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TITLE: "Diagnosing Contributions of Sensory and Cognitive Deficits to Hearing Dysfunction in Blast-Exposed/TBI Service Members"

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14. ABSTRACT <i>brief (~200 word) unclassified summary of most significant finding during the research period</i> The primary focus of Year 2 of the study has been subject recruitment. At the conclusion of Year 2 we have consented 53 (36 male, 17 female) potential study participants of which 38 (25 male, 13 female) were eligible for full participation. After attrition, we currently have data from 25 subjects (19 controls and 6 blast-exposed) who have participated in the auditory (ASA) and visual (VSA) selective attention/frequency-following response (FFR) tasks. Recruitment of subjects for the blast-exposed experimental group has proven to be more challenging than originally anticipated; however, we have made adjustments to our inclusion criteria and have extended our recruitment efforts to audiology clinics outside of the Walter Reed National Military Medical. These new recruitment efforts are being led by new hires Research Audiologist, Dr. Kimberly Jenkins (filling the vacancy left from Dr. Lynn Bielski's departure), and Research Communication Scientist, Dr. Jennifer Myers.					
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## 1. Introduction

Blast-exposed Service Members returning from recent conflicts in Afghanistan and Iraq pose a new and challenging problem for the audiological community—many have near-normal hearing thresholds, but have difficulty understanding speech amidst competing sounds. Many of these Service Members have been diagnosed with Central Auditory Processing Disorder (CAPD) or cognitive deficits. Exposure to blast likely plays a role in hearing dysfunction, and has also been linked to cognitive dysfunction with and without a confirmed diagnosis of traumatic brain injury. These two independent factors likely cause CAPD symptoms, one related to supra-threshold auditory coding fidelity and the other to cortical control, both of which can be adversely affected by exposure to blast. The goals of this study are to use objective electrophysiological tests to quantify specific sensory and cognitive deficits contributing to CAPD, to determine how these are related to blast exposure, and to develop a clinically useful test battery to quantify each of these deficits.

## 2. Keywords

Blast exposure, Central Auditory Processing Disorder (CAPD), traumatic brain injury (TBI), hearing loss, cochlear neuropathy, electroencephalography (EEG), frequency following response (FFR), auditory brainstem response (ABR)

## 3. Accomplishments

With the successful installation and implementation of the EEG hardware and software systems from Year 1, the primary focus of Year 2 of the project has been on subject recruitment, data collection and analysis.

### What were the major goals of the project?

- Hiring and training of Research Audiologist (SOW Major Task 2)
- Participant recruitment and evaluation (SOW Major Task 4)
- Analysis of data (SOW Major Task 5)
- Oversight and administration of the project (SOW Major Task 6)

### What was accomplished under these goals?

#### ***SOW Major Task 2: Hiring and training of Research Audiologist***

- On 17-Jan-2016, the project hired Research Audiologist, Dr. Kimberly Jenkins, to fill the position left vacant by Dr. Lynn Bielski's departure on 02-Dec-2016.
- On 14-Nov-2016, the project hired Research Communications Scientist, Dr. Jennifer Myers to fill the position left vacant by Dr. Lee Ann Horvat's departure in early September 2016.

**2b:** Both Drs. Jenkins and Myers have received multiple training session on the EEG hardware setup and data analysis software from Research Engineer, Scott Bressler, during his four site visits to WRNMMC this year.

#### ***SOW Major Task 4: Participant recruitment and evaluations***

- Total number of subjects consented = 53 (36 male, 17 female)
- Total number of eligible subjects = 38
  - Controls = 29 (16 male, 13 female)
  - Blast-Exposed = 9 male

- Study withdrawals = 6
  - Controls = 4 (3 male, 1 female)
  - Blast-Exposed = 2 male

***SOW Major Task 5: Analyze and Disseminate Data***

**5a:** Monitor data collection rates and data quality: summarized below

Number of subjects who completed the Electrophysiological Test Session (ETS) = 31

- Controls = 25 (13 male, 12 female)
- Blast-Exposed = 6 male

Breakdown summary of the completed datasets from the Electrophysiological Test Session (ETS)

- Auditory Selective Attention (ASA) = 26 (20 controls, 6 blast-exposed) Tests N6, N7
- Visual Selective Attention (VSA) = 21 (16 controls, 5 blast-exposed) Tests N9, N10
- Frequency-Following Response (FFR) = 27 (21 controls, 6 blast-exposed) Test N8

**5d:** Work with data core and dissemination of findings

Auditory, central, and cognitive test results from the Phase II CAPD study were presented at the Collaborative Auditory and Vestibular Research Network (CAVRN) meeting in San Antonio, TX. 13-15 June 2017. *Grant, KW., Bielski, L., Brungart, DS., Cesario, E., and Cripps, D., Fallon, A, Galloza, H., Horvat, L., Jackson, J., Jenkins, K., Kokx-Ryan, M., Krackau, G., Kubli, L., Lee, G., Myers, J., Phatak, SA., Roth, C., Stakhovskaya, OA. (2017). "Hidden Hearing Loss and Assessment of Functional Hearing Deficits in Active-Duty Service Members."*

***SOW Major Task 6: Oversight and administration of the project***

Research Engineer, Scott Bressler, and Research Audiologist, Dr. Kimberly Jenkins continue to be in frequent contact with each other regarding the progress of subject recruitment and data collection.

Mr. Bressler made four trips to WRNMMC to oversee data collection and provide continued training on the EEG hardware and software systems to new hires Research Audiologist, Dr. Kimberly Jenkins, and Research Communications Scientist, Dr. Jennifer Myers. These trips have also provided Mr. Bressler with valuable face time with Drs. Grant and Jenkins to discuss results and data analysis strategies.

Summary of Mr. Bressler's trips to WRNMMC:

- 17-Oct-2016 to 21-Oct-2016
  - EEG data collection training
- 28-Nov-2016 to 02-Dec-2016
  - EEG data collection training
- 18-Apr-2017 to 21-Apr-2017
  - Assembly of a second 32-channel BioSemi EEG system
  - Continued EEG data analysis training
- 30-May-2017 to 02-Jun-2017
  - Follow-up visit to evaluate EEG hardware installation
  - Continued EEG data analysis training

**6b:** Submit quarterly reports for CDMRP submission: all three quarters submitted

**6f:** Develop scripts for analyzing results: MATLAB scripts can summarize individual and group data. Group summarized data can be generated and updated as subjects complete the required measures from the Electrophysiological Test Sessions (ETS).

**What opportunities for training and professional development has the project provided?**

With the addition of Research Audiologist, Dr. Jenkins, and Research Communications Scientist, Dr. Myers, Mr. Bressler's trips to WRNMMC have focused primarily on providing the necessary training on the EEG system. While Drs. Jenkins and Myers have had some background experience with other EEG systems, the setup at WRNMMC provides exposure to another type of system and the data processing streams associated with it. Formalized MATLAB tutorials using the EEGLab toolbox have been created and introduced to Dr. Jenkins. These have proven to be a useful supplement to her current knowledge in MATLAB coding and EEG data analysis.

Mr. Bressler continues to receive exposure to translational research in a clinical setting. His continued interactions with Dr. Grant and his lab continue to broaden Mr. Bressler's knowledge in auditory neuroscience, and provide him the opportunity to interact with other leading researchers in the field of hearing sciences.

**How were the results disseminated to communities of interest?**

Results from Phase II of the CAPD prevalence study were presented as a poster at the Collaborative Auditory and Vestibular Research Network (CAVRN) meeting in San Antonio, TX on 13-15 June 2017.

Dr. Jenkins and Mr. Bressler have also submitted abstracts for consideration for the 41<sup>st</sup> Annual Midwinter Meeting of the Association for Research in Otolaryngology being held 9-14 February, 2018 in San Diego, CA.

**What do you plan to do during the next reporting period to accomplish the goals?**

While recruitment of control subjects is on schedule, finding eligible subjects for the blast-exposed group has been challenging this year. Recent changes to our inclusion criteria and outreach to other audiology clinics appears to be starting to make a difference. We will continue our recruitment efforts, and make adjustments if necessary. We will also pay close attention to how broadening our inclusion criteria may affect the outcome of the various study measures.

As the data continue to be gathered and analyzed, we will also be increasing the number of interactions between the Boston University and Walter Reed sites. We plan on increasing the frequency of conference calls between the two sites to discuss how to begin integrating the data collected from Phase II of the CAPD Prevalence Study with the data collected from the Electrophysiological Test Sessions (ETS). Dr. Grant is also planning to visit the Boston University campus to attend a workshop on cochlear synaptopathy on December 19<sup>th</sup> of this year; the plan is to set aside time for continued discussion of the data, and how to start disseminating our preliminary findings (conference presentations, journal publications).

We will also continue to work closely with LeVon Greer, our liaison at FITBIR who has been helping us figure out which data would be appropriate to share with the FITBIR

database. We are currently focusing on developing unique data elements (UDEs) and new data structures based on the data we have collected from the CAPD prevalence study and the electrophysiological test battery. We expect to have a full complement of shared data structures and elements in place by the end of the next quarter.

#### **4. Impact**

##### **What as the impact on the development of the principal discipline(s) of the project?**

Preliminary findings from the Phase II portion of the CAPD Study are suggesting that even for subjects classified as having normal to near-normal hearing, exposure to blast negatively impacts high frequency pure tone thresholds in a way that is consistent with subject-reported proximity to the blast (close versus far). Furthermore, these increased high frequency thresholds in the blast-exposed subjects are consistent with self-reported complications with hearing in everyday settings as measured by an abbreviated 6-question version of the Speech, Spatial, Qualities Questionnaire (Gatehouse and Noble, 2004), and two objective hearing measures that rely heavily on good neural representation of the temporal information of the auditory stimulus at the sensory periphery— 1)  $N_0S_\pi$  thresholds and 2) a modified version of the Oldenburg Matrix Test ([www.hoertech.de](http://www.hoertech.de)). The  $N_0S_\pi$  test is a standardized test that measures the signal-to-noise ratio at which subjects can detect a 500-Hz pure tone presented in opposing phases to the two ears in the presence of noise presented at identical phase across the two ears. The Oldenburg Matrix Test is a speech-in-noise (speech babble) test where the target speech has been artificially modified to increase the syllabic rate and presented in a simulated reverberant environment. Both of these objective hearing measures can easily be implemented in the clinic, and when combined with the high frequency audiometric thresholds that are already measured during a standard hearing evaluation, we hope to develop a quick and simple screening measure that can identify subjects that are at increased risk of suffering from this sub-clinical type of hearing dysfunction.

##### **What was the impact on other disciplines?**

Nothing to report

##### **What was the impact on technology transfer?**

Nothing to report

##### **What was the impact on society beyond science and technology?**

Nothing to report

#### **5. Changes/Problems**

##### **Changes in approach and reason for change**

Nothing to report

##### **Actual or anticipated problems or delays and actions or plans to resolve them**

In the second quarter of year two of the project, we reported having difficulty recruiting subjects into the experimental blast-exposed group because our inclusion criteria were rather narrow in focus. To address this problem, we expanded our recruitment efforts beyond the referrals we currently receive from the Phase II portion of the CAPD Prevalence Study to include referrals from the audiology clinic at WRNMMC. Additionally, Dr. Kimberly Jenkins began actively recruiting potential study candidates during VA Compensation and Pension evaluations she conducts at the Zybs Medical Group in Largo, MD. To date, Dr. Jenkins' recruitment efforts at the offsite clinic have resulted in an additional four eligible participants (3 control, 1 blast-exposed). While the audiology clinic at WRNMMC has yet to identify study-eligible candidates, we will continue this partnership and remain hopeful these efforts will pay off.

**Changes that had a significant impact on expenditures**

Nothing to report

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

Nothing to report

**Significant changes in use or care of human subjects**

Nothing to report

**Significant changes in use or care of vertebrate animals**

Nothing to report

**Significant changes in use of biohazards and/or select agents**

Nothing to report

**6. Products**

**Publications, conference papers, and presentations**

**Journal publications**

Nothing to report

**Books or other non-periodical, one-time publications**

Nothing to report

**Other publications, conference papers, and presentations**

Auditory, central, and cognitive test results from the Phase II CAPD study were presented at the Collaborative Auditory and Vestibular Research Network (CAVRN) meeting in San Antonio, TX. 13-15 June 2017. *Grant, KW., Bielski, L., Brungart, DS., Cesario, E., and Cripps, D., Fallon, A, Galloza, H., Horvat, L., Jackson, J., Jenkins, K., Kokx-Ryan, M., Krackau, G., Kubli, L., Lee, G., Myers, J., Phatak, SA., Roth, C., Stakhovskaya, OA. (2017). "Hidden Hearing Loss and Assessment of Functional Hearing Deficits in Active-Duty Service Members."*

**Website(s) or other Internet site(s)**

Nothing to report

**Technologies or techniques**

Nothing to report

**Inventions, patent applications, and/or licenses**

Nothing to report

**Other products**

Nothing to report

**7. Participants and Other Collaborating Organizations**

**What individuals have worked on the project?**

Name:	Prof. Barbara Shinn-Cunningham
Project Role:	Principal Investigator
Research Identifier:	0000-0002-5096-5914
Nearest person month worked:	1
Contribution to project:	
Funding support:	



Name:	Dr. Kenneth Grant
Project Role:	Co-Principal Investigator
Research Identifier:	
Nearest person month worked:	1
Contribution to project:	
Funding support:	

Name:	Scott Bressler
Project Role:	Research Engineer/Graduate Student
Research Identifier:	
Nearest person month worked:	12
Contribution to project:	Mr. Bressler is responsible for the procurement and installation the research hardware, development of the experimental and data analysis software, and training Research Audiologist, Dr. Jenkins, and Research Communications Scientist, Dr. Myers, in EEG data collection and analysis techniques. He has also been instrumental in filing the quarterly technical progress reports.
Funding support:	

Name:	Dr. Kimberly Jenkins
Project Role:	Research Audiologist
Research Identifier:	
Nearest person month worked:	9 (hired 17-Jan-2017)
Contribution to project:	Dr. Jenkins is responsible for subject scheduling, evaluation, data collection, and data archiving. She represents the main point of contact for the study participants, and is Mr. Bressler's direct contact for all technical and/or equipment related issues.
Funding support:	

Name:	Dr. Jennifer Myers
Project Role:	Research Communications Scientist
Research Identifier:	
Nearest person month worked:	12 (hired 14-Nov-2016)
Contribution to project:	Dr. Myers is responsible for Phases I & II of the CAPD Prevalence Study to which the BU study is attached. Along with Dr. Jenkins, she is also a main point of contact for the study participants, and a secondary contact for Mr. Bressler on EEG-related hardware, software, and data collection issues.
Funding support:	CAPD Prevalence Study

Name:	Dr. Leonard Varghese
Project Role:	Engineer
Research Identifier:	
Nearest person month worked:	1
Contribution to project:	Dr. Varghese provided valuable technical support and guidance in the acquisition, setup, and calibration of the EEG hardware and software system.
Funding support:	

Name:	Dr. Olga Stakhovskaya
Project Role:	Engineer
Research Identifier:	
Nearest person month worked:	1
Contribution to project:	Dr. Stakhovskaya has provided valuable technical support of the EEG hardware and software infrastructure.
Funding support:	CAPD Prevalence Study

Name:	Tom Heil
Project Role:	Engineer
Research Identifier:	
Nearest person month worked:	1
Contribution to project:	Mr. Heil has provided valuable technical support of the EEG hardware and software infrastructure.
Funding support:	CAPD Prevalence Study

**Has there been a change in the active or support of the PD/PI(s) or senior key personnel since the last reporting period?**

Nothing to report

**What other organizations were involved as partners?**

Nothing to report

## **8. Special Reporting Requirements**

**Collaborative awards**

**Quad charts**

## **9. Appendices**

### **References**

Gatehouse, S., & Noble, W. (2004). The speech, spatial and qualities of hearing scale (SSQ). *International Journal of Audiology*, 43(2), 85–99.

## Quad Chart

# Diagnosing contributions of sensory and cognitive deficits to hearing dysfunction in blast-exposed / mTBI Service Members



PI: Barbara G. Shinn-Cunningham

Org: Boston University (sub: Walter Reed Nat. Mil. Med. Cent.)

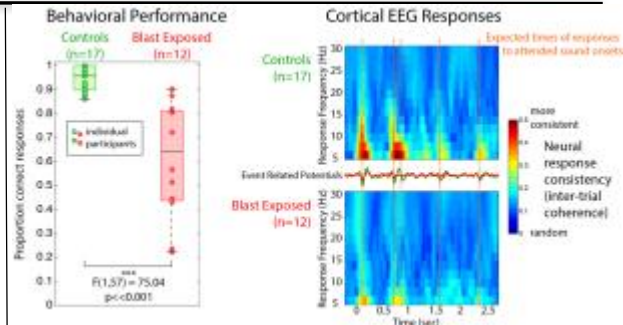
Award Amount: \$1,500,000

### Study/Product Aim(s)

- Understand why roughly 40% of blast-exposed Service Members returning from Iraq or Afghanistan (~15% of all personnel) experience difficulty understanding speech in noisy environments, despite having normal to near-normal hearing thresholds. These individuals are often misdiagnosed as having no hearing deficit, and are thus offered no treatment plan.
- Develop an efficient battery of tests appropriate for clinical use to diagnose patterns of hearing dysfunction in individual Service Members.

### Approach

We will recruit Service Members with varying degrees of blast exposure. Using both behavioral measures and physiological biomarkers, we will quantify 1) supra-threshold coding fidelity (likely related to noise and possibly blast exposure), and 2) cognitive / executive function (likely related to blast exposure). We will quantify the relationships amongst communication deficits, blast exposure history, sensory hearing fidelity, and cognitive / cortical control deficits. We will develop a clinically appropriate test battery to diagnose and tease apart contributions of sensory and cognitive deficits to hearing dysfunction in individual Service Members.



Pilot tests show that blast-exposed Veterans cannot effectively deploy auditory attention, evidenced by behavioral deficits (re: controls, left) and weak cortical responses to attended sounds (right). Both sensory and cognitive deficits likely contribute to this dysfunction.

### Timeline and Cost

Activities	CY	16	17	18
Prepare for data collection				
Recruit and test ~50 subjects				
Model key relationships in results				
Develop efficient diagnostic battery				
Estimated Budget (\$K)		\$537	\$475	\$488

Updated: (4 April 2017)

### Goals/Milestones

**CY16 Goals** – Setup and study initialization

✓ Hire and train research audiologist at WRNMMC

✓ Collect data on ~16 subjects (full set on ~12)

✓ Present preliminary results and solicit feedback

**CY17 Goals** – Data collection and dissemination

□ Collect data on ~36 subjects (full set on ~27)

□ Develop statistical model of key factors leading to hearing dysfunction

□ Present results and solicit feedback

**CY18 Goals** – Wrap up and dissemination

□ Finish data collection on ~18 subjects (full set on ~11)

□ Finalize statistical analysis and modeling

□ Develop efficient test battery for individualized diagnosis of specific sensory and cognitive deficits contributing to auditory dysfunction

### Budget Expenditure to Date

Projected Expenditure: \$817,026

Actual Expenditure: \$893,250