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TITLE: MISSION CONNECT MILD TBI TRANSLATIONAL RESEARCH CONSORTIUM

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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> The purpose of this project is to identify the incidence of post traumatic hypopituitarism (PTH) in mild TBI and develop criteria for assessing which patients with a mild TBI are at risk for developing PTH. This study will also correlate the characteristics of the individuals with PTH by neuropsychological, neurophysiological and imaging testing as they relate to functional outcome.  At 6 months post injury, patients will be screened for anterior pituitary function.  IRB approvals have been obtained and an Integrated Clinical Protocol has been developed. Operational procedures have been developed. Initial recruitment has been slow. Eleven subjects have been recruited as of June 21, 2010; however, none have reached the six month milestone for blood testing					
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**Introduction:**

The purpose of this project will be to study the diagnosis of post traumatic hypopituitarism after MTBI. We will determine the incidence of hypopituitarism following MTBI and develop criteria for assessing which MTBI patients are at high risk for developing posttraumatic hypopituitarism and should have routine post-injury screening. We will also determine the relationship between post-traumatic hypopituitarism and functional outcome, cognitive recovery, and resolution of PCS at six months after MTBI. At 6 months post-injury, patients will be screened for anterior pituitary function by measuring IGF1, total testosterone in males, 17 beta estradiols in females, prolactin, TSH, and morning cortisol. The incidence of single and multiple pituitary hormone deficiencies will be determined. The clinical characteristics, MRI imaging results, EEG and MEG results of the patients who have pituitary deficiency will be compared to those of patients with normal pituitary function. The relationship between pituitary dysfunction and functional outcome, cognitive recovery, and resolution of PCS will be examined.

**Body of report****SA #2.3: To study diagnosis of post-traumatic hypopituitarism after MTBI**

**SA #2.3.1:** To determine the incidence of hypopituitarism following MTBI.

**SA #2.3.2:** To develop criteria for assessing which MTBI patients are at high risk for developing posttraumatic hypopituitarism and should have routine post-injury screening.

Relative to SA #2.3.1 and 2.3.2:

Eleven subjects have been recruited as of June 21, 2010; however, as of this date, none have reached the 6 month endpoint for pituitary testing.

I have been an active participant in the Clinical Working Group as well as at the Partnering PI Quarterly meetings.

My facility holds an invited conference every year. The focus of this year's conference was Translational Research, with the main focus on blast--from the physics to the clinical issues. Many of the speakers and attendees were members of the Mission Connect consortium.

**Key research accomplishments:**

The recruitment of study subject has begun (11 subjects as of June 30, 2010); however, as of this date, there have been no 6 month pituitary studies done.

A paper entitled: *The Effects of Growth Hormone Replacement Therapy on Cognition after Traumatic Brain Injury*, has been accepted for poster and platform presentation at the 27<sup>th</sup> Army Science Conference in Orlando in November, 2010.

**Reportable outcomes:**

A proposal was submitted to the DOD on March 31, 2010. This proposed study would entail screening and treating blast and non-blast injured soldiers with mild TBI recruited from the Neurology Clinic at Camp Lejeune for pituitary dysfunction. These individuals would be invited to participate in this placebo controlled double blind study of growth hormone replacement. This study would include imaging, physical testing and neuropsychological testing.

This study would also include a cohort recruited from the Mission Connect MTBI clinical study. These individuals would have already been screened for pituitary dysfunction and would be invited to participate as well.

Many of the investigators in this study are part of the Mission Connect MTBI Consortium.

**Conclusion:**

As of June 21, 2010, eleven subjects have been recruited for the clinical trials. Dr. Levin's report addresses the fact that recruitment has been slower than anticipated, and discusses the measures taken to improve upon this problem.

Pituitary dysfunction as a result of moderate to severe TBI has been extensively documented in recent studies with approximately 30 to 40% of subjects showing a deficiency of one or more anterior pituitary hormones. Growth hormone deficiency (GHD) is the most common of these at approximately 20%, while the incidence of GHD in the non-brain injured population is <1 %. However, there are no published studies on the prevalence of GHD in mTBI. We estimate that approximately 30% of symptomatic individuals with mTBI will have GHD.

Fatigue is one of the most common complaints following TBI, and is also a common symptom in individuals with GHD. Symptoms of fatigue may hinder civilians from returning to normal life activities or hinder soldiers from returning to active duty. The interplay between psychological fatigue and physical fatigue is variable. Our group has found that individuals with GHD from a moderate-severe TBI have a decreased exercise capacity when compared to a similar TBI cohort with normal GH levels, and in a case report found improvement in muscle force production, body composition and aerobic capacity after rhGH replacement in a subject with mTBI. A recent mTBI literature review stated that "specific to drug interventions, this review has failed to produce solid evidence that any specific drug treatment is effective for one or more symptoms of mTBI" (Comper R, Bisschop SM, Carnide N, Tricco A. A systematic review of treatments for mild traumatic brain injury. *Brain Injury* 2005; 19:863-880.) This research will be the first to identify the incidence of pituitary dysfunction in mTBI, and will hopefully lead to a treatment study that would not only address the complex issue of neuropsychological sequelae of mTBI, but would provide a pharmacological treatment for these symptoms that, to our knowledge, has not been previously identified.



**References:**  
None

**Appendices:**  
None