Among Persian Gulf War Veterans: Case Validation Studies.	C		$2,208,000	$0	$0	$4,264	$267,337	$0	$0			$2,479,601
DoD-059	Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis.	C		$625,000	$0	$0	$0	$0					$625,000
DoD-060	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness.	C		$125,000	$0	$0							$125,000
DoD-061	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid.	C		$1,586,000	$0	$0	$0						$1,586,000
DoD-062	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice.	C		$201,000	$0	$0							$201,000
DoD-063	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity.	C		$1,626,000	$0	$0	$0						$1,626,000
DoD-064	Individual Differences in Neurobehavioral Effects of Pyridostigmine.	C		$1,900,000	$18,516	$0	$190,595	$0					$2,109,111
DoD-065	Multi-Disciplinary Pathophysiologic Studies of Neurotoxic Gulf War-Related Neurologic Syndromes Leading to Diagnosis and Treatment.	C		$3,000,000	$0	$0	$0	$0					$3,000,000
DoD-066	Testing for Mycoplasmal Infection Replicability of Nucleoprotein Gene Tracking and Forensic Polymerase Chain Reaction.	C	$49,940	$100,000	$40,000	$403,000	$140,319	$0					$733,259

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DoD-067	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria.	C		$3,400,000	$0	$0							$3,400,000
DoD-069	Five Year Follow-Up of Army Personnel Potentially Exposed to Chemical Warfare Agents.	O		$946,160	$0	$0	$110,000	$0	$245,910	$0	$0	$0	$1,302,070
DoD-070	War Syndromes from 1900 to the Present: Symptom Patterns and Long Term Health Outcomes.	C		$734,687	$0	$115,000	$0	$0					$849,687
DoD-071	A Comparison of Post-Deployment Hospitalization Incidence between Vietnam and Gulf War Veterans.	C		$566,000	$0	$0	$0						$566,000
DoD-072	Long-Term Effects of Subchronic Exposure to Sarin, Alone and with Stress and Other Chemicals.	C		$996,000	$0	$0	$0	$0	$0				$996,000
DoD-073	Post-Deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes.	C		$500,000	$0	$0	$0	$0					$500,000
DoD-074	Relationship of Stress Exposures to Health in Gulf War Veterans.	C		$161,489	$1,991,330	$0	$0	$0	$0				$2,152,819
DoD-075	Toxic Interactions of Prophylactic Drugs and Pesticides.	C			$1,380,157	$0	$0	$0	$0	$0			$1,380,157
DoD-076	Evaluation of Immunotoxicity Due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel.	C			$448,369	$0	$0	$0	$0	$0			$448,369
DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War.	C			$760,031	$0	$0	$0	$0				$760,031

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DoD-078	Experimental Models of Gulf War Syndrome.	C			$2,179,097	$444,800	$0	$0	$0				$2,623,897
DoD-079	Time-course of Stress-Induced Impairment of the Blood Brain Barrier.	C		$100,200	$0	$0	$0						$100,200
DoD-080	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells.	C		$297,400	$0	$0	$0	$0	$0				$297,400
DoD-081	Immunotoxicity Due to Coexposure of DEET, Pyridostigmine, and Stress.	C		$300,000	$0	$0	$0	$0	$0				$300,000
DoD-082	Feasibility of Developing a Registry of PTSD-Affected Veteran Sib Pairs.	C		$172,000	$0	$0	$0	$0	$0				$172,000
DoD-083	Risk for Stress-Related Substance Abuse: Effects of Family History of Alcoholism.	C		$299,700	$0	$0	$0	$0	$0				$299,700
DoD-084	Psychobiological Alterations Of Persian Gulf War Veterans with and without PTSD.	C		$300,000	$0	$0	$0	$0	$0				$300,000
DoD-085	Central Nervous System Cytokines and CRH in Gulf War Veterans with Multiple Unexplained Symptoms.	C		$149,900	$149,200	$0	$0	$0	$0				$299,100
DoD-086	Effects of Combat Stress on the Structure and Function of the Hippocampus.	C		$300,000	$297,800	$0	$0	$0	$0	$0			$597,800
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		$289,100	$0	$0	$0	$68,044	$0	$0			$357,144
DoD-088	Clinical Relevance of Novel Immunological Markers in PTSD.	C		$242,300	$0	$0	$0	$0	$0				$242,300

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DoD-089	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder.	C		$288,500	$0	$0	$0	$0	$0				$288,500
DoD-090	SPECT Benzodiazepine Receptor and MR Imaging in PTSD.	C		$200,000	$100,000	$0	$0	$0	$0				$300,000
DoD-091	Neurological and Circadian Substrates of PTSD-Like Behaviors.	C		$300,000	$299,000	$0	$0	$0					$599,000
DoD-092	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward and Animal Model of Chronic Stress and Posttraumatic Stress Disorder.	C		$249,700	$0	$0	$0	$0	$0				$249,700
DoD-093	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up.	C				$970,700	$0	$0					$970,700
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				$557,173	$206,727	$0	$0				$763,900
DoD-095	Development of Diagnostic tools and alternative treatment drugs for Leishmania.	C				$1,500,000	$1,500,000	$1,500,000	$1,500,000				$6,000,000
DoD-096	Deployment Health Center.	O				$1,500,000	$1,500,000	$2,250,000	$1,750,000	$1,750,000	$1,750,000	$0	$10,500,000
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				$177,300	$146,742	$151,202	$151,000				$626,244

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DoD-098	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans.	O				$332,500	$188,000	$364,182	$0	$0	$0	$0	$884,682
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				$207,876	$204,205	$224,265	$0	$0			$636,346
DoD-100	Antibodies to Squalene.	O				$582,756		$50,000	$487,333	$0	$0	$0	$1,120,089
DoD-101	Mechanisms in Chronic Multisymptom Illnesses.	O				$2,903,408	$5,542,189	$0	$4,786,192	$644,870	$4,527,000	$0	$18,403,659
DoD-102	Case-control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-deployed Veterans.	C				$249,908	$0	$253,793	$0	$281,950			$785,651
DoD-103	Human Metabolism & Interactions of Deployment-related Chemicals.	O				$583,319	$46,315	$0	$0	$349,994	$242,424	$160,000	$1,382,052
DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome.	C				$1,003,937	$9,311	$0	$0	$40,844			$1,054,092
DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala.	C				$950,490	$0	$0	$0	$0			$950,490
DoD-106	The role of Th1/Th2 cytokine balance in Gulf War-related Illness.	C				$292,411	$0	$0	$0				$292,411
DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity.	C				$875,373	$10,825	$0	$0	$0			$886,198
DoD-108	Health Status of Current National Guard Members.	O				$578,970	$0	$264,375	$174,651	$0	$0	$0	$1,017,996
DoD-109	Disordered responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms.	C				$917,762	$147,523	$397,243	$0	$0			$1,462,528

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DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy.	C				$127,920	$63,705	$0	$0				$191,625
DoD-111	Autonomic Dysfunction in Gulf War Veterans.	O				$999,144	$0	$0	$0	$189,609	$0	$0	$1,188,753
DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?	C				$256,916	$0	$0	$0				$256,916
DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine-Neurochemical, Behavioral, and Physiological Effects.	C				$802,140	$0	$0	$0	$0	$0		$802,140
DoD-114	A Re-Examination of Neuropsychological Functioning in Persian Gulf War Veterans.	C				$593,712	$0	$0	$0				$593,712
DoD-115	A Randomized Multi-Center Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (see also VA-62; formerly VA/DoD-1D).	C				$1,000,000	$2,000,000	$0	$0				$3,000,000
DoD-116	VA/DoD Core Funding of the Medical Follow-up Agency (See also VA-63; formerly VA/DoD-2D).	C	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000			$2,000,000
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

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DoD-116 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly listed as VA/DoD-2DB).	C											$0
DoD-117	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking.	C					$1,232,050	$0	$0				$1,232,050
DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) among GWVs (See also VA-61).	C					$430,824	$832,272	$0				$1,263,096
DoD-119	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT). (see also VA-055)	C				$500,000	$1,000,000	$0	$0				$1,500,000
DoD-120	Assessing Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents.	C				$239,000	$316,000	$0	$0				$555,000
DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel on Pregnancy and Offspring Development.	C		$300,000	$250,000	$25,000	$15,000	$15,000					$605,000
DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys.	C		$25,000	$25,000	$25,000	$30,000	$35,000					$140,000
DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys.	C				$15,000	$20,000	$15,000					$50,000
DoD-124	Randomized, Controlled Trial of Combination Treatment with Pyridostigmine, DEET, and Permethrin.	C				$1,283,218	$0	$0	$0	$0			$1,283,218

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DoD-125	A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (see also VA-074)	O					$445,078	$0	$0	$0	$0	$0	$445,078
DoD-126	Blood-Brain Barrier Transport of Uranium	O					$790,884	$0	$0	$0	$0	$0	$790,884
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	O					$661,156	$0	$0	$328,734	$0	$89,055	$1,078,945
DoD-129	Inhalation of Uranium Oxide Aerosols: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness	O						$1,276,220	$0	$0	$0	$0	$1,276,220
DoD-130	Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents	O						$983,164	$0	$0	$0	$0	$983,164
DoD-131	Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illness	O						$5,377,526	$0	$500,000	$0	$0	$5,877,526
DoD-132	Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness	O						$792,198	$0	$0	$0	$0	$792,198
DoD-133	Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome	O						$884,087	$0	$0	$0	$0	$884,087
DoD-134	Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin	O					$775,155	$0	$0	$0	$0	$0	$775,155

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DoD-135	Biochemical Markers for Exposure to Low Doses of Organophosphorus Insecticides	O					$786,408	$0	$0	$0	$0	$0	$786,408
DoD-136	A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure	O						$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	O						$600,111	$0	$0	$0	$0	$600,111
DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents	O						$434,795	$0	$0	$0	$0	$434,795
DoD-139	Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illness	C					$892,399	$500,885	$0			$0	$1,393,284
DoD-140	US Department of Defense Surveillance for Neoplasms in Infancy	O						$764,879	$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	Illness Among Persian Gulf War Veterans: Case Validation Studies	O								$168,962	$0	$0	$168,962
DoD-143	Millennium Cohort Study (see VA-078)	O					$3,000,000	$1,000,000	$1,250,000	$2,000,000	$1,950,000	$2,880,000	$12,080,000
DoD-144	Psychological Health Screening: Methods & Metrics for Deployed Forces	O				$109,000	$295,000	$250,000	$300,000	$0	$0	$0	$954,000

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DoD-145	Early Intervention Research Program to Enhance Soldier Resilience	O						$250,000	$275,000	$275,000	$0	$0	$800,000
DoD-146	Assessment of Toxicology Assays Methods & Chemical Exposures Among a Cohort of US Marines Deployed in the Gulf War	C						$100,000					$100,000
DoD-147	Development of Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications	O		$105,000	$200,000	$190,000	$260,000	$412,000	$696,111	$292,530	$0	$0	$2,155,641
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	O						$1,689,945	$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	O							$482,274	$0	$0	$0	$482,274
DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents	O							$1,000,000	$1,019,440	$4,500,000	$1,517,839	$8,037,279
DoD-153	Gulf War Illness Research	O						$4,694,500	$4,950,000	$920,838	$2,003,000	$928,000	$13,496,338
DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (see VA-088)	O							$100,000	$566,542	$368,687	$604,372	$1,639,601

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Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS* FY '96-'05
DoD-155	Neuropsychological Functioning in Gulf War Veterans Exposed to Pesticides and Pyridostigmine Bromide	O								$1,021,862	$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	O								$1,519,951	$0	$0	$1,519,951
	DoD Total Funds		**$11,905,214**	**$28,880,536**	**$13,213,232**	**$22,674,338**	**$23,847,679**	**$28,752,084**	**$18,827,819**	**$12,396,126**	**$15,341,111**	**$6,179,266**	**$182,017,405**

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Status: C=Complete; O=Ongoing

Department of Health and Human Services Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
HHS-001	Health Assessment of Persian Gulf War Veterans from Iowa	C	$1,616,755	$0	$0	$162,000	$0	$0					$1,778,755
HHS-002	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18	C	$0	$0	$16,055	$0	$0						$16,055
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			$600,000	$558,000	$660,000	$0	$0	$0			$1,818,000
HHS-006	Defining Gulf War Illness	C			$600,000	$480,000	$719,792	$200,000	$0	$0	$0		$1,999,792
HHS-007	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid	C			$175,706	$192,445	$187,647	$0					$555,798
HHS-008	Strategy to Identify Non-Additive Response to Chemical Mixtures	C			$242,586	$247,933	$0	$0					$490,519
HHS-009	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments	O						$337,693	$339,814	$339,814	$0		$1,017,321
HHS-010	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline	O						$461,177	$460,000	$460,000	$0		$1,381,177
HHS-011	Deployment to the Gulf War and the Subsequent Development of Cancer	O								$164,291	$0		$164,291
HHS-012	Epidemiology of ALS in Veterans										$461,951	$462,071	**$924,022**
	Total HHS Funds		**$1,616,755**	**$0**	**$1,634,347**	**$1,640,378**	**$1,567,439**	**$998,870**	**$799,814**	**$964,105**	**$461,951**	**$462,071**	**$10,145,730**

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
VA-001	Mortality Follow-up Study of Persian Gulf Veterans	C	$1,980,000	$440,032	$178,197	$166,848	$176,440	$171,154	$128,496				$3,241,167
VA-002	National Health Survey of Persian Gulf Veterans	C											
VA-002 A	VA National Survey of Persian Gulf Veterans - Phase I	C			$18,111								$18,111
VA-002 B	VA National Survey of Persian Gulf Veterans - Phase II	C											
VA-002 C	VA National Survey of Persian Gulf Veterans - Phase III	C			$1,601,280	$3,571,932	$3,400,000	$2,344,427	$30,000				$10,947,639
VA-003	Use of Roster of Veterans Who Served in Persian Gulf Area	C											
VA-004 TOTAL	Boston Environmental Hazards Research Center Program.	C	$500,000	$500,000	$500,000	$500,000	$229,500						$2,229,500
VA-004	Boston Environmental Hazards Research Center Program	C											
VA-004 A	Evaluation of Cognitive Functioning of Persian Gulf Veterans	C											
VA-004 B	Evaluation of Neurological Functioning in Persian Gulf Veterans	C											
VA-004 C	Gulf War And Vietnam Veterans Cancer Incidence Surveillance	C											
VA-004 D	Evaluation of Respiratory Dysfunction Among Gulf War Veterans	C											

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
VA-004 E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility	C											
VA-004 F	Validity of Computerized Tests	C											
VA-005 TOTAL	East Orange Environmental Hazards Research Center Program	C	$500,000	$500,000	$500,000	$500,000	$326,900						$2,326,900
VA-005	East Orange Environmental Hazards Research Center Program	C											
VA-005 A	Health and Exposure Survey of Persian Gulf Veterans	C											
VA-005 B	Physiological and Psychological Assessments of Persian Gulf Veterans	C											
VA-005 C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans	C											
VA-005 D	Effects of Genetics and Stress on Responses to Environmental Toxins	C											
VA-006 TOTAL	Portland Environmental Hazards Research Center: Environment, Veterans' Gulf War Syndrome. Core: Clinical and Epidemiology Research.	C	$498,695	$499,198	$499,926	$499,098	$233,290						$2,230,207

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
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											
VA-006 A	Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I)	C											
VA-006 B	Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II)	C											
VA-006 C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III)	C											
VA-006 D	DNA Damage from Chemical Agents and Its Repair (Project IV)	C											
VA-006 E	Clinical and Epidemiology Leishmania Research	C											
VA-007	Desert Storm Reunion Survey	C											
VA-008	Psychological Test Data of Gulf War Veterans Over Time	C											
VA-009	Evaluation of Cognitive Functioning in Persian Gulf War Veterans Reporting War-related Health Problems	C											

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
VA-010	Memory and Attention in PTSD	C	$63,700	$57,000	$57,600	$0							$178,300
VA-011	Neuropsychological Functioning in Veterans	C											
VA-012	Psychological Assessment of Operation Desert Storm Returnees	C											
VA-013	Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot Study	C											
VA-015	Vaccine-Mediated Immunity Against Leishmaniasis	C	$0	$82,600	$80,000	$79,400	$41,540	$114,336	$119,600	$59,800			$577,276
VA-016	Protective Immunity in Experimental Visceral Leishmaniasis	C	$60,700	$54,900									$115,600
VA-017	Immunological Evaluation of Persian Gulf Veterans	C											
VA-018	Chronic Gastrointestinal Illness in Persian Gulf Veterans	C											
VA-020	Psychological Adjustment in Operation Desert Shield/Storm Veterans	C											
VA-021	A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in ODS	C											
VA-036	Stress Symptoms and Their Causal Attribution in Desert Storm Veterans	C											

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
VA-040	Musculoskeletal Symptoms in Gulf War Syndrome	C											
VA-046	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder	C											
VA-047	Retrospective Verification of Mustard Gas Exposure	C		$349,700	$299,700	$299,700	$139,960						$1,089,060
VA-048	Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance	C			$99,900	$89,400	$92,840	$45,000					$327,140
VA-049	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction	C			$112,090	$147,950	$141,696	$144,024	$125,862				$671,622
VA-050	Neuropsychological findings in a sample of Operation Desert Storm veterans	C											
VA-051	Psychobiological Assessment of Desert Storm Veterans	C											
VA-053	Spouses and Children Program	C		$101,360	$98,651	$51,088	$33,655	$12,934	$25,000				$322,688
VA-054	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress	C				$53,400	$90,131	$86,895	$86,350	$72,700	$39,375		$428,851
VA-055	Antibiotic Treatment of Gulf War Veterans' Illnesses (ABT) (See also DoD-119)	C				$447,742	$1,466,375	$1,981,963	$254,000				$4,150,080

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
VA-056	Birmingham's Gulf War Veterans' Illness Demonstration Clinic (13)	C			$54,100	$261,625	$161,175						$476,900
VA-057	Case Management and Residential Rehabilitation for Persian Gulf War Veterans (13)	C			$71,625	$253,625	$174,750						$500,000
VA-058	Implementation and Evaluation of Gulf War Veterans' Demonstration Project (13)	C			$84,714	$349,805	$262,496						$697,015
VA-059	Demonstration Treatment Program for Gulf War Veterans With Unexplained Physical Symptoms (13)	C			$45,750	$348,225	$259,500						$653,475
VA-060	Identification and Management of Sleep Disorders in Gulf War Veterans	C			$121,125	$328,500	$246,375						$696,000
VA-061	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among Gulf War Veterans (See also DoD-118)	C					$0	$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				$788,000	$3,756,826	$1,971,233	$44,250				$6,560,309

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
VA-063	VA/DoD Core funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D)	O	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$2,500,000
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											
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											
VA-064	Boston Environmental Hazards Research Center	O					$112,360	$299,700	$300,000	$297,000	$337,200	$337,200	$1,683,460
VA-064 A	Functional Neuroimaging in Lead Exposed Adults	O											$0
VA-064 B	Quantification and Validation of Structure-Function relationships through visuospatial test performance	O											$0
VA-064 C	Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in veteran populations	O											$0
VA-065	San Antonio Environmental Hazards Research Center	C					$116,750	$350,000	$300,000	$300,000	$337,200		$1,403,950

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
VA-065 A	Does a variant of the human SOD2 gene increase sensitivity to hazards?	C											
VA-065 B	The contribution of FEN-1 to genetic integrity subsequent to oxidative stress	C											
VA-065 C	The importance of hydrogen peroxide detoxification in cellular protection	C											
VA-065 D	Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental hazards?	C											
VA-066	Physiological Responding in Posttraumatic Stress Disorder	C											
VA-067	Olfactory Functioning in Gulf War Veterans	C					$7,500	$7,500					$15,000
VA-068	Family Study of Fibromyalgia	C					$46,700	$50,000	$50,000				$146,700
VA-069	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans	C					$122,243	$135,487	$141,815	$48,947			$448,492
VA-070	A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8	C			$50,051	$19,817	$6,204	$4,884	$4,900				$85,856
VA-071	Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome	C					$125,313	$181,692	$186,524	$47,975			$541,504

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
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	Millennium Cohort Study (see DoD-143)	O					$0	$0	$0	$0	$0	$0	$0
VA-080	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress	O								$203,400	$119,818	$248,458	$$571,676
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	O							$88,000	$135,000	$151,740	$276,112	$650,852

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
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	$232,459		$366,859
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 (see DoD-154)	C								$24,057	$74,222		$71,068
VA-089	National Registry of Veterans with Amyotrophic Lateral Sclerosis	O								$319,229	$625,564	$799,104	$1,743,897
VA-090	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness	O								$250,000	$281,000	$281,000	$812,000

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
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	O											$0
VA-090D	Seizures and Neuroplasticity:Physiology and Biochemistry	O											$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	O								$56,750	$36,080	$163,205	$256,035
VA-094	The Immunology of Chronic Cutaneous Leishmaniasis	O									$192,204	$157,360	$349,564
VA-095	The Role of Signal Regulatory Proteins in Astrocytomas	O								$54,158	$231,566	$238,239	$523,963
VA-096	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain	O									$49,035	$128,698	$177,733

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
VA-097	Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas	O								$99,563	$215,093	$241,957	$556,6136
VA-098	Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas	O									$44,420	$168,600	$213,020
VA-099	Vaccination Against Visceral Leishmaniasis with a multi-epitope vaccine	O							$65,700	$123,413	$116,896	$118,863	$424,872
VA-100	Studies of the Blood-Brain Barrier and its Manipulation	O							$151,875	$151,875	$151,740	$151,740	$607,230
VA-101	Biomarkers Discovery in ALS	O									$50,518	$227,130	$277,648
VA-102	Cholinergic and Monoaminergic Influences on Sleep	O						$60,642	$92,588	$92,588	$134,160	$175,814	$555,792
VA-103	Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal	O								$210,600	$296,657	$307,253	$814,510
VA-104	Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome	O								$114,975	$168,600	$168,600	$452,175
VA-105	Expression of the Major Surface Protease of Leishmania Chagasi	O							$76,613	$135,628	$298,175	$119,535	$629,951
VA-106	Interoceptive Stressor Conditioning: A Model for Gulf War Illness	O										$193,440	$193,440
VA-107	Evaluation of Stress Response Systems in Gulf War Veterans with CMI	O										$192,766	$192,766
VA-108	Telemedicine Treatment for Veterans with Gulf War Illness	O										$185,714	$185,714

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 1996	FY 1997	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	FY2003	FY 2004	FY 2005	TOTALS FY '96-'05
VA-109	Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics	O										$158,372	$158,372
VA-110	Pain Among Gulf War Veterans: Secondary Analysis of CSP#458 Data	O										$96,439	$96,439
VA-111	T Cell Responses to Multiple Immunizations and Stress	O										$112,399	$112,399
VA-112	National VA Amyotrophic Lateral Sclerosis Research Consortium	O										$1,171,208	$1,171,208
VA-113	Novel Cause of Motor Neuron Disease	O										$166,352	$166,352
VA-114	Strategies in Therapeutic Development of Neurodegenerative Diseases	O										$266,950	$266,950
VA-115	Autonomic System Changes Cause Intestinal Symptoms in Gulf War Veterans	O										$275,623	$275,623
VA-116	Quantitative Trait Genes Controlling Circadian and Sleep Behaviors	O										$125,888	$125,888
VA-117	Estimates of Cancer Prevalence in Gulf Veterans Using State Registries	O										$42,206	$42,206
VA-118	Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004	O										$42,262	$42,262
VA-119	Patterns of Microarray Gene Expression in Gulf War Illness	O										$192,204	$192,204
VA-120	Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis	O										$90,988	$90,988
VA-121 (formerly VA-065)	Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders	O										$295,938	$295,938

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Department of Veterans Affairs Gulf War Research Funding

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VA-122	Role of Mitochondrial Oxidative Stress in ALS	O										$55,188	$55,188
VA-123	Interactions Between Maternal Care, Stress and Pyridostigmine Bromide	O										$60,134	$60,134
VA-124	Early Life Determinants of Vulnerability to Pyridostigmine Bromide	O										$213,110	$213,110
VA-125	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla	O										$322,532	$322,532
VA-126	Structural Magnetic Reasonance Imaging in Gulf War-Era Veterans	O										$159,552	$159,552
VA-127	Interactions of the Leishmania sp. with Mammalian Cells	O										$101,216	$101,216
VA-128	MR Tracking of Stem Cells for Replacement Therapy in ALS	O										$236,730	$236,730
VA-129	Glucocorticoid Responsivity in Gulf War Veterans	O										$168,600	$168,600
	Total VA Funds		**$3,853,095**	**$2,834,790**	**$4,722,820**	**$9,006,155**	**$12,020,519**	**$8,576,675**	**$4,512,676**	**$5,746,467**	**$7,671,771**	**$9,484,679**	**$68,429,647**

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