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AWARD NUMBER: DAMD17-02-1-0665

TITLE: Neural Mechanisms of Chronic Fatigue Syndrome

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REPORT DATE: April 2006

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. REPORT DATE (DD-MM-YYYY) 01-04-2006		2. REPORT TYPE Final		3. DATES COVERED (From - To) 1 Apr 2002 – 31 Mar 2006	
4. TITLE AND SUBTITLE Neural Mechanisms of Chronic Fatigue Syndrome				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER DAMD17-02-1-0665	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Guang H. Yue, Ph.D. E-Mail: yueg@ccf.org				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Cleveland Clinic Foundation Cleveland, Ohio 44195				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT Nearly one million Americans suffer from chronic fatigue syndrome (CFS). More than 15% of Gulf War veterans (GWV) were found to have CFS. The disease significantly reduces work 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 central nervous system (CNS). However, little is known about how the CNS is affected by CFS. This study will focus on evaluating brain activities of CFS patients during fatigue and non-fatigue muscle exercises. Our hypothesis is that the brain activation pattern in CFS differs from that of healthy controls. Aim 1 of the study is to determine brain activation patterns during motor activity in CFS patients using functional magnetic resonance imaging. Aim 2 is to examine brain activation patterns during motor activity in CFS patients by analyzing signals of electroencephalograms. Aim 3 is to evaluate signal relationships among different brain regions and between the brain and muscle. Measurements will be made from four groups of participants: a civilian CFS group, a civilian control group, a GWV CFS group, and a GWV control group. We expect that the study will provide objective information for diagnosis of CFS.					
15. SUBJECT TERMS Chronic fatigue syndrome, Gulf War Syndrome, functional MRI, electroencephalogram (EEG) Electromyogram (EMG), brain motor activity, brain activation pattern, EEG frequency					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	6	19b. TELEPHONE NUMBER (include area code)

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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 work of the entire duration of the study. We have had a total of 11 peer-reviewed articles either published (7) in, are in press (2) in, or have been accepted (2) by high-quality scientific or clinical journals (see below for the list of the references). Another manuscript reporting changes of brain signal source locations in chronic fatigue patients is under preparation and we plan to submit this manuscript early next year (see the publication #12 in the Reference below). These studies were either supported solely by this grant or were jointly supported by this grant and other awards (mainly from NIH). Further analyses of data collected in the past four years are still ongoing and more publications are expected in the future.

Key Research Accomplishments

- I. Twelve manuscripts have been published or will be published soon in high-quality clinical and scientific journals (see References).
- II. Twelve presentations related to the topic of this study have been made at regional, national, and international scientific conferences

Reportable Outcomes

- I. Motor performance of the CFS patients was poorer than the controls [3].
- II. Relative power of EEG theta frequency band (4-8 Hz) during performing a non-fatigue (NFT) and fatigue (FT) task was significantly greater in the CFS than control group [3].

- III. The amplitude of negative potential (NP), a major component of EEG-derived movement-related cortical potential for the combined NFT and FT tasks was higher in the CFS than control group [3].
- IV. Within the CFS group, the NP was greater for the FT than NFT task, whereas no such difference between the two tasks was found in the control group [3].
- V. Compared to healthy individuals, the EEG source of the CFS patients shifted towards anterior-inferior location of the brain during the fatigue task [12].
- VI. The source strength was different between the CFS and control groups during both the fatigue and non-fatigue tasks [12].
- VII. In healthy humans, physical activity-induced fatigue occurs mainly in the muscle; there is little fatigue in the central nervous system [1,5,11].
- VIII. Developed methods to quantify physiological connection among brain regions [6] and between the brain and muscle [8].
- IX. Developed methods to quantify brain white matter structures [2,7,9].
- X. Quantified reproducibility of functional magnetic resonance imaging (fMRI) data of the brain [4].
- XI. Found relationship between non-linear EEG and muscle force and fatigue [10].
- XII. Found that cancer related fatigue (CRF) during motor performance is contributed more significantly by the central (brain) than peripheral (muscle) mechanisms [13].

Conclusions

The results show that chronic fatigue syndrome involves altered central nervous system signals in controlling voluntary muscle activities, especially when the activities induce fatigue. Physical activity-induced EEG signal changes may serve as biological/physiological markers for more objective diagnosis of CFS.

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