AD	1	

Award Number: DAMD17-02-1-0665

TITLE: Neural Mechanisms of Chronic Fatigue Syndrome

PRINCIPAL INVESTIGATOR: Guang H. Yue, Ph.D.

CONTRACTING ORGANIZATION: Cleveland Clinic Foundation

Cleveland, Ohio 44195

REPORT DATE: April 2003

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command

Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;

Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT		OMB No. 074-0188								
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existir reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Papers) data sources, gathering and maintaining the data needed, and completing and or reducing this burden to Washington Headquarters Services, Directorate for						
Information Operations and Reports, 1215 Jefferson Davis 1. AGENCY USE ONLY (Leave blank)	Highway, Suite 1204, Arlington, VA 22202-4302, and to the 0	Office of Management and Budget, Paperw 3. REPORT TYPE AND DA	rk Reduction Project (07	04-0188), Washington, DC 20503						
1. AGENCY OSE ONLY (Leave blank)	April 2003	Annual (1 Apr		r 03)						
4. TITLE AND SUBTITLE	1		5. FUNDING N							
	of Chronic Fatigue	Syndrome		02-1-0665						
Nedrai Mechanisms	or chronic racigae	by narounc	DIMIDI	02 1 0005						
6. AUTHOR(S):										
Guang H. Yue, Ph.D)_									
7. PERFORMING ORGANIZATION NAMI	E(S) AND ADDRESS(ES)		8. PERFORMING ORGANIZATION REPORT NUMBER							
Cleveland Clinic F	loundation		,,_,							
Cleveland, Ohio 4	4195									
1										
E-Mail: yueg@ccf.org										
9. SPONSORING / MONITORING AGEN	ICY NAME(S) AND ADDRESS(ES)		10. SPONSORING / MONITORING							
			AGENCY RI	PORT NUMBER						
U.S. Army Medical Research an			•							
Fort Detrick, Maryland 21702-5	5012									
11. SUPPLEMENTARY NOTES										
11. SUPPLEMENTARY NOTES										
12a. DISTRIBUTION / AVAILABILITY ST				12b. DISTRIBUTION CODE						
Approved for Public Re	elease; Distribution Uni	limited								
				.						
13. Abstract (Maximum 200 Words) (abstract should contain no proprieta	ry or confidential informatio	2)							
Nearly one million Ame	ricans suffer from chro	onic fatigue synd	drome (CFS	3). More than 15% of						
Gulf war veterans (GWV) were found to have Ci	ss. The disease s	eignificar of HC mil	Gulf War veterans (GWV) were found to have CFS. The disease significantly reduces work						
Increasing scientific	production of civilian patients and combat ability/readiness of US military forces. Increasing scientific evidence suggests that CFS is a biological illness involving									
pathology of the centr	evidence suggests that	CFS is a biolog:	ical illne	itary forces. ess involving						
is affected by CFS. Th	evidence suggests that cal nervous system (CNS)	CFS is a biolog: . However, littl	ical illne le is know	ess involving on about how the CNS						
during fatigue and non-fatigue muscle exercises. Our hypothesis is that the brain										
1	evidence suggests that ral nervous system (CNS) his study will focus on a-fatigue muscle exercis	CFS is a biolog: . However, little evaluating braines. Our hypothes	ical illne le is know n activiti sis is tha	ess involving on about how the CNS es of CFS patients at the brain						
activation pattern in	evidence suggests that all nervous system (CNS) all study will focus on a fatigue muscle exercise CFS differs from that of	CFS is a biological to the control of the control o	cal illne le is know n activiti sis is tha ols. Aim 1	ess involving on about how the CNS es of CFS patients at the brain of the study is to						
activation pattern in determine brain activa	evidence suggests that ral nervous system (CNS) is study will focus on a-fatigue muscle exercise CFS differs from that of ation patterns during more	CFS is a biological to the control of the control o	cal illne le is know n activiti sis is tha ols. Aim 1 CFS patie	ess involving on about how the CNS des of CFS patients det the brain def the study is to ents using functional						
activation pattern in determine brain activa magnetic resonance ima	evidence suggests that ral nervous system (CNS) is study will focus on a fatigue muscle exercise CFS differs from that of ation patterns during marging. Aim 2 is to examinate the exercise control of the control of th	CFS is a biological to the control of the control o	cal illnet is known activition is is the color of the col	ess involving m about how the CNS es of CFS patients at the brain of the study is to ents using functional erns during motor						
activation pattern in determine brain activa magnetic resonance ima activity in CFS patien	evidence suggests that ral nervous system (CNS) is study will focus on a-fatigue muscle exercise CFS differs from that of ation patterns during more	CFS is a biological to the control of the control o	cal illne is known activities is the ols. Aim 1 CFS pation patte ohalograms	ess involving m about how the CNS es of CFS patients at the brain of the study is to ents using functional erns during motor s. Aim 3 is to						
activation pattern in determine brain activated magnetic resonance impactivity in CFS patient evaluate signal relations muscle. Measurements were made activity in the magnetic magneti	evidence suggests that all nervous system (CNS) all study will focus on a fatigue muscle exercise CFS differs from that all tion patterns during making. Aim 2 is to examinate by analyzing signals onships among different will be made from four of	CFS is a biological control of the c	cal illned is known activities is the color of the color	ess involving m about how the CNS es of CFS patients at the brain of the study is to ents using functional erns during motor e. Aim 3 is to en the brain and civilian CFS group,						
activation pattern in determine brain activation magnetic resonance impactivity in CFS patient evaluate signal relations muscle. Measurements was civilian control groups a civilian control groups with the control groups and the control groups are signal control groups.	evidence suggests that all nervous system (CNS) all study will focus on a fatigue muscle exercise CFS differs from that all tion patterns during make a tion patterns during makes by analyzing signals conships among different will be made from four coup, a GWV CFS group, ar	CFS is a biological control of the c	cal illned is known activities is is the color of the col	ess involving m about how the CNS es of CFS patients at the brain of the study is to ents using functional erns during motor e. Aim 3 is to en the brain and civilian CFS group,						
activation pattern in determine brain activation magnetic resonance impactivity in CFS patient evaluate signal relations muscle. Measurements was civilian control groups a civilian control groups with the control groups and the control groups are signal control groups.	evidence suggests that all nervous system (CNS) all study will focus on a fatigue muscle exercise CFS differs from that all tion patterns during making. Aim 2 is to examinate by analyzing signals onships among different will be made from four of	CFS is a biological control of the c	cal illned is known activities is is the color of the col	ess involving m about how the CNS es of CFS patients at the brain of the study is to ents using functional erns during motor e. Aim 3 is to en the brain and civilian CFS group,						
activation pattern in determine brain activation magnetic resonance impactivity in CFS patient evaluate signal relations muscle. Measurements was civilian control groups a civilian control groups with the control groups and the control groups with the control groups and the control groups with the control groups and the control groups with	evidence suggests that all nervous system (CNS) all study will focus on a fatigue muscle exercise CFS differs from that all tion patterns during make a tion patterns during makes by analyzing signals conships among different will be made from four coup, a GWV CFS group, ar	CFS is a biological control of the c	cal illned is known activities is is the color of the col	ess involving m about how the CNS es of CFS patients at the brain of the study is to ents using functional erns during motor e. Aim 3 is to en the brain and civilian CFS group,						
activation pattern in determine brain activation magnetic resonance impactivity in CFS patient evaluate signal relations muscle. Measurements was civilian control groups a civilian control groups with the control groups and the control groups are signal control groups.	evidence suggests that all nervous system (CNS) all study will focus on a fatigue muscle exercise CFS differs from that all tion patterns during make a tion patterns during makes by analyzing signals conships among different will be made from four coup, a GWV CFS group, ar	CFS is a biological control of the c	cal illned is known activities is is the color of the col	ess involving m about how the CNS es of CFS patients at the brain of the study is to ents using functional erns during motor e. Aim 3 is to en the brain and civilian CFS group,						
activation pattern in determine brain activation magnetic resonance imaterized activity in CFS patient evaluate signal relation muscle. Measurements was civilian control grostudy will provide obj	evidence suggests that all nervous system (CNS) all study will focus on a fatigue muscle exercise CFS differs from that all tion patterns during make a tion patterns during makes by analyzing signals conships among different will be made from four coup, a GWV CFS group, ar	CFS is a biological control of the c	cal illned is known activities is is the color of the col	ess involving on about how the CNS des of CFS patients det the brain def the study is to ents using functional erns during motor def the brain and civilian CFS group, defeated that the						
activation pattern in determine brain activation magnetic resonance imaterized activity in CFS patient evaluate signal relation muscle. Measurements was a civilian control grostudy will provide obj	evidence suggests that cal nervous system (CNS) is study will focus on a fatigue muscle exercise CFS differs from that cation patterns during maging. Aim 2 is to examinate by analyzing signals conships among different will be made from four coup, a GWV CFS group, are ective information for	CFS is a biologic. However, little evaluating brain ses. Our hypothese of healthy control to activity in the brain activate of electroences brain regions a groups of participal a GWV control diagnosis of CFS	cal illned is known activities is is the color of the col	ess involving on about how the CNS des of CFS patients det the brain def the study is to ents using functional erns during motor def. Aim 3 is to en the brain and civilian CFS group, defeate that the						
activation pattern in determine brain activation magnetic resonance imaterized activity in CFS patient evaluate signal relation muscle. Measurements was a civilian control grostudy will provide obj	evidence suggests that all nervous system (CNS) all study will focus on a fatigue muscle exercise CFS differs from that all tion patterns during make a tion patterns during makes by analyzing signals conships among different will be made from four coup, a GWV CFS group, ar	CFS is a biologic. However, little evaluating brain ses. Our hypothese of healthy control to activity in the brain activate of electroences brain regions a groups of participal a GWV control diagnosis of CFS functional MRI,	cal illnete is known activities is the ols. Aim I CFS paties ion patter ohalograms and between pants: a group. West.	ess involving on about how the CNS des of CFS patients det the brain def the study is to ents using functional erns during motor def. Aim 3 is to en the brain and civilian CFS group, defer expect that the						
activation pattern in determine brain activation magnetic resonance imagnetic resonance imagnetic resonance imagnetic resonance imagnetivity in CFS patient evaluate signal relations. Measurements was a civilian control growth study will provide objective. 14. SUBJECT TERMS: Chronic Fatigue Syndrogelectroencephalogram extinity brain active.	evidence suggests that cal nervous system (CNS) is study will focus on a fatigue muscle exercise CFS differs from that cation patterns during more aging. Aim 2 is to examinate by analyzing signals conships among different will be made from four coup, a GWV CFS group, and ective information for the coup, a Gulf War Syndrome, (EEG), electromyogram (EEG	CFS is a biolog: O. However, little evaluating brain ses. Our hypothes of healthy control to activity in the brain activate of electroences brain regions a groups of particular a GWV control diagnosis of CFS functional MRI, EMG), brain motor lency	cal illne is known activities is is the ols. Aim I CFS paties ion patter ohalograms and between pants: a group. We see that it is a group.	m about how the CNS les of CFS patients let the brain let of the study is to ents using functional erns during motor let Aim 3 is to ent the brain and civilian CFS group, expect that the 15. NUMBER OF PAGES 4 16. PRICE CODE						
activation pattern in determine brain activation magnetic resonance imaterial activity in CFS patient evaluate signal relation muscle. Measurements was a civilian control ground study will provide object TERMS: Chronic Fatigue Syndroelectroencephalogram	evidence suggests that ral nervous system (CNS) is study will focus on a fatigue muscle exercise CFS differs from that of a tion patterns during more aging. Aim 2 is to example the state of the state	CFS is a biology. However, little evaluating brain ses. Our hypothes of healthy control to a ctivity in the brain activate of electroences brain regions a groups of particular a GWV control diagnosis of CFS functional MRI, EMG), brain motor	cal illne is known activities is is the ols. Aim I CFS paties ion patter ohalograms and between pants: a group. We see that it is a group.	ess involving m about how the CNS es of CFS patients at the brain of the study is to ents using functional erns during motor. Aim 3 is to en the brain and civilian CFS group, expect that the						

Form Approved

Table of Contents

Cover	1
SF 298	2
Table of Contents	3
Introduction	4
Body	4
Key Research Accomplishments	NA
Reportable Outcomes	NA
Conclusions	NA
References	NA
Appendices	NA

INTRODUCTION

Chronic fatigue syndrome (CFS) is an illness that affects quality of life of both civilian and military populations. However, the diagnosis of CFS is difficult to make because of the absence of specific biomedical markers. Thus, the diagnosis depends primarily on determining whether subjective information provided by the patient meets the clinical case definition of the syndrome. The purpose of this study is to determine whether the central nervous system signals of CFS patients for performing fatigue and non-fatigue motor activities are impaired compared to the signals of healthy volunteers. It is hypothesized that the CNS signals of CFS patients will significantly differ from those of healthy controls. It is expected that at least one or more measurements made by this study will serve as "biological markers" for more objective diagnoses of CFS.

BODY

This report covers the first year of work related to this study. Up to date, there are still no results available yet. The experiments are under way and we expect to report findings of the study by the midterm or the 2nd-year annual report. The tasks that were performed in the first year include:

- I. Ordering equipment and supplies. All pieces of major equipment that were requested have been ordered, tested, and are being used for data collection and analyses.
- II. Filing IRB (Institutional Review Board) applications. Three IRB applications were made. Final IRB approval from the principal investigator's institution, the Cleveland Clinic Foundation was obtained shortly after the grant was awarded. The final approval from the Office of Regulatory Compliance and Quality, U.S. Army Medical Research and Materiel Command was given in September 2002. We also filed an application to the IRB Office of Louis Stokes Cleveland Veteran Affairs (VA) Medical Center in order to recruit the Gulf War veterans as research subjects. This application process has been quite long but the final approval is expected to be offered in May 2003. Despite the slow progress of the VA IRB application, and therefore, slow progress of the Gulf War veteran subject recruitment, we have already began data collection from civilian CFS patients and control subjects (see below).
- III. Recruiting research subjects. Twelve civilian CFS patients have been recruited from the Cleveland Clinic and 6 patients has been tested. Ten civilian control subjects have also been recruited and 4 have been tested. More subjects will be recruited in the coming months. We are currently testing more subjects and performing initial data analysis of the tested subjects. We will begin to recruit the Gulf War veteran subjects as soon as the approval from the IRB Office of Louis Stokes Cleveland VA Medical Center is obtained.
- IV. Data collection and analysis. As indicated in the last paragraph, we have performed data collection from 10 subjects and begun initial data analysis. We expect that preliminary results will be ready for presentation or publication during near the end of the second year of the project.