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TITLE: Plasticity-Based Adaptive Cognitive Remediation (PACR) for OIF/OEF Veterans: A Randomized Controlled Trial

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14. ABSTRACT Our work in the past year has focused on submission of IRB materials for each site training all site study staff on study procedures. In particular, we initiated two clinical trials site – the Boston VA and the Connecticut VA. Both sites now have all relevant regulatory approval to begin enrolling patients. This is a major milestone in the development of the study. The Houston VA is awaiting final HRPO approval of its revised IRB, confirming that it was reviewed by a fully convened IRB. Walter Reed has received IRB approval from HRPO, and will be initiated when the Henry Jackson foundation completes the hiring process for their psychometrician. Tripler is now submitting their IRB now that Walter Reed has completed their process.					
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Table of Contents

	<u>Page</u>
Introduction.....	4
Body.....	4
Key Research Accomplishments.....	5
Reportable Outcomes.....	5
Conclusion.....	5
References.....	n/a
Appendices.....	n/a

Introduction:

Traumatic brain injury (TBI) has been described as “the signature injury” of the war in Iraq and Afghanistan. The long-term impacts of chronic cognitive symptoms following TBI for active military personnel, veterans, their families, and for American society as a whole is only now beginning to be appreciated. We have developed a novel treatment program that can deliver effective brain-plasticity-based cognitive remediation (“PACR”) to veterans and active duty military personnel suffering from persistent post-concussive symptoms (PPCS) following mild traumatic brain injury (mTBI) at any internet-connected computer, under the controlled, monitored, quality-assured remote guidance of trained clinical providers. PACR holds tremendous promise because 1) the *innovative therapeutic approach* differs from current treatments in that it uses the principles of brain plasticity to restore, insofar as is possible, the brain’s capacity to process information with high accuracy and efficiency, 2) it implements a *practical and novel delivery approach* with a web-based implementation that can assure the provision of essential cognitive remediation to active personnel and veterans in need of help wherever they may be, and 3) a *significant body of randomized controlled clinical trial data* demonstrates that PACR improves cognitive and real-world function in people with the mild cognitive impairment typical of PPCS following mTBI. Given the substantial unmet medical need in these patients, the basic science rationale and the demonstrated clinical evidence for a brain-plasticity-based cognitive remediation approach, and the scalable technical solution, we propose a clinical trial of PACR in people with PPCS following mTBI. The final product of the activities funded from this grant will be the establishment of a complete brain-plasticity-based cognitive remediation system for use by the Veterans Affairs (VA) and the military that provides scientifically validated, clinically supervised treatment with demonstrable outcomes, delivered in a highly cost-effective and readily scalable form.

Body: Our work in the past year has focused on submission of IRB materials for each site training all site study staff on study procedures. In particular, we initiated two clinical trials site – the Boston VA and the Connecticut VA. Both sites now have all relevant regulatory approval to begin enrolling patients. This is a major milestone in the development of the study. The Houston VA is awaiting final HRPO approval of its revised IRB, confirming that it was reviewed by a fully convened IRB. Walter Reed has received IRB approval from HRPO, and will be initiated when the Henry Jackson foundation completes the hiring process for their psychometrician. Tripler is now submitting their IRB now that Walter Reed has completed their process.

1. **Task 1:** Update protocol if necessary. We generally completed this activity in year one, and made minor amendments in year 2 to accommodate regulatory requirements.
2. **Task 2:** Prepare sites for clinical trial
 - a. **Task 2a:** Conclude contractual agreements. Complete.
 - b. **Task 2b:** Submit IRB materials. Our most important accomplishment was achieving full coordinating center, HRPO, and site IRB clearance for two out of five sites, and being in progress in the remaining nearly complete

on the fifth site (Tripler). Tripler is awaiting formal notice of its inclusion under the Walter Reed IRB process. This inclusion proved to be more complex than forecast by the Tripler and Walter Reed staff, but is now nearly complete.

- c. **Task 2c:** Train site study staff on study procedures: Complete.
- d. **Task 2d:** Implement study database and electronic data collection system. Complete
- 3. **Task 3:** Collect normative data for co-primary outcome measures: pushed forward.
- 4. **Task 4:** Execute study with 132 enrolled participants at five trial sites: Next focus of activity.
- 5. **Task 5:** Analyze data, prepare study publications: awaiting study completion

Key Research Accomplishments: Beginning enrollment in the clinical trial is a significant research accomplishment, given our extended IRB period. Enrollment is now proceeding smoothly.

Reportable Outcomes: None to date

Conclusions: None to date