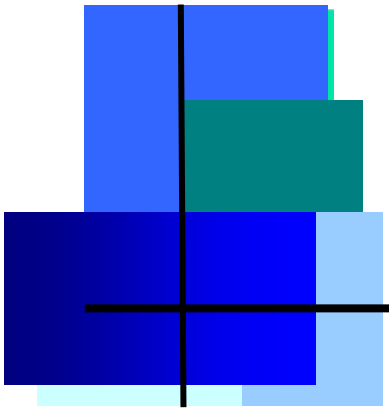
DEPARTMENT OF VETERANS AFFAIRS

ANNUAL SUMMARY

Federally Sponsored Research on Gulf War Veterans' Illnesses for 2015



Annual Summary
FY 2015

Federally Sponsored Research on Gulf War Veterans' Illnesses for 2015

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EXECUTIVE SUMMARY

I. INTRODUCTION

Section 707 of Public Law (P.L.) 102-585, as amended by section 104 of P.L. 105-368 and section 502 of P.L. 111-163, required that an annual report be submitted to the Senate and House Veterans' Affairs Committees through 2014 on the results, status, and priorities of research activities related to the health consequences of military service in the Gulf War (GW) in Operations Desert Shield and Desert Storm, 1990 and 1991. The Research Subcommittee of the interagency Deployment Health Working Group (DHWG) prepared the Annual Report to Congress on Federally Sponsored Research on Gulf War Veterans' Illnesses for 2014, which was the 21st report on Federal research and research activities. This report (2015) follows the general format of previous reports but is not required by Congress.

As in previous annual reports to Congress, the material presented is divided into six sections and three appendices. Section I is an introduction; Section II summarizes the research priorities and organization of the Federal GW research portfolio; Section III highlights and summarizes research progress published since the last annual report to Congress; Section IV summarizes Federal funding trends for GW research during the 10-year period from fiscal year (FY) 2006 through FY 2015; Section V highlights new research projects and initiatives since the last report; Section VI contains literature references; and the Appendices contain listings of federally-funded research projects.

II. RESEARCH PRIORITIES

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

III. PUBLISHED RESULTS AND STATUS OF THE FIELD IN 2015

Section III provides abstracts or summaries of research articles on the health problems of GW Veterans published during calendar year (CY) 2015 or in CY 2014 after the previous annual report to Congress was submitted.

IV. RESEARCH FUNDING TRENDS

VA, the Department of Defense (DoD), and Department of Health and Human Services (HHS) funded 480 distinct projects from FY 1992 through FY 2015 related to health problems affecting GW Veterans. The scope of the Federal research portfolio is broad, from small pilot studies to large-scale epidemiology studies involving large populations and major center-based research programs. Federal funding for research on GWVI totaled almost $245 million for the period from FY 2006 through FY 2015. As of September 30, 2015, 393 projects (82 percent of the 480 projects) were completed, and 87 projects (18 percent) were new or ongoing.

V. NEW RESEARCH PROJECTS AND INITIATIVES

Twenty-six new projects were funded through the FY 2014 appropriation for the Gulf War Illness Research Program (GWIRP) managed by the Congressionally Directed Medical Research Programs (CDMRP) at DoD; these were not initiated until FY 2015. These projects focused on Brain and Nervous System Function (5), Environmental Toxicology (1), Immune Function (2) and Symptoms and General Health (18). VA funded four new projects in FY 2015. One of these projects focused on Brain and Nervous System Function, and three focused on Symptoms and General Health.

I. INTRODUCTION

The Secretary of Veterans Affairs was required by section 707 of P.L. 102-585, as amended by section 104 of P.L. 105-368 and section 502 of P.L. 111-163, to submit an annual report through 2014 on the results, status, and priorities of research activities related to the health consequences of military service in the GW to the Senate and House Committees on Veterans' Affairs. The Research Subcommittee of the interagency DHWG prepared the 2014 annual report to Congress, which was the 21st report on research and research activities (DHWG, 2004; DHWG, 2005; DHWG, 2006a; DHWG, 2006b; DHWG, 2007; DHWG, 2008; DHWG, 2009; DHWG, 2010; DHWG, 2011; DHWG, 2012; DHWG, 2013; DHWG, 2014; DHWG, 2015; MVHCB, 2001; MVHCB, 2002; PGVCB, 1995; PGVCB, 1996b; PGVCB, 1997; PGVCB, 1998; PGVCB, 1999; PGVCB, 2001). This report (2015) follows the general format of previous reports but is not required by Congress.

As in previous annual reports to Congress, the material presented is divided into six sections and three appendices. Section I is an introduction. Section II summarizes the research priorities and organization of the Federal GW research portfolio. Section III highlights and summarizes published research progress since the last report. Section IV summarizes Federal funding trends for GW research during the 10-year period from FY 2006 through FY 2015. Section V highlights new research projects and initiatives since the 2014 Annual Report to Congress. Section VI contains literature references, and the Appendices contain listings of federally-funded research projects.

II. RESEARCH PRIORITIES

A. Nineteen Research Topics

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

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

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

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

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

B. Research Portfolio Descriptors

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

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

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

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

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

- Environmental Toxicology (e.g., studies focused on specific environmental exposures such as pesticides, oil well fires, jet fuel, vaccines, medical prophylactic agents, etc.)
  - Petroleum products and combustion products (original Question 3)

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

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

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

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

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

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

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

- Diagnosis: studies that will improve the ability to diagnose previously unexplained conditions or to better refine diagnoses with new tools
- Exposure: studies that examine individual exposures and/or interactions of exposures (chemical, biological, pharmacological, physiological, etc.)
- Interactions: interactions of combined exposures (chemical, biological, pharmacological, physiological, etc.)

- Prevention: studies that will produce knowledge that could lead to disease prevention strategies
- Symptoms: prevalence and risk factors for symptoms and alterations in general health status
- Treatment: development or testing of new therapies

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

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

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

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

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

The research database on GWVI catalogs only research and development activities that either directly involve GW Veterans or answer specific questions about risk factors.

C. Portfolio Criteria

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

1. Studies of CMI affecting GW Veterans, including case definitions for CMI in GW Veterans and the general population.
   a) Case definitions of multisymptom illnesses affecting GW Veterans (Fukuda et al., 1998; Haley et al., 1997a; Haley et al., 1997b; Haley et al., 2002; Steele, 2000; Wolfe et al., 2002; IOM, 2014)
   b) Chronic fatigue syndrome (Dunphy et al., 2003; Eisen et al., 2005; Gray et al., 2002; The Iowa Persian Gulf Study Group, 1997; Unwin et al., 1999)
   c) Fibromyalgia (Eisen et al., 2005; The Iowa Persian Gulf Study Group, 1997)
   d) Irritable bowel syndrome (Dunphy et al., 2003; Gray et al., 2002; The Iowa Persian Gulf Study Group, 1997)
   e) Multiple chemical sensitivity (MCS) (Fiedler et al., 2004; Gray et al., 2002; The Iowa Persian Gulf Study Group, 1997)

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

1999; Kang et al., 2000; Knoke et al., 2000; Pierce, 1997; Proctor et al., 1998; Wolfe et al., 2002)

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

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

III. PUBLISHED RESULTS AND STATUS OF THE FIELD IN 2015

A. Summary

Since the 2014 *Annual Report to Congress,* numerous research studies have provided new and detailed information on the health problems of GW Veterans. A PubMed search retrieved 60 relevant articles published in English in calendar year 2015 or in 2014 after the last report was submitted. These articles include federally and non-federally funded research, as well as international research. Most of the articles are related to more than one of the five Research Focus Areas described in Section II. B., above. However, twenty-two can be characterized as Brain and Nervous System Function, twenty as Symptoms and General Health, twelve as Environmental Toxicology, and six as Immune Dysfunction. No articles regarding Reproductive Health were found for 2015.

B. Abstracts/Summaries from Published Research

Albertini RJ, Vacek PM, Carter EW, Nicklas JA, Squibb KS, Gucer PW, Engelhardt SM, McDiarmid MA (2015 Aug) Mutagenicity monitoring following battlefield exposures: Longitudinal study of HPRT mutations in Gulf War I veterans exposed to depleted uranium. Environ Mol Mutagen. 56(7):581-93. doi: 10.1002/em.21955.

A total of 70 military Veterans have been monitored for HPRT T-cell mutations in five separate studies at 2-year intervals over an 8-year period. Systemic depleted uranium (DU) levels were measured at the time of each study by determining urinary uranium (uU) excretion. Each HPRT study included 30-40 Veterans, several with retained DU-containing shrapnel. Forty-nine Veterans were evaluated in multiple studies, including 14 who were in all five studies. This permitted a characterization of the HPRT mutation assay over time to assess the effects of age, smoking and non-selected cloning efficiencies, as well as the inter- and intra-individual variability across time points. Molecular analyses identified the HPRT mutation and T-cell receptor (TCR) gene rearrangement in 1,377 mutant isolates. An unexpected finding was that in vivo clones of HPRT mutant T-cells were present in some Veterans, and could persist over several years of the study. The calculated HPRT mutant frequencies (MFs) were repeatedly elevated in replicate studies in three outlier Veterans with elevated urinary uranium excretion levels. However, these three outlier Veterans also harbored large and persistent in vivo HPRT mutant T-cell clones, each of which was represented by a single founder mutation. Correction for in vivo clonality allowed calculation of HPRT T-cell mutation frequencies (MutFs). Despite earlier reports of DU associated increases in HPRT MFs in some Veterans, the results presented here demonstrate that HPRT mutations are not increased by systemic DU exposure. Additional battlefield exposures were also evaluated for associations with HPRT mutations and none were found.

Alijotas-Reig J (2015 Sep) Human adjuvant-related syndrome or autoimmune/inflammatory syndrome induced by adjuvants. Where have we come from? Where are we going? A proposal for new diagnostic criteria. Lupus 24(10):1012-8. doi: 10.1177/0961203315579092.

In 1964, Miyoshi reported a series of patients with diverse symptoms after receiving treatment with silicone or paraffin fillers. Miyoshi named this condition 'human adjuvant disease'. Since then, the literature has been flooded with case reports and case series of granulomatous and systemic autoimmune disorders related to vaccines, infection or other adjuvants such as silicone and other biomaterials. A new term -autoimmune/inflammatory syndrome induced by adjuvants--has recently been coined for a process that includes several clinical features previously described by Miyoshi plus other clinical and laboratory parameters related to exposure to diverse external stimuli. Disorders such as siliconosis, Gulf War syndrome, macrophagic myofasciitis syndrome, sick building syndrome and post-vaccination syndrome have been included in autoimmune/inflammatory syndrome induced by adjuvants. Disorders such as Spanish toxic oil syndrome and Ardystil syndrome could also be included. Furthermore, biomaterials other than silicone should also be considered as triggering factors for these adjuvant-related syndromes. New diagnostic criteria in this field have been proposed. Nevertheless, many of these criteria are too subjective, leading to some patients being diagnosed with chronic fatigue syndrome or other 'central

sensitization syndromes'. Diagnostic criteria based only on objective clinical and laboratory data to be further discussed and validated are proposed herein.

Al-Shammri SN, Hanna MG, Chattopadhyay A, Akanji AO (2015 Jul 1) Sociocultural and Demographic Risk Factors for the Development of Multiple Sclerosis in Kuwait: A Case - Control Study. PLoS One 10(7):e0132106. doi: 10.1371/journal.pone.0132106.

INTRODUCTION: Immunological, genetic and environmental factors are believed to play important roles in the pathogenesis of Multiple Sclerosis (MS). There have been many studies on risk factors for MS but these have been mainly in Caucasian populations; robust studies in Arab populations remain relatively uncommon. This study therefore aimed to identify behavioral, socio-cultural, and demographic factors associated with development of MS in Kuwait, a high income Arab country, currently undergoing a demographic transition. SUBJECTS AND METHODS: In this case-control study, 195 Kuwaiti MS patients and 146 healthy age and sex-matched controls were recruited. Both groups of subjects were interviewed using a structured questionnaire, in relation to anthropometric, socio-cultural and demographic data, residence during the 1990/91 Gulf War and current and past medical history, including medications. We also clinically evaluated, and retrospectively reviewed medical records of patients to derive appropriate clinical information, including associated chronic medical illness requiring long-term treatment. RESULTS: On multiple logistic regression analysis after adjustment for potential confounders including age, gender and BMI, in all the subjects, a positive associations prevail with presence of MS and some sociocultural and demographic factors, which included non-Bedouin ethnicity (AOR 2, 95% CI 1.0-3.9, p 0.049), positive family history of MS (AOR 10.6, 95% CI 3.0-36.9), $p < 0.001$), and low daily sunlight exposure of < 15min/day (AOR 5.3, 95% CI 2.7-10.5 $p < 0.001$). In addition, while 41.8% of MS patients indicated at least one comorbidity, only 26.8% of the controls reported any associated physical illness, with the suggestion that presence of certain comorbidities might increase MS risk (AOR 2.4, 95% CI 1.3-4.7, $p < 0.001$). Other risk variables such as smoking status and mode of routine outdoor dressing were not significant in all the MS subjects taken as a whole, but demonstrated variably positive associations in the MS subgroup classified as those with established disease and those who were newly diagnosed and drug naïve. CONCLUSIONS: This study suggests that a positive family history of MS and presence of certain comorbidities appeared to be associated with an increased risk of developing MS. In contrast, relatively increased amount of daily sunlight exposure and Bedouin ethnicity appear to somewhat be protective. It is speculated that the relationship of sunlight exposure with MS might be due to vitamin D availability, and is deserving of further study.

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

Rates of amyotrophic lateral sclerosis (ALS) have been reported to be higher among US military veterans, who currently number more than 21 million, but the causal factor(s) has not been identified. We conducted a review to examine the weight of evidence for

associations between military service, deployments, and exposures and ALS etiology and survival. Thirty articles or abstracts published through 2013 were reviewed. Although the current evidence suggests a positive association with ALS etiology, it is too limited to draw firm conclusions regarding associations between military service and ALS etiology or survival. Some evidence suggests that deployment to the 1990-1991 Persian Gulf War may be associated with ALS etiology, but there is currently no strong evidence that any particular military exposure is associated with ALS etiology. Future studies should address the limitations of previous ones, such as reliance on mortality as a surrogate for incidence, a dearth of survival analyses, lack of clinical data, low statistical power, and limited exposure assessment. The Genes and Environmental Exposures in Veterans with Amyotrophic Lateral Sclerosis (GENEVA) Study is one such study, but additional research is needed to determine whether military-related factors are associated with ALS and to assess potential prevention strategies.

Bergman BP, Mackay DF, Pell JP (2015 Dec) Motor neurone disease and military service: evidence from the Scottish Veterans Health Study. Occup Environ Med. 72(12):877-9. doi: 10.1136/oemed-2015-103066.

OBJECTIVES: In 2003, it was reported that motor neurone disease was linked to military service in the 1990-1991 Gulf War. A large study in the US confirmed an association with military service but found no association with specific conflicts or length of service. Non-veteran studies have suggested an association with physical activity, smoking and other risk factors. We used data from the Scottish Veterans Health Study to investigate the association between motor neurone disease and military service in UK veterans. METHODS: Retrospective cohort study of 57,000 veterans born 1945-1985, and 173,000 demographically matched civilians, using Cox proportional hazard models to compare the risk of motor neurone disease overall, and by sex, birth cohort, length of service and year of recruitment. We had no data on smoking prevalence. RESULTS: Veterans had an increased risk of motor neurone disease compared with non-veterans (adjusted HR 1.49, 95% CI 1.01 to 2.21, p=0.046). The increase was independent of birth cohort, length or period of service, or year of recruitment. Risk was associated with a history of trauma or road traffic accident in veterans and non-veterans. CONCLUSIONS: We confirmed an increased risk of motor neurone disease in military veterans, although the absolute risk is extremely low. We found no evidence that the increased risk was associated with any specific conflict. We could not rule out that smoking (and perhaps other lifestyle factors) may be responsible for our findings. Trauma may play a role in the increased risk but further studies are needed.

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

BACKGROUND: Gulf War veterans were exposed to environmental toxins not present in other combat theaters resulting in a unique biological signature that only partially resembles that seen in other combat veterans with PTSD. Thus it is important to determine

if brain abnormalities seen in non-Gulf War veterans with PTSD are also present in Gulf War veterans. In this pilot study, diffusion tensor imaging (DTI) tractography was used to assess the ultra-structural integrity of fronto-limbic white matter connections in Gulf War veterans with and without PTSD. The effects of chronic multisymptom illness on DTI measures was also evaluated. METHODS: Subjects were 20 previously studied Gulf War veterans on whom MRIs had been obtained. Mean diffusivity (MD) and fractional anisotropy (FA) were determined for left and right cingulum bundle by DTI tractography and compared in separate analyses for 12 veterans with, and 8 without PTSD. The effect of chronic multisymptom illness and it's interaction with PTSD, were similarly investigated using multivariate ACOVA. Partial correlations were used to test the associations of both DTI indices with PTSD severity and plasma cortisol, controlling for whole brain volume. RESULTS: Significantly lower MD was demonstrated in the right cingulum bundle among Gulf War veterans with PTSD. There were no significant differences in MD or FA in the left cingulum bundle. The presence of chronic multisymptom illness significantly attenuated the PTSD associated decrement in right cingulum MD. Clinician and self-rated PTSD symptom severity scores were significantly associated with reduced MD and increased FA in the right cingulum. Similar associations were observed for 8am plasma cortisol in a subset of participants. CONCLUSIONS: The preliminary findings indicate increased structural integrity - supporting enhanced connectivity - between right amygdala and anterior cingulate cortex in PTSD. This effect was strongest among Gulf War veterans without chronic multisymptom illness. The association of both MD and FA in the right cingulum with PTSD severity, and with heightened glucocorticoid responsivity, suggests that these DTI findings are a reflection of current PTSD illness expression. Although based on a small sample, these microstructural observations are consistent with a functional model suggesting increased amygdala responsivity in association with anterior cingulate modulation in PTSD.

Blore JD, Sim MR, Forbes AB, Creamer MC, Kelsall HL (2015 Jun) Depression in Gulf War veterans: a systematic review and meta-analysis. Psychol Med 45(8):1565-1580. doi: 10.1017/S0033291714001913.

BACKGROUND: Although post-traumatic stress disorder (PTSD) has been a focus of attention in 1990/1991 Gulf War veterans, the excess risk of depression has not been clearly identified. We investigated this through a systematic review and meta-analysis of studies comparing depression in Gulf War veterans to depression in a comparison group of non-deployed military personnel. METHOD: Multiple electronic databases and grey literature were searched from 1990 to 2012. Studies were assessed for eligibility and risk of bias according to established criteria. RESULTS: Of 14 098 titles and abstracts assessed, 14 studies met the inclusion criteria. Gulf War veterans had over twice the odds of experiencing depression [odds ratio (OR) 2.28, 95% confidence interval (CI) 1.88-2.76] and dysthymia or chronic dysphoria (OR 2.39, 95% CI 2.0-2.86) compared to non-deployed military personnel. This finding was robust in sensitivity analyses, and to differences in overall risk of bias and psychological measures used. CONCLUSIONS: Despite divergent methodologies between studies, depression and dysthymia were twice as common in Gulf War veterans and are important medical conditions for clinicians and policymakers to be aware of in managing Gulf War veterans' health.

Burkhart L, Hogan N (2015 Mar 4) Being a Female Veteran: A Grounded Theory of Coping With Transitions. Soc Work Ment Health 13(2):108-127.

Female veterans, the fastest growing segment in the military, have unique pre-military histories and military experiences that are associated with post-military physical and mental health service needs. Successful treatment is contingent on a clearer understanding of the processes underlying these experiences. Data from 20 female veterans who served post-Gulf War were analyzed to generate a substantive theory of the process of women who entered, served in, and transitioned out of the military. Coping with transitions emerged as the basic psychosocial process used by female veterans. The Coping with transitions process is comprised of seven categories: Choosing the Military, Adapting to the Military, Being in the Military, Being a Female in the Military, Departing the Military, Experiencing Stressors of Being a Civilian, and Making Meaning of Being a Veteran-Civilian. The results of this study provide a theoretical description of the process female veterans experience when transitioning from a civilian identity, through military life stressors and adaptations, toward gaining a dual identity of being a veteran-civilian.

Chao LL, Zhang Y, Buckley S (2015 May) Effects of low-level sarin and cyclosarin exposure on white matter integrity in Gulf War Veterans. Neurotoxicology 48:239-48. doi: 10.1016/j.neuro.2015.04.005.

BACKGROUND: We previously found evidence of reduced gray and white matter volume in Gulf War (GW) veterans with predicted low-level exposure to sarin (GB) and cyclosarin (GF). Because loss of white matter tissue integrity has been linked to both gray and white matter atrophy, the current study sought to test the hypothesis that GW veterans with predicted GB/GF exposure have evidence of disrupted white matter microstructural integrity. METHODS: Measures of fractional anisotropy and directional (i.e., axial and radial) diffusivity were assessed from the 4T diffusion tensor images (DTI) of 59 GW veterans with predicted GB/GF exposure and 59 "matched" unexposed GW veterans (mean age: 48 ± 7 years). The DTI data were analyzed using regions of interest (ROI) analyses that accounted for age, sex, total brain gray and white matter volume, trauma exposure, posttraumatic stress disorder, current major depression, and chronic multisymptom illness status. RESULTS: There were no significant group differences in fractional anisotropy or radial diffusivity. However, there was increased axial diffusivity in GW veterans with predicted GB/GF exposure compared to matched, unexposed veterans throughout the brain, including the temporal stem, corona radiata, superior and inferior (hippocampal) cingulum, inferior and superior fronto-occipital fasciculus, internal and external capsule, and superficial cortical white matter blades. Post hoc analysis revealed significant correlations between higher fractional anisotropy and lower radial diffusivity with better neurobehavioral performance in unexposed GW veterans. In contrast, only increased axial diffusivity in posterior limb of the internal capsule was associated with better psychomotor function in GW veterans with predicted GB/GF exposure. CONCLUSIONS: The finding that increased axial diffusivity in a region of the brain that contains descending corticospinal fibers was associated with better psychomotor function and the lack of significant neurobehavioral deficits in veterans with predicted GB/GF

exposure hint at the possibility that the widespread increases in axial diffusivity that we observed in GW veterans with predicted GB/GF exposure relative to unexposed controls may reflect white matter reorganization after brain injury (i.e., exposure to GB/GF).

Chong SJ, Jiang L, Chow WE (2015 Aug) Challenges of Forward Naval Surgical Support for Maritime Forces. Mil Med 180(8):888-891. doi: 10.7205/MILMED-D-14-00532.

The emphasis of naval operations has shifted from conventional naval warfare since World War II to Operations Other than War such as Peace Support Operations and Humanitarian Aid and Disaster Relief. Maritime forces are increasingly deployed in distant areas of operations such as the Somali Basin and Gulf of Aden for longer durations, in a possibly higher threat environment against nonconventional threats such as in counter piracy operations. There is therefore a need to balance the challenges of providing adequate forward naval surgical support with limitations in medical manpower, logistics as well as the need for a suitable surgical platform for these deployments. This article aims to share the Republic of Singapore Navy's experience in overcoming some of these challenges. This includes the ability to deploy surgical containers onboard the Landing Ship Tank and Civil Resource vessels, and the ability to convert existing spaces onboard the endurance class Landing Ship Tank and other platforms such as the formidable class Frigate into surgical facilities. The key success factors such as the development of deep expertise in naval operational medicine, operationalization of third generation surgical stores, and enhanced interoperability among maritime forces will also be highlighted.

Conard P, Scott-Tilley D (2015 Oct-Dec) The Lived Experience of Female Veterans Deployed to the Gulf War II. Nurs Forum 50(4):228-40. doi: 10.1111/nuf.12097.

PURPOSE: The purpose of this inquiry is to discover the experiences of female veterans in order to understand the impacts of combat on their physical and mental health, and to shed light on directions for future research. The research question for this inquiry is: What is the lived experience of female combat veterans who deployed to Iraq and Afghanistan from 2001 through 2013? METHODS: The methodology used in this qualitative inquiry is a descriptive phenomenological approach using Husserl's philosophical framework. Colaizzi's method was used for data analysis. FINDINGS: Analysis revealed seven themes: living in constant fear while deployed, combat has different meanings, bringing the war home, fear of being forever changed, disrespect from fellow military members, physical health-for better or worse, and combat has rewarding experiences. CONCLUSION: Early detection and assessment is crucial to providing interventions to military veterans to reduce the invisible wound of war, posttraumatic stress disorder, and ultimately increase the quality of life.

Conard PL, Armstrong ML (2015 Jun 10) Deployed Women Veterans: Important Culturally Sensitive Care. Nurs Forum doi: 10.1111/nuf.12142. [Epub ahead of print]

PROBLEM: Today, with almost 23 million veterans in the nation, and currently only about 10 million, or less, of them seeking active services associated with the Veterans

Administration (VA) health facilities, these men and women veterans will be seeking some, more, or even all of their health care over their life time in civilian-based facilities. METHODS: Pertinent literary sources were reviewed to gather applicable data about the problem. FINDINGS: Every patient that enters your health facility should be asked an essential assessment question: "Have you served in the military?" Importantly, to gain effective rapport when they present, civilian nurses will need to anticipate their health needs and provide culturally sensitive care. Specific issues of deployed women veterans are provided in a series of two articles. CONCLUSION: This article provides a snapshot of the uniquely entrenched military culture, as well as women service member experiences in wartime, including the Global War on Terror (Iraq and Afghanistan). The next article discusses the various healthcare differences (e.g., post-traumatic stress disorder and military sexual trauma), difficulties (e.g., reproductive, gynecologic, urinary, employment, homelessness issues), and gender disparities (varied treatment patterns) so the civilian nurse can better advocate for women veterans.

Conard PL, Armstrong ML (2015 Jun 11) Advocating for Deployed Women Veterans' Health Differences, Difficulties, and Disparities. Nurs Forum doi: 10.1111/nuf.12143. [Epub ahead of print]

PROBLEM: The preceding article presented a glimpse of deployed women veterans, their military culture, and their experiences in the Global War on Terror (Iraq and Afghanistan) to assist civilian nurses to gain significant rapport and provide important culturally sensitive care. METHODS: Pertinent literary sources were reviewed to gather applicable data about the problem. FINDINGS: A confirmatory answer from the assessment question of "Have you served in the military?" and the use of the Military Health History Pocket Card for Clinicians (available at http://www.va.gov.oaa/pocketcard) will assist with revealing possible health risks from the increased amounts of military men and women veterans seeking (and/or returning to) a variety of community-based health services. This article about deployed women veterans examines their specific health differences (e.g., research literature, post-traumatic stress disorder, and military sexual trauma), difficulties (e.g., reproductive, gynecologic, urinary, suicide), and gender disparities (varied treatment patterns). CONCLUSION: Understanding these gender situations, civilian nurses can better advocate with increasing evidence-based decisions that their physical and behavioral responses were different from their male counterparts. Continual assessment, knowledgeable care, ongoing literature review, interdisciplinary health team development, and the presence of resourceful community agencies should be a significant part of their holistic care.

Conard PL, Armstrong ML, Young C, Hogan LM (2015 Mar) Nursing advocacy for women veterans and suicide. J Psychosoc Nurs Ment Health Serv 53(3):24-30. doi: 10.3928/02793695-20150220-01.

Little is known about suicide variables in women Veterans. The authors reviewed numerous applicable health care and military literary sources regarding suicide in this population. The current article describes the surrounding circumstances, military war/conflict culture, and potential effects on women Veterans, including major collection

problems with current Veteran data. Women Veterans are increasingly reporting more behavioral health issues (e.g., posttraumatic stress disorder) and attempting suicide upon civilian reintegration. Outcomes from this literature review suggest the importance of nursing advocacy to create better rapport and communication with women Veterans from Vietnam, Gulf I, Iraq, and Afghanistan wars seeking care at civilian health facilities, as some may present with suicidal ideologies.

Craddock TJ, Del Rosario RR, Rice M, Zysman JP, Fletcher MA, Klimas NG, Broderick G (2015 Jul 20) Achieving Remission in Gulf War Illness: A Simulation-Based Approach to Treatment Design. PLoS One 10(7):e0132774. doi: 10.1371/journal.pone.0132774. Gulf War Illness (GWI) is a chronic multi-symptom disorder affecting up to one-third of the 700,000 returning veterans of the 1991 Persian Gulf War and for which there is no known cure. GWI symptoms span several of the body's principal regulatory systems and include debilitating fatigue, severe musculoskeletal pain, cognitive and neurological problems. Using computational models, our group reported previously that GWI might be perpetuated at least in part by natural homeostatic regulation of the neuroendocrine-immune network. In this work, we attempt to harness these regulatory dynamics to identify treatment courses that might produce lasting remission. Towards this we apply a combinatorial optimization scheme to the Monte Carlo simulation of a discrete ternary logic model that represents combined hypothalamic-pituitary-adrenal (HPA), gonadal (HPG), and immune system regulation in males. In this work we found that no single intervention target allowed a robust return to normal homeostatic control. All combined interventions leading to a predicted remission involved an initial inhibition of Th1 inflammatory cytokines (Th1Cyt) followed by a subsequent inhibition of glucocorticoid receptor function (GR). These first two intervention events alone ended in stable and lasting return to the normal regulatory control in 40% of the simulated cases. Applying a second cycle of this combined treatment improved this predicted remission rate to 2 out of 3 simulated subjects (63%). These results suggest that in a complex illness such as GWI, a multi-tiered intervention strategy that formally accounts for regulatory dynamics may be required to reset neuroendocrine-immune homeostasis and support extended remission.

Craddock TJ, Harvey JM, Nathanson L, Barnes ZM, Klimas NG, Fletcher MA, Broderick G (2015 Jul 9) Using gene expression signatures to identify novel treatment strategies in gulf war illness. BMC Med Genomics. 8:36. doi: 10.1186/s12920-015-0111-3.

BACKGROUND: Gulf War Illness (GWI) is a complex multi-symptom disorder that affects up to one in three veterans of this 1991 conflict and for which no effective treatment has been found. Discovering novel treatment strategies for such a complex chronic illness is extremely expensive, carries a high probability of failure and a lengthy cycle time. Repurposing Food and Drug Administration approved drugs offers a cost-effective solution with a significantly abbreviated timeline. METHODS: Here, we explore drug re-purposing opportunities in GWI by combining systems biology and bioinformatics techniques with pharmacogenomic information to find overlapping elements in gene expression linking GWI to successfully treated diseases. Gene modules were defined based on cellular function and their activation estimated from the differential expression of each module's

constituent genes. These gene modules were then cross-referenced with drug atlas and pharmacogenomic databases to identify agents currently used successfully for treatment in other diseases. To explore the clinical use of these drugs in illnesses similar to GWI we compared gene expression patterns in modules that were significantly expressed in GWI with expression patterns in those same modules in other illnesses. RESULTS: We found 19 functional modules with significantly altered gene expression patterns in GWI. Within these modules, 45 genes were documented drug targets. Illnesses with highly correlated gene expression patterns overlapping considerably with GWI were found in 18 of the disease conditions studied. Brain, muscular and autoimmune disorders composed the bulk of these. CONCLUSION: Of the associated drugs, immunosuppressants currently used in treating rheumatoid arthritis, and hormone based therapies were identified as the best available candidates for treating GWI symptoms.

Currie J, Chipps J (2015 Oct) Mapping the field of military nursing research 1990-2013: A bibliometric review. Int J Nurs Stud. 52(10):1607-16. doi:10.1016/j.ijnurstu.2015.06.008.

BACKGROUND: Over the past 20 years, military forces worldwide have been engaged in a number of conflicts and humanitarian operations and the impact of this on the field of military nursing research is unknown. The aim of this bibliometric review was to investigate the research field of military nursing in the main databases with the purpose to describe trends in military nursing research since 1990. OBJECTIVES: To identify military nursing papers in the main databases and to describe the field of military nursing research for the period 1990-2013 in terms of research productivity, trends in topic focus, trends in authorship and country of publication. METHOD: Bibliometric review of published military nursing research papers was undertaken in March 2014 and data was extracted and coded and trends were analyzed using SPSSv21. RESULTS: In total 237 articles were included in the review. The majority of publications emanating from America (n=175, 73.8%) and the quantity of papers has increased significantly since the commencement of the second Gulf War in Iraq from 2003 onwards (n=156, 65.8%). This has been accompanied by a shift in topic focus from professional (n=16, 20.3%) and occupational issues (n=17, 21.5%) pre 2003, to clinical (n=48, 30.4%) and an increase in multidisciplinary research from 4% in 1990-94 to 29% in 2010-13. The mean citations were 10.6 (sd 17.0) and the mean references per paper post 2003 showed a marked increase from 23.5 to 25.4. CONCLUSION: The military nursing research field appears stronger than it has been in the past twenty years and has demonstrated increased transferability to other fields. To maintain this momentum and further develop the field of military nursing research, military forces worldwide need to devise focused nursing research strategies that involve international and multidisciplinary collaboration.

Dickstein BD, Weathers FW, Angkaw AC, Nievergelt CM, Yurgil K, Nash WP, Baker DG, Litz BT; Marine Resiliency Study Team (2015 Jun) Diagnostic Utility of the Posttraumatic Stress Disorder (PTSD) Checklist for Identifying Full and Partial PTSD in Active-Duty Military. Assessment 22(3):289-297. doi: 10.1177/1073191114548683.

The aim of this study was to determine optimally efficient cutoff scores on the Posttraumatic Stress Disorder Checklist (PCL) for identifying full posttraumatic stress disorder (PTSD) and partial PTSD (P-PTSD) in active-duty Marines and Sailors. Participants were 1,016 Marines and Sailors who were administered the PCL and Clinician-Administered PTSD Scale (CAPS) 3 months after returning from Operations Iraqi and Enduring Freedom. PCL cutoffs were tested against three CAPS-based classifications: full PTSD, stringent P-PTSD, and lenient P-PTSD. A PCL score of 39 was found to be optimally efficient for identifying full PTSD. Scores of 38 and 33 were found to be optimally efficient for identifying stringent and lenient P-PTSD, respectively. Findings suggest that the PCL cutoff that is optimally efficient for detecting PTSD in active-duty Marines and Sailors is substantially lower than the score of 50 commonly used by researchers. In addition, findings provide scores useful for identifying P-PTSD in returning service members.

Friedl KE (2014 Jun) Introduction: Evolution of military and veterans brain health research. Alzheimers Dement 10(3 Suppl):S94-6. doi: 10.1016/j.jalz.2014.05.001.

Recent military conflicts have resulted in a new focus on brain injury and brain health of service members and aging veterans. The wars in Iraq and Afghanistan have been characterized by injuries from improvised explosive devices, including nearly a quarter million cases of mild traumatic brain injury (mTBI) since 2000. Brain injuries represent a higher proportion of injuries compared with previous conflicts such as the Vietnam War, in part because the modern body armor has altered the pattern of combat injuries.

Georgopoulos AP, James LM, Mahan MY, Joseph J, Georgopoulos A, Engdahl BE (2015 Nov 22) Reduced Human Leukocyte Antigen (HLA) Protection in Gulf War Illness (GWI). EBioMedicine. 3:79-85. doi: 10.1016/j.ebiom.2015.11.037.

BACKGROUND: Gulf War Illness (GWI) is a disease of unknown etiology with symptoms suggesting the involvement of an immune process. Here we tested the hypothesis that Human Leukocyte Antigen (HLA) composition might differ between veterans with and without GWI. METHODS: We identified 144 unique alleles of Class I and II HLA genes in 82 veterans (66 with and 16 without GWI). We tested the hypothesis that a subset of HLA alleles may classify veterans in their respective group using a stepwise linear discriminant analysis. In addition, each participant rated symptom severity in 6 domains according to established GWI criteria, and an overall symptom severity was calculated. FINDINGS: We found 6 Class II alleles that classified participants 84.1% correctly (13/16 control and 56/66 GWI). The number of copies of the 6 alleles was significantly higher in the control group, suggesting a protective role. This was supported by a significant negative dependence of overall symptom severity on the number of allele copies, such that symptom severity was lower in participants with larger numbers of allele copies. INTERPRETATION: These results indicate a reduced HLA protection (i.e. genetic susceptibility) in veterans with GWI.

Golier JA, Caramanica K, Michaelides AC, Makotkine I, Schmeidler J, Harvey PD, Yehuda R (2016 Feb) A randomized, double-blind, placebo-controlled, crossover

trial of mifepristone in Gulf War veterans with chronic multisymptom illness. Psychoneuroendocrinology 64:22-30. doi: 10.1016/j.psyneuen.2015.11.001.

No pharmacological treatments have been demonstrated to effectively treat chronic multisymptom illness (CMI) in Gulf War veterans (GWV). This study assessed the effect of the glucocorticoid receptor antagonist mifepristone in GWV with CMI. A randomized, double-blind, cross-over trial of mifepristone, with two six-week treatment phases separated by a one-month washout period, was conducted at a Veterans Affairs (VA) hospital between 2008 and 2011. Participants were randomized to receive either 200mg of mifepristone per day or matched placebo first. The primary clinical outcome measure was change in self-reported physical health. Neurocognitive functioning and self-reported measures of depression, PTSD, and fatigue were secondary outcomes. Sixty-five participants enrolled, of whom 36 were randomized and 32 (mean age, 49.1 (7.2) years) completed the study. Physical and mental health status and neurocognitive functioning were poor at baseline. Mifepristone treatment was not associated with improvement in self-reported physical health (p=0.838) or in other self-reported measures of mental health. Mifepristone treatment was significantly associated with improvements in verbal learning (p=0.008, d=0.508), in the absence of improvement in other cognitive measures (working memory (p=0.914), visual learning (p=0.643) and a global composite measure (p=0.937). Baseline morning cortisol levels and lysozyme IC50-DEX, a measure of peripheral glucocorticoid sensitivity, displayed a significant relationship with endpoint verbal learning scores (p=0.012 and p=0.007, respectively). The magnitude of cortisol change during treatment mediated the improvement in verbal learning. This study was negative for the primary and secondary clinical outcomes. However, the data suggest a moderate dose of mifepristone may have circumscribed cognitive-enhancing effects in CMI. Further study is warranted to determine whether and through which mechanisms mifepristone treatment can yield clinically meaningful improvement in cognitive function in CMI or other neuropsychiatric conditions associated with HPA axis dysregulation.

Gwini SM, Forbes AB, Kelsall HL, Ikin JF, Sim MR (2015 Dec) Increased symptom reporting persists in 1990-1991 Gulf War veterans 20 years post deployment. Am J Ind Med. 58(12):1246-54. doi: 10.1002/ajim.22490.

BACKGROUND: Following the 1990-1991 Gulf War, Gulf War veterans (veterans) reported health symptoms more commonly than non-deployed groups. This article examines symptom persistence, incidence and prevalence 20 years on. METHODS: In 2000-2003 and 2011-2012, a 63-item symptom checklist was administered to 697 veterans and 659 comparison group. Symptomatology was compared using log-binomial regression. RESULTS: Both veterans and comparison group reported significantly increased prevalence (3-52%) over time in more than half the symptoms, with a similar overall rate of increase. Half the symptoms had higher incidence (risk-ratios ranged 1.43-1.50) and a quarter were more persistent (risk-ratios ranged 1.12-1.20) in veterans than the comparison group. CONCLUSIONS: Symptomatology increased in both groups over time, but persisted to a similar extent and had higher incidence among veterans than the comparison group. The gap in symptom prevalence between the two groups remained unchanged. These findings suggest enduring health consequences of Gulf War service.

Hammond KW, Ben-Ari AY, Laundry RJ, Boyko EJ, Samore MH (2015 Dec) The Feasibility of Using Large-Scale Text Mining to Detect Adverse Childhood Experiences in a VA-Treated Population. J Trauma Stress. 28(6):505-514. doi: 10.1002/jts.22058. Free text in electronic health records resists large-scale analysis. Text records facts of interest not found in encoded data, and text mining enables their retrieval and quantification. The U.S. Department of Veterans Affairs (VA) clinical data repository affords an opportunity to apply text-mining methodology to study clinical questions in large populations. To assess the feasibility of text mining, investigation of the relationship between exposure to adverse childhood experiences (ACEs) and recorded diagnoses was conducted among all VA-treated Gulf war veterans, utilizing all progress notes recorded from 2000-2011. Text processing extracted ACE exposures recorded among 44.7 million clinical notes belonging to 243,973 veterans. The relationship of ACE exposure to adult illnesses was analyzed using logistic regression. Bias considerations were assessed. ACE score was strongly associated with suicide attempts and serious mental disorders (ORs = 1.84 to 1.97), and less so with behaviorally mediated and somatic conditions (ORs = 1.02 to 1.36) per unit. Bias adjustments did not remove persistent associations between ACE score and most illnesses. Text mining to detect ACE exposure in a large population was feasible. Analysis of the relationship between ACE score and adult health conditions yielded patterns of association consistent with prior research.

Hao Y, Liu C, Huang J, Gu Y, Li H, Yang Z, Liu J, Wang W, Li R (2016 Jan 1) Ghrelin protects against depleted uranium-induced apoptosis of MC3T3-E1 cells through oxidative stress-mediated p38-mitogen-activated protein kinase pathway. Toxicol Appl Pharmacol 290:116-125. doi: 10.1016/j.taap.2015.10.022. Depleted uranium (DU) mainly accumulates in the bone over the long term. Osteoblast cells are responsible for the formation of bone, and they are sensitive to DU damage. However, studies investigating methods of reducing DU damage in osteoblasts are rarely reported. Ghrelin is a stomach hormone that stimulates growth hormones released from the hypothalamic-pituitary axis, and it is believed to play an important physiological role in bone metabolism. This study evaluates the impact of ghrelin on DU-induced apoptosis of the osteoblast MC3T3-E1 and investigates its underlying mechanisms. The results show that ghrelin relieved the intracellular oxidative stress induced by DU, eliminated reactive oxygen species (ROS) and reduced lipid peroxidation by increasing intracellular GSH levels; in addition, ghrelin effectively suppressed apoptosis, enhanced mitochondrial membrane potential, and inhibited cytochrome c release and caspase-3 activation after DU exposure. Moreover, ghrelin significantly reduced the expression of DU-induced phosphorylated p38-mitogen-activated protein kinase (MAPK). A specific inhibitor (SB203580) or specific siRNA of p38-MAPK could significantly suppress DU-induced apoptosis and related signals, whereas ROS production was not affected. In addition, ghrelin receptor inhibition could reduce the anti-apoptosis effect of ghrelin on DU and reverse the effect of ghrelin on intracellular ROS and p38-MAPK after DU exposure. These results suggest that ghrelin can suppress DU-induced apoptosis of MC3T3-E1 cells, reduce DU-induced oxidative stress by interacting with its receptor, and inhibit downstream p38-MAPK activation, thereby suppressing the mitochondrial-dependent apoptosis pathway.

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

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

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

The toxicity of the class of chemicals known as the organophosphates (OP) is most commonly attributed to the inhibition of the enzyme acetylcholinesterase. However, there is significant evidence that this mechanism may not account for all of the deleterious neurologic and neurobehavioral symptoms of OP exposure, especially those associated with levels that produce no overt signs of acute toxicity. In the study described here we evaluated the effects of the commonly used OP-pesticide, chlorpyrifos (CPF) on axonal transport in the brains of living rats using manganese (Mn2+)-enhanced magnetic resonance imaging (MEMRI) of the optic nerve (ON) projections from the retina to the superior colliculus (SC). T1-weighted MEMRI scans were evaluated at 6 and 24h after intravitreal injection of Mn2+. As a positive control for axonal transport deficits, initial studies were conducted with the tropolone alkaloid colchicine administered by intravitreal injection. In subsequent studies both single and repeated exposures to CPF were evaluated for effects on axonal transport using MEMRI. As expected, intravitreal injection of colchicine (2.5μg) produced a robust decrease in transport of Mn2+ along the optic

nerve (ON) and to the superior colliculus (SC) (as indicated by the reduced MEMRI contrast). A single subcutaneous (s.c.) injection of CPF (18.0mg/kg) was not associated with significant alterations in the transport of Mn2+. Conversely, 14-days of repeated s.c. exposure to CPF (18.0mg/kg/day) was associated with decreased transport of Mn2+ along the ONs and to the SC, an effect that was also present after a 30-day (CPF-free) washout period. These results indicate that repeated exposures to a commonly used pesticide, CPF can result in persistent alterations in axonal transport in the living mammalian brain. Given the fundamental importance of axonal transport to neuronal function, these observations may (at least in part) explain some of the long term neurological deficits that have been observed in humans who have been repeatedly exposed to doses of OPs not associated with acute toxicity.

Ikin JF, McKenzie DP, Gwini SM, Kelsall HL, Creamer M, McFarlane AC, Clarke DM, Wright B, Sim M (2016 Jan 1) Major depression and depressive symptoms in Australian Gulf War veterans 20 years after the Gulf War. J Affect Disord 189:77-84. doi: 10.1016/j.jad.2015.09.016.

BACKGROUND: Risk of major depression (depression) was elevated in Australia's Gulf War veterans in a 2000-2002 (baseline) study. A follow up study has measured the Gulf War-related risk factors for depression, also the current prevalence and severity of depression, use of anti-depressant medication, and persistence, remittance or incidence of depression since baseline in Gulf War veterans and a military comparison group. METHODS: Participants completed the Composite International Diagnostic Interview v.2.1, the 9-item Patient Health Questionnaire and the Military Service Experience Questionnaire, and consented to Repatriation Pharmaceutical Benefits Scheme (RPBS) and PBS linkage. RESULTS: Prevalence of depression (9.7% Gulf War veterans and 7.7% comparison group; adj RR=1.2, 95% CI 0.8-1.7), and pattern of persistence, remittance and incidence of depression since baseline, were similar in the two groups, however veterans reported slightly more severe symptoms (adj median difference 1, 95% CI 0.26-1.74) and were more likely to have been dispensed anti-depressant medication (adj RR=1.56, 95% CI 1.05-2.32). Depression amongst veterans was associated with self-reported Gulf War-related stressors in a dose-response relationship (adj RR 1.06, 95% CI 1.02-1.09). LIMITATIONS: Lower participation rates at follow up resulted in reduced statistical power compared with baseline, Gulf War related stressor data collected at baseline was at risk of recall bias, and RPBS and PBS databases do not capture all dispensed Nervous System medications. CONCLUSIONS: More than 20 years after the Gulf War, veterans are experiencing slightly more severe depressive symptoms than a military comparison group, and depression continues to be associated with Gulf War-related stressors.

Institute of Medicine, National Academies of Sciences, Engineering, and Medicine, Board on the Health of Select Populations (2015 Dec 11) Committee on Designing and Epidemiologic Study for Multiple Sclerosis and Other Neurologic Disorders in Veterans of the Persian Gulf and Post 9/11 Wars. National Academies Press (US), Washington (DC).

https://www.nap.edu/catalog/21870/considerations-for-designing-an-epidemiologic-study-for-multiple-sclerosis-and-other-neurologic-disorders-in-pre-and-post-911-gulf-war-veterans

Jitnarin N, Poston WS, Haddock CK, Jahnke S (2015 May) Health in the news: an analysis of magazines coverage of health issues in veterans and military service organizations. Mil Med 180(5):539-546. doi: 10.7205/MILMED-D-14-00210.

The purpose of this study was to conduct a content analysis of Veterans and Military Service Organizations (VMSOs) magazines to determine what health-related topics VMSOs target and how they inform their constituencies about health issues. Health-related topics in 288 VMSOs' magazines from 21 VMSOs published in 2011 and 2012 were coded by trained raters using a standardized manual. The top three most addressed health topics were Health Services (Health care, Insurance), Disability and Disability benefits, and post-traumatic stress disorder. Topics least frequently covered were Tobacco and Smoking cessation, Illegal drugs, Alcohol, Gulf War Syndrome, and Weight and Body composition. VMSOs are concerned about the health and well-being of their members given the considerable amount of content devoted to certain health topics such as health insurance concerns, disability, and post-traumatic stress disorder. However, other health concerns that affect a considerable number of both current military personnel and veterans and cost both the Department of Veterans Affairs and the Department of Defense millions annually, such as drug and alcohol problems, and tobacco use and smoking cessation, are infrequently covered. The results of this study improve our understanding of the health-related information that reaches the military and veteran populations through this important media outlet.

Kearney DJ, Simpson TL, Malte CA, Felleman B, Martinez ME, Hunt SC (2016 Feb) Mindfulness-based Stress Reduction in Addition to Usual Care Is Associated with Improvements in Pain, Fatigue, and Cognitive Failures Among Veterans with Gulf War Illness. Am J Med 129(2):204-14. doi: 10.1016/j.amjmed.2015.09.015.
BACKGROUND: Many Gulf War I veterans report ongoing negative health consequences. The constellation of pain, fatigue, and concentration/memory disturbances is referred to as "Gulf War illness." Prior research suggests that mindfulness-based stress reduction may be beneficial for these symptoms, but mindfulness-based stress reduction has not been studied for veterans with Gulf War illness. The objective of this trial was to conduct a pilot study of mindfulness-based stress reduction for veterans with Gulf War illness.
METHODS: Veterans (N = 55) with Gulf War illness were randomly assigned to treatment as usual plus mindfulness-based stress reduction or treatment as usual only. Mindfulness-based stress reduction was delivered in 8 weekly 2.5-hour sessions plus a single 7-hour weekend session. Pain, fatigue, and cognitive failures were the primary outcomes, assessed at baseline, after mindfulness-based stress reduction, and 6 months follow-up. Secondary outcomes included symptoms of posttraumatic stress disorder and depression.
RESULTS: In intention-to-treat analyses, at 6-month follow-up, veterans randomized to mindfulness-based stress reduction plus treatment as usual reported greater reductions in pain ($f = 0.33$; $P = .049$), fatigue ($f = 0.32$; $P = .027$), and cognitive failures ($f = 0.40$; $P < .001$). Depressive symptoms showed a greater decline after mindfulness-based stress

reduction (f = 0.22; P = .050) and at 6 months (f = 0.27; P = .031) relative to treatment as usual only. Veterans with posttraumatic stress disorder at baseline randomized to mindfulness-based stress reduction plus treatment as usual experienced significantly greater reductions in symptoms of posttraumatic stress disorder after mindfulness-based stress reduction (f = 0.44; P = .005) but not at 6 months follow-up (f = 0.31; P = .082). CONCLUSIONS: Mindfulness-based stress reduction in addition to treatment as usual is associated with significant improvements in self-reported symptoms of Gulf War illness, including pain, fatigue, cognitive failures, and depression.

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

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

Ker J (2015 Mar) Of poppies and men – from trench nephritis to Gulf War syndrome. J R Coll Physicians Edinb 45(1):91-92.

In 2008, another editorial was published in the Lancet4 stating that: ‘a congressionally mandated group has concluded that Gulf War syndrome is a real, serious and in many cases, deadly illness.’ This statement acknowledged that more than 174,000 US veterans and 6,000–12,000 UK soldiers suffered from chronic headaches, fatigue, cognitive problems, pain and chronic digestive, respiratory and skin disorders, which were initially attributed to pesticides and pyridostigmine bromide. However, Gulf War syndrome is still a topic of heated debate and no consensus on its cause has yet been reached.

Kerr KJ (2015) Gulf War illness: an overview of events, most prevalent health outcomes, exposures, and clues as to pathogenesis. Rev Environ Health. 30(4):273-86. doi: 10.1515/reveh-2015-0032.

INTRODUCTION: During or very soon after the 1990-1991 Persian Gulf War, veterans of the conflict began to report symptoms of illness. Common complaints included combinations of cognitive difficulties, fatigue, myalgia, rashes, dyspnea, insomnia, gastrointestinal symptoms and sensitivity to odors. Gradually in the USA, and later in the UK, France, Canada, Denmark and Australia, governments implemented medical assessment programs and epidemiologic studies to determine the scope of what was popularly referred to as "the Gulf War syndrome". Attention was drawn to numerous potentially toxic deployment-related exposures that appeared to vary by country of deployment, by location within the theater, by unit, and by personal job types. Identifying a single toxicant cause was considered unlikely and it was recognized that outcomes were influenced by genetic variability in xenobiotic metabolism. METHODS: Derived from primary papers and key reports by the Research Advisory Committee on Gulf War Veterans' Illnesses and the Institute of Medicine, a brief overview is presented of war related events, symptoms and diagnostic criteria for Gulf War illness (GWV), some international differences, the various war-related exposures and key epidemiologic studies. Possible exposure interactions and pathophysiologic mechanisms are discussed. RESULTS: Exposures to pyridostigmine bromide, pesticides, sarin and mustard gas or combinations thereof were most associated with GWI, especially in some genotype subgroups. The resultant oxidant stress and background exposome must be assumed to have played a role. CONCLUSION: Gulf War (GW) exposures and their potential toxic effects should be considered in the context of the human genome, the human exposome and resultant oxidant stress to better characterize this unique environmentally-linked illness and, ultimately, provide a rationale for more effective interventions and future prevention efforts.

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

Gulf War illness (GWI) is a chronic disease of unknown etiology characterized by persistent symptoms such as cognitive impairment, unexplained fatigue, pervasive pain, headaches, and gastrointestinal abnormalities. Current reports suggest that as many as 200,000 veterans who served in the 1990-1991 Persian Gulf War were afflicted. Several potential triggers of GWI have been proposed including chemical exposure, toxins, vaccines, and unknown infectious agents. However, a definitive cause of GWI has not been identified and a specific biological marker that can consistently delineate the disease has not been defined. Myalgic encephalomyelitis (ME) is a disease with similar and overlapping symptomology, and subjects diagnosed with GWI typically fit the diagnostic criteria for ME. For these reasons, GWI is often considered a subgroup of ME. To explore this possibility and identify immune parameters that may help to understand GWI pathophysiology, we measured 77 serum cytokines in subjects with GWI and compared these data to that of subjects with ME as well as healthy controls. Our analysis identified a group of cytokines that identified ME and GWI cases with sensitivities of 92.5% and 64.9%, respectively. The five most significant cytokines in decreasing order of importance

were IL-7, IL-4, TNF-α, IL-13, and IL-17F. When delineating GWI and ME cases from healthy controls, the observed specificity was only 33.3%, suggesting that with respect to cytokine expression, GWI cases resemble control subjects to a greater extent than ME cases across a number of parameters. These results imply that serum cytokines are representative of ME pathology to a greater extent than GWI and further suggest that the two diseases have distinct immune profiles despite their overlapping symptomology.

Llabre MM, Hadi F, La Greca AM, Lai BS (2015) Psychological distress in young adults exposed to war-related trauma in childhood. J Clin Child Adolesc Psychol. 44(1):169-80. doi: 10.1080/15374416.2013.828295.

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

McDiarmid MA, Gaitens JM, Hines S, Condon M, Roth T, Oliver M, Gucer P, Brown L, Centeno JA, Streeten E, Squibb KS (2015 Jun) Biologic monitoring and surveillance results for the department of veterans affairs' depleted uranium cohort: Lessons learned from sustained exposure over two decades. Am J Ind Med 58(6):583-94. doi: 10.1002/ajim.22435.

BACKGROUND: A small group of Gulf War I veterans wounded in depleted uranium (DU) friendly fire incidents have been monitored in a clinical surveillance program at the Veterans Affairs Medical Center, Baltimore since 1994. METHODS: An in-patient clinical surveillance protocol was performed on 35 members of the cohort, including exposure monitoring for total and isotopic uranium concentrations in urine and a comprehensive assessment of health outcomes. RESULTS: Although urine U concentrations continue to be elevated in this group, illustrating on-going in situ mobilization of U from embedded fragments, no consistent U-related health effects have been observed. CONCLUSIONS: Now more than 20 years since first exposure to DU, an aging cohort of military veterans continues to show no U-related health effects in known target organs of U toxicity. As tissue concentrations continue to accrue with exposure duration, critical tissue-specific U concentration thresholds may be reached, thus recommending on-going surveillance of this veteran cohort.

McKenzie DP, Sim MR, Clarke DM, Forbes AB, Ikin JF, Kelsall HL (2015 Dec) Developing a brief depression screen and identifying associations with comorbid physical and psychological illness in Australian Gulf War veterans. J Psychosom Res 79(6):566-73. doi: 10.1016/j.jpsychores.2015.08.003.

OBJECTIVE: Major depression occurs frequently in veterans, and is associated with comorbid psychological and physical disorders and poorer quality of life. Depression can be difficult to detect in primary care, while lengthy assessment instruments can deter use. Our study aimed to develop a brief depression screen that could be used by veterans and caregivers, and then to compare the association between the brief screen and comorbidities and quality of life with that of a longer instrument. METHODS: Our dataset comprised 1204 male Royal Australian Navy veterans of the 1990/91 Gulf War. Depressive symptoms were assessed using the General Health Questionnaire (GHQ-12), health-related quality of life by the Short-Form Health Survey (SF-12), major depression and comorbid psychiatric diagnoses such as posttraumatic disorder (PTSD) using Diagnostic and Statistical Manual (DSM-IV) criteria. Comorbid physical illnesses including musculoskeletal disorders, chronic fatigue and diabetes were examined. RESULTS: A brief depression screen of three key self-reported symptoms was identified. Veterans with major depression present according to the screen were over four times more likely to have multisymptom illness or PTSD, and almost twice as likely to have musculoskeletal disorders. Having depression according to the brief screen and having at least one other physical or psychological condition was associated with poorer quality of life. Similar results were obtained for a longer screen based on all GHQ-12 items. CONCLUSION: A 3 item depression screen performed as well as a 12 item one in identifying major depression, comorbid physical and psychological illness and poorer quality of life in veterans.

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

Cognitive dysfunction is amongst the most conspicuous symptoms in Gulf War illness (GWI). Combined exposure to the nerve gas antidote pyridostigmine bromide (PB), pesticides and stress during the Persian Gulf War-1 (PGW-1) are presumed to be among the major causes of GWI. Indeed, our recent studies in rat models have shown that exposure to GWI-related (GWIR) chemicals and mild stress for 4 weeks engenders cognitive impairments accompanied with several detrimental changes in the hippocampus. In this study, we tested whether reduced numbers of hippocampal gamma-amino butyric acid (GABA)-ergic interneurons are among the pathological changes induced by GWIR-chemicals and stress. Animals were exposed to low doses of GWIR-chemicals and mild stress for 4 weeks. Three months after this exposure, subpopulations of GABA-ergic interneurons expressing the calcium binding protein parvalbumin (PV), the neuropeptide Y (NPY) and somatostatin (SS) in the hippocampus were stereologically quantified. Animals exposed to GWIR-chemicals and stress for 4 weeks displayed reduced numbers of PV-expressing GABA-ergic interneurons in the dentate gyrus and NPY-expressing

interneurons in the CA1 and CA3 subfields. However, no changes in SS+ interneuron population were observed in the hippocampus. Furthermore, GABA-ergic interneuron deficiency in these animals was associated with greatly diminished hippocampus neurogenesis. Because PV+ and NPY+ interneurons play roles in maintaining normal cognitive function and neurogenesis, and controlling the activity of excitatory neurons in the hippocampus, reduced numbers of these interneurons may be one of the major causes of cognitive dysfunction and reduced neurogenesis observed in GWI. Hence, strategies that improve inhibitory neurotransmission in the hippocampus may prove beneficial for reversing cognitive dysfunction in GWI.

Moffett K, Crosson B, Spence JS, Case K, Levy I, Gopinath K, Shah P, Goyal A, Fang Y, Briggs RW, Hart J Jr, Moore A, Haley RW (2015 Aug) Word-finding impairment in veterans of the 1991 Persian Gulf War. Brain Cogn. 98:65-73. doi: 10.1016/j.bandc.2015.05.005. Approximately one quarter of 1991 Persian Gulf War Veterans experience cognitive and physiological sequelae that continue to be unexplained by known medical or psychological conditions. Difficulty coming up with words and names, familiar before the war, is a hallmark of the illness. Three Gulf War Syndrome subtypes have been identified and linked to specific war-time chemical exposures. The most functionally impaired veterans belong to the Gulf War Syndrome 2 (Syndrome 2) group, for which subcortical damage due to toxic nerve gas exposure is the suspected cause. Subcortical damage is often associated with specific complex language impairments, and Syndrome 2 veterans have demonstrated poorer vocabulary relative to controls. 11 Syndrome 1, 16 Syndrome 2, 9 Syndrome 3, and 14 age-matched veteran controls from the Seabees Naval Construction Battalion were compared across three measures of complex language. Additionally, functional magnetic resonance imaging (fMRI) was collected during a covert category generation task, and whole-brain functional activity was compared between groups. Results demonstrated that Syndrome 2 veterans performed significantly worse on letter and category fluency relative to Syndrome 1 veterans and controls. They also exhibited reduced activity in the thalamus, putamen, and amygdala, and increased activity in the right hippocampus relative to controls. Syndrome 1 and Syndrome 3 groups tended to show similar, although smaller, differences than the Syndrome 2 group. Hence, these results further demonstrate specific impairments in complex language as well as subcortical and hippocampal involvement in Syndrome 2 veterans. Further research is required to determine the extent of language impairments in this population and the significance of altered neurologic activity in the aforementioned brain regions with the purpose of better characterizing the Gulf War Syndromes.

Nettleman M (2015) Gulf War Illness: Challenges Persist. Trans Am Clin Climatol Assoc. 126:237-247.

It has been more than 20 years since the United States and coalition forces entered Kuwait and Iraq. Actual combat was of remarkably short duration: less than 1 week of sustained ground activity and 6 weeks of air missions. Thus, it was surprising when approximately 200,000 returning US veterans were affected by a chronic multi-symptom illness that came to be known as Gulf War Illness (GWI). There were many challenges in investigating GWI, not least of which was that it took several years before the condition

was officially taken seriously. There were multiple exposures to potentially causal agents on and off the battlefield, but these exposures were documented incompletely if at all, leaving epidemiologists to rely on self-report for information. In the past 2 years, significant controversy has arisen over the future directions of the field. Despite these challenges, several studies have implicated exposure to acetylcholinesterase inhibitors such as pyridostigmine bromide in the genesis of the condition. The story of GWI can inform research into other conditions and guide future work on veterans' health.

Nicklas JA, Albertini RJ, Vacek PM, Ardell SK, Carter EW, McDiarmid MA, Engelhardt SM, Gucer PW, Squibb KS (2015 Aug) Mutagenicity monitoring following battlefield exposures: Molecular analysis of HPRT mutations in Gulf War I veterans exposed to depleted uranium. Environ Mol Mutagen. 56(7):594-608. doi: 10.1002/em.21956.

Molecular studies that involved cDNA and genomic DNA sequencing as well as multiplex PCR of the HPRT gene were performed to determine the molecular mutational spectrum for 1,377 HPRT mutant isolates obtained from 61 Veterans of the 1991 Gulf War, most of whom were exposed to depleted uranium (DU). Mutant colonies were isolated from one to four times from each Veteran (in 2003, 2005, 2007, and/or 2009). The relative frequencies of the various types of mutations (point mutations, deletions, insertions, etc.) were compared between high versus low DU exposed groups, (based on their urine U concentration levels), with HPRT mutant frequency (as determined in the companion paper) and with a database of historic controls. The mutational spectrum includes all classes of gene mutations with no significant differences observed in Veterans related to their DU exposures.

Nutter TJ, Johnson RD, Cooper BY (2015 Dec) A delayed chronic pain like condition with decreased Kv channel activity in a rat model of Gulf War Illness pain syndrome. Neurotoxicology. 51:67-79. doi: 10.1016/j.neuro.2015.09.010.

Following their return from deployment, Gulf War (GW) veterans reported widespread joint and muscle pain at rates that far exceeded those of soldiers returning from other conflicts. It is widely believed that exposure to insecticides, repellants and nerve gas prophylactics contributed to the symptoms of Gulf War Illness (GWI), but an animal model of GW pain has been elusive. In our previous work, we observed that 4-8 weeks exposure to pyridostigmine bromide (PB), permethrin and chlorpyrifos could produce persistent alterations in the physiology of Nav1.9 and Kv7 expressed in deep tissue nociceptors of the dorsal root ganglion. However, behavioral assessments from these same rats were not consistent with a delayed pain syndrome similar to that of GWI pain. In the present studies, we intensified the exposure to anticholinesterases PB and chlorpyrifos while retaining the same dosages. Animals receiving the intensified protocol for 30 days exhibited significant increases in resting for about 8 weeks after exposure. Thereafter, all measures were comparable to controls. Animals treated with intensified anticholinesterases for 60 days exhibited increased resting and reduced movement 12 weeks post-exposure. In whole cell patch studies, muscle and vascular nociceptor KDR and Kv7 ion channels exhibited increased amplitude relative to controls (e.g., normalized current and/or peak conductance) at 8 weeks post-exposures; however, at 12 weeks post-exposure, the

amplitude of these currents was significantly decreased in muscle nociceptors. In current clamp studies, muscle nociceptors also manifested increased action potential duration, after hyperpolarization and increased discharge to muscarinic agonists 12 weeks post-exposure. The decline in activity of muscle nociceptor KDR and Kv7 channel proteins was consistent with increased nociceptor excitability and a delayed myalgia in rats exposed to GW chemicals.

O'Callaghan JP, Kelly KA, Locker AR, Miller DB, Lasley SM (2015 Jun) Corticosterone primes the neuroinflammatory response to DFP in mice: potential animal model of Gulf War Illness. J Neurochem 133(5):708-721. doi: 10.1111/jnc.13088.

Gulf War Illness (GWI) is a multi-symptom disorder with features characteristic of persistent sickness behavior. Among conditions encountered in the Gulf War (GW) theater were physiological stressors (e.g., heat/cold/physical activity/sleep deprivation), prophylactic treatment with the reversible AChE inhibitor, pyridostigmine bromide (PB), the insect repellent, N,N-diethyl-meta-toluamide (DEET), and potentially the nerve agent, sarin. Prior exposure to the anti-inflammatory glucocorticoid, corticosterone (CORT), at levels associated with high physiological stress, can paradoxically prime the CNS to produce a robust proinflammatory response to neurotoxicants and systemic inflammation; such neuroinflammatory effects can be associated with sickness behavior. Here, we examined whether CORT primed the CNS to mount neuroinflammatory responses to GW exposures as a potential model of GWI. Male C57BL/6 mice were treated with chronic (14 days) PB/DEET, subchronic (7-14 days) CORT, and acute exposure (day 15) to diisopropyl fluorophosphate (DFP), a sarin surrogate and irreversible AChE inhibitor. DFP alone caused marked brain-wide neuroinflammation assessed by qPCR of tumor necrosis factor-α, IL6, chemokine (C-C motif) ligand 2, IL-1β, leukemia inhibitory factor, and oncostatin M. Pre-treatment with high physiological levels of CORT greatly augmented (up to 300-fold) the neuroinflammatory responses to DFP. Anti-inflammatory pre-treatment with minocycline suppressed many proinflammatory responses to CORT+DFP. Our findings are suggestive of a possible critical, yet unrecognized interaction between the stressor/environment of the GW theater and agent exposure(s) unique to this war. Such exposures may in fact prime the CNS to amplify future neuroinflammatory responses to pathogens, injury, or toxicity. Such occurrences could potentially result in the prolonged episodes of sickness behavior observed in GWI. Gulf War (GW) veterans were exposed to stressors, prophylactic medicines and, potentially, nerve agents in theater. Subsequent development of GW Illness, a persistent multi-symptom disorder with features characteristic of sickness behavior, may be caused by priming of the CNS resulting in exaggerated neuroinflammatory responses to pathogens/insults. Nerve agent, diisopropyl fluorophosphate (DFP), produced a neuroinflammatory response that was exacerbated by pre-treatment with levels of corticosterone simulating heightened stressor conditions. While prophylactic treatments reduced DFP-induced neuroinflammation, this effect was negated when those treatments were combined with corticosterone.

O'Donovan A, Chao LL, Paulson J, Samuelson KW, Shigenaga JK, Grunfeld C, Weiner MW, Neylan TC (2015 Jan) Altered inflammatory activity associated with

reduced hippocampal volume and more severe posttraumatic stress symptoms in Gulf War veterans. Psychoneuroendocrinology 51:557-66. doi: 10.1016/j.psyneuen.2014.11.010. (Epub 2014 Nov 18.)

BACKGROUND: Inflammation may reduce hippocampal volume by blocking neurogenesis and promoting neurodegeneration. Posttraumatic stress disorder (PTSD) has been linked with both elevated inflammation and reduced hippocampal volume. However, few studies have examined associations between inflammatory markers and hippocampal volume, and none have examined these associations in the context of PTSD. METHODS: We measured levels of the inflammatory markers interleukin-6 (IL-6) and soluble receptor II for tumor necrosis factor (sTNF-RII) as well as hippocampal volume in 246 Gulf War veterans with and without current and past PTSD as assessed with the Clinician Administered PTSD Scale (CAPS). Enzyme-linked immunosorbent assays were used to measure inflammatory markers, and 1.5Tesla magnetic resonance imaging (MRI) and Freesurfer version 4.5 were used to quantify hippocampal volume. Hierarchical linear regression and analysis of covariance models were used to examine if hippocampal volume and PTSD status would be associated with elevated levels of IL-6 and sTNF-RII. RESULTS: Increased sTNF-RII, but not IL-6, was significantly associated with reduced hippocampal volume (β=-0.14, p=0.01). The relationship between sTNF-RII and hippocampal volume was independent of potential confounds and covariates, including PTSD status. Although we observed no PTSD diagnosis-related differences in either IL-6 or sTNF-RII, higher PTSD severity was associated with significantly increased sTNF-RII (β=0.24, p=0.04) and reduced IL-6 levels (β=-0.24, p=0.04). CONCLUSIONS: Our results indicate that specific inflammatory proteins may be associated with brain structure and function as indexed by hippocampal volume and PTSD symptoms.

Parkitny L, Middleton S, Baker K, Younger J (2015 Sep 30) Evidence for abnormal cytokine expression in Gulf War Illness: A preliminary analysis of daily immune monitoring data. BMC Immunol 16:57. doi: 10.1186/s12865-015-0122-z.
BACKGROUND: Gulf War Illness (GWI) is a clinically heterogeneous chronic condition that affects many veterans of the 1990-1991 Persian Gulf War. One of the most prevalent and debilitating symptoms of GWI is abnormal fatigue. The mechanisms underlying GWI generally, and fatigue symptoms specifically, have yet to be conclusively identified, although immune system abnormalities are suspected to be involved. The first goal of this immune monitoring study was to determine if GWI is associated with higher absolute levels and daily variability of pro-inflammatory immune factors. The second goal was to explore the relationship between day-to-day immune marker fluctuations and daily self-reported fatigue severity. METHODS: We recruited veterans with GWI and healthy veteran control (HV) participants to provide self-reported fatigue severity data and blood samples, over 25 consecutive days. We profiled inflammatory processes by using a longitudinal, daily immune-monitoring approach. For each day, serum cytokine and chemokine concentrations were determined using multiplex assays. RESULTS: Seven veterans with GWI and eight healthy veteran control (HV) participants completed the study protocol. We found that GWI was associated with higher variability in the expression of eotaxin-1 ($p < 0.001$). For GWI participants, higher fatigue severity days were associated with greater IL-1β ($p = 0.008$) and IL-15 ($p < 0.001$). CONCLUSIONS: Our findings provide preliminary

evidence that the immune system is involved in the pathophysiology of GWI. Longitudinal immune profiling approaches may be helpful in discovering targets for novel therapies in conditions such as GWI.

Phillips KF, Deshpande LS (2016 Jan) Repeated low-dose organophosphate DFP exposure leads to the development of depression and cognitive impairment in a rat model of Gulf War Illness. Neurotoxicology. 52:127-33. doi: 10.1016/j.neuro.2015.11.014. Approximately 175,000-250,000 of the returning veterans from the 1991 Persian Gulf War exhibit chronic multi-symptom illnesses that includes neurologic co-morbidities such as depression, anxiety and cognitive impairments. Amongst a host of causative factors, exposure to low levels of the nerve agent Sarin has been strongly implicated for expression of Gulf War Illness (GWI). Nerve agents similar to pesticides are organophosphate (OP) compounds. There is evidence from civilian population that exposure to OPs such as in agricultural workers and nerve agents such as the survivors and first-responders of the Tokyo subway Sarin gas attack suffer from chronic neurological problems similar to GWI symptoms. Given this unique chemical profile, OPs are ideal to study the effects of nerve agents and develop models of GWI in civilian laboratories. In this study, we used repeated low-dose exposure to OP agent diisopropyl fluorophosphate (DFP) over a 5-day period to approximate the duration and level of Sarin exposure during the Persian Gulf War. We tested the rats at 3-months post DFP exposure. Using a battery of behavioral assays, we observed the presence of symptoms of chronic depression, anxiety and memory problems as characterized by increased immobility time in the Forced Swim Test, anhedonia in the Sucrose Preference Test, anxiety in the Elevated Plus Maze, and spatial memory impairments in the Object Location Test, respectively. Chronic low dose DFP exposure was also associated with hippocampal neuronal damage as characterized by the presence of Fluoro-Jade staining. Given that OP exposure is considered a leading cause of GWI related morbidities, this animal model will be ideally suited to study underlying molecular mechanisms for the expression of GWI neurological symptoms and identify drugs for the effective treatment of GWIs.

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

Exposure to high levels of organophosphorus compounds (OP) can induce status epilepticus (SE) in humans and rodents via acute cholinergic toxicity, leading to neurodegeneration and brain inflammation. Currently there is no treatment to combat the neuropathologies associated with OP exposure. We recently demonstrated that inhibition of the EP2 receptor for PGE2 reduces neuronal injury in mice following pilocarpine-induced SE. Here, we investigated the therapeutic effects of an EP2 inhibitor (TG6-10-1) in a rat model of SE using diisopropyl fluorophosphate (DFP). We tested the hypothesis that EP2 receptor inhibition initiated well after the onset of DFP-induced SE reduces the associated neuropathologies. Adult male Sprague-Dawley rats were injected with

pyridostigmine bromide (0.1 mg/kg, sc) and atropine methylbromide (20 mg/kg, sc) followed by DFP (9.5 mg/kg, ip) to induce SE. DFP administration resulted in prolonged upregulation of COX-2. The rats were administered TG6-10-1 or vehicle (ip) at various time points relative to DFP exposure. Treatment with TG6-10-1 or vehicle did not alter the observed behavioral seizures, however six doses of TG6-10-1 starting 80-150 min after the onset of DFP-induced SE significantly reduced neurodegeneration in the hippocampus, blunted the inflammatory cytokine burst, reduced microglial activation and decreased weight loss in the days after status epilepticus. By contrast, astrogliosis was unaffected by EP2 inhibition 4 d after DFP. Transient treatments with the EP2 antagonist 1 h before DFP, or beginning 4 h after DFP, were ineffective. Delayed mortality, which was low (10%) after DFP, was unaffected by TG6-10-1. Thus, selective inhibition of the EP2 receptor within a time window that coincides with the induction of cyclooxygenase-2 by DFP is neuroprotective and accelerates functional recovery of rats.

Roncati L, Gatti AM, Pusiol T, Barbolini G, Maiorana A (2015 Jun) Acquired immunodeficiency similar to Gulf War illness in a dead former serviceman. J R Army Med Corps 161(2):153-155. doi: 10.1136/jramc-2014-000345.

A 38-year-old non-commissioned officer was certified unfit for military duty several months before his death. The forensic autopsy revealed a severe bone marrow aplasia and a pulmonary angioinvasive aspergillosis. Moreover, the presence of inorganic foreign particles in the pulmonary macrophages and intestinal endothelia was observed. The microanalysis implemented on these last selected specimens revealed the presence of silica particles microimpregnated by lanthanides and steel. The patient's acquired immunodeficiency appears comparable with that of Iraqi civilians suffering from Gulf War illness. This is the first report in the literature of the presence of intestinal endothelia engulfed by foreign war particulates; the silica particles may have entered the intestinal endothelia via the blood stream or by ingestion of impregnated fruit and vegetable foodstuffs. This finding provides new perspectives in the assessment of war-associated diseases and includes electron probe microanalysis among the new techniques of military and forensic medicine.

Schiehser DM, Twamley EW, Liu L, Matevosyan A, Filoteo JV, Jak AJ, Orff HJ, Hanson KL, Sorg SF, Delano-Wood L (2015 Jul-Aug) The Relationship Between Postconcussive Symptoms and Quality of Life in Veterans With Mild to Moderate Traumatic Brain Injury. J Head Trauma Rehabil. 30(4):E21-8. doi: 10.1097/HTR.0000000000000065.

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

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

Sharkey JM, Abraham JH (2015) Evaluation of Postdeployment Cancers Among Active Duty Military Personnel. US Army Med Dep J. 2015 Jul-Sep:68-75.
The military population presents a unique opportunity to study links between environmental exposures and cancer. Advantageous aspects of studying cancer among military personnel include well characterized person-time, occupation, and, though not always the case, environmental hazards. Access to routine healthcare including recommended cancer screenings at no cost to the service member and robust electronic medical record systems also facilitate assessments of cancer outcomes in the military population. Furthermore, exposures associated with military deployments may influence cancer risk among military personnel.

Shiu J, Gaitens J, Squibb KS, Gucer PW, McDiarmid MA, Gaspari AA (2015 May-Jun) Significance of dermatologic findings in a cohort of depleted uranium-exposed veterans of Iraqi conflicts. Dermatitis. 26(3):142-7. doi: 10.1097/DER.0000000000000110

BACKGROUND: Depleted uranium (DU)-containing weapons have been used in military operations since 1991. There is interest in following veterans who were occupationally exposed to DU by either inhalation or retention of fragments. A cohort of DU-exposed Gulf War I veterans has been followed longitudinally at the Baltimore Veterans Administration Medical Center since 1993. OBJECTIVE: The aim was to monitor chronic dermatological findings associated with occupational DU exposure in the 2013 cohort. METHODS: Thirty-five veterans were evaluated. This study was reviewed and approved by the institutional review board and the Baltimore Veterans Administration Medical Center research service. Depleted uranium exposure was measured using creatinine-adjusted urine uranium concentrations (micrograms of uranium per gram of creatinine [μgU/gCrea]). Detailed medical histories, physical examinations, and exposure histories were performed. RESULTS: Using a cutoff level of 0.1 μgU/gCrea, 11 veterans were placed in the high-uranium exposure group, whereas 23 veterans were placed in the low-uranium exposure group. Retained fragments were documented in 91% of the high-exposure group versus that in 13% of the low-exposure group ($P < 0.001$), and fragment-related scarring was significantly increased in the high-exposure group ($P = 0.002$). Other dermatological findings such as dermatitis were also assessed. CONCLUSIONS: Fragment retainment and related scarring was significantly increased in veterans exposed to high levels of DU.

Continuous monitoring of this cohort will yield interesting dermatological findings related to DU exposure.

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

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

Thorne MC, Wilson J (2015 Dec) Generally applicable limits on intakes of uranium based on its chemical toxicity and the radiological significance of intakes at those limits. J Radiol Prot. 35(4):743-62. doi: 10.1088/0952-4746/35/4/743.

Uranium is chemically toxic and radioactive, and both considerations have to be taken into account when limiting intakes of the element, in the context of both occupational and public exposures. Herein, the most recent information available on the chemical toxicity and biokinetics of uranium is used to propose new standards for limiting intakes of the element. The approach adopted allows coherent standards to be set for ingestion and inhalation of different chemical forms of the element by various age groups. It also allows coherent standards to be set for occupational and public exposures (including exposures of different age groups) and for various exposure regimes (including short-term and chronic exposures). The proposed standards are more restrictive than those used previously, but

are less restrictive than the Minimal Risk Levels proposed recently by the US Agency for Toxic Substances and Disease Registry. Having developed a set of proposed limits based solely on chemical toxicity considerations, the radiological implications of exposure at those proposed limits are investigated for natural, depleted and enriched uranium.**Wang WF, Guo XX, Yang YS (2015 Jun 24) Gastrointestinal problems in modern wars: clinical features and possible mechanisms. Mil Med Res. 2:15. doi: 10.1186/s40779-015-0042-5**.

Gastrointestinal problems are common during wars, and they have exerted significant adverse effects on the health of service members involved in warfare. The spectrum of digestive diseases has varied during wars of different eras. At the end of the 20th century, new frontiers of military medical research emerged due to the occurrence of high-tech wars such as the Gulf War and the Kosovo War, in which ground combat was no longer the primary method of field operations. The risk to the military personnel who face trauma has been greatly reduced, but disease and non-battle injuries (DNBIs) such as neuropsychological disorders and digestive diseases seemed to be increased. Data revealed that gastrointestinal symptoms such as constipation, diarrhea, dyspepsia, and non-cardiac chest pain are common among military personnel during modern wars. In addition, a large number of deployed soldiers and veterans who participated in recent wars presented with chronic gastrointestinal complaints, which fulfilled with the Rome III criteria for functional gastrointestinal disorders (FGIDs). It was also noted that many veterans who returned from the Gulf War suffered not only from chronic digestive symptoms but also from neuropsychological dysfunction; however, they also showed symptoms of other systems. Presently, this broad range of unexplained symptoms is known as "Gulf War syndrome". The mechanism that underlies Gulf War syndrome remains unclear, but many factors have been associated with this syndrome such as war trauma, stress, infections, immune dysfunction, radiological factors, anthrax vaccination and so on. Some have questioned if the diagnosis of FGIDs can be reached given the complexity of the military situation. As a result, further studies are needed to elucidate the pathogenesis of gastrointestinal disease among military personnel.

White HD, Robinson TD (2015 Aug) A novel use for testosterone to treat central sensitization of chronic pain in fibromyalgia patients. Int Immunopharmacol 27(2):244-248. doi: 10.1016/j.intimp.2015.05.020.

Fibromyalgia is a diffuse chronic pain condition that occurs predominantly in women and may be under-reported in men. Symptoms include a loss of feeling of well-being and generalized widespread flu-like muscle aches and pain that fail to resolve due to central sensitization of nociceptive neurons. It has commonalities with a myriad of other chronic pain conditions which include PTSD, "Gulf War Syndrome", and various stress-induced conditions caused, for example, by viral infection, emotional or physical stress, trauma, combat, accident or surgery. It is not understood why some individuals are susceptible to this condition and others are not. White et al., elsewhere in this issue, present a clinical feasibility study designed to test the hypothesis that 1) low or deficient testosterone serum levels are linked to a high risk for an inflamed nociceptive nervous system and resultant chronic pain states, and 2) a testosterone transdermal gel applied once a day by

fibromyalgia patients can be an effective therapeutic against chronic pain. Here, a short profile of fibromyalgia is provided along with a brief summary of best practices currently recommended by clinical specialists. The link between testosterone and pain is then discussed, with an overview of scientific studies that lay the foundation for testosterone as a possible important additional therapeutic that has the potential to be safely administered and effective but also avoid the adverse effects of other therapeutics. Finally, novel mechanisms by which testosterone therapy is likely to down-modulate pain signaling are proposed.

White RF, Steele L, O'Callaghan JP, Sullivan K, Binns JH, Golomb BA, Bloom FE, Bunker JA, Crawford F, Graves JC, Hardie A, Klimas N, Knox M, Meggs WJ, Melling J, Philbert MA, Grashow R (2016 Jan) Recent research on Gulf War illness and other health problems in veterans of the 1991 Gulf War: Effects of toxicant exposures during deployment. Cortex 74:449-475. doi: 10.1016/j.cortex.2015.08.022.

Veterans of Operation Desert Storm/Desert Shield - the 1991 Gulf War (GW) - are a unique population who returned from theater with multiple health complaints and disorders. Studies in the U.S. and elsewhere have consistently concluded that approximately 25-32% of this population suffers from a disorder characterized by symptoms that vary somewhat among individuals and include fatigue, headaches, cognitive dysfunction, musculoskeletal pain, and respiratory, gastrointestinal and dermatologic complaints. Gulf War illness (GWI) is the term used to describe this disorder. In addition, brain cancer occurs at increased rates in subgroups of GW veterans, as do neuropsychological and brain imaging abnormalities. Chemical exposures have become the focus of etiologic GWI research because nervous system symptoms are prominent and many neurotoxicants were present in theater, including organophosphates (OPs), carbamates, and other pesticides; sarin/cyclosarin nerve agents, and pyridostigmine bromide (PB) medications used as prophylaxis against chemical warfare attacks. Psychiatric etiologies have been ruled out. This paper reviews the recent literature on the health of 1991 GW veterans, focusing particularly on the central nervous system and on effects of toxicant exposures. In addition, it emphasizes research published since 2008, following on an exhaustive review that was published in that year that summarizes the prior literature (RACGWI, 2008). We conclude that exposure to pesticides and/or to PB are causally associated with GWI and the neurological dysfunction in GW veterans. Exposure to sarin and cyclosarin and to oil well fire emissions are also associated with neurologically based health effects, though their contribution to development of the disorder known as GWI is less clear. Gene-environment interactions are likely to have contributed to development of GWI in deployed veterans. The health consequences of chemical exposures in the GW and other conflicts have been called "toxic wounds" by veterans. This type of injury requires further study and concentrated treatment research efforts that may also benefit other occupational groups with similar exposure-related illnesses.

Wojcik W, Lawrie SM (2015 Dec 23) Towards a Biopsychosocial Model of Gulf War Illness? EBioMedicine. 3:6-7. doi: 10.1016/j.ebiom.2015.12.021. No Abstract

Wright BK, McFarlane AC, Clarke DM, Sim MR, Kelsall HL (2015 Dec) Symptom attribution and symptom reporting in Australian Gulf War veterans. J Psychosom Res 79(6):674-679. doi: 10.1016/j.jpsychores.2015.04.012.

OBJECTIVE: To better understand the consistent elevated symptom reporting by Gulf War veterans; we compared Australian Gulf War veterans and military-comparison group on symptom attributional styles and the relationship with total number and grouping of somatic and psychological symptoms. METHOD: Postal questionnaires were completed by Australian Gulf War veterans (n=697) and military-comparison group (n=659) in 2000-2002 and 2011-2012. Data were collected on deployments, military-psychological stressors, symptom reporting, symptom factors and attributional style (normalising, psychologising, somatising, mixed-attribution). RESULTS: Gulf War veterans did not differ in attributional style from comparison group (p>0.05); normalising was the predominant style. Groups were combined for analyses. Psychologisers reported the highest overall symptoms (mean(M)=10.95, standard deviation(SD)=9.15), the most psychophysiological (M=1.71, SD=2.82), cognitive (M=5.79, SD=5.09) and arthro-neuromuscular symptoms (M=1.53, SD=1.73). Psychologisers and somatisers reported significantly more symptoms across overall symptoms, all three symptom factors and psychological distress than normalisers. Normalisers consistently reported fewest overall symptoms (M=2.85, SD=4.49), psychophysiological (M=0.40, SD=0.98), cognitive (M=1.14, SD=2.22), and arthro-neuromuscular symptoms (M=0.72, SD=1.31). Persistent symptoms, rather than remitted, between baseline and follow-up were associated with increased rates of psychologising and mixed-attribution compared with normalising. For incident symptoms a similar pattern was observed, some symptoms also showed increased rates of somatising. CONCLUSIONS: In veterans, psychologising was associated with higher symptom reporting, whilst somatisers and mixed-attribution also demonstrated higher reporting than normalisers. Symptom persistence and incidence were associated with symptom attribution. The findings indicate that attributional style is associated with patterns of symptom reporting and highlights both past and present symptoms may influence attributional style.

Zakirova Z, Crynen G, Hassan S, Abdullah L, Horne L, Mathura V, Crawford F, Ait-Ghezala G (2016 Jan 12) A Chronic Longitudinal Characterization of Neurobehavioral and Neuropathological Cognitive Impairment in a Mouse Model of Gulf War Agent Exposure. Front Integr Neurosci. 9:71. doi: 10.3389/fnint.2015.00071.

Gulf War Illness (GWI) is a chronic multisymptom illness with a central nervous system component that includes memory impairment as well as neurological and musculoskeletal deficits. Previous studies have shown that in the First Persian Gulf War conflict (1990-1991) exposure to Gulf War (GW) agents, such as pyridostigmine bromide (PB) and permethrin (PER), were key contributors to the etiology of GWI. For this study, we used our previously established mouse model of GW agent exposure (10 days PB+PER) and undertook an extensive lifelong neurobehavioral characterization of the mice from 11 days to 22.5 months post exposure in order to address the persistence and chronicity of effects suffered by the current GWI patient population, 24 years post-exposure. Mice were evaluated using a battery of neurobehavioral testing paradigms, including Open Field Test

(OFT), Elevated Plus Maze (EPM), Three Chamber Testing, Radial Arm Water Maze (RAWM), and Barnes Maze (BM) Test. We also carried out neuropathological analyses at 22.5 months post exposure to GW agents after the final behavioral testing. Our results demonstrate that PB+PER exposed mice exhibit neurobehavioral deficits beginning at the 13 months post exposure time point and continuing trends through the 22.5 month post exposure time point. Furthermore, neuropathological changes, including an increase in GFAP staining in the cerebral cortices of exposed mice, were noted 22.5 months post exposure. Thus, the persistent neuroinflammation evident in our model presents a platform with which to identify novel biological pathways, correlating with emergent outcomes that may be amenable to therapeutic targeting. Furthermore, in this work we confirmed our previous findings that GW agent exposure causes neuropathological changes, and have presented novel data which demonstrate increased disinhibition, and lack of social preference in PB+PER exposed mice at 13 months after exposure. We also extended upon our previous work to cover the lifespan of the laboratory mouse using a battery of neurobehavioral techniques.

Zakirova Z, Tweed M, Crynen G, Reed J, Abdullah L, Nissanka N, Mullan M, Mullan MJ, Mathura V, Crawford F, Ait-Ghezala G (2015 Mar 18) Gulf War agent exposure causes impairment of long-term memory formation and neuropathological changes in a mouse model of Gulf War Illness. PLoS One. 10(3):e0119579. doi: 10.1371/journal.pone.0119579.

Gulf War Illness (GWI) is a chronic multisymptom illness with a central nervous system component such as memory deficits, neurological, and musculoskeletal problems. There are ample data that demonstrate that exposure to Gulf War (GW) agents, such as pyridostigmine bromide (PB) and pesticides such as permethrin (PER), were key contributors to the etiology of GWI post deployment to the Persian GW. In the current study, we examined the consequences of acute (10 days) exposure to PB and PER in C57BL6 mice. Learning and memory tests were performed at 18 days and at 5 months post-exposure. We investigated the relationship between the cognitive phenotype and neuropathological changes at short and long-term time points post-exposure. No cognitive deficits were observed at the short-term time point, and only minor neuropathological changes were detected. However, cognitive deficits emerged at the later time point and were associated with increased astrogliosis and reduction of synaptophysin staining in the hippocampi and cerebral cortices of exposed mice, 5 months post exposure. In summary, our findings in this mouse model of GW agent exposure are consistent with some GWI symptom manifestations, including delayed onset of symptoms and CNS disturbances observed in GWI veterans.

IV. RESEARCH FUNDING TRENDS

This section provides a quantitative overview of the current research portfolio on GWVI and the evolution of the portfolio since 2006. Topics that are covered include research expenditures by VA, DoD, and HHS from FY 2006-2015, and the number of research projects in which the Federal Government has invested.

The appropriated funds for FY 2006 through 2015, centrally obligated to each project, are shown in Appendix C and summarized in Table IV-1. Federal funding for GW research totaled more than $245 million during this period. Funds obligated for these projects prior to FY 2006 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 2006 are listed with no associated obligation ($0) in Appendix C. Federal funds for these earlier projects were reported in prior annual reports to Congress.

Table IV-1. 10-Year (FY 2006-2015) Funding Trends for GW Research in Millions of Dollars

Department	FY '06	FY '07	FY '08	FY '09	FY '10	FY '11	FY '12	FY '13	FY '14	FY '15	Total Costs FY '06-'15
DoD	$ 10.1	$ 3.4	$ 11.7	$ 10.4	$ 10.4	$ 10.3	$ 11.7	$ 19.5	$ 22.5	$ 5.4	**$ 115.4**
HHS	$ 0.5	$ 0.4	$ 0.4	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	**$ 1.3**
VA	$ 13.0	$ 22.1	$ 21.9	$16.6	$13.9	$ 5.6	$ 6.7	$ 7.9	$ 9.7	$ 11.6	**$ 129.0**
Total	**$ 23.6**	**$25.9**	**$ 34.0**	**$ 27.0**	**$ 24.3**	**$ 15.9**	**$ 18.4**	**$ 27.4**	**$ 32.2**	**$ 17.0**	**$ 245.7**

The funding level for FY 2014 in the table above differs from the value reported in the 2014 annual report to Congress due to the delayed start of 26 projects funded through the FY 2014 appropriation for the Gulf War Illness Research (GWIRP) managed by the Congressionally Directed Medical Research Programs (CDMRP) at DoD. DoD did not receive final approval until FY 2015. DoD funding listed for FY 2015 is only $5.4 million for the same reason and will be updated after the CDMRP projects selected for funding in FY 2015 have begun.

VA, DoD, and HHS sponsored a total of 480 distinct research projects on GWVI during the period of FY 1992 through FY 2015. Appendix A lists all of the research and development projects and programs supported now or in the past by each of the three Federal agencies. Nine projects have been dual-funded by VA and DoD, and each agency has given the project its own unique project number (DoD-115/VA-062; DoD-116/VA-063; DoD-116A/VA-063A; DoD-116B/VA-063B; D0D-118/VA-061; DoD-119/VA-055; DoD-125/VA-074; DoD-143/VA-078; and DoD-154/VA-088). In prior annual reports to Congress, the total number of funded projects was corrected for the number of dual-funded projects. Starting with the 2005 annual report to Congress, this practice has been discontinued since VA and DoD may start or end funding of their portion of these projects independent of each other. Any dual-funded project is, therefore, treated as two distinct projects.

The numbers of new, ongoing, and completed projects for FY 2006 - FY 2015 are shown in Figure IV-1. As of September 30, 2015, 393 projects (82 percent of the 480 projects) were completed, and 87 projects (18 percent) were new or ongoing.

The annual distribution of new and ongoing projects within the five major Research Focus Areas is shown in Figure IV-2. From FY 2006 through 2015, new and ongoing research assigned to the Brain and Nervous System Function, Environmental Toxicology, and General Health and Symptoms categories represent 96.6 ± 0.9 percent of all new and ongoing projects.

Figure IV-1. Cumulative Number of Funded Projects (FY 2006 - FY 2015)

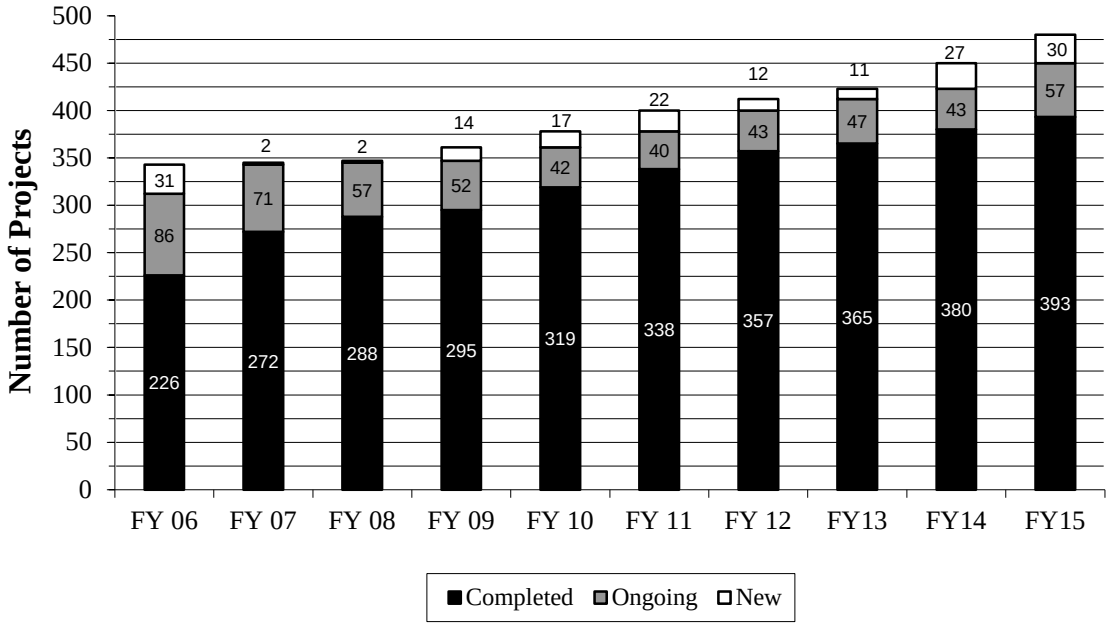
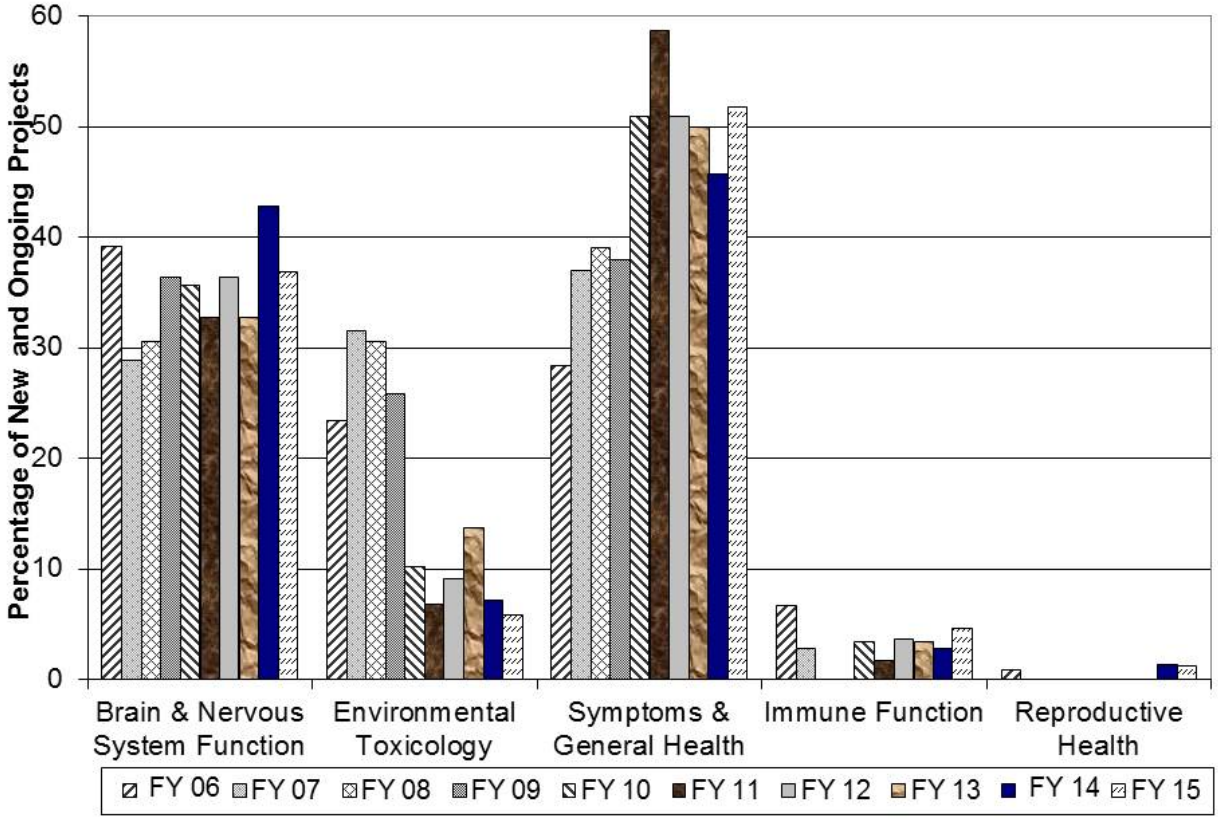


Figure IV-2. Annual Distribution of Topic Areas for New and Ongoing Projects



V. NEW RESEARCH PROJECTS AND INITIATIVES

A. New Initiatives

Program Announcements (PAs) and Requests for Applications (RFAs) were issued by CDMRP and VA in FY 2015. Proposals received for review in response to these PAs and RFAs were reviewed, and projects selected for funding will begin in FY 2016. As more investigators engage in GW research, there has been an increase in applications for funding and increases in the number of newly-approved treatment trials and biomarker studies. In 2015, 30 new projects were added to the 57 ongoing projects.

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

Two CDMRP-funded research consortia combine the talents and expertise of GW researchers who focus on different aspects of GWI. One consortium studies brain-immune interactions to monitor neurotoxic and neuroinflammatory reactions as the investigators try to understand the underlying causes of the health problems in GW Veterans. The other

consortium is focused on a “systems biology” approach to combining basic research with clinical results to identify biomarkers and possible treatments for GW Veterans.

The Institute of Medicine (IOM; renamed National Institute of Medicine in July, 2015) released a study for VA entitled “Considerations for Designing an Epidemiologic Study for Multiple Sclerosis and Other Neurologic Disorders in Pre and Post 9/11 Gulf War Veterans” on December 12, 2015. The report provided useful recommendations for GW research.

B. Portfolio Review

VA and DoD each review their portfolios of GW research on a regular basis in order to determine research gaps and to expand successful research topic areas. The Federal GW research portfolio is increasingly focused on identifying potential new treatments (clinical trials, including complementary medicine approaches) for ill GW Veterans and identifying new diagnostic markers of disease and potential therapeutic targets to develop new therapies. VA and DoD program managers meet regularly to share information regarding funded GW research projects and coordinate activities, whenever possible, to maximize combined program impact. To formalize this process, the GW research programs have been integrated into the ongoing Department-wide VA-DoD Joint Program Reviews. The second such GW review was held in May 2015, and the next review will be in 2017.

C. New Projects

This section highlights the new research projects that have been approved since last year’s 2014 annual report to Congress; these projects represent an investment of more than $30 million by the time they are completed. They are described below and incorporated into the tables in Appendices A, B, and C.

DoD Projects

Twenty-six new projects were recommended for funding through the FY 2014 appropriation for the GWIRP managed by CDMRP, but were not finalized and funded until FY 2015. These projects focused on Brain and Nervous System Function (5), Environmental Toxicology (1), Immune Function (2) and Symptoms and General Health (18).

*DoD-243, “Vascular and Skeletal Muscle Function in Gulf War Veterans Illness” is designed to assess blood vessel responses (normal bloodflow vs. abnormal) to several short-term medications using standard catheterization. Biopsies of the thigh muscle will also be performed to examine the muscle cells and genes that control muscle strength and fatigue. Secondarily, fatigue with muscle strength tests and a stress test will be examined.

*DoD-244, “Neurovascular and Autonomic Dysfunction Associated with Gulf War Illness Pain” will use a rat model of GWI to determine the persistence of autonomic, behavioral, cellular, and molecular consequences of chronic exposure to Gulf War toxicants DEET,

pyridostigmine bromide, permethrin, and chlorpyrifos. The Principal Investigator will investigate the physiology of proteins expressed in pain system neurons that innervate blood vessels, which appear to be highly vulnerable to Gulf War pesticides. Treatment studies examining the capacity of drugs targeting misregulated proteins to reverse the established pain and autonomic signs of GWI in the rat model will also be undertaken.

*DoD-245, “Biomarkers and Brain Mechanisms of Gulf War Illness” will use a multimodal approach, including advanced brain scanning techniques like MRI (magnetic resonance imaging), to examine neuroinflammation, oxidative stress, and mitochondrial dysfunction in the brains of 20 patients with Gulf War illness. Investigators will also compare metabolic data from cerebral spinal fluid between ill GW patients and controls to elucidate underlying pathophysiology in GWI.

*DoD-246, “Novel Autoantibody Serum and Cerebrospinal Fluid Biomarkers in Veterans with Gulf War Illness” will determine whether Veterans with GWI have higher levels of blood autoantibodies compared to healthy Veterans or disease controls. Investigators will also examine whether the pattern or levels of autoantibodies expressed are associated with exposures during the war, including pesticides, sarin nerve gas, anti-nerve gas pills, or prior mild traumatic brain injuries in GW Veterans. Autoantibodies against brain proteins in the stored blood samples from Veterans with GWI will be compared with healthy GW Veteran controls. As a second comparison group, individuals with either irritable bowel syndrome or chronic fatigue syndrome, two chronic disorders that also occur in GW Veterans and with similarities to GWI, will be compared.

*DoD-247, “Novel Autoantibody Serum and Cerebrospinal Fluid Biomarkers in Veterans with Gulf War Illness” will determine whether Veterans with GWI have higher levels of blood autoantibodies compared to healthy Veterans or disease controls. Investigators will also examine whether the pattern or levels of autoantibodies expressed are associated with exposures during the war, including pesticides, sarin nerve gas, anti-nerve gas pills, or prior mild traumatic brain injuries in GW Veterans. Autoantibodies against brain proteins in the stored blood samples from Veterans with GWI will be compared with healthy GW Veteran controls. As a second comparison group, individuals with either irritable bowel syndrome or chronic fatigue syndrome, two chronic disorders that also occur in GW Veterans and with similarities to GWI, will be compared.

*DoD-248, “Preclinical Treatment of an Organophosphate Model of Gulf War Illness” aims to validate an animal model treatment for cognitive impairment associated with Gulf War illness using human growth factor IGF-1, a treatment already FDA-approved for other neurological disorders. This preclinical study will evaluate the effectiveness of human growth factor IGF-1, at the maximum clinical dose, to reverse dendritic spine loss in the CA3-CA1 region of the hippocampus.

*DoD-249, “Gulf War Illness as a Brain Autoimmune Disorder” will comprehensively assess the association of GWI to autoimmune disorders using cutting-edge measures of brain structure and function, genetic analysis, and laboratory tests. Preliminary studies suggest that GWI possesses a distinct functional brain pattern that is very close to that

observed in a well-known autoimmune disorder, Sjogren's syndrome. The main goal of this proposal is to test the hypothesis that GWI is an autoimmune disorder. The Principal Investigator will compare the results of brain, genetic, and laboratory tests in subjects with GWI to those to be obtained from subjects with known autoimmune disorders and determine the extent to which GWI reflects autoimmune abnormalities.

*DoD-250, “An Integrated Genomics and Cell Biology Approach to Correlate Novel GWI Indicators of Infections and Neuroinflammatory Mechanisms with Targeted Drug Therapy” will combine the latest state-of-art genomics, cell and computational biology methods to find unknown, more comprehensive mechanisms of GWI pathobiology and indicators of chronic infections, as well as test drugs capable of nucleocytoplasmic homeostasis restoration. Further understanding of the genomic alterations and immune modulation will provide a more comprehensive understanding of aberrant underlying pathways of GWI disease activation and progression. The project will examine PBMCs already isolated from patients recruited for another DoD-funded research project.

*DoD-251, “Muscle Mitochondrial Assessments in Gulf War Illness” will investigate the character of mitochondrial impairments in symptomatic Gulf War Veterans to better understand the pathobiology of GWI and to identify objective signatures of GWI that may aid diagnosis. Muscle biopsies from 27 symptomatic Veterans and the same number of matched controls will be examined for mitochondrial appearance (density, elongation, networks, cristae patterning) and function (energy production), plus oxidative stress measures.

*DoD-252, “START and STOPP in GWI” will verify and extend previously reported objective biomarkers and phenotypes of Gulf War illness to provide a mechanistic basis for GWI. The study will also use informatics tools to identify new drug targets. The study incorporates an Exercise Stressor Paradigm, MRI and blood oxygenation level dependent (BOLD) signaling as well as cerebrospinal fluid miRNA, proteomics, and metabolomics to identify potential dysfunctional pathway interactions and pathogenic mechanisms.

*DoD-253, “D-cycloserine: A Novel Treatment for Gulf War Illness” is a pilot study comparing D-cycloserine treatment to placebo for efficacy in improving cognitive functioning in 50 symptomatic ill Gulf War Veterans. The primary outcome measures will be tests of verbal memory of word-pairs and tests of computerized focused or sustained attention and a test of more selective attention. Other outcomes will include self-report questionnaires of physical health and mood.

*DoD-254, “Effect of Diet on Gulf War Illness: A Pilot Study” is a randomized clinical trial to compare low FODMAPs (Fermentable Oligo-, Di- and Mono-saccharides And Polyols, carbohydrates that are poorly absorbed in the small intestine) diet to a high FODMAP diet. Both diets will be healthy. The Principal Investigator has shown that Veterans with IBS are more likely to report fatigue, joint pain, general stiffness, and headache as common clinical features of GW illness. The majority of patients with IBS believe that diet plays a significant role in their symptoms. This pilot trial will demonstrate the safety and effectiveness of low FODMAP diet in the treatment Gulf War illness.

*DoD-255, “Microtubule Abnormalities Underlying Gulf War Illness in Neurons from Human-Induced Pluripotent Cells” will develop human neuron or glial cell cultures derived from human induced pluripotent stem cells (hiPSCs) originating from GW Veterans with GWI and healthy GW Veteran controls. The purpose of the research is to develop microtubule-based strategies for treating Veterans suffering from Gulf War illness, with emphasis on available drugs that can be readily translated into the clinic once shown to be helpful in these human cell studies.

*DoD-256, “Vagus Nerve Stimulation as a Treatment Strategy for Gulf War Illness” ” will examine vagus nerve stimulation as a potential therapeutic strategy to treat Gulf War illness (GWI). The proposal aims to demonstrate proof of concept showing that vagus nerve stimulation (VNS) will reverse GWI-like symptomology in an established animal model of exposure compounds that Gulf War Veterans encountered in the theater.

*DoD-257, “Designing a Successful Acupuncture Treatment Program for Gulf War Illness” has three objectives: (1) Gather follow-up data from former Veteran participants on current symptom levels and use of services to explore the long-term effects of an acupuncture treatment program. (2) Develop suggestions for how an acupuncture program may be implemented using the viewpoints of multiple stakeholders. (3) Develop a treatment manual for acupuncture practitioners explaining the most effective methods of treating the symptoms of GWI. Two aims support these goals. Aim 1: Survey Veteran participants for their current symptom levels and use of acupuncture and other services using approved surveys to all participants. Aim 2: Conduct effectiveness research/program evaluation of the acupuncture treatments and study design from the viewpoint of multiple stakeholders: Veterans, acupuncturists/clinicians, and scientists.

*DoD-258, “High-Fidelity Design of Multimodal Restorative Interventions in Gulf War Illness” builds on an existing DoD-funded bioinformatics platform modeling Gulf War illness as dysregulated homeostasis resulting from a chronic imbalance in co-regulation between the nervous, endocrine and immune systems. The current project emphasizes translation to immediately deployable therapies by incorporating pharmacokinetic and pharmacodynamic data of currently available drugs. Improvements in the model will include discrete probabilistic simulation that accounts for the timescale of dynamic processes and better represents intracellular and cell-cell signaling and increasing the scale of tractable simulation models as well as improving the speed and thoroughness of current search capabilities to deliver much more realistic treatment designs that can be directly validated through traditional projects.

*DoD-259, “High Fidelity Design of Multimodal Restorative Interventions in Gulf War Illness” builds on an existing DoD-funded bioinformatics platform modeling Gulf War illness as dysregulated homeostasis resulting from a chronic imbalance in co-regulation between the nervous, endocrine and immune systems. The current project emphasizes translation to immediately deployable therapies by incorporating pharmacokinetic and pharmacodynamic data of currently available drugs. Improvements in the model will include discrete probabilistic simulation that accounts for the timescale of dynamic

processes and better represents intracellular and cell-cell signaling and increasing the scale of tractable simulation models as well as improving the speed and thoroughness of current search capabilities to deliver much more realistic treatment designs that can be directly validated through traditional projects.

*DoD-260, “Extending Benefits of Q10: Mitochondrial Cocktail for Gulf War Illness” aims to secure preliminary information to support that a full trial of this mitochondrial cocktail is justified in GWI and to develop the critical information to ensure a successful large-scale trial, e.g., to select outcomes, duration, and sample size. Thirty-two symptomatic ill GW Veterans will be randomly allocated to either a mitochondrial cocktail with individualized treatment (for impaired bioenergetics) or a sham treatment in identical capsules.

*DoD-261, “Testing the Model: A Phase I/II Randomized Double Blind Placebo Control Trial of Targeted Therapeutics: Liposomal Glutathione and Curcumin” will study glutathione and curcumin, both in formulations that optimize bioavailability, and compare them to placebo in a classic double blind placebo control study. These studies are termed Phase I/II, to acknowledge that the interventions have not been tested before in GWI, but they will be evaluated in a way that allows conclusions on feasibility and safety (Phase I), as well as efficacy (Phase II). The primary goal of the study is to test the utility of a previously developed computational model of the illness in an intervention setting. The proposed intervention will be used to assess the established in silico modeling and the impact of the intervention on the implicated homeostatic networks.

*DoD-262, “Testing the Model: A Phase I/II Randomized Double Blind Placebo Control Trial of Targeted Therapeutics: Liposomal Glutathione and Curcumin” will study glutathione and curcumin, both in formulations that optimize bioavailability, and compare them to placebo in a classic double blind placebo control study. These studies are termed Phase I/II, to acknowledge that the interventions have not been tested before in GWI, but they will be evaluated in a way that allows conclusions on feasibility and safety (Phase I), as well as efficacy (Phase II). The primary goal of the study is to test the utility of a previously developed computational model of the illness in an intervention setting. The proposed intervention will be used to assess the established in silico modeling and the impact of the intervention on the implicated homeostatic networks.

*DoD-263, “Vagus Nerve Stimulation: A Noninvasive Treatment to Improve the Health of Gulf Veterans with Gulf War Illness.” Vagus nerve stimulation (VNS) is approved by the Food and Drug Administration (FDA) to treat treatment-resistant epilepsy and depression. This study will test the utility of VNS for Gulf War Veterans with GWI, which is characterized by widespread pain. Besides their pain, the effect of VNS in alleviating migraine headache, another complaint of ill Gulf War Veterans which is common in the presence of widespread pain, will be assessed.

*DoD-264, “An Objective Blood Test from Stimulated Gene Expression for Classification and Outcome Assessment in Clinical Trials of Gulf War Illness” aims to identify new targets for rational development of new diagnostic and treatment approaches for Gulf War illness by performing a second whole genome gene expression study of a validated case

definition of GWI in a developmental sample and then a representative replication sample of Gulf War Veterans. To address high variability in the source material, gene expression will be measured in pure suspensions of T lymphocytes after stimulating aliquots with lipopolysaccharide (LPS) or acetylcholine (ACh). The Principal Investigator will measure gene expression of the whole transcriptome and perform a bioinformatics analysis for differences in gene expression among four clinical groups (the 3 GWI variants from the Haley Factor case definition and a control group).

*DoD-265, “An Objective Blood Test from Stimulated Gene Expression for Classification and Outcome Assessment in Clinical Trials of Gulf War Illness” aims to identify new targets for rational development of new diagnostic and treatment approaches for Gulf War illness by performing a second whole genome gene expression study of a validated case definition of GWI in a developmental sample and then a representative replication sample of Gulf War Veterans. To address high variability in the source material, gene expression will be measured in pure suspensions of T lymphocytes after stimulating aliquots with lipopolysaccharide (LPS) or acetylcholine (ACh). The Principal Investigator will measure gene expression of the whole transcriptome and perform a bioinformatics analysis for differences in gene expression among four clinical groups (the 3 GWI variants from the Haley Factor case definition and a control group).

*DoD-266, “A Randomized, Double-Blind, Placebo-Controlled Crossover Study of the Anti-Inflammatory Compound Anatabine to Treat Pain in GWI Patients” is a pilot clinical evaluation of the anti-inflammatory agent anatabine to mitigate the chronic pain and fatigue experienced with GWI. If successful, this trial will lead to a larger scale trial of GWI patients across multiple sites, which in turn would support an application to the Food and Drug Administration (FDA) for anatabine as a treatment for GWI.

*DoD-267, “Diagnosis of Late-Stage, Early-Onset, Small-Fiber Polyneuropathy.” The Principal Investigator’s prior work suggested that some Veterans with Gulf War illness may have longstanding, persistent early-onset SFPN contracted during the 1990-1991 Gulf War. The current project aims to translate those findings into generally applicable tools that clinicians can use to better diagnose and treat Veterans with GWI. This project will develop and evaluate screening tools for diagnosis and monitoring of longstanding eoSFPN, develop and evaluate simple biotechnology devices for diagnosing and monitoring longstanding eoSFPN, and develop methods for identifying gene polymorphisms that convey risk for eoSFPN. Diagnostic performance (sensitivity, specificity, predictive value) of these new tools will be evaluated in a cohort of those confirmed with longstanding eoSFPN, matched controls, and Veterans with GWI with unknown eoSFPN status.

*DoD-268, “Diagnosis of Late-Stage, Early-Onset, Small-Fiber Polyneuropathy.” The Principal Investigator’s prior work suggested that some Veterans with Gulf War illness may have longstanding, persistent early-onset SFPN contracted during the 1990-1991 Gulf War. The current project aims to translate those findings into generally applicable tools that clinicians can use to better diagnose and treat Veterans with GWI. This project will develop and evaluate screening tools for diagnosis and monitoring of longstanding

eoSFPN, develop and evaluate simple biotechnology devices for diagnosing and monitoring longstanding eoSFPN, and develop methods for identifying gene polymorphisms that convey risk for eoSFPN. Diagnostic performance (sensitivity, specificity, predictive value) of these new tools will be evaluated in a cohort of those confirmed with longstanding eoSFPN, matched controls, and Veterans with GWI with unknown eoSFPN status.

VA Funded Projects

VA initiated funding for four new projects during FY 2015. These four projects focused on Brain and Nervous System Function (1) and Symptoms and General Health (3).

VA-194 “National Health Survey of Veterans and Family Members: Secondary Analysis of CSP #458 Data” is a follow-up study to determine the prevalence of Gulf War-related health conditions in spouses and children of deployed Veterans (DV) and non-deployed Veterans (NDV) and whether Veterans’ health conditions are associated with similar problems in family members.

VA-195 “RCT of Duloxetine and Pregabalin for the Treatment of Gulf War Illness in Veterans” is a randomized, double-blind, controlled trial of Veterans who meet defining criteria for GWI and whose symptom profile includes chronic widespread pain and fatigue. They will be treated with Duloxetine, Pregabalin, or placebo, and compared to a control group to evaluate the efficacy of these medications for the treatment of pain and safety and tolerability.

VA-196 “Immune Basis for Hippocampal Cholinergic Deficits in Pyridostigmine-Treated Rats” will investigate the hypothesis that the combined effects of stress and pyridostigmine bromide (PB) exposure in a rat model result in altered immune function, which then leads to modifications in cholinergic responses in key brain areas that lead to cognitive deficits. Successful completion of the proposed studies will identify loci for therapeutic interventions.

VA-197 “Genomics of Gulf War Illness in Veterans” will address potential genetic risk factors for GWI utilizing single-nucleotide polymorphism (SNP) genotyping data on confirmed GWI cases and controls in a genomewide association study that will also facilitate genomic studies of the relationships between genetic variations and Gulf War environmental exposures.

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Appendices

Federally Funded Research Projects

Appendix A

Project Index By Department

DEPARTMENT OF DEFENSE PROJECTS

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

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

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

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

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

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

DoD-143 Millennium Cohort Study (See also VA-78)

DoD-144 Psychological Health Screening: Methods and Metrics for Deployed Forces

DoD-145 Early Intervention Research Program to Enhance Soldier Resilience

DoD-146 Assessment of Toxicology Assays Methods & Chemical Exposures Among a Cohort of US Marines

DoD-147 Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications

DoD-148 Predicting operational readiness for deployed Army National Guard and Army Reserve soldiers and families

DoD-149 Longitudinal Health Study of GW Veterans

DoD-150 Validation Study of Gulf War Deployment Files

DoD-151 Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in GW Veterans

DoD-152 Characterization of Intracellular Signaling Pathways Activated by Nerve Agents

DoD-153 Gulf War Illness Research

DoD-154 Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-88)

DoD-155 Neuropsychological Functioning in GW Veterans Exposed to Pesticides and Pyridostigmine Bromide

DoD-156 The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant

DoD-157 Novel Leishmania and Malaria Potassium Channels: Candidate Therapeutic Targets

DoD-158 Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission of Genetic Damage to Offspring

DoD-159 Neurotoxicity from Chronic Exposure to Depleted Uranium

DoD-160 Characterization of the Reproductive Toxicity of Depleted Uranium

DoD-161 Glutamate Receptor Aptamers and ALS

DoD-162 Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function

DoD-163 Neuroimmune Effects of Inhaling Low Dose Sarin

DoD-164 Efficacy of Adjunct Sleep Interventions for PTSD (EASI-PTSD)

DoD-165 Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military – BALSAM

DoD-166 A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance

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

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

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

DoD-240	Novel Therapeutic Approaches for the Treatment of Depression and Cognitive Deficits in a Rodent Model of Gulf War Veterans' Illness
DoD-241	Gulf War Illness Inflammation Reduction Trial
DoD-242	Epigenetic Mediation of Endocrine and Immune Response in an Animal Model for Gulf War Illness
DoD-243	Vascular and Skeletal Muscle Function in Gulf War Veterans Illness
DoD-244	Neurovascular and Autonomic Dysfunction Associated with Gulf War Illness Pain
DoD-245	Biomarkers and Brain Mechanisms of Gulf War Illness
DoD-246	Novel Autoantibody Serum and Cerebrospinal Fluid Biomarkers in Veterans with Gulf War Illness
DoD-247	Novel Autoantibody Serum and Cerebrospinal Fluid Biomarkers in Veterans with Gulf War Illness
DoD-248	Preclinical Treatment of an Organophosphate Model of Gulf War Illness
DoD-249	Gulf War Illness as a Brain Autoimmune Disorder
DoD-250	An Integrated Genomics and Cell Biology Approach to Correlate Novel GWI Indicators of Infections and Neuroinflammatory Mechanisms with Targeted Drug Therapy
DoD-251	Muscle Mitochondrial Assessments in Gulf War Illness
DoD-252	START and STOPP in GWI
DoD-253	D-cycloserine: A Novel Treatment for Gulf War Illness
DoD-254	Effect of Diet on Gulf War Illness: A Pilot Study
DoD-255	Microtubule Abnormalities Underlying Gulf War Illness in Neurons from Human-Induced Pluripotent Cells
DoD-256	Vagus Nerve Stimulation as a Treatment Strategy for Gulf War Illness
DoD-257	Designing a Successful Acupuncture Treatment Program for Gulf War Illness
DoD-258	High-Fidelity Design of Multimodal Restorative Interventions in Gulf War Illness
DoD-259	High Fidelity Design of Multimodal Restorative Interventions in Gulf War Illness
DoD-260	Extending Benefits of Q10: Mitochondrial Cocktail for Gulf War Illness
DoD-261	Testing the Model: A Phase I/II Randomized Double Blind Placebo Control Trial of Targeted Therapeutics: Liposomal Glutathione and Curcumin
DoD-262	Testing the Model: A Phase I/II Randomized Double Blind Placebo Control Trial of Therapeutics: Liposomal Glutathione and Curcumin
DoD-263	Vagus Nerve Stimulation: A Noninvasive Treatment to Improve the Health of Gulf Veterans with Gulf War Illness
DoD-264	An Objective Blood Test from Stimulated Gene Expression for Classification and Outcome Assessment in Clinical Trials of Gulf War Illness

DoD-265	An Objective Blood Test from Stimulated Gene Expression for Classification and Outcome Assessment in Clinical Trials of Gulf War Illness
DoD-266	A Randomized, Double-Blind, Placebo-Controlled Crossover Study of the Anti-Inflammatory Compound Anatabine to Treat Pain in GWI Patients
DoD-267	Diagnosis of Late-Stage, Early-Onset, Small-Fiber Polyneuropathy
DoD-268	Diagnosis of Late-Stage, Early-Onset, Small-Fiber Polyneuropathy

DEPARTMENT OF HEALTH AND HUMAN SERVICES PROJECTS

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

DEPARTMENT OF VETERANS AFFAIRS PROJECTS

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

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

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

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

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

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

VA-156 Gulf War Era Cohort and Biorepository (CSP 585)

VA-157 A Clinical Demonstration of an EEG Brain-Computer Interface for ALS Patients (CSP 567)

VA-158 Testing the Feasibility of MC CBT for Veterans with IBS

VA-159 Somatic hypersensitivity in Veterans with IBS

VA-160 Lipoic Acid Therapy for Experimental Autoimmune Encephalomyelitis

VA-161 Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease

VA-162 Transcription factors regulating sensory gene expression and pain pathways

VA-163 Immunoregulation of Myelin Specific T Lymphocytes

VA-164 Central Mechanisms Modulating Visceral Sensitivity (renewal of VA-136)

VA-165 A Pilot Study of CPAP Adherence Promotion by Peer Buddies with Sleep Apnea

VA-166 A Randomized Controlled Trial of a Mindfulness-Based Intervention for Gulf War Syndrome

VA-167 Neuroprotection and Myelin Repair Mechanisms in Multiple Sclerosis

VA-168 Sleep Neurobiology and Circuitry

VA-169 Prevention of Hippocampal Neurodegeneration Due to Age and Apnea

VA-170 Epigenetic Mechanisms Relevant to the Pathogenesis of ALS

VA-171 Nanoparticle Coupled Antioxidants for Respiratory Illness in Veterans

VA-172 Understanding Pain of Gastrointestinal Origin in Women that Serve in OEF/OIF

VA-173 Impact of Exercise Training on Pain and Brain Function in GW Veterans

VA-174 VA GW Veterans' Illnesses Biorepository

VA-175 Memory and Mood Enhancing Therapiesfor Gulf War Illness

VA-176 MEG Synchronous Neural Interactions (SNI) in GW Veterans

VA-177 Somatic Hypersensitivity in Veterans with IBS

VA-178 rTMS for the Treatment of Chronic Pain in GW1 Veterans

VA-179 Vascular and Skeletal Muscle Function in Gulf War Veterans Illness

VA-180 Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with GWI

VA-181 Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI

VA-182 Consensus Case Definition for Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans

VA-183 Examination of Cognitive Fatigue in Gulf War Illness Using fMRI

VA-184	Longitudinal Assessment of Gulf War Veterans with Suspected Sarin Exposure
VA-185	Identification of Plasma Biomarkers of Gulf War Illness Using “omic” Technology
VA-186	Gulf War Exposures and the Molecular Mechanisms of Paternal Reproductive Risk
VA-187	Multimodal Biological Assessment of Gulf War Illness
VA-188	Complementary Neurosteroid Intervention in Gulf War Veterans’ Illnesses
VA-189	CAM in Veterans with Gulf War Illnesses
VA-190	Cognitive Rehabilitation for Gulf War Illness
VA-191	Novel Neurotrophic Therapies in an Optimized Mouse Model of GWVI
VA-192	Women vs. Men with GWI: Differences in Computational Models and Therapeutic Targets
VA-193	Neuroinflammation, Oxidative Stress, and Hippocampal Defects in Gulf War Illness
VA-194	Health of Family Members: Secondary Analysis of CSP #458 Data
VA-195	RCT of Duloxetine and Pregabalin for the Treatment of Gulf War Illness in Veterans
VA-196	Immune Basis for Hippocampal Cholinergic Deficits in Pyridostigmine-Treated Rats
VA-197	Genomics of Gulf War Illness in Veterans

Appendix B

Project List by Research Focus Areas

Brain and Nervous System Function

Clinical

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

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

			with PTSD
Symptoms and General Health	Symptoms	VA-077	HPA Axis Reactivity in Men and Women with Chronic PTSD
Symptoms and General Health	Symptoms	VA-083	Neuropsychological Assessment of a Population-Based Sample of Persian GW Veterans and Controls
Symptoms and General Health	Symptoms	VA-084	Neurobiology of Severe Psychological Trauma in Women
Symptoms and General Health	Symptoms	VA-085	Associative Learning in Veterans with and without Combat Experience
Symptoms and General Health	Treatment	VA-089	National Registry of Veterans with Amyotrophic Lateral Sclerosis
Symptoms and General Health	Symptoms	VA-093	HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans
Symptoms and General Health	Treatment	VA-112	National VA Amyotrophic Lateral Sclerosis Research Consortium
Symptoms and General Health	Diagnosis	VA-125	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla
Symptoms and General Health	Diagnosis	DoD-238	Restoring the Brain's Lipid Homeostasis as a Therapeutic Avenue for Treating the CNS Symptoms of Gulf War Illness
Symptoms and General Health	Treatment	VA-181	Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI
Symptoms and General Health	Treatment	DoD-240	Novel Therapeutic Approaches for the Treatment of Depression and Cognitive Deficits in a Rodent Model of Gulf War Veterans' Illness
Symptoms and General Health	Symptoms	DoD-243	Vascular and Skeletal Muscle Function in Gulf War Veterans Illness
Symptoms and General Health	Symptoms	DoD-246	Novel Autoantibody Serum and Cerebrospinal Fluid Biomarkers in Veterans with Gulf War Illness
Symptoms and General Health	Symptoms	DoD-247	Novel Autoantibody Serum and Cerebrospinal Fluid Biomarkers in Veterans with Gulf War Illness
Symptoms and General Health	Symptoms; Diagnosis	DoD-065	Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment
Symptoms and General Health	Symptoms; Exposure	DoD-057	Physiologic Effects of Stress in GW Veterans
Symptoms and General Health	Symptoms; Exposure	DoD-133	Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome
Symptoms and General Health	Diagnosis; Symptoms	DoD-087	Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related Quality of Life among PGWVs
Symptoms and General Health	Treatment; Symptoms	DoD-125	A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74)
Symptoms and General Health	Diagnosis; Symptoms	DoD-131	Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses
Symptoms and General Health	Diagnosis; Symptoms	DoD-144	Psychological Health Screening: Methods and Metrics for Deployed Forces
Symptoms and General Health	Diagnosis; Symptoms	DoD-153	Gulf War Illness Research
Symptoms and General Health	Treatment; Symptoms	DoD-164	Efficacy of Adjunct Sleep Interventions for PTSD (EASI- PTSD)

Symptoms and General Health	Treatment; Symptoms	VA-060	Identification and Management of Sleep Disorders in Gulf War Veterans
Symptoms and General Health	Diagnosis; Symptoms	VA-064 B	Quantification and Validation of Structure-Function relationships through visuospatial test performance
Symptoms and General Health	Diagnosis; Symptoms	VA-067	Olfactory Functioning in GW Veterans
Symptoms and General Health	Treatment; Symptoms	VA-074	A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125)
Symptoms and General Health	Treatment; Symptoms	VA-086	A Clinical Trial of Magnetic Stimulation in Depression
Symptoms and General Health	Treatment	VA-087	Improving Outcomes of Depression in Primary Care
	Symptoms		
Symptoms and General Health	Treatment; Symptoms	VA-138	Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP
Symptoms and General Health;	Symptoms; Environmental Toxicology	VA-008	Psychological Test Data of GW Veterans Over Time
Symptoms and General Health;	Symptoms; Diagnosis	DoD-197	Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness?

Development

Research Focus	Project Focus	Project	Project Title
	Diagnosis	HHS-013	ALS Biomarkers in the Cerebrospinal Fluid
	Diagnosis	VA-184	Longitudinal Assessment of Gulf War Veterans with Suspected Sarin Exposure
	Treatment	DoD-189	Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers
	Treatment	VA-160	Lipoic Acid Therapy for Experimental Autoimmune Encephalomyelitis
	Treatment	DoD-231	Use of a Portable Stimulator to Treat GWI
	Symptoms	VA-183	Examination of Cognitive Fatigue in Gulf War Illness Using fMRI
Environmental Toxicology	Treatment; Exposure; Symptoms	DoD-184	Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the GW Veterans' Illnesses
Symptoms and General Health	Diagnosis	VA-113	Novel Cause of Motor Neuron Disease
Symptoms and General Health	Diagnosis	DoD-245	Biomarkers and Brain Mechanisms of Gulf War Illness
Symptoms and General Health	Treatment; Prevention	VA-097	Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas
Symptoms and General Health	Diagnosis; Symptoms	VA-101	Biomarkers Discovery in ALS
Symptoms and General Health	Treatment; Symptoms	VA-128	MR Tracking of Stem Cells for Replacement Therapy in ALS

Epidemiology

Department of Veterans Affairs Gulf War Research Funding

Research Focus	Project Focus	Project	Project Title
Symptoms and General Health	Symptoms	DoD-023	Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families
Symptoms and General Health	Symptoms	DoD-082	Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs
Symptoms and General Health	Symptoms	DoD-114	A Re-examination of Neuropsychological Functioning in Persian GW Veterans
Symptoms and General Health	Symptoms	DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also VA-61)
Symptoms and General Health	Symptoms	HHS-006	Defining Gulf War Illness
Symptoms and General Health	Diagnosis	HHS-012	Genetic Epidemiology of ALS in Veterans
Symptoms and General Health	Symptoms	VA-036	Stress Symptoms and Their Causal Attribution in Desert Storm Veterans
Symptoms and General Health	Symptoms	VA-061	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also DoD-118)
Symptoms and General Health	Symptoms	VA-068	Family Study of Fibromyalgia
Symptoms and General Health	Symptoms	VA-075	ALS and Veterans: Are Veterans at Increased Risk?
Symptoms and General Health	Symptoms	VA-110	Pain Among GW Veterans: Secondary Analysis of CSP#458 Data
Symptoms and General Health	Symptoms	VA-150	GW Veterans Illnesses' Research IDIQ Contract
Symptoms and General Health	Diagnosis	VA-151	Genetic Epidemiology of ALS Veterans
Symptoms and General Health	Symptoms	VA-152	Multiple Sclerosis in GW Veterans
Symptoms and General Health	Symptoms	DoD-227	Monosodium Luminol for Improving Brain Function in Gulf War Illness
Symptoms and General Health	Symptoms; Diagnosis	DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome
Symptoms and General Health	Treatment; Prevention	DoD-145	Early Intervention Research Program to Enhance Soldier Resilience
Symptoms and General Health	Diagnosis; Symptoms	DoD-052	Female Gender and Other Potential Predictors of Functional Health Status Among Persian GW Veterans
Symptoms and General Health	Diagnosis; Symptoms	DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also VA-088)
Symptoms and General Health	Diagnosis; Symptoms	HHS-002	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18
Symptoms and General Health	Diagnosis; Symptoms	VA-088	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study (See also DoD-154)

Mechanistic

Department of Veterans Affairs Gulf War Research Funding

Research Focus	Project Focus	Project	Project Title
	Diagnosis	VA-174	VA GW Veterans' Illnesses Biorepository
	Diagnosis	VA-176	MEG Synchronous Neural Interactions (SNI) in GW Veterans
	Diagnosis	VA-187	Multimodal Biological Assessment of Gulf War Illness
	Diagnosis	VA-193	Neuroinflammation, Oxidative Stress, and Hippocampal Defects in Gulf War Illness
	Symptoms	VA-091	The Role of Dietary Choline in Neuroprotection
	Symptoms	VA-120	Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis
	Symptoms	VA-139	Sleep Neurobiology and Circuitry
	Symptoms	VA-141	Genetic Analysis of an Invertebrate Model of Amyotrophic Lateral Sclerosis
	Treatment	DoD-161	Glutamate Receptor Aptamers and ALS
	Treatment	VA-140	Integrated Neuroimaging and Neuropathological Analysis of the Effects of Physical Activity on Progression and Therapy in ALS
	Treatment	VA-163	Immunoregulation of Myelin Specific T Lymphocytes
	Treatment	VA-191	Novel Neurotrophic Therapies in an Optimized Mouse Model of GWVI
	Treatment; Symptoms	VA-161	Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease
Environmental Toxicology	Exposure; Interactions; Treatment	VA-175	Memory and Mood Enhancing Therapies for Gulf War Illness
Environmental Toxicology	Symptoms	VA-126	Structural Magnetic Resonance Imaging in Gulf War-Era Veterans
Environmental Toxicology	Symptoms; Exposure	DoD-176	Studies on Axonal Transport in an Animal Model for Gulf War Syndrome
Environmental Toxicology	Exposure; Symptoms	DoD-190	Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness
Environmental Toxicology Chemical Weapons	Exposure; Symptoms	DoD-219	Organophosphate-Related Alterations in Myelin and Axonal Transport in the Living Mammalian Brain
Environmental Toxicology;	Treatment; Exposure; Immune Function	DoD-185	Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model
Environmental Toxicology	Exposures; Symptoms	DoD-244	Neurovascular and Autonomic Dysfunction Associated with Gulf War Illness Pain
Environmental Toxicology; Symptoms and General Health	Symptoms; Exposure	DoD-170	Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I
Environmental Toxicology; Symptoms and General Health	Symptoms; Exposure	DoD-198	Oxidative Stress
Symptoms and General Health	Symptoms	DoD-080	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells
Symptoms and General Health	Symptoms	DoD-091	Neurological and Circadian Substrates of PTSD-like Behaviors
Symptoms and General Health	Symptoms	DoD-092	Traumatic Experiences Persistently Enhance Cue-dependent Learning:

			Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder
Symptoms and General Health	Symptoms	DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala
Symptoms and General Health	Treatment; Diagnosis	DoD-205	The HPA Axis and Metabolic Outcomes in GW Veterans
Symptoms and General Health	Symptoms	VA-081	Stress, Pro-Inflammatory Cytokines and Coping Behavior
Symptoms and General Health	Symptoms	VA-090	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness
Symptoms and General Health	Symptoms	VA-090A	Neuronal Hyperexcitability and Motor Neuron Regeneration
Symptoms and General Health	Symptoms	VA-090B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders
Symptoms and General Health	Symptoms	VA-090C	Developmental Differences in Alcohol Withdrawal Sensitivity
Symptoms and General Health	Symptoms	VA-090D	Seizures and Neuroplasticity: Physiology and Biochemistry
Symptoms and General Health	Symptoms	VA-092	Acetylcholinesterase Activity in GW Veterans
Symptoms and General Health	Symptoms	VA-095	The Role of Signal Regulatory Proteins in Astrocytomas
Symptoms and General Health	Symptoms	VA-098	Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas
Symptoms and General Health	Symptoms	VA-103	Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal
Symptoms and General Health	Symptoms	VA-109	Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics
Symptoms and General Health	Treatment	VA-114	Strategies in Therapeutic Development of Neurodegenerative Diseases
Symptoms and General Health	Symptoms	VA-116	Quantitative Trait Genes Controlling Circadian and Sleep Behaviors
Symptoms and General Health	Symptoms	VA-121	Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders
Symptoms and General Health	Symptoms	VA-122	Role of Mitochondrial Oxidative Stress in ALS
Symptoms and General Health	Symptoms	VA-129	Glucocorticoid Responsivity in GW Veterans
Symptoms and General Health	Diagnosis; Symptoms	DoD-214	Abnormalities in Human Brain Creatine Metabolism in Gulf War Illness Probed with MRS
Symptoms and General Health	Treatment; Symptoms	VA-100	Studies of the Blood-Brain Barrier and its Manipulation
Symptoms and General Health	Prevention; Symptoms	VA-102	Cholinergic and Monoaminergic Influences on Sleep
Symptoms and General Health	Treatment	VA-167	Neuroprotection and Myelin Repair Mechanisms in Multiple Sclerosis
Symptoms and General Health	Treatment	VA-168	Sleep Neurobiology and Circuitry
Symptoms and General Health	Treatment; Prevention	VA-169	Prevention of Hippocampal Neurodegeneration Due to Age and Apnea
Symptoms and General Health	Diagnosis; Prevention	VA-170	Epigenetic Mechanisms Relevant to the Pathogenesis of ALS
Immune Function	Treatment	DoD-202	Brain-Immune Interactions as Basis of Gulf War Illness: Consortium Development
Immune Function	Diagnosis; Symptoms	DoD-222	Brain Immune Interactions as the Basis of Gulf War Illness: Gulf War Illness Consortium (GWIC)
Immune Function; Pyridostigmine	Exposure	VA-196	Immune Basis for Hippocampal Cholinergic Deficits in Pyridostigmine-Treated Rats

Environmental Toxicology

Clinical

Research Focus	Project Focus	Project	Project Title
Brain and Nervous System Function	Interactions; Exposure; Symptoms	VA-048	Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance
Brain and Nervous System Function; Symptoms and General Health	Exposure; Symptoms	VA-005 C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans
Chemical Weapons	Symptoms	DoD-060	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness
Chemical Weapons	Exposure	DoD-146	Assessment of Toxicology Assay Methods and Chemical Exposures Among a Cohort of US Marines Deployed in the Gulf War
Pyridostigmine Bromide	Exposure; Prevention	DoD-011	Male/Female Differential Tolerances to Pyridostigmine Bromide
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-124	Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure Interactions	DoD-155	Neuropsychological Functioning in GW Veterans Exposed to Pesticides and Pyridostigmine Bromide Symptoms
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms	DoD-064	Individual Differences in Neurobehavioral Effects of Pyridostigmine
Symptoms and General Health	Exposure; Symptoms	VA-004 D	Evaluation of Respiratory Dysfunction Among GW Veterans
Symptoms and General Health; Brain and Nervous System Function	Exposure; Symptoms	DoD-156	The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant

Development

Research Focus	Project Focus	Project	Project Title
	Interactions; Exposure	DoD-034	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents
	Diagnosis; Exposure	DoD-134	Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin
	Exposure; Interactions	HHS-008	Strategy to Identify Non-Additive Response to Chemical Mixtures
Brain and Nervous System Function; Symptoms and General Health	Diagnosis; Exposure; Symptoms	VA-064 C	Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in Veteran populations
Chemical Weapons	Diagnosis	DoD-049	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts
Chemical Weapons	Exposure; Diagnosis	DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents

Chemical Weapons	Diagnosis; Exposure	DoD-050	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways
Chemical Weapons	Diagnosis; Exposure	DoD-137	Low Level Exposure to Sulfur Mustard: Development of an SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin
Chemical Weapons	Diagnosis; Exposure	DoD-167	Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure
Symptoms and General Health	Diagnosis; Exposure	DoD-018	Kuwait Oil Fires Troop Exposure Assessment Model (TEAM)
Symptoms and General Health	Diagnosis; Exposure	DoD-019	Persian Gulf Veterans Health Tracking System
Symptoms and General Health	Diagnosis; Exposure	DoD-100	Antibodies to Squalene
Symptoms and General Health	Diagnosis; Exposure; Symptoms	DoD-016	Kuwait Oil Fire Health Risk Assessment
Symptoms and General Health	Diagnosis	DoD-221	Role of microRNAs in the Pathobiology of Gulf War Illness: Identification of Potential Novel Therapeutic Targets

Epidemiology

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

Symptoms and General Health	Exposure; Symptoms	VA-006	Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Exposure	DoD-248	Preclinical Treatment of an Organophosphate Model of Gulf War Illness
	Exposure; Interactions	DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals
	Exposure; Interactions	VA-145	Proteomic Analysis of Cellular Response to Biological Warfare Agents
	Exposure; Prevention	HHS-003	Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires
	Exposure; Prevention	VA-004 E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility
	Exposure; Prevention	VA-171	Nanoparticle Coupled Antioxidants for Respiratory Illness in Veterans
	Exposure; Symptoms	DoD-223	Persistent Neural Membrane Protein Misregulation Following Neurotoxicant Exposure
Brain and Nervous System Function	Exposure	DoD-175	Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium
Brain and Nervous System Function	Interactions; Exposure; Symptoms	DoD-178	Analysis of Paraoxonase Status among US Navy GW Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions
Brain and Nervous System Function	Exposure; Interactions	VA-146	Direct Delivery of Neurotoxins to the Brain by an Intranasal Route
Brain and Nervous System Function	Exposure; Prevention	DoD-159	Neurotoxicity from Chronic Exposure to Depleted Uranium
Brain and Nervous System Function	Exposure; Symptoms	VA-144	Testing the Role of Permethrin on the Progression of ALS
Brain and Nervous System Function	Exposure; Symptoms	VA-149	Behavior of Neural Stem Cells in a Rat Model of GWS
Brain and Nervous System Function; Chemical Weapons	Exposure; Symptoms	DoD-022	Chronic Organophosphorus Exposure and Cognition
Brain and Nervous System Function; Immune Function	Exposure; Interactions; Symptoms	DoD-037	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats
Brain and Nervous System Function;	Exposure	DoD-126	Blood-Brain Barrier Transport of Uranium
Brain and Nervous System Function;	Exposure; Symptoms	DoD-128	Multifactorial Assessment of Depleted Uranium Neurotoxicity
Brain and Nervous System Function;	Exposure; Symptoms	DoD-129	Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness

Brain and Nervous System Function; Pyridostigmine Bromide	Exposure; Interactions	DoD-201	Synergistic Actions of Pyridostigmine Bromide and Insecticides on Muscle and Vascular Nociceptors
Brain and Nervous System Function; Pyridostigmine Bromide	Exposure; Symptoms	VA-143	The Role of Protein Oxidation in the Progression of ALS
Brain and Nervous System Function; Symptoms and General Health	Exposure; Symptoms	DoD-007 A	Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling
Brain and Nervous System Function	Exposure; Interactions	DoD-225	The Role of Protein Radicals in Chronic Neuroimmune Dysfunction and Neuropathology in Response to a Multiple-Hit Model of Gulf War Exposures
Chemical Weapons	Exposure; Diagnosis	DoD-136	A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure
Chemical Weapons; Brain and Nervous System Function	Exposure	VA-006 D	DNA Damage from Chemical Agents and Its Repair (Project IV)
Chemical Weapons; Brain and Nervous System Function	Exposure; Diagnosis	DoD-135	Biochemical Markers for Exposure to Low Doses of Organophosphorus Exposure
Chemical Weapons; Brain and Nervous System Function	Prevention; Exposure	DoD-051	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-054	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-055	Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-056	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-061	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-062	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-072	Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals
Chemical Weapons; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects
Chemical Weapons; Brain and Nervous System Function	Exposure; Symptoms	DoD-053	Long-Term Effects of Subclinical Exposures to Sarin
Chemical Weapons; Brain and Nervous System Function	Exposure; Symptoms	DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents
Immune Function	Exposure; Interactions	HHS-007	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid
Immune Function	Exposure; Symptoms	DoD-163	Neuroimmune Effects of Inhaling Low Dose Sarin
Immune Function and Infectious Diseases	Exposure; Symptoms	DoD-191	Neuroimmune Interactions, Low-Dose Sarin Inhalation, and Gulf War Syndrome
Immune Function	Exposure	DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys
Immune Function Pyridostigmine Bromide	Exposure; Interactions	DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War

Immune Function Symptoms and General Health	Exposure; Symptoms	DoD-130	Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents
Pyridostigmine Bromide	Prevention; Exposure	DoD-033	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity
Pyridostigmine Bromide	Exposure; Interactions	DoD-010	Pyridostigmine Synergistic Toxicity Study
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions	DoD-002	Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions	DoD-075	Toxic Interactions of Prophylactic Drugs and Pesticides
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions	DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-078	Experimental Models of Gulf War Syndrome
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-079	Time Course of Stress-induced Impairment of Blood Brain Barrier
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	DoD-139	Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	VA-006 C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III)
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Interactions; Symptoms	VA-080	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms	DoD-059	Pyridostigmine-induced Neurodegeneration: Role of Neuronal Apoptosis
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms	VA-049	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms	VA-106	Interoceptive Stressor Conditioning: A Model for Gulf War Illness
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms	VA-123	Interactions Between Maternal Care, Stress and Pyridostigmine Bromide
Pyridostigmine Bromide; Brain and Nervous System Function	Exposure; Symptoms	VA-124	Early Life Determinants of Vulnerability to Pyridostigmine Bromide
Pyridostigmine Bromide; Symptoms and General Health	Exposure; Interactions; Symptoms	VA-005 D	Effects of Genetics and Stress on Responses to Environmental Toxins
Reproductive Health;	Exposure; Symptoms	DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development
Symptoms and General Health	Exposure	VA-065	San Antonio Environmental Hazards Research Center
Symptoms and General Health	Exposure	VA-065 A	Does a variant of the human SOD2 gene increase sensitivity to hazards?
Symptoms and General Health	Exposure	VA-065 B	The contribution of FEN-1 to genetic integrity subsequent to oxidative stress
Symptoms and General Health	Exposure	VA-065 C	The importance of hydrogen peroxide detoxification in cellular

			protection
Symptoms and General Health	Exposure	VA-065 D	Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental hazards?
Symptoms and General Health	Symptoms	VA-155	Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis
Symptoms and General Health	Exposure; Symptoms	DoD-160	Characterization of the Reproductive Toxicity of Depleted Uranium
Symptoms and General Health	Exposure; Symptoms	DoD-192	Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome
Symptoms and General Health;	Exposure	DoD-007 B	Carcinogenicity of Depleted Uranium Fragments
Symptoms and General Health;	Exposure; Symptoms	DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys
Symptoms and General Health;	Exposure; Symptoms	DoD-127	Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man

Immune Function and Infectious Diseases

Clinical

Research Focus	Project Focus	Project	Project Title
	Diagnosis	DoD-047	Study of Mycoplasmal Infections in GW Veterans
	Symptoms	DoD-048	Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs. Selected Control Groups
	Diagnosis	VA-147	The Diagnosis and Pathogenesis of Occult Leishmaniasis
	Diagnosis; Treatment	VA-006 E	Clinical and Epidemiology Leishmania Research
Brain and Nervous System Function	Symptoms	DoD-088	Clinical Relevance of Novel Immunological Markers in PTSD
Brain and Nervous System Function	Symptoms	VA-017	Immunological Evaluation of Persian Gulf Veterans
Environmental Toxicology	Exposure; Interactions; Symptoms	DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War-related illness
Symptoms and General Health	Treatment; Diagnosis	DoD-067	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria
Symptoms and General Health	Symptoms; Exposure	VA-006 B	Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II)
Symptoms and General Health	Exposure; Interactions	DoD-162	Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function
Symptoms and General Health	Exposure; Symptoms	DoD-042	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment
Symptoms and General Health	Treatment; Symptoms	DoD-119	Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also VA-55)
Symptoms and General Health	Treatment; Symptoms	VA-055	Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also DoD-119)

Symptoms and General Health	Symptoms	DoD-249	Gulf War Illness as a Brain Autoimmune Disorder

Development

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

Mechanistic

Research Focus	Project Focus	Project	Project Title
	Treatment	DoD-009	Identification of the Genetic Factors Which Control Tropism in Leishmania
	Treatment	DoD-157	Novel Leishmania and Malaria Potassium Channels: Candidate Therapeutic Targets
	Prevention	VA-015	Vaccine-Mediated Immunity Against Leishmaniasis
	Prevention	VA-016	Protective Immunity in Experimental Visceral Leishmaniasis
	Symptoms	VA-127	Interactions of the Leishmania sp. with Mammalian Cells
	Symptoms	DoD-215	Identifying Immune Drivers of Gulf War Illness Using a Novel Daily Sampling Approach
	Prevention; Treatment	VA-094	The Immunology of Chronic Cutaneous Leishmaniasis
Brain and Nervous System Function	Symptoms	DoD-195	Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness
Environmental Toxicology	Diagnosis	DoD-242	Epigenetic Mediation of Endocrine and Immune Response in an Animal Model for Gulf War Illness
Environmental Toxicology	Exposure	DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in GW Veterans
Environmental Toxicology	Exposure; Interactions	DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?
Environmental Toxicology; Pyridostigmine Bromide	Exposure; Interactions	DoD-076	Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel
Environmental Toxicology; Pyridostigmine Bromide	Exposure; Interactions; Symptoms	DoD-081	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress
Symptoms and General Health	Symptoms	VA-111	T Cell Responses to Multiple Immunizations and Stress

Symptoms and General Health	Treatment; Symptoms	VA-105	Expression of the Major Surface Protease of Leishmania Chagasi
Symptoms and General Health	Treatment; Symptoms	DoD-250	An Integrated Genomics and Cell Biology Approach to Correlate Novel GWI Indicators of Infections and Neuroinflammatory Mechanisms with Targeted Drug Therapy

Reproductive Health

Clinical

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

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Prevention	DoD-001 C	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among Gulf War Veterans and other active-duty personnel
	Prevention	DoD-001 D	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in GW Veterans
	Symptoms	DoD-001 G	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian GW Veterans
	Prevention; Symptoms	DoD-035	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War.
	Prevention; Symptoms	HHS-004	Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian GW Veterans in Mississippi

Mechanistic

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

Symptoms and General Health

Clinical

Department of Veterans Affairs Gulf War Research Funding

Research Focus	Project Focus	Project	Project Title
	Symptoms	DoD-001 A	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees
	Diagnosis	DoD-109	Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms
	Symptoms	VA-018	Chronic Gastrointestinal Illness in Persian Gulf Veterans
	Symptoms	VA-040	Musculoskeletal Symptoms in Gulf War Syndrome
	Treatment; Diagnosis; Symptoms	DoD-172	CNDP1 Polymorphisms and Carnosine Therapy in GWI
	Treatment; Symptoms	DoD-171	Q10 for GW Veterans
	Treatment; Symptoms	DoD-181	Effectiveness of Acupuncture in the Treatment of Gulf War Illness
	Treatment; Symptoms	DoD-186	Small Intestinal Microbial Community in Gulf War Illness
	Treatment	DoD-204	Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Syndrome
	Treatment	VA-189	CAM in Veterans with Gulf War Illnesses
	Treatment	DoD-229	Bench to Bedside: Understanding Symptom Response to Acupuncture Treatment and Designing a Successful Acupuncture Treatment Program
	Treatment	DoD-234	A Prospective Open-Label Clinical Trial of Methylphenidate plus a GWI-Specific Nutrient Formula in Patients with Gulf War Illness and Concentration Disturbances
	Treatment	DoD-235	Treating Gulf War Illness with Novel Anti-Inflammatories: A Screening of Botanical Microglia Modulators
	Treatment	DoD-236	Development of Dietary Polyphenol Preparations for Treating Veterans with Gulf War Illness
	Treatment	DoD-241	Gulf War Illness Inflammation Reduction Trial
	Treatment; Symptoms	DoD-206	Investigating Clinical Benefits of a Novel Sleep-Focused, Mind-Body Program on Gulf War Illness Symptoms: An Exploratory Randomized Controlled Trial
	Treatment; Symptoms	DoD-216	Intranasal Insulin: A Novel Treatment for Gulf War Multisymptom Illness
	Treatment; Symptoms	VA-056	Birmingham's GW Veterans' Illness Demonstration Clinic
	Treatment; Symptoms	VA-058	Implementation and Evaluation of GW Veterans' Demonstration Project
	Diagnosis; Symptoms	VA-104	Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome
	Treatment; Symptoms	VA-137	Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans
	Treatment; Symptoms	VA-153	Bacterial Overgrowth Associated with Chronic Multi- Symptom Illness Complex
	Treatment; Symptoms	VA-158	Testing the Feasibility of MC CBT for Veterans with IBS
	Treatment	VA-165	A Pilot Study of CPAP Adherence Promotion by Peer Buddies with Sleep Apnea

	Diagnosis	DoD-251	Muscle Mitochondrial Assessments in Gulf War Illness
	Diagnosis	DoD-252	START and STOPP in GWI
	Treatment	DoD-253	D-cycloserine: A Novel Treatment for Gulf War Illness
	Treatment	DoD-254	Effect of Diet on Gulf War Illness: A Pilot Study
	Treatment	DoD-260	Extending Benefits of Q10: Mitochondrial Cocktail for Gulf War Illness
	Treatment	DoD-261	Testing the Model: A Phase I/II Randomized Double Blind Placebo Control Trial of Targeted Therapeutics: Liposomal Glutathione and Curcumin
	Treatment	DoD-262	Testing the Model: A Phase I/II Randomized Double Blind Placebo Control Trial of Targeted Therapeutics: Liposomal Glutathione and Curcumin
	Treatment	DoD-263	Vagus Nerve Stimulation: A Noninvasive Treatment to Improve the Health of Gulf Veterans with Gulf War Illness
	Diagnosis	DoD-264	An Objective Blood Test from Stimulated Gene Expression for Classification and Outcome Assessment in Clinical Trials of Gulf War Illness
	Diagnosis	DoD-265	An Objective Blood Test from Stimulated Gene Expression for Classification and Outcome Assessment in Clinical Trials of Gulf War Illness
	Treatment	DoD-266	A Randomized, Double-Blind, Placebo-Controlled Crossover Study of the Anti-Inflammatory Compound Anatabine to Treat Pain in GWI
	Diagnosis	DoD-267	Diagnosis of Late-Stage, Early-Onset, Small-Fiber Polyneuropathy
	Diagnosis	DoD-268	Diagnosis of Late-Stage, Early-Onset, Small-Fiber Polyneuropathy
	Diagnosis	VA-197	Genomics of Gulf War Illness in Veterans
	Treatment	VA-195	RCT of Duloxetine and Pregabalin for the Treatment of Gulf War Illness in Veterans
Brain and Nervous System Function	Symptoms	DoD-036	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms
Brain and Nervous System Function	Symptoms	DoD-041	Evaluation of Muscle Function in Persian Gulf Veterans
Brain and Nervous System Function	Symptoms	DoD-058	Illness Among Persian GW Veterans: Case Validation Studies
Brain and Nervous System Function	Symptoms	DoD-085	CNS Cytokines and CRH in GW Veterans with Multiple Unexplained Symptoms
Brain and Nervous System Function	Symptoms	DoD-101	Mechanisms in Chronic Multisymptom Illnesses
Brain and Nervous System Function	Symptoms	VA-069	Cardiovascular Hyporeactivity and Fatiguing Illness in Gulf War Veterans
Brain and Nervous System Function	Symptoms	VA-071	Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome
Brain and Nervous System Function	Symptoms	VA-073	Pain Sensitivity in GW Veterans with Medically Unexplained Musculoskeletal Pain
Brain and Nervous System Function	Symptoms	VA-082	Pituitary Adrenal Function in People with Fatiguing Illness
Brain and Nervous System Function	Symptoms	VA-096	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain
Brain and Nervous System Function	Symptoms	VA-107	Evaluation of Stress Response Systems in GW Veterans with CMI

Brain and Nervous System Function	Symptoms	VA-134	Autonomic Functions of GW Veterans with Unexplained Illnesses
Brain and Nervous System Function	Symptoms	VA-135	Motor Neuron Function of GW Veterans with Excessive Fatigue
Brain and Nervous System Function	Symptoms	VA-154	Imaging Pain Modulation in GW Veterans with Chronic Muscle Pain
Brain and Nervous System Function	Symptoms; Diagnosis	DoD-180	Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of Fatigue
Brain and Nervous System Function	Diagnosis; Symptoms	DoD-111	Autonomic Dysfunction in GW Veterans
Brain and Nervous System Function	Treatment; Symptoms	DoD-115	A Randomized, Multi-Center, Controlled Trial of Multi- Modal Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D)
Brain and Nervous System Function	Treatment; Symptoms	DoD-173	A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in GW Veterans with Chronic Multisymptom Illness
Brain and Nervous System Function	Treatment; Symptoms	DoD-182	Trial of Naltrexone and Dextromethorphan for GW Veterans' Illness
Brain and Nervous System Function	Treatment; Symptoms	VA-057	Case Management and Residential Rehabilitation for Persian Gulf War Veterans
Brain and Nervous System Function	Treatment; Symptoms	VA-059	Demonstration Treatment Program for GW Veterans With Unexplained Physical Symptoms (13)
Brain and Nervous System Function	Treatment; Symptoms	VA-062	A Randomized, Multi-Center, Controlled Trial of Multi- Modal Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V)
Brain and Nervous System Function	Treatment; Symptoms	VA-108	Telemedicine Treatment for Veterans with Gulf War Illness
Brain and Nervous System Function	Treatment	VA-166	A Randomized Controlled Trial of a Mindfulness-Based Intervention for Gulf War Syndrome
Brain and Nervous System Function	Treatment	VA-173	Impact of Exercise Training on Pain and Brain Function in Gulf War Veterans
Brain and Nervous System Function;	Diagnosis; Symptoms	DoD-031	Dysregulation of the Stress Response in the Persian Gulf Syndrome
Brain and Nervous System Function	Treatment; Symptoms	DoD-199	Gulf War Illness: Evaluation of an Innovative Detoxification Program
Brain and Nervous System Function	Treatment	VA-178	rTMS for the Treatment of Chronic Pain in GW1 Veterans
Brain and Nervous System Function	Treatment	DoD-256	Vagus Nerve Stimulation as a Treatment Strategy for Gulf War Illness
Environmental Toxicology	Treatment	DoD-177	Randomized Trial of an Environmental Medicine Approach to Gulf War Veterans' Illness
Immune Function	Symptoms	DoD-187	The Use of Comprehensive Molecular Profiling with Network and Control Theory to Better Understand GWI and Model Therapeutic Strategies
Immune Function	Symptoms	DoD-188	Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War Illness
Other Topics	Treatment; Symptoms	DoD-196	Probiotic (Bifidobacterium Infantis) for Gulf War Illness

Development

Research Focus	Project Focus	Project	Project Title
	Treatment; Symptoms	DoD-169	Development of Novel Therapy for Chronic Neuropathic Pain
	Treatment; Symptoms	DoD-257	Designing a Successful Acupuncture Treatment Program for Gulf War Illness

	Treatment	DoD-258	High-Fidelity Design of Multimodal Restorative Interventions in Gulf War Illness
	Treatment	DoD-259	High-Fidelity Design of Multimodal Restorative Interventions in Gulf War Illness
	Diagnosis	DoD-210	Assessment of Diverse Biological Indicators in Gulf War Illness: Are They Replicable? Are They Related?
	Diagnosis	VA-182	Consensus Case Definition for Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans
Brain and Nervous System Function	Diagnosis; Symptoms	DoD-168	Developing Biomarkers for Fibromyalgia
Brain and Nervous System Function	Diagnosis; Treatment	DoD-209	Proteomic Immune Profiling for the Therapeutic Modulation of Cognitive Impairment in a Novel GWI Mouse Model
Immune Function	Symptoms; Diagnosis	DoD-183	Biomarkers of GW Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation

Epidemiology

Research Focus	Project Focus	Project	Project Title
	Symptoms	DoD-001 B	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not.
	Symptoms	DoD-001 E	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study
	Symptoms	DoD-001 F	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: GWV vs. NDV
	Symptoms	DoD-004	The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey
	Symptoms	DoD-014	Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry
	Symptoms	DoD-046	Exploratory Data Analysis with the CCEP Database
	Symptoms	DoD-070	War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes
	Symptoms	DoD-071	A Comparison of Post Deployment Hospitalization between Vietnam and GW Veterans
	Symptoms	DoD-098	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans
	Prevention	DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy
	Symptoms	DoD-116 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking,

		Pilot Study (See also VA-63B; formerly VA/DoD-2DB)
Symptoms	DoD-120	Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents
Diagnosis	DoD-140	US DOD Surveillance for Neoplasms in Infancy
Symptoms	DoD-148	Predicting Operational Readiness for Deployed Army National Guard and Army Reserve Soldiers and Families
Symptoms	DoD-150	Validation Study of Gulf War Deployment Files
Symptoms	DoD-203	Redefining Gulf War Illness Using Longitudinal Health Data: The Devens Cohort
Symptoms	HHS-001	Health Assessment of Persian GW Veterans from Iowa
Prevention	HHS-009	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments
Symptoms	HHS-011	Deployment to the Gulf War and the Subsequent Development of Cancer
Symptoms	VA-002	National Health Survey of Persian Gulf Veterans
Symptoms	VA-002 A	VA National Survey of Persian Gulf Veterans - Phase I
Symptoms	VA-002 B	VA National Survey of Persian Gulf Veterans - Phase II
Symptoms	VA-004 C	Gulf War and Vietnam Veterans Cancer Incidence Surveillance
Symptoms	VA-046	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder
Symptoms	VA-063 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB)
Symptoms	VA-070	A Clinical Evaluation of the Health Status of Persian Gulf War Veterans in VISN 8
Symptoms	VA-117	Estimates of Cancer Prevalence in Gulf Veterans Using State Registries
Symptoms	DoD-218	Establishing a 1991 Veterans Research Network To Improve Characterization of Gulf War Illness and Provide a National Resource for Veterans and Investigators
Symptoms; Exposure	DoD-073	Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes
Diagnosis; Exposure	DoD-208	Genome-Wide Association Study of a Validated Case Definition of Gulf War Illness in a Population-Representative Sample
Prevention; Symptoms	DoD-108	Health Status of Current National Guard Members
Prevention; Symptoms	DoD-117	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking
Prevention; Treatment	HHS-010	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline
Symptoms	DoD-015	Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm
Prevention	DoD-102	Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War

			and Non-Deployed Veterans
	Symptoms	VA-001	Mortality Follow-up Study of Persian Gulf Veterans
	Symptoms	VA-148	Profile of GW Veterans Who Applied for Undiagnosed Illness Compensation
	Symptoms	DoD-217	Efficacy of Treatments Tried: A Survey of GW Veterans
	Symptoms	VA-194	National Health Survey of Veterans and Family Members: Secondary Analysis of CSP #458 Data
Brain and Nervous System Function	Symptoms	DoD-039	A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces
Brain and Nervous System Function	Symptoms	DoD-141	Physical, Mental, Social, and Family Health Outcomes of Gulf War Veterans
Brain and Nervous System Function	Symptoms	DoD-142	Illnesses Among Persian GW Veterans: Case Validation Studies (Iowa / Great Britain)
Brain and Nervous System Function	Symptoms	DoD-143	Millennium Cohort Study
Brain and Nervous System Function	Symptoms	DoD-149	Longitudinal Health Study of GW Veterans
Brain and Nervous System Function	Symptoms	VA-002 C	VA National Survey of Persian Gulf Veterans - Phase III
Brain and Nervous System Function	Symptoms	VA-005 A	Health and Exposure Survey of Persian Gulf Veterans
Brain and Nervous System Function	Symptoms	VA-078	Millenium Cohort Study
Brain and Nervous System Function	Symptoms	VA-118	Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004
Brain and Nervous System Function	Symptoms; Exposure	VA-156	Gulf War Era Cohort and Biorepository (CSP 585)
Brain and Nervous System Function; Reproductive Health	Symptoms	DoD-045	Air Force Women's Health Surveillance Study
Environmental Toxicology	Symptoms	VA 156	Gulf War Era Cohort and Biorepository (CSP 585)
Environmental Toxicology	Symptoms; Exposure	DoD-074	Relationship of Stress Exposures to Health in GW Veterans
Environmental Toxicology; Chemical Weapons	Exposure; Symptoms	DoD-116	VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V)
Environmental Toxicology; Chemical Weapons	Exposure; Symptoms	VA-063	VA/DoD Core funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D)
Reproductive Health	Symptoms	DoD-030	Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study
Reproductive Health	Symptoms; Diagnosis; Prevention	DoD-096	Deployment Health Center
Reproductive Health	Symptoms; Prevention	DoD-001	Naval Health Study Program

Mechanistic

Research Focus	**Project Focus**	**Project**	**Project Title**
	Diagnosis	DoD-193	Genome Instability: A Common Link in Gulf War Illness Patients
	Diagnosis	DoD-220	Biomarker Discovery in GW Veterans: Development of a War Illness

			Diagnostic Panel
	Diagnosis	VA-185	Identification of Plasma Biomarkers of Gulf War Illness Using "omic" Technology
	Diagnosis	DoD-239	Mitochondrial and Nuclear Genetics in Gulf War Illness
	Diagnosis	DoD-255	Microtubule Abnormalities Underlying Gulf War Illness in Neurons from Human-Induced Pluripotent Cells
	Diagnosis; Symptoms	VA-179	Vascular and Skeletal Muscle Function in Gulf War Veterans Illness
	Diagnosis: Symptoms	VA-180	Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with GWI
	Diagnosis; Treatment	DoD-224	Understanding Gulf War Illness: An Integrative Modeling Approach
	Symptoms	DoD-179	Mechanisms of Mitochondrial Defects in Gulf War Syndrome
	Symptoms	VA-130	Tissue Factor and Gulf War-Associated Chronic Coagulopathies
	Symptoms	VA-131	Neuroendocrine Regulators and Proteomics in GW Veterans with CMI
	Symptoms	VA-136	Central Mechanisms Modulating Visceral Sensitivity
	Symptoms	VA-159	Somatic hypersensitivity in Veterans with IBS
	Symptoms	VA-162	Transcription factors regulating sensory gene expression and pain pathways
	Symptoms	VA-177	Somatic hypersensitivity in Veteraans with IBS
	Symptoms; Treatment	VA-164	Central Mechanisms Modulating Visceral Sensitivity (renewal of VA-136)
	Symptoms; Treatment	VA-172	Understanding Pain of Gastrointestinal Origin in Women that Serve in OEF/OIF
	Treatment	VA-192	Women vs. Men with GWI: Differences in Computational Models and Therapeutic Targets
Brain and Nervous System Function	Symptoms	VA-115	Autonomic System Changes Cause Intestinal Symptoms in Gulf War Veterans
Brain and Nervous System Function	Symptoms	VA-119	Patterns of Microarray Gene Expression in Gulf War Illness
Brain and Nervous System Function	Symptoms	DoD-194	Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome
Brain and Nervous System Function	Symptoms; Treatment	DoD-213	Effectiveness of Accupressure Treatment for Pain Management and Fatigue Relief in GW Veterans
Brain and Nervous System Function	Treatment	DoD-207	Gulf War Illness Research Development Consortium (GWIC)
Brain and Nervous System Function	Diagnosis; Symptoms	DoD-226	Gulf War Illness: Assessment of Bioenergetics in Brain and Muscle
Environmental Toxicology	Exposure; Symptoms	DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness
Immune Function	Diagnosis	DoD-200	XMRV and GWI: Is There an Association?
Immune Function	Diagnosis Symptoms	DoD-211	Detection of Xenotropic Murine Leukemia Virus-Related Virus (XMRV) in Gulf War Illness: Role in Pathogenesis or Biomarker?
Immune Function	Symptoms	VA-132	Immunologic Mechanisms and Biomarkers in Gulf War Illness

Immune Function	Symptoms	VA-133	Longitudinal Study of Gene Expression and Gene Products in Veterans with Gulf War Illness

Appendix C
Project Funding

(As of September 30, 2015)

NOTES ON REVISED TABLE OF SPENDING FOR GULF WAR VETERANS' ILLNESSES RESEARCH FROM FY 2006-2015

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 1992-2015 are listed, only the financial data for FY 2006-2015 (a 10-year window) are shown in Appendix C; Totals for FY 2006-2015 do not include funds obligated in FY 1992-2005. Projects that received all of their obligated funds prior to FY 2006 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 was 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 were 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	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-001	Naval Health Study Program	C											$0
DoD-001 A	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; A Study of Symptoms Among 1500 Seabees	C											$0
DoD-001 B	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 2: A Comparative Study of Hospitalizations among Active-Duty Personnel Who Participated in the Gulf War and Similar Personnel Who Did Not.	C											$0
DoD-001 C	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 3: A comparative study of pregnancy outcomes among GW Veterans and other active-duty personnel	C											$0
DoD-001 D	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 4: Infertility and Miscarriage in GW Veterans	C											$0
DoD-001 E	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 5: Seabee Health Study	C											$0
DoD-001 F	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 6: A Comparison of Nonfederal Hospitalization Experience Among Veterans in California who have separated from active service: GWV vs. NDV	C											$0
DoD-001 G	Epidemiologic Studies of Morbidity Among GW Veterans: A Search for Etiologic Agents and Risk Factors; Study 7: Prevalence of Congenital Anomalies Among Children of Persian GW Veterans	C											$0

*****Totals for FY '06 -'15 do not include funds obligated in FY 1992 -2005

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-002	Physiological and Neurobehavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET	C											$0
DoD-004	The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey	C											$0
DoD-007 A	Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling	C											$0
DoD-007 B	Carcinogenicity of Depleted Uranium Fragments	C											$0
DoD-008	Program DoD-8.	C											$0
DoD-008 A	Serologic Diagnosis of Viscerotropic Leishmaniasis (VTL)	C											$0
DoD-008 B	Development of a Leishmania Skin Test Antigen (LSTA)	C											$0
DoD-009	Identification of the Genetic Factors Which Control Tropism in Leishmania	C											$0
DoD-010	Pyridostigmine Synergistic Toxicity Study	C											$0
DoD-011	Male/Female Differential Tolerances to Pyridostigmine Bromide	C											$0
DoD-013	Effects of Persian Gulf War Service on Military Working Dogs	C											$0
DoD-014	Risk Factors Among US Army Soldiers for Enrolling on the Department of Veterans Affairs Gulf War Registry	C											$0
DoD-015	Comparative Mortality Among US Military Personnel Worldwide During Operations Desert Shield and Desert Storm	C											$0
DoD-016	Kuwait Oil Fire Health Risk Assessment	C											$0
DoD-017	Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning	C											$0
DoD-018	Kuwait Oil Fires Troop Exposure Assessment Model (TEAM)	C											$0
DoD-019	Persian Gulf Veterans Health Tracking System	C											$0

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Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-021	Study of Variability In Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals With Symptoms Following Participation in Operation Desert Storm	C											$0
DoD-022	Chronic Organophosphorus Exposure and Cognition	C											$0
DoD-023	Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and their Families	C											$0
DoD-030	Epidemiological Studies Persian Gulf War Illnesses, PG Women's Health Linkage Study	C											$0
DoD-031	Dysregulation of the Stress Response in the Persian Gulf Syndrome	C											$0
DoD-032	Neuropsychological Functioning in Persian Gulf Era Veterans	C											$0
DoD-033	Effects of Pyridostigmine in Flinders Line Rats Differing in Cholinergic Sensitivity	C											$0
DoD-034	Characterization of Emissions from Heaters Burning Leaded Diesel Fuel in Unvented Tents	C											$0
DoD-035	Feasibility of Investigating Whether There is a Relationship Between Birth Defects and Service in the Gulf War.	C											$0
DoD-036	Fatigue in Persian Gulf Syndrome-Physiologic Mechanisms	C											$0
DoD-037	Neurobehavioral and Immunological Toxicity of Pyridostigmine, Permethrin, and DEET in Male and Female Rats	C											$0
DoD-038	Diagnostic Antigens of Leishmania tropica	C											$0
DoD-039	A Controlled Epidemiological and Clinical Study into the Effect of Gulf War Service on Servicemen and Women of the United Kingdom Armed Forces	C											$0
DoD-040	Psychological and Neurobiological Consequences of the Gulf War Experience	C											$0
DoD-041	Evaluation of Muscle Function in Persian Gulf Veterans	C											$0

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Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-042	The Symptomatic Persian Gulf Veterans Protocol: An Analysis of Risk Factors with an Immunologic and Neuropsychiatric Assessment	C											$0
DoD-044	Investigation of Seminal Plasma Hypersensitivity Reactions	C											$0
DoD-045	Air Force Women's Health Surveillance Study	C											$0
DoD-046	Exploratory Data Analysis with the CCEP Database	C											$0
DoD-047	Study of Mycoplasmal Infections in GW Veterans	C											$0
DoD-048	Assessment of Genomic Instability via Chromosome 7 Inversion Frequency in a Gulf-War Syndrome Cohort vs. Selected Control Groups	C											$0
DoD-049	Diagnosis and Dosimetry of Exposure to Sulfur Mustard: Development of Standard Operating Procedures and Exploratory Research on Protein Adducts	C											$0
DoD-050	Toxicokinetics of 0-Ethyl S-(2-Diisopropylaminoethyl) Methylphosphonothioate [(+)-VX] in Rats, Hairless Guinea Pigs and Marmosets - Identification of Metabolic Pathways	C											$0
DoD-051	Transgenic Engineering of Cholinesterases: Tools for Exploring Cholinergic Responses	C											$0
DoD-052	Female Gender and Other Potential Predictors of Functional Health Status Among Persian GW Veterans	C											$0
DoD-053	Long-Term Effects of Subclinical Exposures to Sarin	C											$0
DoD-054	Assessment of Subchronic Neurobehavioral and Neuropathologic Effects in Rats Following Low-Level Sarin Exposure	C											$0
DoD-055	Low-Level Exposure to GB Vapor in Air: Diagnosis/Dosimetry, Lowest Observable Effect Levels, Performance-Incapacitation, and Possible Delayed Effects	C											$0

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Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-056	Low-Level Sarin Neurotoxicity and Its Modulation by Pyridostigmine	C											$0
DoD-057	Physiologic Effects of Stress in GW Veterans	C											$0
DoD-058	Illness Among Persian GW Veterans: Case Validation Studies	C											$0
DoD-059	Pyridostigmine-induced Neurodegeneration: Role of neuronal Apoptosis	C											$0
DoD-060	Butyrylcholinesterase Genetic Variants in Persons with Gulf War Illness	C											$0
DoD-061	Neurophysiologic and Neuropathologic Effects in Monkeys of Low Level Exposures to Sarin, Pyridostigmine, Pesticides, and Botulinum Toxoid	C											$0
DoD-062	Sarin and Pyridostigmine Interaction under Physical Stress: Neurotoxic Effects in Mice	C											$0
DoD-063	PGW Veterans: Epidemiological and Clinical Evidence for Residual Organophosphate Neurotoxicity	C											$0
DoD-064	Individual Differences in Neurobehavioral Effects of Pyridostigmine	C											$0
DoD-065	Multi-disciplinary Pathophysiologic Studies of Neurotoxic Gulf War Related Syndromes Leading to Diagnosis and Treatment	C											$0
DoD-066	Testing for mycoplasmal infection replicability of nucleoprotein gene tracking and forensic polymerase chain reaction	C											$0
DoD-067	Antibacterial Treatment Method Based Upon the Excretion of Dead and Decaying Spherical Bacteria	C											$0
DoD-069	Five Year Follow-Up of Army Personnel Exposed to Chemical Warfare Agents	C	$0										$0
DoD-070	War Syndromes from 1900 to the Present: Symptom Patterns and Long-term Health Outcomes	C											$0

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-071	A Comparison of Post Deployment Hospitalization Between Vietnam and GW Veterans	C											$0
DoD-072	Long-term Effects of Subchronic Exposure to Sarin, Alone and with Stress or Other Chemicals	C											$0
DoD-073	Post-deployment Morbid Stress, Behavior and Health: Developing a Model for Predicting Morbidity, Mortality, and other Adverse Outcomes	C											$0
DoD-074	Relationship of Stress Exposures to Health in GW Veterans	C											$0
DoD-075	Toxic Interactions of Prophylactic Drugs and Pesticides	C											$0
DoD-076	Evaluations of Immunotoxicity due to Concurrent Exposure to DEET, Pyridostigmine, and JP-8 Jet Fuel	C											$0
DoD-077	Percutaneous Absorption of Chemical Mixtures Relevant to the Gulf War	C											$0
DoD-078	Experimental Models of Gulf War Syndrome	C											$0
DoD-079	Time Course of Stress-induced Impairment of Blood Brain Barrier	C											$0
DoD-080	Molecular Regulation of Corticosteroid Receptor Expression in Stress-Responsive Cells	C											$0
DoD-081	Immunotoxicity due to Coexposure to DEET, Pyridostigmine, and Stress	C											$0
DoD-082	Feasibility of Developing a Registry of PTSD Affected Veteran Sib Pairs	C											$0
DoD-083	Risk for Stress-related Substance Abuse: the Effects of Family History of Alcoholism	C											$0
DoD-084	Psychobiologic Alterations in Persian GW Veterans with and without PTSD	C											$0
DoD-085	CNS Cytokines and CRH in GW Veterans with Multiple Unexplained Symptoms	C											$0
DoD-086	Effects of Combat Stress on Structure and Function of the Hippocampus	C											$0
DoD-087	Measurement and Validation of Psychosocial Risk and Resilience Factors Accounting for Physical and Mental Health and Health-Related	C											$0

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Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
	Quality of Life among PGWVs												
DoD-088	Clinical Relevance of Novel Immunological Markers in PTSD	C											$0
DoD-089	Limbic Blood Flow and Opiate Receptor PET in Posttraumatic Stress Disorder	C											$0
DoD-090	SPECT Benzodiazepine Receptor and MR Imaging in PTSD	C											$0
DoD-091	Neurological and Circadian Substrates of PTSD-like Behaviors	C											$0
DoD-092	Traumatic Experiences Persistently Enhance Cue-dependent Learning: Toward an Animal Model of Chronic Stress and Posttraumatic Stress Disorder	C											$0
DoD-093	Troops Exposed to Nerve Agents at Aberdeen Proving Ground: Follow-Up	C											$0
DoD-094	Combined Analysis of the VA and DoD Gulf War Clinical Registries: A Study of Clinical Findings from Systematic Medical Examinations of 100,000 U.S. GW Veterans	C											$0
DoD-095	Development of Diagnostic tools and alternative treatment drugs for Leishmania	C											$0
DoD-096	Deployment Health Center	C											$0
DoD-097	Surveillance of B. pertussis among Military Trainees with Respiratory Disease: Development and Validation of a Highly Sensitive PCR and Beacon Probe based Method for Diagnosis of Pertussis	C											$0
DoD-098	Investigation of a Baseline Medical Database to Evaluate the Health of Military Forces and Veterans	C	$0	$0	$0	$0							$0
DoD-099	DoD-wide Medical Surveillance for Potential Long-Term Adverse Events associated with Anthrax Immunization in Active Duty Service Members, Proposal 1:	C											$0

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Status: C=Complete; O=Ongoing

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
	Hospitalizations												
DoD-100	Antibodies to Squalene	C	$0	$0									$0
DoD-101	Mechanisms in Chronic Multisymptom Illnesses	C	$0	$0	$0	$0							$0
DoD-102	Case-Control Study of Fatal Motor Vehicle Crashes Among Gulf War and Non-Deployed Veterans	C											$0
DoD-103	Human Metabolism and Interactions of Deployment-related Chemicals	C	$326,570	$166,570	$0	$0							$493,140
DoD-104	Clinical Evaluation of a Proposed New Gulf War Syndrome	C											$0
DoD-105	Neuroplasticity and Calcium Signaling in Stressed Rat Amygdala	C											$0
DoD-106	The Role of Th1/Th2 cytokine balance in Gulf War-related illness	C											$0
DoD-107	Stress, Organophosphates and Blood Brain Barrier Integrity	C											$0
DoD-108	Health Status of Current National Guard Members	C											$0
DoD-109	Disordered Responses to Orthostatic Stress in the Pathogenesis of Gulf War Syndrome Symptoms	C											$0
DoD-110	Predictors of Career and Family Dysfunction in Young Adults Enlisting in the United States Navy	C											$0
DoD-111	Autonomic Dysfunction in GW Veterans	C											$0
DoD-112	Role of Respirable Saudi Arabian Sand and Pyridostigmine in the Gulf War Syndrome: An Autoimmune Adjuvant Disease?	C											$0
DoD-113	Interactions of Subsymptomatic Doses of Sarin with Pyridostigmine: Neurochemical, Behavioral, and Physiological Effects	C											$0
DoD-114	A Re-examination of Neuropsychological Functioning in Persian GW Veterans	C											$0
DoD-115	A Randomized, Multi-Center, Controlled Trial of Multi-Model	C											$0

*****Totals for FY '06 -'15 do not include funds obligated in FY 1992 -2005

Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
	Therapy in Veterans with Gulf War Illnesses (EBT) (See also VA-62; formerly VA/DoD 1D)												
DoD-116	VA/DoD Core Funding of the Medical Follow-Up Agency (See also VA-63; formerly VA-DoD-2D/2V)	C											$0
DoD-116 A	Follow-Up Investigation of Troops Exposed to Nerve Agents at Aberdeen Proving Ground (Pilot Study) (See also VA-63A; formerly VA/DoD-2DA)	C											$0
DoD-116 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking, Pilot Study (See also VA-63B; formerly VA/DoD- 2DB)	C											$0
DoD-117	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking	C											$0
DoD-118	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also VA-61)	C											$0
DoD-119	Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also VA-55)	C											$0
DoD-120	Assessing the Potential Health Impact of the Gulf War on Saudi Arabia National Guard Members and Their Dependents	C											$0
DoD-121	Evaluation of the Health Risks of Embedded Depleted Uranium Shrapnel During Pregnancy and Offspring Development	C											$0
DoD-122	Carcinogenic Potential of Depleted Uranium and Tungsten Alloys	C											$0
DoD-123	Immunotoxicity of Depleted Uranium and Heavy Metal Tungsten Alloys	C											$0
DoD-124	Randomized, Controlled Trial for Combination Treatment with Pyridostigmine, DEET, and Permethrin	C	$0										$0
DoD-125	A Randomized Clinical Trial of Cognitive-Behavioral Treatment for PTSD in Women (See VA-74)	C	$0										$0
DoD-126	Blood-Brain Barrier Transport of Uranium	C	$0	$0	$0	$0							$0

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-127	Depleted Uranium Fragment Carcinogenicity: Extrapolation of Findings in Rodents to Man	C											$0
DoD-128	Multifactorial Assessment of Depleted Uranium Neurotoxicity	C	$0	$0	$0	$0							$0
DoD-129	Inhalation of Uranium Oxide Aerosol: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness	C	$0	$0	$0	$0							$0
DoD-130	Carcinogenicity and Immunotoxicity of Embedded Depleted Uranium and Heavy-Metal Tungsten Alloys in Rodents	C	$0	$0	$0	$0							$0
DoD-131	Magnetic Resonance and Spectroscopy of the Human Brain in Gulf War Illnesses	C	$0	$0	$0	$0							$0
DoD-132	Impaired Auditory Sensory Gating, Acoustic Startle Response: Effects of Long and Short Deployments on Army Combat Readiness	C	$0	$0									$0
DoD-133	Odors, Deployment Stress, and Health: A Conditioning Analysis of Gulf War Syndrome	C	$0	$0									$0
DoD-134	Identification and Development of Biological Markers of Human Exposure to the Insecticide Permethrin	C	$0	$0									$0
DoD-135	Biochemical Markers for Exposure to Low Doses of Organophosphorus Exposure	C											$0
DoD-136	A Mechanism-Based, Molecular Fingerprint Strategy for Detecting Biomarkers of Organophosphate Exposure	C											$0
DoD-137	Low Level Exposure to Sulfur Mustard: Development of a SOP for Analysis of Albumin Adducts and of a System for Non-Invasive Diagnosis on Skin	C	$0										$0
DoD-138	Improving Blood Monitoring of Enzymes as Biomarkers of Risk from Anticholinergic Pesticides and Chemical Warfare Agents	C	$0	$0									$0
DoD-139	Assessment of the Role of Stress-Activated Kinase in the Pathogenesis of Gulf War Illnesses	C											$0

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-140	US DOD Surveillance for Neoplasms in Infancy	C	$0										$0
DoD-141	Physical, Mental, Social, and Family Health Outcomes of GW Veterans	C											$0
DoD-142	Illnesses Among Persian GW Veterans: Case Validation Studies (Iowa / Great Britain)	C											$0
DoD-143	Millennium Cohort Study	O	$2,893,000	$3,251,000	$3,160,000	$3,145,000	$3,306,000	$3,347,000	$3,676,000	$3,535,000	$4,073,000	$5,390,000	$35,776,000
DoD-144	Psychological Health Screening: Methods and Metrics for Deployed Forces	C	$0	$0	$0	$0							$0
DoD-145	Early Intervention Research Program to Enhance Soldier Resilience	C	$0	$0	$0	$0	$0						$0
DoD-146	Assessment of Toxicology Assay Methods and Chemical Exposures Among a Cohort of US Marines Deployed in the Gulf War	C											$0
DoD-147	Development and Validation of the Automated Neuropsychological Assessment Metric (ANAM) for Deployment Health Monitoring Applications	C	$0										$0
DoD-148	Predicting Operational Readiness for Deployed Army National Guard and Army Reserve Soldiers and Families	C											$0
DoD-149	Longitudinal Health Study of GW Veterans	C	$0										$0
DoD-150	Validation Study of Gulf War Deployment Files	C											$0
DoD-151	Mechanisms and Consequences of Vaccine Effects on Th1/Th2 Balance in GW Veterans	C	$0										$0
DoD-152	Characterization of Intracellular Signaling Pathways Activated by Nerve Agents	C	$0	$0	$0	$0							$0
DoD-153	Gulf War Illness Research	C	$0										$0
DoD-154	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study	C	$0	$0	$0	$0	$0						$0
DoD-155	Neuropsychological Functioning in GW Veterans Exposed to Pesticides and Pyridostigmine Bromide	C	$0	$0	$0								$0

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-156	The Effects of Diesel Exhaust and Stress on the Acute Phase Response and Symptoms in the Chemically Intolerant	C	$0	$0	$0								$0
DoD-157	Novel Leishmania And Malaria Potassium Channels: Candidate Therapeutic Targets	C											$0
DoD-158	Preconceptional Paternal Exposure to Embedded Depleted Uranium Fragments: Transmission Of Genetic Damage To Offspring	C											$0
DoD-159	Neurotoxicity from Chronic Exposure to Depleted Uranium	C											$0
DoD-160	Characterization of the Reproductive Toxicity of Depleted Uranium	C											$0
DoD-161	Glutamate Receptor Aptamers and ALS	C	$0	$0	$0								$0
DoD-162	Evaluation of the Effects of Multiple Immunizations Administered in a Stressful Environment on Immunologic Function	C	$0	$0	$0								$0
DoD-163	Neuroimmune Effects of Inhaling Low Dose Sarin	C	$0	$0	$0								$0
DoD-164	Efficacy of Adjunct Sleep Interventions For PTSD (EASI-PTSD)	C	$0	$0	$0								$0
DoD-165	Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military - BALSAM	C	$0	$0	$0								$0
DoD-166	A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance	C	$0	$0	$0								$0
DoD-167	Mass Spectrometry to Identify New Biomarkers of Nerve Agent Exposure	C	$637,848	$0	$0	$0							$637,848
DoD-168	Developing Biomarkers for Fibromyalgia	C	$936,067	$0	$0	$0							$936,067
DoD-169	Development of Novel Therapy for Chronic Neuropathic Pain	C	$840,574	$0	$0	$0							$840,574
DoD-170	Structural MRI and Cognitive Correlates in Pest-Control Personnel from Gulf War I	C	$208,353	$0	$0	$0							$208,353
DoD-171	Q10 for GW Veterans	C	$718,261	$0	$0	$0							$718,261
DoD-172	CNDP1 Polymorphisms and	C	$831,200	$0	$0	$0							$831,200

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
	Carnosine Therapy in GWI												
DoD-173	A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial of Mifepristone in GW Veterans with Chronic Multisymptom Illness	C	$650,279	$0	$0	$0							$650,279
DoD-174	Autonomic Biomarkers and Treatment for Gulf War Illness	C	$687,530	$0	$0	$0							$687,530
DoD-175	Novel Pharmacological Approaches for Treatment of Neurotoxicity Induced by Chronic Exposure to Depleted Uranium	C	$767,061	$0	$0	$0							$767,061
DoD-176	Studies on Axonal Transport in an Animal Model for Gulf War Syndrome	C	$112,500	$0	$0	$0							$112,500
DoD-177	Randomized Trial of an Environmental Medicine Approach to GW Veterans' Illness	C	$445,865	$0	$0	$0							$445,865
DoD-178	Analysis of Paraoxonase Status among US Navy GW Veterans with Increased Postwar Symptoms, Psychological Morbidity and Medical Conditions	C	$73,153	$0	$0	$0							$73,153
DoD-179	Mechanisms of Mitochondrial Defects in Gulf War Syndrome	C			$440,674	$0	$0	$0					$440,674
DoD-180	Exercise-Induced Cerebrospinal Fluid Proteomic Biomarkers of Fatigue	C			$921,000	$0	$0	$0					$921,000
DoD-181	Effectiveness of Acupuncture in the Treatment of Gulf War Illness	C			$1,015,733	$0	$0	$0					$1,015,733
DoD-182	Trial of Naltrexone and Dextromethorphan for GW Veterans' Illness	C			$1,063,641	$0	$0	$0					$1,063,641
DoD-183	Biomarkers of GW Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation	C			$653,460	$0	$0	$0					$653,460
DoD-184	Treatment of Memory Impairment and Sensorimotor Deficits in an Animal Model for the GW Veterans' Illnesses	C			$311,135	$0	$0	$0					$311,135
DoD-185	Neuroinflammatory Pathobiology in Gulf War Illness: Characterization with an Animal Model	C			$718,326	$0	$0	$0					$718,326
DoD-186	Small Intestinal Microbial Community in Gulf War Illness	C			$634,142	$0	$0	$0					$634,142

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-187	The Use of Comprehensive Molecular Profiling with Network and Control Theory to Better Understand GWI and Model Therapeutic Strategies	C			$715,456	$0	$0	$0					$715,456
DoD-188	Epithelial Cell TRPV1-Mediated Airway Sensitivity as a Mechanism for Respiratory Symptoms Associated with Gulf War Illness	C			$842,400	$0	$0	$0					$842,400
DoD-189	Discovery of AMPA Receptor Potentiating Aptamers as Cognitive Enhancers	C			$303,000	$0	$0	$0					$303,000
DoD-190	Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness	C			$894,000	$0	$0	$0					$894,000
DoD-191	Neuroimmune Interactions, Low-Dose Sarin Inhalation, and Gulf War Syndrome	C				$1,247,995	$0	$0	$0				$1,247,995
DoD-192	Exhaled Gas Frequency Comb Spectroscopy Distinguishing Biomarkers in Gulf War Illness Syndrome	C				$742,296	$0	$0	$0				$742,296
DoD-193	Genome Instability: A Common Link in Gulf War Illness Patients	C				$904,364	$0	$0	$0				$904,364
DoD-194	Homeostatic and Circadian Abnormalities in Sleep and Arousal in Gulf War Syndrome	C				$705,654	$0	$0	$0				$705,654
DoD-195	Theory-Driven Models for Correcting "Fight or Flight" Imbalance in Gulf War Illness	C				$678,953	$0	$0	$0				$678,953
DoD-196	Probiotic (Bifidobacterium Infantis) for Gulf War Illness	C				$466,260	$0	$0	$0				$466,260
DoD-197	Undiagnosed Small Fiber Polyneuropathy: Is It a Component of Gulf War Illness?	C				$929,224	$0	$0	$0				$929,224
DoD-198	Oxidative Stress	C				$927,000	$0	$0	$0				$927,000
DoD-199	Gulf War Illness: Evaluation of an Innovative Detoxification Program	C				$633,677	$0	$0	$0				$633,677
DoD-200	XMRV and GWI: Is There an Association?	C					$565,794	$0	$0	$0	$0		$565,794
DoD-201	Synergistic Actions of Pyridostigmine Bromide and Insecticides on Muscle and Vascular Nociceptors	C					$852,157	$0	$0	$0			$852,157
DoD-202	Brain-Immune Interactions as Basis	C					$262,052	$0	$0	$0			$262,052

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
	of Gulf War Illness: Consortium Development												
DoD-203	Redefining Gulf War Illness Using Longitudinal Health Data: The Devens Cohort	C					$708,169	$0	$0	$0	$0		$708,169
DoD-204	Nasal Irrigation for Chronic Rhinosinusitis and Fatigue in Patients with Gulf War Syndrome	C					$668,072	$0	$0	$0	$0		$668,072
DoD-205	The HPA Axis and Metabolic Outcomes in GW Veterans	C					$699,933	$0	$0	$0	$0		$699,933
DoD-206	Investigating Clinical Benefits of a Novel Sleep-Focused, Mind-Body Program on Gulf War Illness Symptoms: An Exploratory Randomized Controlled Trial	C					$606,496	$0	$0	$0	$0		$606,496
DoD-207	Gulf War Illness Research Development Consortium (GWIC)	C					$251,475	$0	$0	$0			$251,475
DoD-208	Genome-Wide Association Study of a Validated Case Definition of Gulf War Illness in a Population-Representative Sample	C					$140,357	$0	$0	$0			$140,357
DoD-209	Proteomic Immune Profiling for the Therapeutic Modulation of Cognitive Impairment in a Novel GWI Mouse Model	C					$925,368	$0	$0	$0	$0		$925,368
DoD-210	Assessment of Diverse Biological Indicators in Gulf War Illness: Are They Replicable? Are They Related?	C					$741,013	$0	$0	$0	$0		$741,013
DoD-211	Detection of Xenotropic Murine Leukemia Virus-Related Virus (XMRV) in Gulf War Illness: Role in Pathogenesis or Biomarker?	C					$403,050	$0	$0	$0			$403,050
DoD-212	Integrative Physiology of Gulf War Illness: Role of Autonomic Function, Central Neural Processing, and Sleep	C					$254,295	$0	$0	$0			$254,295
DoD-213	Effectiveness of Acupressure Treatment for Pain Management and Fatigue Relief in GW Veterans	C						$677,280	$0	$0	$0		$677,280
DoD-214	Abnormalities in Human Brain Creatine Metabolism in Gulf War Illness Probed with MRS	C						$878,051	$0	$0	$0		$878,051
DoD-215	Identifying Immune Drivers of Gulf War Illness Using a Novel Daily Sampling Approach	O						$900,642	$0	$0	$0		$900,642
DoD-216	Intranasal Insulin: A Novel Treatment	O						$1,492,571	$0	$0			$1,492,571

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
	for Gulf War Multisymptom Illness										$0		
DoD-217	Efficacy of Treatments Tried: A Survey of GW Veterans	O						$527,365	$0	$0	$0		$527,365
DoD-218	Establishing a 1991 Veterans Research Network To Improve Characterization of Gulf War Illness and Provide a National Resource for Veterans and Investigators	O						$814,165	$0	$0	$0		$814,165
DoD-219	Organophosphate-Related Alterations in Myelin and Axonal Transport in the Living Mammalian Brain	O						$859,673	$0	$0	$0		$859,673
DoD-220	Biomarker Discovery in GW Veterans: Development of a War Illness Diagnostic Panel	O						$784,175	$0	$0	$0		$784,175
DoD-221	Role of microRNAs in thePathobiology of Gulf War Illness: Identification of Potential Novel Therapeutic Targets	O							$339,305	$0	$0		$339,305
DoD-222	Brain Immune Interactions as the Basis of Gulf War Illness: Gulf War Illness Consortium (GWIC)	O							$2,642,203	$2,141,930	$0		$4,784,133
DoD-223	Persistent Neural Membrane Protein Misregulation Following Neurotoxicant Exposure	O							$881,479	$0	$0		$881,479
DoD-224	Understanding Gulf War Illness: An Integrative Modeling Approach	O							$2,361,185	$1,741,342	$0		$4,102,527
DoD-225	The Role of Protein Radicals in Chronic Neuroimmune Dysfunction and Neuropathology in Response to a Multiple-Hit Model of Gulf War Exposures	O							$884,129	$0	$0		$884,129
DoD-226	Gulf War Illness: Assessment of Bioenergetics in Brain and Muscle	O							$930,000	$0	$0		$930,000
DoD-227	Monosodium Luminol for Improving Brain Function in Gulf War Illness	O								$872,357	$0		$872,357
DoD-228	A Multimodal Evaluation of the Comparative Efficacy of Yoga versus a Patient-Centered Support Group for Treating Chronic Pain in Gulf War Illness	O								$603,663	$0		$603,663
DoD-229	Bench to Bedside: Understanding Symptom Response to Acupuncture Treatment and Designing a Successful Acupuncture Treatment Program	O								$395,880	$0		$395,880

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-230	An In Vivo Investigation of Brain Inflammation in Gulf War Illness with Integrated PET/MR Imaging	O								$1,026,352	$0		$1,026,352
DoD-231	Use of a Portable Stimulator to Treat GWI	O								$553,095	$0		$553,095
DoD-232	Characterizing Treatable Causes of Small Fiber Polyneuropathy in Gulf War Veterans	O								$1,031,355	$0		$1,031,355
DoD-233	Assessment of MRI-Based Markers of Dopaminergic Integrity as a Biological Indicator of Gulf War Illness	O								$425,471	$0		$425,471
DoD-234	A Prospective Open-Label Clinical Trial of Methylphenidate plus a GWI-Specific Nutrient Formula in Patients with Gulf War Illness and Concentration Disturbances	O								$580,981	$0		$580,981
DoD-235	Treating Gulf War Illness with Novel Anti-Inflammatories: A Screening of Botanical Microglia Modulators	O								$652,496	$0		$652,496
DoD-236	Development of Dietary Polyphenol Preparations for Treating Veterans with Gulf War Illness	O								$540,039	$0		$540,039
DoD-237	Direct Test for Neuroinflammation with [11C]DAP-713-PET Scanning	O								$849,827	$0		$849,827
DoD-238	Restoring the Brain's Lipid Homeostasis as a Therapeutic Avenue for Treating the CNS Symptoms of Gulf War Illness	O								$954,000	$0		$954,000
DoD-239	Mitochondrial and Nuclear Genetics in Gulf War Illness	O								$930,000	$0		$930,000
DoD-240	Novel Therapeutic Approaches for the Treatment of Depression and Cognitive Deficits in a Rodent Model of Gulf War Veterans' Illness	O								$884,066	$0		$884,066
DoD-241	Gulf War Illness Inflammation Reduction Trial	O								$1,044,682	$0		$1,044,682
DoD-242	Epigenetic Mediation of Endocrine and Immune Response in an Animal Model of Gulf War Illness	O								$774,746	$0		$774,746
DoD-243	Vascular and Skeletal Muscle Function in Gulf War Veterans Illness	O									$870,642		
DoD-244	Neurovascular and Autonomic Dysfunction Associated with Gulf War Illness Pain	O									$1,023,883		

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-245	Biomarkers and Brain Mechanisms of Gulf War Illness	O									$741,578		
DoD-246	Novel Autoantibody Serum and Cerebrospinal Fluid Biomarkers in Veterans with Gulf War Illness	O									$424,901		
DoD-247	Novel Autoantibody Serum and Cerebrospinal Fluid Biomarkers in Veterans with Gulf War Illness	O									$665,930		
DoD-248	Preclinical Treatment of an Organophosphate Model of Gulf War Illness	O									$542,092		
DoD-249	Gulf War Illness as a Brain Autoimmune Disorder	O									$881,448		
DoD-250	An Integrated Genomics and Cell Biology Approach to Correlate Novel GWI Indicators of Infections and Neuroinflammatory Mechanisms with Targeted Drug Therapy	O									$805,882		
DoD-251	Muscle Mitochondrial Assessments in Gulf War Illness	O									$1,085,000		
DoD-252	START and STOPP in GWI	O									$1,088,499		
DoD-253	D-cycloserine: A Novel Treatment for Gulf War Illness	O									$739,525		
DoD-254	Effect of Diet on Gulf War Illness: A Pilot Study	O									$524,557		
DoD-255	Microtubule Abnormalities Underlying Gulf War Illness in Neurons from Human-Induced Pluripotent Cells	O									$734,265		
DoD-256	Vagus Nerve Stimulation as a Treatment Strategy for Gulf War Illness	O									$607,717		
DoD-257	Designing a Successful Acupuncture Treatment Program for Gulf War Illness	O									$288,261		
DoD-258	High-Fidelity Design of Multimodal Restorative Interventions in Gulf War Illness	O									$810,466		
DoD-259	High Fidelity Design of Multimodal Restorative Interventions in Gulf War Illness	O									$353,236		
DoD-260	Extending Benefits of Q10: Mitochondrial Cocktail for Gulf War Illness	O									$1,085,000		

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Department of Defense Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY2014	FY2015	TOTALS FY 06-15
DoD-261	Testing the Model: A Phase I/II Randomized Double Blind Placebo Control Trial of Targeted Therapeutics: Liposomal Glutathione and Curcumin	O									$560,788		
DoD-262	Testing the Model: A Phase I/II Randomized Double Blind Placebo Control Trial of Therapeutics: Liposomal Glutathione and Curcumin	O									$512,460		
DoD-263	Vagus Nerve Stimulation: A Noninvasive Treatment to Improve the Health of Gulf Veterans with Gulf War Illness	O									$703,272		
DoD-264	An Objective Blood Test from Stimulated Gene Expression for Classification and Outcome Assessment in Clinical Trials of Gulf War Illness	O									$967,068		
DoD-265	An Objective Blood Test from Stimulated Gene Expression for Classification and Outcome Assessment in Clinical Trials of Gulf War Illness	O									$369,511		
DoD-266	A Randomized, Double-Blind, Placebo-Controlled Crossover Study of the Anti-Inflammatory Compound Anatabine to Treat Pain in GWI Patients	O									$710,843		
DoD-267	Diagnosis of Late-Stage, Early-Onset, Small-Fiber Polyneuropathy	O									$1,174,728		
DoD-268	Diagnosis of Late-Stage, Early-Onset, Small-Fiber Polyneuropathy	O									$189,257		
	DoD Totals		$10,128,261	$3,417,570	$11,672,967	$10,380,423	$10,384,231	$10,280,922	$11,714,301	$19,537,282	$22,533,809	$5,390,000	$115,439,766

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Department of Health and Human Services Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	TOTALS FY 06-15
HHS-001	Health Assessment of Persian GW Veterans from Iowa	C											$0
HHS-002	Disease Cluster in a Pennsylvania Air National Guard Unit, EPI-AID 95-18	C											$0
HHS-003	Biomarkers of Susceptibility and Polycyclic Aromatic Hydrocarbon (PAH) Exposure in Urine and blood Cell DNA from U.S. Army Soldiers Exposed to Kuwaiti Oil Well Fires	C											$0
HHS-004	Suspected Increase of Birth Defects and Health Problems Among Children Born to Persian GW Veterans In Mississippi	C											$0
HHS-005	Cognitive Function and Symptom Patterns in Persian Gulf Veterans	C											$0
HHS-006	Defining Gulf War Illness	C											$0
HHS-007	Immunotoxicity of Dermal Permethrin and Cis-Urocanic Acid	C											$0
HHS-008	Strategy to Identify Non-Additive Response to Chemical Mixtures	C											$0
HHS-009	Improving Health Risk Communications to Prevent Unexplained Illnesses Related to Military Deployments	C	$0	$0									$0
HHS-010	Health-e Voice: Optimized Implementation of a Stepped Clinical Risk Communications Guideline	C	$0	$0									$0
HHS-011	Deployment to the Gulf War and the Subsequent Development of Cancer	C	$0	$0									$0
HHS-012	Genetic Epidemiology of ALS in Veterans	C	$455,587	$441,974	$433,467	$0	$0	$0					$1,331,028
	HHS Totals		$455,587	$441,974	$433,467	$0	$0	$0	$0	$0	$0	$0	$1,331,028

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Department of Veterans Affairs Gulf War Research Funding

PROJECT NO	PROJECT TITLE	STATUS	FY 2006	FY2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	TOTALS FY 06-15
VA-001	Mortality Follow-up Study of Persian Gulf Veterans	C											$0
VA-002	National Health Survey of Persian Gulf Veterans	C											$0
VA-002 A	VA National Survey of Persian Gulf Veterans - Phase I	C											$0
VA-002 B	VA National Survey of Persian Gulf Veterans - Phase II	C											$0
VA-002 C	VA National Survey of Persian Gulf Veterans - Phase III	C											$0
VA-003	Use of Roster of Veterans Who Served in Persian Gulf Area	C											$0
VA-004	Boston Environmental Hazards Research Center Program	C											$0
VA-004 A	Evaluation of Cognitive Functioning of Persian Gulf Veterans	C											$0
VA-004 B	Evaluation of Neurological Functioning in Persian Gulf Veterans	C											$0
VA-004 C	Gulf War And Vietnam Veterans Cancer Incidence Surveillance	C											$0
VA-004 D	Evaluation of Respiratory Dysfunction Among GW Veterans	C											$0
VA-004 E	The Aromatic Hydrocarbon Receptor (AhR) as a Biomarker of Susceptibility	C											$0
VA-004 F	Validity of Computerized Tests	C											$0
VA-005	East Orange Environmental Hazards Research Center Program	C											$0
VA-005 A	Health and Exposure Survey of Persian Gulf Veterans	C											$0
VA-005 B	Physiological and Psychological Assessments of Persian Gulf Veterans	C											$0
VA-005 C	Effects of Exertion and Chemical Stress on Persian Gulf Veterans	C											$0
VA-005 D	Effects of Genetics and Stress on Responses to Environmental Toxins	C											$0
VA-006	Core Program: Portland Environmental Hazards Research Center: Environment, Veterans Health and the Gulf War Syndrome. Core Project for Clinical and Epidemiology Research	C											$0
VA-006 A	Psychosocial, Neuropsychological and Neurobehavioral Assessment (Project I)	C											$0

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PROJECT NO	PROJECT TITLE	STATUS	FY 2006	FY2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	TOTALS FY 06-15
VA-006 B	Clinical and Neuroendocrine Aspects of Fibromyalgia (Project II)	C											$0
VA-006 C	Neurotoxicity of Environmental Pollutants and Warfare Agents (Project III)	C											$0
VA-006 D	DNA Damage from Chemical Agents and Its Repair (Project IV)	C											$0
VA-006 E	Clinical and Epidemiology Leishmania Research	C											$0
VA-007	Desert Storm Reunion Survey	C											$0
VA-008	Psychological Test Data of GW Veterans Over Time	C											$0
VA-009	Evaluation of Cognitive Functioning in Persian GW Veterans Reporting War-related Health Problems	C											$0
VA-010	Memory and Attention in PTSD	C											$0
VA-011	Neuropsychological Functioning in Veterans	C											$0
VA-012	Psychological Assessment of Operation Desert Storm Returnees	C											$0
VA-013	Neurobehavioral Aspects of Persian Gulf Experiences: A Pilot Study	C											$0
VA-015	Vaccine-Mediated Immunity Against Leishmaniasis	C											$0
VA-016	Protective Immunity in Experimental Visceral Leishmaniasis	C											$0
VA-017	Immunological Evaluation of Persian Gulf Veterans	C											$0
VA-018	Chronic Gastrointestinal Illness in Persian Gulf Veterans	C											$0
VA-020	Psychological Adjustment in Operation Desert Shield/Storm Veterans	C											$0
VA-021	A Comparison of PTSD Symptomatology among Three Army Medical Units Involved in ODS	C											$0
VA-036	Stress Symptoms and Their Causal Attribution in Desert Storm Veterans	C											$0
VA-040	Musculoskeletal Symptoms in Gulf War Syndrome	C											$0
VA-046	Diarrhea in Persian Gulf Veterans: An Irritable Bowel-Like Disorder	C											$0

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VA-047	Retrospective Verification of Mustard Gas Exposure	C											$0
VA-048	Cross-Sensitization as a CNS Model for Gulf War Chemical Intolerance	C											$0
VA-049	Sensitivity to Pyridostigmine Bromide: Persistent Neural Dysfunction	C											$0
VA-050	Neuropsychological findings in a sample of Operation Desert Storm Veterans	C											$0
VA-051	Psychobiological Assessment of Desert Storm Veterans	C											$0
VA-053	Spouses and Children Program	C											$0
VA-054	Follow-up of Psychological and Neurocognitive Gulf War Outcome: Relation to Stress	C											$0
VA-055	Antibiotic Treatment of GW Veterans' Illnesses (ABT) (See also DoD-119)	C											$0
VA-056	Birmingham's GW Veterans' Illness Demonstration Clinic (13)	C											$0
VA-057	Case Management and Residential Rehabilitation for Persian GW Veterans (13)	C											$0
VA-058	Implementation and Evaluation of GW Veterans' Demonstration Project (13)	C											$0
VA-059	Demonstration Treatment Program for GW Veterans With Unexplained Physical Symptoms (13)	C											$0
VA-060	Identification and Management of Sleep Disorders in GW Veterans	C											$0
VA-061	An Epidemiological Investigation into the Occurrence of Amyotrophic Lateral Sclerosis (ALS) Among GW Veterans (See also DoD-118)	C											$0
VA-062	A Randomized, Multi-Center, Controlled Trial of Multi-Model Therapy in Veterans with Gulf War Illness (EBT) (See also DoD-115; formerly VA/DoD 1V)	C											$0
VA-063	VA/DoD Core funding of the Medical Follow-Up Agency (See also DoD-116; formerly VA/DoD-2V/2D)	C	$250,000	$250,000									$500,000

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VA-063 A	Follow-Up Investigation of troops exposed to nerve agents at Aberdeen Proving Ground (Pilot Study) (See also DoD-116A; formerly VA/DoD-2VA/2DA)	C											$0
VA-063 B	Patterns of Pre-Persian Gulf War Illness and Health Care Seeking Pilot Study (See also DoD-116B; previously VA/DoD-2VB)	C											$0
VA-064	Boston Environmental Hazards Research Center	C	$337,200										$337,200
VA-064 A	Functional Neuroimaging in Lead Exposed Adults	C											$0
VA-064 B	Quantification and Validation of Structure-Function relationships through visuospatial test performance	C											$0
VA-064 C	Development of a structured neurotoxicant assessment checklist (SNAC) for clinical use in Veteran populations	C											$0
VA-065	San Antonio Environmental Hazards Research Center	C											$0
VA-065 A	Does a variant of the human SOD2 gene increase sensitivity to hazards?	C											$0
VA-065 B	The contribution of FEN-1 to genetic integrity subsequent to oxidative stress	C											$0
VA-065 C	The importance of hydrogen peroxide detoxification in cellular protection	C											$0
VA-065 D	Do defective Gpx1 and ALDH2 genes increase sensitivity to environmental hazards?	C											$0
VA-066	Physiological Responding in Posttraumatic Stress Disorder	C											$0
VA-067	Olfactory Functioning in GW Veterans	C											$0
VA-068	Family Study of Fibromyalgia	C											$0
VA-069	Cardiovascular Hyporeactivity and Fatiguing Illness in GW Veterans	C											$0
VA-070	A Clinical Evaluation of the Health Status of Persian GW Veterans in VISN 8	C											$0
VA-071	Central Nervous System Modulation of Visceral Pain in the Persian Gulf Syndrome	C											$0

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VA-072	Roles of Paraoxonase, Butyrylcholinesterase and Stress in Unexplained Illnesses	C											$0
VA-073	Pain Sensitivity in GW Veterans with Medically Unexplained Musculoskeletal Pain	C											$0
VA-074	A Randomized Clinical Trial for Cognitive-Behavioral Treatment for PTSD in Women (See DoD-125)	C											$0
VA-075	ALS and Veterans: Are Veterans at Increased Risk?	C											$0
VA-076	Analysis of Hippocampal Volume in Aging Combat Veterans with PTSD	C											$0
VA-077	HPA Axis Reactivity in Men and Women with Chronic PTSD	C											$0
VA-078	Millenium Cohort Study	C											$0
VA-080	Neurochemical and Neurobehavioral Impact of Pyridostigmine Bromide Treatment and Stress	C	$253,277	$252,602									$505,879
VA-081	Stress, Pro-Inflammatory Cytokines and Coping Behavior	C											$0
VA-082	Pituitary Adrenal Function in People with Fatiguing Illness	C	$121,842										$121,842
VA-083	Neuropsychological Assessment of a Population-Based Sample of Persian GW Veterans and Controls	C											$0
VA-084	Neurobiology of Severe Psychological Trauma in Women	C											$0
VA-085	Associative Learning in Veterans with and without Combat Experience	C											$0
VA-086	A Clinical Trial of Magnetic Stimulation in Depression	C											$0
VA-087	Improving Outcomes of Depression in Primary Care	C											$0
VA-088	Prospective Assessment of Neurocognition in Future Gulf-deployed and Gulf-nondeployed Military Personnel: A Pilot Study	C											$0
VA-089	National Registry of Veterans with Amyotrophic Lateral Sclerosis	C	$863,951										$863,951
VA-090	Differential Gene Expression in Pathologies Associated with Neuronal Hyperexcitability: Links to Gulf War Illness	C	$449,990	$449,990	$0	$0	$0	$281,000	$70,250				$1,251,230

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VA-090A	Neuronal Hyperexcitability and Motor Neuron Regeneration	C											$0
VA-090B	Gene Expression and Proteomic Strategies in Severe Psychiatric Disorders	C											$0
VA-090C	Developmental Differences in Alcohol Withdrawal Sensitivity	C											$0
VA-090D	Seizures and Neuroplasticity: Physiology and Biochemistry	C											$0
VA-091	The Role of Dietary Choline in Neuroprotection	C											$0
VA-092	Acetylcholinesterase Activity In GW Veterans	C											$0
VA-093	HPA Axis Alterations in PTSD: A Comparison of Gulf War and Vietnam Veterans	C	$127,405										$127,405
VA-094	The Immunology of Chronic Cutaneous Leishmaniasis	C	$202,320										$202,320
VA-095	The Role of Signal Regulatory Proteins in Astrocytomas	C	$178,679										$178,679
VA-096	Functional Imaging of Pain in Veterans with Unexplained Muscle Pain	C	$70,302	$135,127	$95,382								$300,811
VA-097	Improving a mM-CSF Tumor Vaccine for Established Intracranial Gliomas	C	$246,355	$134,628									$380,983
VA-098	Post-Transcriptional Gene Regulation of VEGF in Malignant Gliomas	C	$168,600										$168,600
VA-099	Vaccination Against Visceral Leishmaniasis with a multi-epitope vaccine	C	$117,908										$117,908
VA-100	Studies of the Blood-Brain Barrier and its Manipulation	C	$151,740										$151,740
VA-101	Biomarkers Discovery in ALS	C	$151,555	$112,009	$299,165	$274,432							$837,161
VA-102	Cholinergic and Monoaminergic Influences on Sleep	C	$134,328										$134,328
VA-103	Hypothalamic and Basal Forebrain Regulation of Sleep and Arousal	C	$317,845										$317,845
VA-104	Characterization of Pain Processing Mechanisms in the Irritable Bowel Syndrome	C	$84,300										$84,300
VA-105	Expression of the Major Surface Protease of Leishmania Chagasi	C	$92,817										$92,817
VA-106	Interoceptive Stressor Conditioning: A Model for Gulf War Illness	C	$198,161										$198,161

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VA-107	Evaluation of Stress Response Systems in GW Veterans with CMI	C	$117,412	$210,637	$173,321	$93,226	$0						$594,596
VA-108	Telemedicine Treatment for Veterans with Gulf War Illness	C	$238,616	$224,916	$11,100								$474,632
VA-109	Effects of Stress on Memory: Brain Circuits, Mechanisms and Therapeutics	C	$306,912	$317,503	$321,148	$241,520							$1,187,083
VA-110	Pain Among GW Veterans: Secondary Analysis of CSP#458 Data	C	$48,557										$48,557
VA-111	T Cell Responses to Multiple Immunizations and Stress	C	$112,399										$112,399
VA-112	National VA Amyotrophic Lateral Sclerosis Research Consortium	C	$734,590										$734,590
VA-113	Novel Cause of Motor Neuron Disease	C	$110,152	$110,152	$110,152	$0							$330,456
VA-114	Strategies in Therapeutic Development of Neurodegenerative Diseases	C	$370,920										$370,920
VA-115	Autonomic System Changes Cause Intestinal Symptoms in GW Veterans	C	$275,623										$275,623
VA-116	Quantitative Trait Genes Controlling Circadian and Sleep Behaviors	C	$228,734										$228,734
VA-117	Estimates of Cancer Prevalence in Gulf Veterans Using State Registries	C	$151,740	$115,772	$66,597	$0							$334,109
VA-118	Post War Mortality from Neurologic Diseases in Gulf Veterans, 1991-2004	C	$160,535	$119,453									$279,988
VA-119	Patterns of Microarray Gene Expression in Gulf War Illness	C	$168,600	$168,600									$337,200
VA-120	Arginase NO Synthase and Cell Death in Amyotrophic Lateral Sclerosis	C	$165,116										$165,116
VA-121	Genes, Environment, and Oxidative Stress in Neurodegenerative Disorders	C	$441,612										$441,612
VA-122	Role of Mitochondrial Oxidative Stress in ALS	C	$271,896										$271,896
VA-123	Interactions Between Maternal Care, Stress and Pyridostigmine Bromide	C	$48,332	$178,447									$226,779
VA-124	Early Life Determinants of Vulnerability to Pyridostigmine Bromide	C	$195,688										$195,688
VA-125	Effects of Gulf War Illness on Brain Structure, Function and Metabolism: MRI/MRS at 4 Tesla	C	$479,892	$743,778	$653,747	$560,455	$5,135,117						$7,572,989
VA-126	Structural Magnetic Resonance Imaging in Gulf War-Era Veterans	C	$165,565	$165,565									$331,130

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VA-127	Interactions of the Leishmania sp. with Mammalian Cells	C	$166,464										$166,464
VA-128	MR Tracking of Stem Cells for Replacement Therapy in ALS	C	$236,730										$236,730
VA-129	Glucocorticoid Responsivity in GW Veterans	C	$167,164	$168,600									$335,764
VA-130	Tissue Factor and Gulf War-Associated Chronic Coagulopathies	C	$194,826	$217,055	$248,741	$273,861	$158,089	$161,644					$1,254,216
VA-131	Neuroendocrine Regulators and Proteomics in GW Veterans with CMI	C	$60,767	$163,579									$224,346
VA-132	Immunologic Mechanisms and Biomarkers in Gulf War Illness	C	$64,630	$112,400	$112,400	$56,200	$56,200						$401,830
VA-133	Longitudinal Study of Gene Expression and Gene Products in Veterans with Gulf War Illness	C	$112,400	$112,400									$224,800
VA-134	Autonomic Functions of GW Veterans with Unexplained Illnesses	C	$8,880	$0	$0	$25,880	$101,863	$72,667					$209,290
VA-135	Motor Neuron Function of GW Veterans with Excessive Fatigue	C	$6,744	$0	$0	$79,242	$103,549	$25,712					$215,247
VA-136	Central Mechanisms Modulating Visceral Sensitivity	C	$83,288	$81,715	$121,055								$286,058
VA-137	Diarrhea-Predominant Irritable Bowel Syndrome in Persian Gulf Veterans	C	$161,968	$224,294	$217,325	$0	$104,982						$708,569
VA-138	Inspiratory Flow Dynamics During Sleep in GWS and the Effect of CPAP	C	$226,773	$235,240	$258,136	$9,819							$729,968
VA-139	Sleep Neurobiology and Circuitry	C	$33,720										$33,720
VA-140	Integrated Neuroimaging and Neuropathological Analysis of the Effects of Physical Activity on Progression and Therapy in ALS	C	$232,553										$232,553
VA-141	Genetic Analysis of an Invertebrate Model of Amyotrophic Lateral Sclerosis	C	$243,779										$243,779
VA-142	VA Gulf War Biorepository Trust	C	$991,510	$991,510	$1,091,547	$5,664,976	$754,942	$948,168	$592,544	$471,756			$11,506,953
VA-143	The Role of Protein Oxidation in the Progression of ALS	C	$112,400	$112,400									$224,800
VA-144	Testing the Role of Permethrin on the Progression of ALS	C	$112,400	$112,400									$224,800
VA-145	Proteomic Analysis of Cellular Response to Biological Warfare Agents	C	$129,260	$224,800	$224,800	$112,400	$67,752						$759,012

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VA-146	Direct Delivery of Neurotoxins to the Brain by an Intranasal Route	C	$161,687	$256,159	$245,295	$195,214							$858,355
VA-147	The Diagnosis and Pathogenesis of Occult Leishmaniasis	C	$98,350										$98,350
VA-148	Profile of GW Veterans Who Applied for Undiagnosed Illness Compensation	C	$24,307	$71,008									$95,315
VA-149	Behavior of Neural Stem Cells in a Rat Model of GWS	C		$129,861	$268,901	$273,801	$136,900						$809,463
VA-150	GW Veterans Illnesses' Research IDIQ Contract with UTSW	C		$15,000,000	$15,000,000	$6,972,481	$2,288,755	$31,472					$39,292,708
VA-151	Genetic Epidemiology of ALS Veterans (CSP #500B)	C			$2,116,602	$377,557	$377,557	$242,775					$3,114,491
VA-152	Multiple Sclerosis in GW Veterans	C			$122,010	$137,791	$120,866						$380,667
VA-153	Bacterial Overgrowth Associated with Chronic Multi-Symptom Illness Complex	C				$8,377	$168,600	$94,681	$158,219	$43,278	$49,504		$522,659
VA-154	Imaging Pain Modulation in GW Veterans with Chronic Muscle Pain (renewal of VA-096)	C				$300,782	$258,076	$259,657	$262,184				$1,080,699
VA-155	Bacterial Host Defense Mechanisms in Polyaromatic Hydrocarbon Carcinogenesis	C	$71,486	$156,461	$176,790	$165,790	$165,790	$222,552	$168,600	$168,600	$168,600		$1,464,669
VA-156	Gulf War Era Cohort and Biorepository (CSP #585)	O					$28,361	$5,110	$2,157,664	$2,155,789	$2,292,081	$2,887,228	$9,526,233
VA-157	A Clinical Demonstration of an EEG Brain-Computer Interface for ALS Patients (CSP #567)	C					$2,368,460	$965,519	$26,296	$84,236			$3,444,511
VA-158	Testing the Feasibility of MC CBT for Veterans with IBS	C					$17,953	$93,153					$111,106
VA-159	Somatic hypersensitivity in Veterans with IBS	C				$56,200	$112,400	$112,400	$56,200				$337,200
VA-160	Lipoic Acid Therapy for Experimental Autoimmune Encephalomyelitis	C					$224,126	$168,600	$168,600	$168,600			$729,926
VA-161	Multiple Antigenic Peptides to Alter the Course of Autoimmune Disease	C					$332,743	$168,600	$168,600	$168,600	$84,300		$922,843
VA-162	Transcription factors regulating sensory gene expression and pain pathways	C				$94,416	$168,600						$263,016
VA-163	Immunoregulation of Myelin Specific T Lymphocytes	O				$371,209	$361,972	$168,600	$168,600	$42,150	$168,600	$168,600	$1,449,731
VA-164	Central Mechanisms Modulating Visceral Sensitivity (renewal of VA-136)	O				$255,170	$267,687	$119,256	$90,574	$112,982	$168,600	$148,368	$1,162,637

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VA-165	A Pilot Study of CPAP Adherence Promotion by Peer Buddies with Sleep Apnea	C						$94,838					$94,838
VA-166	A Randomized Controlled Trial of a Mindfulness-Based Intervention for Gulf War Syndrome	C						$106,898	$112,394				$219,292
VA-167	Neuroprotection anf Myelin Repair Mechanisms in Multiple Sclerosis	O						$267,287	$259,707	$259,707	$259,707	$50,165	$1,096,573
VA-168	Sleep Neurobiology and Circuitry	O						$244,063	$303,406	$168,600	$168,600	$202,320	$1,086,989
VA-169	Prevention of Hippocampal Neurodegeneration Due to Age and Apnea	O						$202,742	$270,322	$270,322	$270,322	$143,872	$1,157,580
VA-170	Epigenetic Mechanisms Relevant to the Pathogenesis of ALS	O						$182,650	$168,600	$168,600	$168,600	$42,150	$730,600
VA-171	Nanoparticle Coupled Antioxidants for Respiratory Illness in Veterans	O						$140,500	$168,600	$168,600	$168,600	$84,300	$730,600
VA-172	Understanding Pain of Gastrointestinal Origin in Women that Serve in OEF/OIF	O						$84,300	$168,600	$168,600	$123,640	$129,260	$674,400
VA-173	Impact of Exercise Training on Pain and Brain Function in GW Veterans	O						$104,167	$202,910	$386,948	$371,321	$329,743	$1,395,089
VA-174	GW Veterans' Illnesses Biorepository	O							$237,878	$263,848	$197,250	$275,762	$974,738
VA-175	Memory and Mood Enhancing Therapies for Gulf War Illness	O							$266,950	$281,000	$281,000	$281,000	$1,109,950
VA-176	MEG Synchronous Neural Interactions (SNI) in GW Veterans	C							$406,888	$397,334	$397,334		$1,201,556
VA-177	Somatic Hypersensitivity in Veterans with IBS (renewal of VA-159)	O							$68,970	$197,998	$159,121	$30,256	$456,345
VA-178	rTMS for the Treatment of Chronic Pain in GW1 Veterans	O								$309,100	$309,100	$309,100	$927,300
VA-179	Vascular and Skeletal Muscle Function in Gulf War Veterans Illness	O								$111,330	$168,257	$168,148	$447,735
VA-180	Diagnostic Utility of mtDNA Content and Exercise Challenge in Veterans with GWI	O								$92,453	$174,769	$47,269	$314,491
VA-181	Transcranial, Light-Emitting Diode (LED) Therapy to Improve Cognition in GWVI	O								$427,447	$774,029	$785,867	$1,987,343
VA-182	Consensus Case Definition for Chronic Multisymptom Illness in 1990-1991 Gulf War Veterans	C								$850,000			$850,000
VA-183	Examination of Cognitive Fatigue in Gulf War Illness Using fMRI	O									$279,149	$263,866	$543,015

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VA-184	Longitudinal Assessment of Gulf War Veterans with Suspected Sarin Exposure	O									$268,201	$455,994	$724,195
VA-185	Identification of Plasma Biomarkers of Gulf War Illness Using "omic" Technology	O									$511,947	$569,235	$1,081,182
VA-186	Gulf War Exposures and the Molecular Mechanisms of Paternal Reproductive Risk	O									$300,433	$373,865	$674,298
VA-187	Multimodal Biological Assessment of Gulf War Illness	O									$477,509	$561,936	$1,039,445
VA-188	Complementary Neurosteroid Intervention in Gulf War Veterans' Illnesses	O									$230,005	$421,204	$651,209
VA-189	CAM in Veterans with Gulf War Illnesses	O									$140,533	$222,332	$362,865
VA-190	Cognitive Rehabilitation for Gulf War Illness	O									$142,910	$392,929	$535,839
VA-191	Novel neurotrophic therapies in an optimized mouse model of GWVI	O									$195,947	$602,157	$798,104
VA-192	Women vs. Men with GWI: Differences in Computational Models and Therapeutic Targets	O									$189,365	$534,460	$723,825
VA-193	Neuroinflammation, Oxidative Stress, and Hippocampal Defects in Gulf War Illness	O									$70,250	$168,600	$238,850
VA-194	National Health Survey of Veterans and Family Members: Secondary Analysis of CSP #458 Data	O										$173,622	$173,622
VA-195	RCT of Duloxetine and Pregabalin for the Treatment of Gulf War Illness in Veterans	O										$384,754	$384,754
VA-196	Immune Basis for Hippocampal Cholinergic Deficits in Pyridostigmine-Treated Rats	O										$136,069	$136,069
VA-197	Genomics of Gulf War Illness in Veterans	O										$288,367	$288,367
	VA Totals		$13,013,552	$22,059,061	$21,934,214	$16,600,799	$13,881,340	$5,569,011	$6,723,556	$7,937,878	$9,729,584	$11,632,798	$129,081,793

*****Totals for FY '06 -'15 do not include funds obligated in FY 1992 -2005

Status: C=Complete; O=Ongoing