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

PRINCIPAL INVESTIGATOR: Dr. Barbara Shinn-Cunningham

CONTRACTING ORGANIZATION: Boston University  
1 Silber Way  
Boston, MA 02215-1703

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<b>14. ABSTRACT</b> <i>brief (~200 word) unclassified summary of most significant finding during the research period</i> The primary focus of Year 3 of the study has been subject recruitment and data collection. Recruitment for the blast-exposed experimental group continues to be challenging; however, we have adjusted our inclusion criteria and have extended our recruitment efforts to audiology clinics and other facilities outside of the Walter Reed National Military Medical Center. At the conclusion of Year 3 we have consented 167 (122 male, 45 female) potential study participants of which 109 (73 male, 36 female) were eligible for full participation. After attrition, we currently have data from 62 subjects (50 controls and 12 blast-exposed) who have participated in the auditory (ASA) and visual (VSA) selective attention/frequency-following response (FFR) tasks. Preliminary results show both control and blast-exposed groups perform equally well in the ASA and VSA tasks. Audiological data suggests subtle differences in cochlear function between blast-exposed Service Members and non-blast controls.					
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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 may have a Central Auditory Processing Disorder (CAPD) or cognitive deficits, but this is seldom assessed clinically. Exposure to blast likely plays a role in hearing dysfunction, and has been linked to cognitive dysfunction with and without a confirmed diagnosis of traumatic brain injury. Two independent factors may play a role in understanding CAPD, 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

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

The primary focus of Year 3 was subject recruitment and data collection. Although we are still struggling to find blast-exposed participants, we were able to exceed our recruitment goals for the non-blast control group this year.

With the completion of data collection for the control group, we also began the process of compiling and analyzing data across the different behavioral and electrophysiological test measures with the goal of identifying an optimal test battery that correlates with an individual's clinical hearing status.

### **What was accomplished under these goals?**

#### ***SOW Major Task 4b: Data collection of control group complete***

As of the writing of this report 56 control participants have completed both the Behavioral (BTS) and Electrophysiological Test Sessions (ETS) yielding between 48 to 53 complete and usable datasets depending on the type of electrophysiological test (see SOW Task 5a below).

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

- Total number of subjects consented = 167 (122 male, 45 female)
- Total number of eligible subjects = 105
  - Controls = 79 (43 male, 36 female)
  - Blast-Exposed = 25 male
  - Blast-Exposed (BU only) = 5 male
- Study withdrawals = 7
  - Controls = 6 (3 male, 3 female)
  - Blast-Exposed = 1 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) = 69

- Controls = 57 (29 male, 27 female)
- Blast-Exposed = 13 male

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

- Auditory Selective Attention (ASA) = 61(50 controls, 11 blast-exposed) <sup>Tests N6, N7</sup>
  - Usable data (49 controls, 11 blast-exposed)
- Visual Selective Attention (VSA) = 59 (48 controls, 11 blast-exposed) <sup>Tests N9, N10</sup>
  - Usable data (46 controls, 11 blast-exposed)
- Frequency-Following Response (FFR) = 65 (53 controls, 12 blast-exposed) <sup>Test N8</sup>
  - Usable data (52 controls, 12 blast-exposed)

It is not unusual to exclude datasets due to the presence of excessive noise artifact during the recording session. The “Usable data” category summarizes the number of quality datasets used in the analysis of the individual electrophysiological tests.

**5b:** Analyze research data

Research audiologist, Dr. Kimberly Jenkins, research communications scientist, Dr. Jennifer Myers, and research engineer Scott Bressler have started work on integrating the numerous datasets produced from the BTS and ETS sessions. Along with Co-PIs Drs. Barbara Shinn-Cunningham and Ken Grant, the team is in continuous discussions as to how best to analyze and interpret the study findings.

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

Poster presented at the 41<sup>st</sup> MidWinter Meeting of the Association for Research in Otolaryngology, 2018 entitled “**Evaluating Hidden Hearing Loss in the Military: Objective and Physiologic Responses of Blast and Non-Blast Exposed Service Members**” by Kimberly Jenkins, AuD; Scott Bressler, MS; Sandeep Phatak, PhD; Barbara Shinn-Cunningham, PhD; Ken W. Grant, PhD

***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.

To this end, Mr. Bressler made two trips to WRNMMC to discuss data collection and analysis with to Research Audiologist, Dr. Kimberly Jenkins, and Research Communications Scientist, Dr. Jennifer Myers. These trips have also provided Mr. Bressler with valuable face time with the team at Walter Reed to discuss recent results and data analysis strategies.

Summary of Mr. Bressler’s trips to WRNMMC:

- 31-Jan-2018 to 02-Feb-2018
  - EEG data analysis and review
- 29-May-2018 to 01-Jun-2018
  - EEG data analysis and review

**6b:** Submit quarterly reports for CDMRP submission  
All three quarterly technical reports were submitted.

**6f:** Develop scripts for analyzing results

Mr. Bressler continues to develop new and refine existing MATLAB data analysis scripts for summarizing 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?**

The EEG setup at WRNMMC continues to provide Drs. Jenkins and Myers opportunities to refine their EEG data collection techniques. Additionally, Dr. Jenkins has also become more experienced scripting in MATLAB and has started performing her own data analysis in parallel with Mr. Bressler's.

Mr. Bressler continues to receive exposure to translational research in a clinical setting. His interactions with Dr. Grant and his lab continue to broaden his knowledge in auditory neuroscience, audiology, and psychoacoustics.

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

Dr. Jenkins and Mr. Bressler presented a poster at 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.

PS 0345 "Evaluating Hidden Hearing Loss in the Military: Objective and Physiologic Responses of Blast and Non-Blast Exposed Service Members."

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

We are constantly trying to find creative solutions to increase our blast-exposed subject recruitment numbers. To reach our recruitment goal:

- We have eliminated the SSQ, NoS $\pi$  + OMT combined screeners from the inclusion criteria for the blast group. The current criteria now permit all normal hearing blast-exposed active duty Service Members to participate in the Boston University electrophysiological test session.
- Dr. Kimberly Jenkins has been granted credentialing privileges as a staff audiologist at the National Intrepid Center of Excellence (NICoE), an on-base traumatic brain injury research center. This will allow her face-to-face time with a patient population that has mild TBI caused by blast exposure. This will give the team the opportunity to inform the patients of the research study and see if they would like to participate
- We are in continued talks with the Center for Neuroscience and Regenerative Medicine (CNRM) whose mission is to conduct research to improve outcomes for military Service Members who suffer from TBI. CNRM maintains a large database of potential subjects that have been blast-exposed with and without TBI. Access to this population should allow for the opportunity to recruit the remaining number of blast-exposed Service Members.

Although we do not quite yet have the numbers in the blast-exposed group to make statistically meaningful comparisons with the non-blast control group, some trends in a subset of measures are starting to develop.

- Tests of the auditory periphery (pure tone audiometric thresholds, distortion product otoacoustic emissions, and to some extent the frequency following response) are hinting at differences between the two groups. We will continue to monitor these outcomes as we collect more data from new blast-exposed study participants.
- For both the Auditory (ASA) and Visual Selective Attention (VSA) tasks, behavioral and electrophysiological measures do not appear to be showing significant differences between control and blast-exposed groups. With the relaxation of the inclusion criteria for the blast group, we expect to come across Service Members that may be less affected by blast exposure as determined by their audiometric threshold data and scores on the SSQ and OMT screeners. In preparation for this possibility, we plan to investigate individual differences across the different test measures independent of blast exposure status. Findings from this analysis will be written up for consideration for publication in an appropriate peer-reviewed journal and will be included as a chapter in Mr. Bressler's doctoral dissertation.
- Data from the parent protocol entitled "Prevalence and Objective Verification of Central Auditory Processing Disorders in Blast-Exposed Warfighters (Phase II) include a number of additional hearing and cognitive tests have been collected on the same subject population as described above. These standardized tests of attention, working memory, and speed of processing are available for comparison with the ASA and VSA tests.

#### **4. Impact**

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

The preliminary findings we reported in the Year 2 Annual Report continue to hold through Year 3. Results suggest that even for subjects classified as having normal to near-normal hearing, exposure to blast negatively impacts cochlear function as indicated in poorer high frequency pure tone thresholds and distortion product otoacoustic emissions (DPOAEs) in a way that is consistent with subject-reported proximity to the blast (close versus far). Furthermore, this reduction in cochlear function in the blast-exposed subjects is 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)).

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

Preliminary analysis of our data seems to be suggesting that current audiological standards for classifying "normal hearing" may be too general. It appears that pure tone thresholds of 15-20 dB HL, while still technically normal, may in fact be affecting a person's ability to communicate in complex listening environments. If confirmed, this may lead to changes in the way sub-clinical hearing loss is categorized and treated in the clinic.

##### **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

Due to complications finding eligible blast-exposed active duty Service Members, we relaxed the inclusion criteria into the blast-exposed group. The original criteria were based on a combination of the Speech, Spatial, and Qualities (SSQ) Questionnaire and the combined screener of the rapid version of the Oldenburg Matrix Test (speech-in-noise test) and threshold values from the NoS $\pi$  condition of the Masking Level Difference (MLD) test. We have removed these screeners as a barrier into the blast-exposed group, effectively accepting any Service Member reporting exposure to blast with normal to near-normal hearing thresholds. Based on preliminary results from the ASA and VSA behavioral and electrophysiological test that show no discernible difference between blast and non-blast controls, we are now looking at individual differences in the correlation across our numerous test measures.

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

- Subject recruitment into the blast-exposed group continues at a much slower than anticipated pace. To address this problem, we have applied and receive a one year no-cost extension, which should give us enough time to increase the numbers in the experimental group. Drs. Jenkin and Myers have been actively searching for other recruitment opportunities within and outside the Walter Reed National Military Medical Center. As of the writing of this report, Dr. Jenkins is now credentialed at the National Intrepid Center of Excellence (NICoE), the national traumatic brain injury research center located at Walter Reed. Her presence there should provide us with more recruitment opportunities.
- At the beginning of September of 2018, PI Dr. Shinn-Cunningham accepted a new position at Carnegie Mellon University in Pittsburgh, PA. Her departure from Boston University means Mr. Bressler and Dr. Shinn-Cunningham will have to rely on video conferencing to conduct meetings to review the latest results and overall progress of the project. Plans are in place to ensure these video conference meetings take place on a weekly basis.
- Additionally, Mr. Bressler has recently accepted a six-month internship position at Apple, Inc. in Cupertino, CA. He has assured both PIs Shinn-Cunningham and Grant that he remains committed to completing this project and has arranged to be in regular contact with all team members at Carnegie Mellon University and Walter Reed.

### 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**

Poster presented at the 41<sup>st</sup> MidWinter Meeting of the Association for Research in Otolaryngology, 2018 entitled “**Evaluating Hidden Hearing Loss in the Military: Objective and Physiologic Responses of Blast and Non-Blast Exposed Service Members**” by Kimberly Jenkins, AuD; Scott Bressler, MS; Sandeep Phatak, PhD; Barbara Shinn-Cunningham, PhD; Ken W. Grant, PhD

**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**

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)	Behavioral Performance	Frontal Cortical EEG Responses
<ul style="list-style-type: none"> <li>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.</li> <li>Develop an efficient battery of tests appropriate for clinical use to diagnose patterns of hearing dysfunction in individual Service Members.</li> </ul> <p><b>Approach</b></p> <p>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.</p>		
	<p>Preliminary results from the Auditory Selective Attention (ASA) task suggest no apparent deficit in executive control in either the behavioral or cortical measures even in blast-exposed subjects with normal to near-normal audiometric thresholds.</p>	

### 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				■
<b>Estimated Budget (\$K)</b>		<b>\$537</b>	<b>\$475</b>	<b>\$488</b>

Updated: (15 Jun 2018)

### 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: \$1,477,944

Actual Expenditure: \$1,153,944

## 9. Appendices

### Conference Presentations

**Abstract ID:** 384445

**Abstract Title:** *Evaluating Hidden Hearing Loss in the Military: Objective and Physiologic Responses of Blast and Non-Blast Exposed Service Members*

#### **Author(s)**

Kimberly Jenkins - Walter Reed National Military Medical Center (Role: Presenting Author)

Sandeep Phatak - Walter Reed National Military Medical Center (Role: Co-Author)

Scott Bressler - Boston University (Role: Co-Author)

Kenneth Grant - Walter Reed National Military Medical Center (Role: Co-Author)

#### **Topic**

Auditory Pathways: Midbrain

#### **Abstract**

VA centers and military treatment facilities across the country are noting an increase in the number of service members (SMs) seeking care for perceived hearing difficulties, particularly in the presence of noise. However, diagnostic test batteries indicate that many of these individuals present with clinically normal or near-normal hearing and are not typical candidates for treatment methods such as hearing aids. Concerns regarding the prevalence of this phenomenon within the military population gave rise to a multi-site investigation of hearing difficulties in a non-clinical population of more than 3,500 active duty military personnel. SMs found to have normal to near-normal hearing thresholds were given a hearing screening battery that consisted of surveys (history of blast exposure, & Speech, Spatial, and Qualities of Hearing), a speech-in-noise test that contained speeded speech and speech in reverberation, and the Binaural Masking Level Difference test. It was found that 31% of listeners exposed to one or more blasts had abnormally low performance on binaural and speech tests. Moreover, experiencing blasts close enough to feel the heat or pressure wave increased the prevalence of hearing deficits by a factor of 2.5 compared to a non-blast group. This study clearly indicates that blast exposure results in auditory dysfunction that may go undetected by traditional diagnostic hearing tests.

To better understand the effects of blast on hearing and communication, the current study compared differences between service members who have been exposed to blasts and those who have not on a test battery that included subjective surveys, hearing tests, and cognitive measures. This discussion will focus on comparisons of the objective, physiologic measures of both groups. The two groups underwent measures of distortion product otoacoustic emissions (DPOAEs), click-evoked auditory brainstem responses (ABRs), frequency following responses (FFRs) to speech and tonal stimuli, and EEG cortical potentials in response to a selected melody attention task. It was found that DPOAEs, ABR and FFR amplitudes were less robust for the blast-exposed group than the nonblast-exposed group. EEG responses to the selected attention task showed no differences between the two groups, consistent with other cognitive tests of attention. This leads us to believe that blast exposure preferentially affects primarily cochlear, auditory brainstem, and certain aspects of binaural processing as opposed to the central auditory system. This information will help improve the diagnostic test battery and guide more effective treatment options for those experiencing functional hearing deficits.



**References**

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