2000 NIH Funded CFS Research

NHLBI

TITLE	RBC MASS, ANS INTEGRITY & SYNCOPE SUSCEPTIBILITY IN CFS
P.I.	HURWITZ, BARRY E
GRANT NO.	1R01HL065668-01
INSTITUTION	UNIVERSITY OF MIAMI-MEDICAL

ABSTRACT: *The pathogenesis of the chronic fatigue syndrome (CFS) includes severe and debilitating fatigue, orthostatic intolerance, and the disruption of hematological, autonomic, and cardiovascular function. Our preliminary findings suggest that: 1) reduced red blood cell (RBC) mass is a critical hematological marker of CFS; and 2) RBC mass expansion improves orthostatic tolerance and fatigue beyond that ascribed to plasma volume expansion alone. However, the physiologic mechanisms underlying the RBC mass treatment effect and the relationship of such mechanisms to individual differences in treatment response have not been elucidated. This proposed 5-year study will screen 150 CDC-defined CFS men and women and classify them into low and normal RBC mass groups. The CFS subjects (90 of 105 enrolled) will be studied before and after a 3-month intervention in a randomized double-blind, placebo-controlled study of pharmacotherapy to expand RBC mass; specifically, two CFS groups with low RBC (RBC-treated and placebo-treated) will be compared to another CFS group with normal RBC mass (standard and usual care). To assess whether the diminished cardiac function, characteristic of CFS orthostatic intolerance, is a consequence of myocardial origin, echocardiographic evaluation of left ventricular structure and function (left ventricular mass and wall thickness, compliance, and contractility) will be performed. In addition, autonomic integrity will be assessed during a standardized battery of tests (supine rest, paced respiration, Valsalva maneuver, lying-to standing, and sustained handgrip); baroreceptor sensitivity and alpha- and beta-adrenoceptor sensitivity will he tested using adrenoceptor pharmacologic challenge (phenylephrine, isoproterenol). To determine orthostatic susceptibility, a 70 head-up tilt (HUT) test combined with beta-adrenoceptor infusion at 2 mug/min (and then again at 5 mug/min, if the previous HUT failed to induce orthostatic hypotension) will be performed. We will further examine the treatment effect on exertional fatigue and hemodynamic and autonomic physiologic response to the HUT tests. Finally, the relation between the criterion (orthostatic hypotension susceptibility) and the predictors (hemodynamic, autonomic, cardiac structure/function and baroreceptor, alpha-adrenoceptor and beta-adrenoceptor sensitivities) will be evaluated to determine the extent to which the predictors are mediating the treatment effects on orthostatic hypotension susceptibility.*

TITLE	ORTHOSTATIC INTOLERANCE IN CFS
P.I.	FREEMAN, ROY
GRANT NO.	5R01HL059459-03
INSTITUTION	BETH ISRAEL DEACONESS MEDICAL CENTER

ABSTRACT: *The over-all objectives of this proposal are: (1) to delineate the pathophysiology and pathogenesis of orthostatic intolerance in the chronic fatigue syndrome (CFS) (2) to investigate the role of orthostatic intolerance in producing the symptoms of CFS and (3) to use this information to apply physiologically appropriate therapeutic interventions and thereby decrease the symptoms of fatigue. The investigators plan to determine the physiological characteristics of orthostatic intolerance in CFS patients and healthy controls, characterize the differences in functional exercise capacity among CFS patients and between CFS patients and controls; and identify the relationships between the physiological measures of orthostatic intolerance, measures of functional exercise capacity, symptoms of orthostatic intolerance and symptoms of fatigue. Cardiovascular autonomic functions are to be assessed using standard tests of the sympathetic and parasympathetic nervous system; arterial baroreflex gain is to be measured using the heart rate and muscle sympathetic nerve activity response to pharmacological provocations; the cardiopulmonary baroreflex functions is to be assessed in response to graded central hypovolemia elicited by lower body negative pressure; plasma volume will be measured using the Evans Blue dye method; venous compliance assessed with venous occlusion plethysmography, Assessment of neurohumoral status and the functional exercise capacity is also to be included. These measures, which comprise the elements of orthostatic tolerance, will be compared with matched healthy controls. The relationships between these variables and the role of covariates such as the level of physical activity and psychiatric state, determined with standardized instruments, are to be analyzed using multivariate statistics.*

TITLE	CIRCULATORY CONTROL IN YOUNG PEOPLE WITH CHRONIC FATIGUE
P.I.	SAUL, J P.
GRANT NO.	5R01HL062385-03
INSTITUTION	MEDICAL UNIVERSITY OF SOUTH CAROLINA
ABSTRACT: *This abstract is not available.*	

TITLE	MUSCLE BLOOD FLOW AND CFS
P.I.	MCCULLY, KEVIN K.
GRANT NO.	5R01HL065179-02
INSTITUTION	UNIVERSITY OF GEORGIA
ABSTRACT: *This abstract is not available.*	

NINCDR

TITLE	COMPREHENSIVE CENTER FOR INFLAMMATORY DISORDERS
P.I.	FLOOD, PATRICK M.
GRANT NO.	3P60DE013079-01S1
INSTITUTION	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL

ABSTRACT: *Chronic inflammatory disorders are one of the biggest health problems in America today. This application describes the Comprehensive Center for Inflammatory Disorders whose mission is to support the identification and implementation of the full range of discovery from research on the basic mechanisms of inflammation to improved methods in the prevention and treatment of oral and systemic inflammatory diseases and disorders. The goals of the Center are to: 1) integrate studies on the fundamental mechanisms of cellular responses to inflammatory stimuli to better understand the basis of cellular activation, motility, and function that occur during inflammatory responses; 2) integrate basic research studies on inflammation with animal, patient-based and population research to better understand the cellular and molecular basis of oral inflammatory disorders; 3) identify several new and innovative approaches to the prevention, diagnosis, and treatment of chronic inflammation and facilitate their development into effective interventions for the treatment of oral and systemic inflammatory diseases and disorders within 5 years; 4) utilize and expand ongoing research on community education, screening, counseling, and related service programs to find better ways to expand public implementation of new advances in the prevention, diagnosis, and treatment of chronic oral and systemic inflammatory diseases and disorders; 5) integrate discovery from laboratory, clinical, population, education or community-based research into ongoing Center activities or new Center initiatives; and 6) promote programs for the education of health professionals and the public on the etiology, prevention, diagnosis, and treatment of chronic inflammatory diseases and disorders. The Center consists of 4 workgroups in the areas of fundamental, clinical, epidemiologic, and community outreach and outcomes research which are supported by an administrative, educational, technology transfer, and research support core. This Center core is designed to: 1) stimulate sharing, mutual interpretation, and integration of information on inflammation or inflammatory disorders obtained through research discovery; 2) provide mechanisms that allow the rapid development of discovery into new research projects, therapies, interventions, or potentially marketable products; 3) educate health professionals and the public on health issues of oral and systemic inflammatory disorders; and 4) make available to each product essential administrative support, research facilities, research services, coordination, and scientific leadership.*

TITLE	Clinical Neurocardiology: Catecholamine Systems in Stress and Disease
P.I.	GOLDSTEIN, DAVID S.
GRANT NO.	1Z01NS002979-02
INSTITUTION	

ABSTRACT: *We conducted patient-oriented clinical research in neurocardiology. Studies focused on elucidating pathophysiologic mechanisms and developing novel diagnostic approaches for disorders involving altered regulation of catecholamine systems. These conditions result from dysfunction of the autonomic nervous system (dysautonomia) or abnormally decreased or increased production of the catecholamines, norepinephrine (NE), epinephrine (EPI), or dopamine (DA). Patients with autonomic failure in the setting of Parkinson's disease all had cardiac sympathetic denervation, detected by 6-[18F]fluorodopamine positron-emission tomographic scanning. In contrast, patients with multiple system atrophy, which can be difficult to distinguish clinically from Parkinson's disease, all had evidence for intact cardiac sympathetic nerve terminals. Even in the absence of autonomic failure, most patients with Parkinson's disease had evidence for localized or diffuse loss of cardiac sympathetic nerve terminals. In the diagnostic evaluation of pheochromocytoma, a clinically important tumor that produces catecholamines, plasma levels of metanephrines, metabolites of NE and EPI made in the tumor, provided a uniquely and virtually perfectly sensitive screening test. 6-[18F]Fluorodopamine positron-emission tomographic scanning successfully localized the tumor even in difficult cases. A combined neurogenetic and neurochemical approach holds great promise for understanding how particular mutations in familial diseases associated with increased production of NE (pheochromocytoma) or decreased production of NE (Menkes disease) relate to particular neurochemical and clinical manifestations.*

NIAID

TITLE	Brain and Cardiovascular Studies
P.I.	NATELSON, BENJAMIN H.
GRANT NO.	5U01AI032247-100006
INSTITUTION	UNIV OF MED/DENT NJ NEWARK
ABSTRACT: *There is no text on file for this abstract.*	

TITLE	Physiological Challenges in CFS
P.I.	LA MANCA, JOHN
GRANT NO.	5U01AI032247-100007
INSTITUTION	UNIV OF MED/DENT NJ NEWARK
ABSTRACT: *There is no text on file for this abstract.*	

TITLE	Core--Patient Accrual and Data Analysis Facility
P.I.	NATELSON, BENJAMIN H.
GRANT NO.	5U01AI032247-109003
INSTITUTION	UNIV OF MED/DENT NJ NEWARK
ABSTRACT: *There is no text on file for this abstract*	

TITLE	POPULATION BASED TWIN STUDY OF CHRONIC FATIGUE SYNDROME
P.I.	SULLIVAN, PATRICK F.
GRANT NO.	5U19AI038429-060006
INSTITUTION	UNIVERSITY OF WASHINGTON

ABSTRACT: *Despite considerable research, fundamental questions about CFS-like illness remain at best partially answered. These questions include its definition, validity, the degree to which it results from genetic versus environmental factors, and the nature of the substantial comorbidity observed with other conditions. The overarching aim of this Project is to shed light on a number of basic questions about CFS via a large population-based classical twin study. First, we will screen approximately 13,000 same-sex twin pairs who are members of the Mid-Atlantic Twin Registry for the lifetime presence of CFS-like illness (and several overlapping conditions such as fibromyalgia and major depression). Second, all twins who screen positive and a subset of twins who screen negative will be directly and blindly interviewed. The interviews will collect information about CFS symptoms, psychiatric disorders, stress life events, and medical history, and medical history. We will obtain additional standardized medical data via the subject's physician(s). Third, all screening, direct interview and medical data will be independently reviewed by three of the study investigators to determine the certainty than an individual meets criteria for "presumptive CFS" plus approximations of the Centers for Disease Control, British, and Australian CFS case definitions. Obtaining these unique data will allow us to address a set of critical questions regarding CFS-like illness. First, using the direct interview data will allow us to address a set of critical questions regarding CFS-like illness. First, using the direct interview data, we will use multivariate techniques to derive and empirical typology of prolonged fatigue and to assess how this typology compares to the major CFS case definitions to answer the question: "Is there a point of rarity that distinguishes the common symptom of fatigue from case definitions of CFS"? Next, we will quantify the role of genetic predisposition and environmental sources of variation from different definitions of CFS-like illness. This will allow us to address 2 important questions. Because the degree to which a complex and idiopathic condition is heritable is an important validator, we can address the question: "Do these definitions yield similar or different estimates of heritability?" In addition, examining the extent to which liability to CFS- like illness is due to additive genetic, shared environmental, and individual-specific environmental precipitating effects will yield glimpses into the fundamental nature of CFS. Finally, using multivariate twin analyses, we address the question: "To what extent to the genetic and environmental sources of variation of these other conditions overlap with CFS?"*

TITLE	MODEL FOR INDUCTION OF CFS
P.I.	JONES, JAMES F.
GRANT NO.	5R01AI040990-03
INSTITUTION	NATIONAL JEWISH MEDICAL & RES CTR AND RESEARCH CENTER

ABSTRACT: *This is an amended application that was previously reviewed October/November 1996. The application was proceeded by an introduction that addressed critique from the first review. Changes and additions were bolded in this re-submitted application. Dr. Jones and colleagues at National Jewish Medical and Research Center in Denver, Colorado propose a case control study of adult patients (18-45 years) with CFS, half of whom have atopic disease compared to matched control groups. They plan to challenge with exercise and nasal allergy provocation 60 CFS patients and controls to determine if such provocation will evoke CFS symptoms as well as induce changes in inflammatory laboratory parameters. Their proposal would be used to define a model that would be usually for future pathophysiological studies and possible intervention trials for adults with CFS.*

TITLE	COGNITIVE BEHAVIORAL STRESS MANAGEMENT INTERVENTION FOR CFS
P.I.	ANTONI, MICHAEL H.
GRANT NO.	5U01AI045940-020002
INSTITUTION	UNIVERSITY OF MIAMI-MEDICAL

ABSTRACT: *The proposed 5-year study examines the effects of a cognitive behavioral stress management (CBSM) intervention (including relaxation training and cognitive restructuring) on physical health status and illness burden in 150 (after attrition) patients diagnosed with Chronic Fatigue Syndrome (CFS). The study tests the efficacy of a conceptual model which holds that the interaction of psychological factors (distress and depression associated with either CFS related symptoms or other stressful life events) and immunologic dysfunction (elevations in cytokines such as tumor necrosis factor [TNF]-alpha and the macrophage activation marker, neopterin) contribute to: (a) the exacerbation of physical symptoms associated with CFS (e.g., fatigue, joint pain, fever) and subsequent increases in illness burden (operationalized as disruptions in daily activities due to fatigue and related physical symptoms); and (b) further dysfunction in the immune system (e.g., impaired lymphocyte proliferative responses to phytohemagglutinin [PHA] and natural killer cell cytotoxicity [NKCC]). The proposed revised study tests this model experimentally by first evaluating the effects of a 10 week group CBSM intervention upon the primary health outcome variables: physical health status (CFS symptoms), fatigue severity, CFS-related illness burden and functional quality of life. Secondly, this study examines the role of two sets of hypothesized mediator variables: (l) reductions in psychological distress and depression levels; and (2) immune system modulation (less impaired NKCC and PHA responsivity, lowered TNF-alpha peptides and TNF-type II receptors in serum, reduced neopterin levels, reduced numbers of lymphocyte subsets expressing activation markers). To bring about these effects the intervention is hypothesized to directly modulate a set of psychosocial intervention targets that we hypothesize will influence the mediator variables. These intervention targets include reductions in distorted cognitive appraisals, greater use of active and engaging coping strategies, increased coping self-efficacy and increased perceptions of social support provisions. This is a randomized experiment with a 12-week CBSM (plus education and standard care) condition vs. an Education plus standard care (ED/SC) control condition, At the end of the 12-week CBSM intervention, the experimental group will continue on a standard of care regimen and will be monitored for their adherence to the techniques learned in the CBSM intervention and for intercurrent medical treatment. At the end of the 12-week ED/SC period the control group will be subsequently monitored as they continue on their standard of care. We will follow subjects at 6 and 12 months post-CBSM to assess treatment carryover and to correlate prospectively pre-post CBSM changes in mediator and health outcome variables measured at these follow-up points.*

TITLE	EFFECT OF STRESS AND CBSM ON NATURAL KILLER CELL ACTIVITY IN CFS
P.I.	FLETCHER, MARY A.
GRANT NO.	5U01AI045940-020004
INSTITUTION	UNIVERSITY OF MIAMI-MEDICAL

ABSTRACT: *Natural cell mediated immunity is frequently decreased in individuals who meet the case definition of chronic fatigue syndrome (CFS). Our research group and others have noted that exposures of healthy individuals as well as immunocompromised persons to acute and chronic stressors have an adverse effect on natural killer (NK) cell function, and that this adverse stress effect is susceptible to amelioration by behavioral interventions in which cognitive restructuring and relaxation training are taught. In this Multidisciplinary Research Center, Project 2 will carry out such an intervention for individuals who meet the diagnosis criteria for CFS. The intervention will be carried out over a 12 week period. Blood samples from both pre-intervention and post-intervention will be available for study in Project 4. Also available will be 2 samples collected 12 weeks apart on CFS subjects who do not receive the intervention, but are in an education/control condition. The Administrative Core will enroll healthy, sedentary controls for both Project l and Project 4 and for the Laboratory Core as normal subjects for all assays being done. The proposed Center will provide a mechanism to advance our understanding of NK cells and CFS. A detailed comparison will be made of markers of NK cell cytotoxic capacity as well as actual killing of tumor cell target cells. The differences between effect of the intervention on NK cell function can be evaluated. In addition to the traditional chromium release cytotoxicity assay, Project 4 will look at important markers of NK cell functional status not yet evaluated in CFS. These will include flow cytometric determination of intracellular perforin and determination of degree of expression on NK cells of the surface membrane adhesion molecules, L-selectin (CD62L), LFA-1 (CDlla) and CD56 by fluorescence intensity measurements. These substances are associated with the ability of NK cells to-kill target cells and/or to interact with vascular epithelial cells and pass from peripheral circulation into tissue. The relationship of these markers to the low NK cell activity associated with CFS, to effects of acute and chronic stress on NK cell function or to the modulation of life stress by behavioral interventions has not previously been studied. We will examine the effects on NK cell cytotoxicity, intracellular perforin levels and surface markers of in vitro exposure of peripheral blood cells to stress hormones (epinephrine, norepinephrine, cortisol) and tumor necrosis factor-o:. All of these studies will be done pre/post intervention in the 2 CFS groups of subjects and one time in the healthy, sedentary controls. This design will allow the determination of differences between CFS and healthy controls as well as the impact of the behavioral intervention by comparing findings before and following the intervention relative to CFS control subjects.*

TITLE	Core--Biological assessment laboratory
P.I.	FLETCHER, MARY A.
GRANT NO.	5P50CA084944-029002
INSTITUTION	UNIVERSITY OF MIAMI CORAL GABLES

ABSTRACT: *The Laboratory Core will provide the assessments of soluble mediators, lymphocyte surface markers, hematological parameters and lymphocyte function in support of the scientific agenda of this Center. The following assays will be done by the Laboratory Core: Cortisol and catecholamines, norepinephrine (NE) and epinephrine (E) in urine. Testosterone, estradiol,. Estrone, sex hormone binding globulin (SHBG) and dehydroepiandrosterone-sulfate (DHEA-S) and NPY in plasma. Natural killer cell cytotoxicity (NKCC) against the tumor cell target, K562. NKCC against the tumor cell target, K562, after ex vivo exposure to interferon-gamma (IFN-gamma). Number and percent of NK (C56+CD3-), CD3+CD4+ and CD3+CD8+ lymphocytes using 4 color flow cytometry.*

TITLE	Brain and Cardiovascular Studies
P.I.	NATELSON, BENJAMIN H
GRANT NO.	5U01AI032247-100006
INSTITUTION	UNIV OF MED/DENT NJ NEWARK

ABSTRACT: *There is no text on file for this abstract.*

TITLE	Physiological Challenges in CFS
P.I.	LA MANCA, JOHN
GRANT NO.	5U01AI032247-100007
INSTITUTION	UNIV OF MED/DENT NJ NEWARK

ABSTRACT: *There is no text on file for this abstract.*

TITLE	Core--Patient Accrual and Data Analysis Facility
P.I.	NATELSON, BENJAMIN H
GRANT NO.	5U01AI032247-109003
INSTITUTION	UNIV OF MED/DENT NJ NEWARK
ABSTRACT: *There is no text on file for this abstract*	

TITLE	MECHANISMS OF IMMUNOLOGICALLY MEDIATED FATIGUE
P.I.	PETERSON, PHILIP K.
GRANT NO.	5R01AI035110-06
INSTITUTION	MINNEAPOLIS MEDICAL RESEARCH FDN, INC.

ABSTRACT: *Fatigue is a common clinical manifestation of infectious and autoimmune diseases; it is also the chief complaint of patients with chronic fatigue syndrome (CFS). Cytokines, which are produced during immune activation, have been hypothesized to affect brain cell function resulting in fatigue. The work proposed, which is potentially relevant to und erstanding CFS, will test the cytokine hypothesis of immunologically mediated chronic fatigue using recently developed murine models of whole cell Corynebacterium parvum antigen inoculation. The specific aims of this research proposal are to: (1) characterize a murine model of immunologically mediated chronic fatigue (Specific Aim 1); (2) evaluate the association between selected cytokine expression in splenic and brain tissues of mice and chronic fatigue development (Specific Aim 2); and (3) investigate the effects of drugs known to inhibit cytokine production on immunologically mediated chronic fatigue (Specific Aim 3). For these studies, fatigue will be quantified by measuring the degree and duration of reduction in spontaneous daily running activity on an exercise wheel following whole cell C. parvum antigen inoculation in C57BL/6 female mice. Serum cytokine levels (interleukin [IL]-1, IL-6, transforming growth factor-beta, interferon-alpha, and tumor necrosis factor-alpha) and cytokine mRNA expression in splenic and brain tissues of inoculated mice will be correlated with the development of chronic fatigue. Treatment of mice which display immunologically mediated chronic fatigue with drugs known to inhibit cytokine expression will be performed to assess their impact on development of chronic fatigue and their therapeutic potential in disorders involving immunologically mediated fatigue. These studies will enhance our understanding of the pathophysiology of immunologically mediated fatigue and will foster the development of new treatment strategies, particularly for patients with CFS.*

TITLE	MONOZYGOTIC TWINS WITH CHRONIC FATIGUE SYNDROME--PREDISPOSITION OR PERCEPTION?
P.I.	BUCHWALD, DEDRA S.
GRANT NO.	5U19AI038429-060005
INSTITUTION	UNIVERSITY OF WASHINGTON

ABSTRACT: *CFS may be associated with the disruption of several physiological processes such as exercise capacity, sleep, cognition and immune function. Most investigations of CFS have used a case-control design with patients recruited from referral centers and controls often matched only of age and sex. Thus, these disorders have not adjusted for genetic and environmental influences. The study of monozygotic (MZ) twins discordant for CFS (i.e., one has CFS, one doesn't) adjusts for genetic variability and common familial exposures. We have constructed a large registry of twins in which at least one member has CFS or a similar illness. All Twin Registry members complete a comprehensive Registry Booklet and a structured psychiatric interview. Using this information and medical records, 21 pairs of CFS discordant twins (CFS-HY) have been selected for a 6-day evaluation that includes polysomnography, exercise capacity testing, neuropsychological assessment, SPECT imaging, a psychiatric and life events interview, tests of viral replication and the immune system (Phase 1). Data from the 17 CFS-HY twin pairs who have completed this evaluation demonstrate remarkably disrupted sleep, poor performance on the several cognitive tests and severely impaired exercise capacity in both twins, as well as intriguing differences in immune function and perceptual style. In Phase 2, the twins will return to Seattle 24-30 months after Phase 1 for further intensive study that will include polysomnography, neuropsychological testing, exercise capacity testing and measurement and measurement of immune function and perception. We will also examine 10 pairs of twins in which both members are health (HY-HY) to clarify the interpretation of the abnormalities documented in the healthy member of the CFS-HY pairs. Our aims are to confirm the Phase 1 results and to assess their stability and reproducibility; 2) improve the interpretation of Phase 1 abnormalities by expanded data collection using challenge studies and other approaches to bring out differences between the CFS-HY twins; 3) compare the results in the CFS-HY pairs with those obtained from HY- HY twins. If abnormalities are not found in HY-HY twins then the impairments in exercise, cognition and sleep may represent predisposing factors that place the healthy member of the CFS-HY pair at risk for illness; 4) establish the extent to which alterations in perception account for dysfunction in CFS.*

TITLE	POPULATION BASED TWIN STUDY OF CHRONIC FATIGUE SYNDROME
P.I.	SULLIVAN, PATRICK F.
GRANT NO.	5U19AI038429-060006
INSTITUTION	UNIVERSITY OF WASHINGTON

ABSTRACT: *Despite considerable research, fundamental questions about CFS-like illness remain at best partially answered. These questions include its definition, validity, the degree to which it results from genetic versus environmental factors, and the nature of the substantial comorbidity observed with other conditions. The overarching aim of this Project is to shed light on a number of basic questions about CFS via a large population-based classical twin study. First, we will screen approximately 13,000 same-sex twin pairs who are members of the Mid-Atlantic Twin Registry for the lifetime presence of CFS-like illness (and several overlapping conditions such as fibromyalgia and major depression). Second, all twins who screen positive and a subset of twins who screen negative will be directly and blindly interviewed. The interviews will collect information about CFS symptoms, psychiatric disorders, stress life events, and medical history, and medical history. We will obtain additional standardized medical data via the subject's physician(s). Third, all screening, direct interview and medical data will be independently reviewed by three of the study investigators to determine the certainty than an individual meets criteria for "presumptive CFS" plus approximations of the Centers for Disease Control, British, and Australian CFS case definitions. Obtaining these unique data will allow us to address a set of critical questions regarding CFS-like illness. First, using the direct interview data will allow us to address a set of critical questions regarding CFS-like illness. First, using the direct interview data, we will use multivariate techniques to derive and empirical typology of prolonged fatigue and to assess how this typology compares to the major CFS case definitions to answer the question: "Is there a point of rarity that distinguishes the common symptom of fatigue from case definitions of CFS"? Next, we will quantify the role of genetic predisposition and environmental sources of variation from different definitions of CFS-like illness. This will allow us to address 2 important questions. Because the degree to which a complex and idiopathic condition is heritable is an important validator, we can address the question: "Do these definitions yield similar or different estimates of heritability?" In addition, examining the extent to which liability to CFS- like illness is due to additive genetic, shared environmental, and individual-specific environmental precipitating effects will yield glimpses into the fundamental nature of CFS. Finally, using multivariate twin analyses, we address the question: "To what extent to the genetic and environmental sources of variation of these other conditions overlap with CFS?"*

TITLE	CHILDREN OF CHRONIC FATIGUE SYNDROME PATIENTS
P.I.	SMITH, MARK
GRANT NO.	5U19AI038429-060007
INSTITUTION	UNIVERSITY OF WASHINGTON

ABSTRACT: *The debilitating effects of CFS on the health of afflicted persons has been well-documented. This study broadens the scope of CFS research beyond the level of the individual to the family. Our primary purpose is to compare the fatigue study, functional performance and psychological health of children who have a parent with CFS with that of children of parents without CFS. A secondary goal is to examine the relationship between a parental CFS and a selected set of vulnerability markers in children. Perturbations in these indicators could serve as a mechanism for the inter-generational transmission of fatiguing illnesses. Probands will be married adult patients from the University of Washington Chronic Fatigue Clinic who meet diagnostic criteria for CFS and have at least one child between the ages of 10 and 17 living at home. The comparison group will be non-fatigued, married friends of CFS probands who are same sex and who have children in the same age range. All adults and children will be evaluated using a broad range of fatigue, functional performance, physical and mental health measures and selected vulnerability markers. These data will be used to address the following questions: Are children of CFS probands more likely to report high fatigue levels than children. of non-CFS probands? Are there differences in pain thresholds or cognitive functioning in the children of CFS probands? Are there higher rates of psychiatric disorders and psychosocial distress among children of CFS probands compared to children of non-CFS probands? Does having a parent with CFS impair the functioning of children and adolescents, or conversely, do the offspring of adults with CFS assume a disproportionate burden of responsibilities? For each of these questions the potential differential effects of age and sex of the proband and age, sex and pubertal status of the children will be investigated. This project elucidate several elements in our conceptual models for the pathophysiology of CFS. The examination of the effects on children of having a parent with CFS is focused on a familial predisposition to fatiguing illness. This predisposition may derive from the familial environment or genetics. Similarly, the targeted potentially pre-morbid perceptual may derive from the familial environment or genetics. Similarly, the targeted potentially pre-morbid perceptual vulnerability markers ask if there are subclinical alterations in the pain threshold and cognition of children of CFS parents; these children may be especially vulnerable for the development of fatiguing illnesses.*

TITLE	CORE--CLINICAL FACILITY
P.I.	BUCHWALD, DEDRA S.
GRANT NO.	5U19AI038429-069002
INSTITUTION	UNIVERSITY OF WASHINGTON

ABSTRACT: *The Clinical Core, will serve as a reservoir of well-characterized study subjects, both patients and controls, for behavioral, clinical and basic research studies. As such, the Clinical Core will serve as the source of patients for Chronic Fatigue Syndrome Clinical Research Center (CFS CRC). This Core has 4 major specific aims 1) to prospectively evaluate and follow a referral clinic-based cohort of patients with chronic fatigue and CFS; 2) to utilize this population as the basis for investigations on CFS; 3) to maintain databases and banks of biological specimens on a variety fatigued and control populations and to recruit new comparison groups to improve our understanding of CFS; and 4) to examine the operating characteristics of clinical evaluation instruments already collected and patient subgroups using available data. The results of a comprehensive evaluation, including information on demographic, medical, psychological, functional and social features on almost 1,200 patients seen in a referral clinic are currently in our data base. Ethnic/racial minorities comprise about 8% and women 77% of patients. Information on new patients is entered weekly and patients are re- evaluated periodically. Control groups available for comparison to CFS patients include healthy individuals and those with medical disorders post-mononucleosis fatigue, the symptom of fatigue but not CFS, major depression, multiple chemical sensitivities, rheumatoid arthritis, fibromyalgia and temporomanidubular joint disorder. Besides descriptive studies, other questions amenable to study using the Clinical Core include the development of a battery of appropriate assessment measures for use in CFS and the evaluation of diagnostic tests or objective markers. In fact, the use of the Clinical Core resources has resulted in the development of a promising test for CFS and in the submission of 5 R01 and many other grant applications.*

TITLE	FACILITY CORE--BIOSTATISTICAL AND DATA MANAGEMENT
P.I.	ZEH, JUDITH
GRANT NO.	5U19AI038429-069001
INSTITUTION	UNIVERSITY OF WASHINGTON

ABSTRACT: *The Biostatistical and Data Management Core, will provide the statistical expertise and data entry and data management support needed by Chronic Fatigue Syndrome Clinical Research Center (CFS CRC) investigators. Its specific aims are to 1) provide consultation and collaboration on study design, methodology, and data analysis; 2) assist with the design of study forms and the evaluation of pre-testing and pilot data; 3) perform and supervise data entry; 4) maintain data bases and perform data management and quality control procedures; and 5) collaborate in the preparing and writing of manuscripts. The establishment of a Biostatistical and Data Management Core will allow new investigators to obtain valuable advice on CFS-related Projects, and established investigators involved in the CFS CRC to get advanced biostatistical consultation and evaluate novel approaches to research relevant to this CRC. A particular strength of this Core will be the availability of methodologists and analysts who have worked with the CFS CRC over the preceding 4 years, have gained extensive knowledge about the problems encountered in the classification of CFS and the appropriate biostatistical methods required to analyze complex data produced by this CFS CRC.*

TITLE	MODEL FOR INDUCTION OF CFS
P.I.	JONES, JAMES F.
GRANT NO.	5R01AI040990-03
INSTITUTION	NATIONAL JEWISH MEDICAL & RES CTR AND RESEARCH Center

Abstract: *This is an amended application that was previously reviewed October/November 1996. The application was proceeded by an introduction that addressed critique from the first review. Changes and additions were bolded in this re-submitted application. Dr. Jones and colleagues at National Jewish Medical and Research Center in Denver, Colorado propose a case control study of adult patients (18-45 years) with CFS, half of whom have atopic disease compared to matched control groups. They plan to challenge with exercise and nasal allergy provocation 60 CFS patients and controls to determine if such provocation will evoke CFS symptoms as well as induce changes in inflammatory laboratory parameters. Their proposal would be used to define a model that would be usually for future pathophysiological studies and possible intervention trials for adults with CFS.*

TITLE	AUTOANTIBODIES TO CELLULAR MATRIX ANTIGENS IN CFS
P.I.	TAN, ENG M.
GRANT NO.	5R01AI041033-04
INSTITUTION	SCRIPPS RESEARCH INSTITUTE

ABSTRACT: *On the basis of recent studies it has been shown that CFS sera contain antibodies to relatively insoluble cellular matrix antigens. Cellular structures (nuclear envelope, vimentin-containing intermediate filaments and a nuclear matrix particle visualized in immunofluorescence as reticulated speckles) associated with these antigens contain proteins that are part of the nuclear or cytoplasmic matrix. In collaboration with investigators at the University of Washington and at Harvard University, the PI and co-investigators at Scripps Research Institute will examine four research aims: 1) using previously collected blood samples from CFS patients from the two CFS center clinics and using currently developed assays the blood samples will be analyzed for the antibodies. They will be compared with patients with primary Sjogren's syndrome and primary fibromyalgia to determine whether differences in autoantibody specificities exist between different diseases and between CFS patients from different clinics; 2) ELISA assays will be developed for anti-lamin B1 and anti-vimentin using recombinant proteins expressed from cDNA clones, so that differences in antibody levels could be quantitated. This would be used in longitudinal studies of CFS patients to determine the role of humoral immunity in the natural history of the illness; 3) the possibility that there might be CFS-specific epitopes on lamin B1 and vimentin will be explored with expression products of PCR constructs, because if CFS-specific epitopes are detected, synthetic peptides of these regions could be used in highly specific immunological assays; 4) antibody screening of cDNA expression libraries will be performed to isolate the reticulated speckles nuclear antigen and a 45 kDa antigen. The antibody to the reticulated speckles could be a new or unique marker for CFS. The antibody to the 45 kDa antigen is present in Sjogren's syndrome but not in CFS-sicca and appears to be a distinguishing feature between the two clinical entities. Overall, these studies are aimed at rigorously defining autoantibody reactivities in CFS and may have etiologic implications.*

TITLE	COGNITIVE BEHAVIORAL STRESS MANAGEMENT INTERVENTION FOR CFS
P.I.	ANTONI, MICHAEL H.
GRANT NO.	5U01AI045940-020002
INSTITUTION	UNIVERSITY OF MIAMI-MEDICAL

ABSTRACT: *The proposed 5-year study examines the effects of a cognitive behavioral stress management (CBSM) intervention (including relaxation training and cognitive restructuring) on physical health status and illness burden in 150 (after attrition) patients diagnosed with Chronic Fatigue Syndrome (CFS). The study tests the efficacy of a conceptual model which holds that the interaction of psychological factors (distress and depression associated with either CFS related symptoms or other stressful life events) and immunologic dysfunction (elevations in cytokines such as tumor necrosis factor [TNF]-alpha and the macrophage activation marker, neopterin) contribute to: (a) the exacerbation of physical symptoms associated with CFS (e.g., fatigue, joint pain, fever) and subsequent increases in illness burden (operationalized as disruptions in daily activities due to fatigue and related physical symptoms); and (b) further dysfunction in the immune system (e.g., impaired lymphocyte proliferative responses to phytohemagglutinin [PHA] and natural killer cell cytotoxicity [NKCC]). The proposed revised study tests this model experimentally by first evaluating the effects of a 10 week group CBSM intervention upon the primary health outcome variables: physical health status (CFS symptoms), fatigue severity, CFS-related illness burden and functional quality of life. Secondly, this study examines the role of two sets of hypothesized mediator variables: (l) reductions in psychological distress and depression levels; and (2) immune system modulation (less impaired NKCC and PHA responsivity, lowered TNF-alpha peptides and TNF-type II receptors in serum, reduced neopterin levels, reduced numbers of lymphocyte subsets expressing activation markers). To bring about these effects the intervention is hypothesized to directly modulate a set of psychosocial intervention targets that we hypothesize will influence the mediator variables. These intervention targets include reductions in distorted cognitive appraisals, greater use of active and engaging coping strategies, increased coping self-efficacy and increased perceptions of social support provisions. This is a randomized experiment with a 12-week CBSM (plus education and standard care) condition vs. an Education plus standard care (ED/SC) control condition, At the end of the 12-week CBSM intervention, the experimental group will continue on a standard of care regimen and will be monitored for their adherence to the techniques learned in the CBSM intervention and for intercurrent medical treatment. At the end of the 12-week ED/SC period the control group will be subsequently monitored as they continue on their standard of care. We will follow subjects at 6 and 12 months post-CBSM to assess treatment carryover and to correlate prospectively pre-post CBSM changes in mediator and health outcome variables measured at these follow-up points.*

TITLE	EFFECT OF STRESS AND CBSM ON NATURAL KILLER CELL ACTIVITY IN CFS
P.I.	FLETCHER, MARY A.
GRANT NO.	5U01AI045940-020004
INSTITUTION	UNIVERSITY OF MIAMI-MEDICAL

ABSTRACT: *Natural cell mediated immunity is frequently decreased in individuals who meet the case definition of chronic fatigue syndrome (CFS). Our research group and others have noted that exposures of healthy individuals as well as immunocompromised persons to acute and chronic stressors have an adverse effect on natural killer (NK) cell function, and that this adverse stress effect is susceptible to amelioration by behavioral interventions in which cognitive restructuring and relaxation training are taught. In this Multidisciplinary Research Center, Project 2 will carry out such an intervention for individuals who meet the diagnosis criteria for CFS. The intervention will be carried out over a 12 week period. Blood samples from both pre-intervention and post-intervention will be available for study in Project 4. Also available will be 2 samples collected 12 weeks apart on CFS subjects who do not receive the intervention, but are in an education/control condition. The Administrative Core will enroll healthy, sedentary controls for both Project l and Project 4 and for the Laboratory Core as normal subjects for all assays being done. The proposed Center will provide a mechanism to advance our understanding of NK cells and CFS. A detailed comparison will be made of markers of NK cell cytotoxic capacity as well as actual killing of tumor cell target cells. The differences between effect of the intervention on NK cell function can be evaluated. In addition to the traditional chromium release cytotoxicity assay, Project 4 will look at important markers of NK cell functional status not yet evaluated in CFS. These will include flow cytometric determination of intracellular perforin and determination of degree of expression on NK cells of the surface membrane adhesion molecules, L-selectin (CD62L), LFA-1 (CDlla) and CD56 by fluorescence intensity measurements. These substances are associated with the ability of NK cells to-kill target cells and/or to interact with vascular epithelial cells and pass from peripheral circulation into tissue. The relationship of these markers to the low NK cell activity associated with CFS, to effects of acute and chronic stress on NK cell function or to the modulation of life stress by behavioral interventions has not previously been studied. We will examine the effects on NK cell cytotoxicity, intracellular perforin levels and surface markers of in vitro exposure of peripheral blood cells to stress hormones (epinephrine, norepinephrine, cortisol) and tumor necrosis factor-o:. All of these studies will be done pre/post intervention in the 2 CFS groups of subjects and one time in the healthy, sedentary controls. This design will allow the determination of differences between CFS and healthy controls as well as the impact of the behavioral intervention by comparing findings before and following the intervention relative to CFS control subjects.*

TITLE	CORE--LABORATORY FACILITY
P.I.	FLETCHER, MARY A.
GRANT NO.	5U01AI045940-029003
INSTITUTION	UNIVERSITY OF MIAMI-MEDICAL

ABSTRACT: *The LABORATORY CORE will provide the assessments of soluble mediators, lymphocyte surface markers, hematological parameters and lymphocyte function in support of the scientific agenda of this Center. For the intervention study, Project l, measurements of plasma and inducible tumor necrosis factor-alpha: (TNF-alpha:), soluble tumor necrosis factor receptor type II (sTNFII), interleukin-1-alpha (IL-1alpha), and IL-6, adrenocorticotropic hormone (ACTH) cortisol, norepinepherine (NE), epinephrine (E), erythropoitin, renin, reticulocytes, red blood cell (RBC) indices and electrolytes will be made at the time points defined in the experimental design for this studies. For Project 3, selected subjects from Project 1 will undergo a laboratory study of hemodynamics and autonomic mechanisms both pre- and post- intervention and serial measurements of plasma catecholamines will be made. For the Cognitive Behavioral Stress Management (CBSM) intervention study, Project 2, the following immunology assays will be done on the serial samples collected on subjects at T0, Tl, T2 and T3 as stipulated in the study design for that project: lymphocyte proliferation assays (LPA) and inducible cytokines in response to the mitogen, phytohemagglutinin (PHA); natural killer cell cytotoxicity (NKCC) against the tumor cell target, K562; number and percent of CD4, CD8 and activated sunsets of these, and NK cells (CD56+CD3-) using 4 color flow cytometry; plasma levels of neopterin, TNF-alpha and sTNFRII. Project 4 will study NK cells in a subset of subjects from Project 2 and will make use of the NKCC data done for that protocol. The Administrative Core will recruit 50 healthy sedentary controls. Blood samples from these controls will be assessed for all of the variables determined in this core, at a rate of 10 controls per year.*

TITLE	VENOUS DYSFUNCTION IN CHRONIC FATIGUE SYNDROME
P.I.	STEWART, JULIAN M.
GRANT NO.	5R03AI045954-02
INSTITUTION	NEW YORK MEDICAL COLLEGE
ABSTRACT: *This abstract is not available*	

TITLE	SIBERIAN GINSENG FOR THE TREATMENT OF CHRONIC FATIGUE
P.I.	HARTZ, ARTHUR J
GRANT NO.	5R03AI045982-02
INSTITUTION	UNIVERSITY OF IOWA
ABSTRACT: *This abstract is not available.*	

TITLE	ACTIVITY INTERVENTION FOR CHRONIC FATIGUE SYNDROME
P.I.	JASON, LEONARD
GRANT NO.	1R01AI049720-01
INSTITUTION	DE PAUL UNIVERSITY

ABSTRACT: *The primary purpose of this study is to evaluate the efficacy of the nurse delivered behavioral interventions of graded activity with cognitive therapy and graded activity alone in comparison to a cognitive therapy alone control condition in a target sample of 120 persons with CFS. This study will: 1) test the hypothesis that graded activity with cognitive therapy will yield significant improvements in physical and role functioning in comparison to the cognitive therapy alone control condition; and 2) test the hypothesis that graded activity alone will yield significant improvements in physical and role functioning in comparison to the cognitive therapy alone control condition. In addition, this study will test, as a secondary Aim, that graded activity alone will be as effective as graded activity with cognitive therapy in improving physical and role functioning in CFS. Since medical utilization rates for CFS patients are high and medical therapies for CFS have been largely unsuccessful, the study of a potentially effective behavioral intervention for the illness may offer an opportunity for a substantially improved quality of life in these debilitated patients.*

TITLE	COORD CTR FOR CLIN & EPIDEM STDYS IN INFEC DISEASES
P.I.	KLEIN, HUGH
GRANT NO.	3N01AI015131-020
INSTITUTION	TECHNICAL RESOURCES INTERNATIONAL, INC.
ABSTRACT: *This abstract is not available.*	

TITLE	FLUDROCORTISONE FOR INDIVIDUALS WITH CHRONIC FATIGUE SYNDROME AND HYPOTENSION
P.I.	STRAUS, STEPHEN E.
GRANT NO.	1Z01AI000812-04
INSTITUTION	

ABSTRACT: *Chronic fatigue syndrome (CFS) is a serious health problem in the United States. It is estimated that the prevalence rate in the United States is as much as 250/100,000 persons. No specific treatment has been identified. Recent observations suggest a strong association between CFS and a treatable disorder in the regulation of blood pressure known as neurally-mediated hypotension (NMH). In small unblinded studies, treatment with fludrocortisone and other medications directed against NMH has appeared to be beneficial, with 40% of treated patients reporting an almost complete resolution of symptoms and another 30% reporting some improvement. The specific aim of this randomized double blind, placebo-controlled trial is to determine whether fludrocortisone is efficacious for those with CFS. In this study, we randomized 100 adults with CFS and NMH, as defined by abnormal responses to postural challenge (tilt table test), to receive either fludrocortisone or placebo. The participants completed self-assessment forms on mood, energy, activity, and performance. The primary indicator of efficacy is a 15-point improvement (on a scale of 1 to 100) in the general sense of well being score. All subjects were 18-49 years of age who satisfy the 1994 CDC criteria for CFS, had undergone a medical evaluation to exclude other causes of CFS, and had hypotension provoked during stage 1 or 2 of an upright tilt table test. Together with our collaborators at Johns Hopkins, we screened 171 subjects, finding 62% of them to have abnormal tilt tests. All 100 eligible subjects were enrolled. The blinded treatment was well tolerated with no serious adverse reactions, nor concerns of our Data and Safety Monitoring Board. The study data were analyzed and were reported at the American College of Cardiology annual scientific meeting in March, 2000. The work has been submitted for publication. The study is, otherwise, terminated.*

NIMH

TITLE	AUDITORY WORKING MEMORY IN CFS--AN FMRI STUDY
P.I.	LANGE, GUDRUN
GRANT NO.	5R01MH057272-02
INSTITUTION	UNIV OF MED/DENT NJ NEWARK
ABSTRACT: *There is no text on file for this abstract.*	

NIAMS

TITLE	HPA AXIS DYSREGULATION IN FIBROMYALGIA
P.I.	CROFFORD, LESLIE J.
GRANT NO.	5R01AR043148-06
INSTITUTION	UNIVERSITY OF MICHIGAN AT ANN ARBOR

ABSTRACT: *Fibromyalgia (FM) and chronic fatigue syndrome (CFS) share many clinical features; however, we believe the difference in the dominant symptomatic manifestations, pain in FM and fatigue in CFS, reflect divergence of their biological phenotype. The onset and course of both syndromes appear to be influenced by physical or emotional stress. The physiologic response to stress is characterized by activation of the hypothalamic-pituitary-adrenal (HPA)* ***axis****. Ongoing studies of the HPA* ***axis*** *have uncovered perturbations of the pulsatile and circadian architecture of pituitary-adrenal secretion that may yield clues to the biologic divergence between FM and CFS. The findings in FM suggest psychophysiological arousal, while those in CFS suggest hypoarousal. Both syndromes are also characterized by non-restorative sleep, which is likely to be related, in a bi-directional manner, to the observed HPA* ***axis*** *disturbances. Analysis of the relationships between neuroendocrine secretory patterns and sleep-wake physiology provides a means to test the functional integrity of neural systems responsible for circadian rhythmicity, sleep regulation and hormonal release. The specific hypotheses to be tested in this proposal are: a) HPA* ***axis*** *abnormalities in FM and CFS are mediated centrally at the level of the hypothalamus through failure of integration of neurochemical systems controlling basal and stimulated hormone secretion, b) a relationship exists between mechanisms controlling sleep and HPA* ***axis*** *activity, such that correlations between neuroendocrine and sleep parameters will be present, and c) although abnormal HPA* ***axis*** *activity occurs in both FM and CFS, there are distinctions in the central inputs to the* ***axis*** *resulting in psychophysiological arousal in FM patients and hypoarousal in patients with CFS that may be revealed by close examination of specific components of the HPA* ***axis*** *and provocative testing of sleep architecture. The applicants propose to measure the dynamic pulsatile and circadian characteristics of the basal pituitary adrenal rhythm in FM and CFS patients under the influence of metyrapone, to inhibit glucocorticoid negative feedback and emphasize divergence in the central components of the HPA* ***axis****. they will examine the effects of the exogenously administered pituitary corticotroph secretagogues on pituitary-adrenal response in the study groups. They wll analyze sleep regulation and correlate sleep parameters with neuroendocrine hormone secretion. The results of these studies should further our understanding of the role of the HPA* ***axis*** *in the pathogenesis and clinical expression of FM and CFS, enlarge our understanding of the relationship between these two syndromes, and in so doing, make the informed development of reasonable diagnostic approaches and treatment interventions more likely.*

NIAMS

TITLE	HPA AXIS DYSREGULATION IN FIBROMYALGIA
P.I.	CROFFORD, LESLIE J.
GRANT NO.	5R01AR043148-06
INSTITUTION	UNIVERSITY OF MICHIGAN AT ANN ARBOR

ABSTRACT: *Fibromyalgia (FM) and chronic fatigue syndrome (CFS) share many clinical features; however, we believe the difference in the dominant symptomatic manifestations, pain in FM and fatigue in CFS, reflect divergence of their biological phenotype. The onset and course of both syndromes appear to be influenced by physical or emotional stress. The physiologic response to stress is characterized by activation of the hypothalamic-pituitary-adrenal (HPA)* ***axis****. Ongoing studies of the HPA* ***axis*** *have uncovered perturbations of the pulsatile and circadian architecture of pituitary-adrenal secretion that may yield clues to the biologic divergence between FM and CFS. The findings in FM suggest psychophysiological arousal, while those in CFS suggest hypoarousal. Both syndromes are also characterized by non-restorative sleep, which is likely to be related, in a bi-directional manner, to the observed HPA* ***axis*** *disturbances. Analysis of the relationships between neuroendocrine secretory patterns and sleep-wake physiology provides a means to test the functional integrity of neural systems responsible for circadian rhythmicity, sleep regulation and hormonal release. The specific hypotheses to be tested in this proposal are: a) HPA* ***axis*** *abnormalities in FM and CFS are mediated centrally at the level of the hypothalamus through failure of integration of neurochemical systems controlling basal and stimulated hormone secretion, b) a relationship exists between mechanisms controlling sleep and HPA* ***axis*** *activity, such that correlations between neuroendocrine and sleep parameters will be present, and c) although abnormal HPA* ***axis*** *activity occurs in both FM and CFS, there are distinctions in the central inputs to the* ***axis*** *resulting in psychophysiological arousal in FM patients and hypoarousal in patients with CFS that may be revealed by close examination of specific components of the HPA* ***axis*** *and provocative testing of sleep architecture. The applicants propose to measure the dynamic pulsatile and circadian characteristics of the basal pituitary adrenal rhythm in FM and CFS patients under the influence of metyrapone, to inhibit glucocorticoid negative feedback and emphasize divergence in the central components of the HPA* ***axis****. they will examine the effects of the exogenously administered pituitary corticotroph secretagogues on pituitary-adrenal response in the study groups. They wll analyze sleep regulation and correlate sleep parameters with neuroendocrine hormone secretion. The results of these studies should further our understanding of the role of the HPA* ***axis*** *in the pathogenesis and clinical expression of FM and CFS, enlarge our understanding of the relationship between these two syndromes, and in so doing, make the informed development of reasonable diagnostic approaches and treatment interventions more likely.*

NIMR

TITLE	ACTIVITY INTERVENTION FOR CHRONIC FATIGUE SYNDROME
P.I.	JASON, LEONARD
GRANT NO.	1R01AI049720-01
INSTITUTION	DE PAUL UNIVERSITY

ABSTRACT: *The primary purpose of this study is to evaluate the efficacy of the nurse delivered behavioral interventions of graded activity with cognitive therapy and graded activity alone in comparison to a cognitive therapy alone control condition in a target sample of 120 persons with CFS. This study will: 1) test the hypothesis that graded activity with cognitive therapy will yield significant improvements in physical and role functioning in comparison to the cognitive therapy alone control condition; and 2) test the hypothesis that graded activity alone will yield significant improvements in physical and role functioning in comparison to the cognitive therapy alone control condition. In addition, this study will test, as a secondary Aim, that graded activity alone will be as effective as graded activity with cognitive therapy in improving physical and role functioning in CFS. Since medical utilization rates for CFS patients are high and medical therapies for CFS have been largely unsuccessful, the study of a potentially effective behavioral intervention for the illness may offer an opportunity for a substantially improved quality of life in these debilitated patients.*

NCRR

TITLE	MUSCLE BLOOD FLOW AND CFS
P.I.	MCCULLY, KEVIN K
GRANT NO.	5R01HL065179-02
INSTITUTION	UNIVERSITY OF GEORGIA
ABSTRACT: *This abstract is not available.*	

TITLE	STRESS, ADRENERGIC & INFLAMMATORY FACTORS IN RA, CFS
P.I.	LIGHT, KATHLEEN C.
GRANT NO.	5M01RR000046-401141
INSTITUTION	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL

ABSTRACT: *The purpose of Study 1 is to investigate the underlying biological mechanisms associated with stress-related reactivity in subjects presenting with clinical symptoms of chronic pain, fatigue, and inflammation. The outcome may provide insight into some of the mechanisms that contribute to these common and debilitating chronic disorders. Study 2 is to investigate the effects of 6 weeks of taking propranolol, a beta-blocker (a drug generally used to treat hypertension and which decreases the pumping actions of the heart), on the underlying biological mechanisms associated with stress-related physical changes in subjects presenting with clinical symptoms of chronic pain, fatigue and inflammation. The outcome may provide insights into some of the mechanisms that contribute to these common and debilitating chronic disorders.*

TITLE	MODEL FOR INDUCTION OF CHRONIC FATIGUE STUDY
P.I.	JONES, JIM
GRANT NO.	5M01RR000051-391090
INSTITUTION	UNIVERSITY OF COLORADO HLTH SCIENCES CTR
ABSTRACT: *The purpose of this project is to study the effects of an exercise challenge and exposure to allergen on the symptoms of CFS. Our aim is to induce the symptoms of CFS with these challenges and record any abnormalities in the immune response over 24 hours. As of February 1, 2000, 54 total subjects have been enrolled in the study. 35 CFS subjects and 19 control subjects. CFS 35 31F 4M(Average age 40 y) Control 19 11F 8M(Average age 31 y) The recruitment of new control subjects is going to be limited to ages 30-45 to increase the average age within that group. To date the following challenges have been completed: Exercise 16 CFS 15 Control Total: 31 Histamine 14 CFS 13 Control Total: 27 Allergen 8 CFS 8 Control Total: 16*	

TITLE	TRIAL OF FLUDROCORTISONE FOR CHRONIC FATIGUE SYNDROME
P.I.	ROWE, PETER C.
GRANT NO.	2M01RR000052-390751
INSTITUTION	JOHNS HOPKINS UNIVERSITY
ABSTRACT: *The trial is based on preliminary data showing that upright tilt table testing can provoke a drop in blood pressure consistent with neurally mediated hypotension (NMH) in a high proportion of those with chronic fatigue syndrome (CFS), and that unblinded treatment of the NMH leads to an improvement in CFS symptoms in 40-70% of CFS patients. The specific aim of this study is to determine whether patients aged 18 to 50 years with CFS and NMH will have a greater improvement in (1) self-reported general sense of well being and (2) objective orthostatic tolerance when treated with fludrocortisone than when treated with placebo. Eligible subjects are randomized to receive either fludrocortisone (escalating to 0.1 mg/day) or placebo for nine weeks. In week 8-9 of treatment, subjects undergo repeat tilt testing. The primary outcome measure is the proportion with a 15 point improvement in wellness on a 100 point wellness score, and a secondary outcome is the proportion with improvement in the number of minutes before the development of hypotension during upright tilt.*	

TITLE	CHRONIC FATIGUE IN POST LYME DISEASE
P.I.	KRUPP, LAUREN
GRANT NO.	5M01RR010710-030029
INSTITUTION	STATE UNIVERSITY NEW YORK STONY BROOK
ABSTRACT: *The primary objective of STOP-LD is to determine if parenteral antibotic treatment is an effective treatment for patients with chronic fatigue following Lyme Disease. If the study fundings indicate that patients improve with antibiotic therapy according to the STOP-LD outcome measures, it will set an important precedent for treatment of Post Lyme Syndrome (PLS) and provide support for a syndrome pathogenesis involving chronic infection. If no difference between antibiotic and placebo therapy is observed, this will be important objective data suggesting the inappropriateness of repeated courses of antibiotic therapy for PLS.*	

TITLE	NASAL STEROIDS & CHRONIC FATIGUE SYNDROME INDUCED SLEEP DISTURBANCE
P.I.	CRAIG, TIMOTHY J.
GRANT NO.	2M01RR010732-060186
INSTITUTION	PENNSYLVANIA STATE UNIV HERSHEY MED CTR
ABSTRACT: *The purpose of this study is to compare the effectiveness of Nasarel and placebo in adults with Chronic Fatigue Syndrome with nasal congestion and sleep disturbances to determine if use of inhaled nasal steroids makes a difference in sleep disturbances*	