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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 over year 3 of this project has focused on completing IRB issues required to launch a multi-site trial with VA and military hospital sites funded through the CDMRP process, and launching patient enrollment. As expected, this process has been time-consuming; however four out of five sites are now IRB approved, and the fifth (Tripler) is awaiting final approval. Below is a list of research-related activities, organized by the key activities in our approved statement of work.						
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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 over year 3 of this project has focused on completing IRB issues required to launch a multi-site trial with VA and military hospital sites funded through the CDMRP process, and launching patient enrollment. As expected, this process has been time-consuming; however four out of five sites are now IRB approved, and the fifth (Tripler) is awaiting final approval. Below is a list of research-related activities, organized by the key activities in our approved statement of work.

1. **Task 1:** Update protocol if necessary. We generally completed this activity in year one, and made minor amendments in years 2 and 3 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 four out of five sites, and being 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 [months 11-34]: see below enrollment table. Current focus of activity.
- 5. **Task 5:** Analyze data, prepare study publications: awaiting study completion

Enrollment Table:

Site	IRB Status	Participants Consented	Participants Randomized	Participants Completed
ALL (total)		105	49	15
VA Connecticut	Fully approved	23	12	6
VA Houston	Fully approved	14	12	7
VA Boston	Fully approved	26	16	2
Walter Reed	Fully approved	25	4	0
Tripler	Awaiting approval	17	5	0

Key Research Accomplishments: Enrollment is now proceeding smoothly with all five trial sites active.

Reportable Outcomes: None to date

Conclusions: None to date