

AD _____
(Leave blank)

Award Number: W81XWH-08-2-0211

TITLE: Deep Brain Stimulation Deep Brain Stimulation of Treatment of Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: Imad Najm, MD

CONTRACTING ORGANIZATION: Cleveland Clinic Foundation
Cleveland, OH 44195

REPORT DATE: October 2009

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 DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188		
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE (DD-MM-YYYY) 25-10-2009		2. REPORT TYPE Annual		3. DATES COVERED (From - To) 26 Sept 2008 - 25 Sept 2009	
4. TITLE AND SUBTITLE Deep Brain Stimulation of Treatment of Traumatic Brain Injury			5a. CONTRACT NUMBER W81XWH-08-2-0211		
			5b. GRANT NUMBER		
			5c. PROGRAM ELEMENT NUMBER		
6. AUTHOR(S) Imad Najm, MD Email: Najmi@ccf.org			5d. PROJECT NUMBER		
			5e. TASK NUMBER		
			5f. WORK UNIT NUMBER		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Cleveland Clinic 9500 Euclid Avenue Cleveland, OH 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 This document explains the change in Principal Investigator for the award as of 13 Jul 2009. The initial Principal Investigator has relocated to another institution, and has relinquished the award back to Cleveland Clinic. Subsequent conversations with TATRC have led to a new project focus, utilizing deep brain stimulation (DBS) for the treatment of traumatic brain injury-related epilepsy. The new Principal Investigator, Dr. Imad Najm, is in the process of finalizing his protocol and obtaining final institution approval to commence the study.					
15. SUBJECT TERMS Epilepsy, epileptogenesis, deep brain stimulation					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 5	
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19a. NAME OF RESPONSIBLE PERSON USAMRMC
					19b. TELEPHONE NUMBER (include area code)

Table of Contents

	<u>Page</u>
Introduction.....	1
Body.....	N/A
Key Research Accomplishments.....	N/A
Reportable Outcomes.....	N/A
Conclusion.....	N/A
References.....	N/A
Appendices.....	N/A

Introduction

This award (W81XWH-08-2-0211) was initially focused on investigating the use of deep brain stimulation (DBS) on traumatic brain injured patients in a minimally conscious state. However in July of 2009, the initial Principal Investigator left the institution for another position. The individual ceded the award back to Cleveland Clinic.

At that time, Cleveland Clinic (with approval of the Telemedicine & Advanced Technology Research Center) decided to alter the focus of the award to take better advantage of the unique resources and capabilities at Cleveland Clinic to focus on the application of deep brain stimulation (DBS) for the treatment of post-traumatic brain injury (TBI) epilepsy.

One of the aforementioned resources at Cleveland Clinic is our Epilepsy Center. Cleveland Clinic has one of the largest and most comprehensive programs in the world for the evaluation and medical and surgical treatment of epilepsy in children and adults.

The Epilepsy Center was established at the Cleveland Clinic to meet the unique needs of patients with pediatric and adult epilepsy. Very few medical centers in the United States, and in the world, provide the range of care that is available here.

Our project melds the talents of the epileptologists and clinical neurophysiologists within the Epilepsy Center with the DBS expertise located in the Clinic's Center for Neurological Restoration. The intellectual and physical resources found within these two centers will be brought to bear on epilepsy, a condition which has been shown to develop in an increased frequency for individuals having suffered a TBI.

The goal of our highly multidisciplinary and translational proposal is to detect surrogate markers of potentially epileptogenic regions non-invasively (through neurophysiologic/EEG and imaging/MRI studies), prevent epileptogenesis, and control epilepsy by selectively applying electrical stimulation (ES) of brain structures directly involved in the generation and/or spread of paroxysmal activity. Based on the results of the animal studies, we will design a pilot clinical study using chronic low frequency deep brain electrical stimulation of the thalamus on a small number of patients with non-surgically remediable medically intractable epilepsy secondary to traumatic brain injury.

We will accomplish our goals through the use of our unique and highly multidisciplinary translational resources within the Neurological Institute (Epilepsy Center, Center for Neurological Restoration, and Neuroimaging Center). Specifically, we plan to accomplish the following in a rat model of TBI and patients with TBI-induced medically intractable epilepsy:

Aim 1: To study the imaging (MRI) and acute/subacute electroencephalographic (EEG) changes following TBI in the rat and assess the predictive value of the changes in the later development of epilepsy (imaging and neurophysiological surrogates of epileptogenesis)

Aim 2: To test the effect of continuous, chronic stimulation (LFS and HFS) of the central thalamus on FPI-induced epileptogenesis in the rat. We hypothesize that continuous LFS of the central thalamus will prevent the development of FPI-induced epileptogenesis through its

neuromodulatory effect on its cortical target areas (in particular the frontal cortical regions which are the most affected by TBI), and will prevent the later recurrence of spontaneous seizures in animals after they develop spontaneous seizures (neuromodulatory effect of the DBS on epileptogenesis following TBI).

Aim 3: To test the effect of thalamic chronic electrical stimulation on TBI-induced seizures in the rat. Because we have recently shown that thalamic stimulation alone significantly reduces seizure severity in a model of generalized seizures, we hypothesize that thalamic stimulation will suppress seizures following TBI (antiepileptic effect of DBS following TBI).

Aim 4: To design a pilot study to assess the effect of DBS on a small group of patients who suffer from medically intractable epilepsy following TBI.

To date, no funds have been expended on research for either the previous project or the final project concept focusing on epilepsy. We are now in the process of finalizing our protocol and obtaining final institutional approval. We anticipate beginning our study no later than the first quarter of 2010, and for the data acquisition portion of the study to occur within 24 months.