AWARD NUMBER: W81XWH-20-1-0485

TITLE: Rapid, Multileveled Assessment of Hearing Dysfunction in Operational and Postdeployment Environments

PRINCIPAL INVESTIGATOR: Lee M. Miller

CONTRACTING ORGANIZATION: University of California, Davis, CA

REPORT DATE: July 2022

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
July 2022	Annual	01Jul2021-30Jun2022

4. TITLE AND SUBTITLE

Rapid, Multileveled Assessment of Hearing Dysfunction in Operational and Postdeployment Environments

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-20-1-0485

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Miller, Lee M.

E-Mail: leemiller@ucdavis.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

University of California,
Davis
1850 Research Park Dr., Ste
300
Davis,CA 95618-6153

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)
USAMRAA - CDMRP

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Fitness-for-duty requires good hearing and speech communication ability, especially in complex and noisy environments. But despite its crucial role in operational performance, medical and support personnel have no means to rapidly and reliably assess the integrated functioning of the auditory-speech processing system, either in the clinic or in forward remote settings. Furthermore after deployment, over a million Veterans with Service-related hearing disability – many of whom are older as well – struggle to understand speech in noisy environments such as work meetings or family gatherings, leading to a cascade of physical and mental/emotional health decline. However, because auditory dysfunctions are complex and multi-leveled they remain largely "hidden" audiologically. Measures using simple sounds and detection-threshold tasks, which inform the present US Army H1-H4 fitness-for-duty profile, fail to predict speech comprehension and job performance in Service members. For this profound military operational need, no assessment tool exists. This research will validate a powerful new EEG diagnostic – applicable in austere deployed settings – to assess auditory dysfunction as related to hidden hearing loss and central auditory processing disorders (US Patent No. 10,729,387). Our rapid (5-10min) brain-behavior assessment of listening uses continuous, uniquely engineered speech to differentiate multiple levels of dysfunction from the auditory periphery to cognition, including how these levels interact. This will enable quick screening of Service members in the field for auditory combat-readiness.

15. SUBJECT TERMS
fitness-for-duty, hearing loss, EEG

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON** USAMRDC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified	14	

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1. **INTRODUCTION:**
Fitness-for-duty requires good hearing and speech communication ability, especially in complex and noisy environments. But despite its crucial role in operational performance, medical and support personnel have no means to rapidly and reliably assess the integrated functioning of the auditory-speech processing system, either in the clinic or in forward remote settings. Furthermore after deployment, over a million Veterans with Service-related hearing disability – many of whom are older as well – struggle to understand speech in noisy environments such as work meetings or family gatherings, leading to a cascade of physical and mental/emotional health decline. However, because auditory dysfunctions are complex and multi-leveled they remain largely "hidden" audiologically. Measures using simple sounds and detection-threshold tasks, which inform the present US Army H1-H4 fitness-for-duty profile, fail to predict speech comprehension and job performance in Service members. For this profound military operational need, no assessment tool exists. This research will validate a powerful new EEG diagnostic – applicable in austere deployed settings – to assess auditory dysfunction as related to hidden hearing loss and central auditory processing disorders (US Patent No. 10,729,387). Our rapid (5-10min) brain-behavior assessment of listening uses continuous, uniquely engineered speech to differentiate multiple levels of dysfunction from the auditory periphery to cognition, including how these levels interact. This will enable quick screening of Service members in the field for auditory combat-readiness. Our Specific Aims include: AIM 1: Relate objective measures of hearing ability – from the brainstem through cognition – to relevant behavioral measures of operational performance (comprehension, ignoring distractions) and readiness (listening fatigue). AIM 2: Establish the test-retest reliability of the measures, within individual listeners over time (months to years). This will enable an "Early Warning" system to detect any decline in listening ability. AIM 3: Demonstrate that non-specialists can use the test to classify fitness-for-duty with durable, off-the-shelf hardware and minimal training in noisy or remote environments.

2. **KEYWORDS:**
hearing loss, speech perception, auditory dysfunction, fitness-for-duty, selective attention, audiology, electroencephalography, EEG, auditory brainstem response, ABR, speech tracking

3. **ACCOMPLISHMENTS:**

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

The major goals that overlap with this period of the project are shown below. (Note that several timeline entries extend into the third award period.) As detailed below, all human subjects-related goals continued to be severely impacted by the COVID-19 related research shutdown extending from the first project period into the present period (winter 2022). Currently, our Office of Research is allowing operation under near-pre-Covid protocols and we are proceeding rapidly with human subjects research and all project goals:

	Proposed Timeline	**Completion Date**	**% Complete**
Specific AIM 1: Performance-based neurobehavioral fitness-for-duty classifier	Months		
Pilot EEG-task sessions	4-5	(Begun as COVID-19	50%

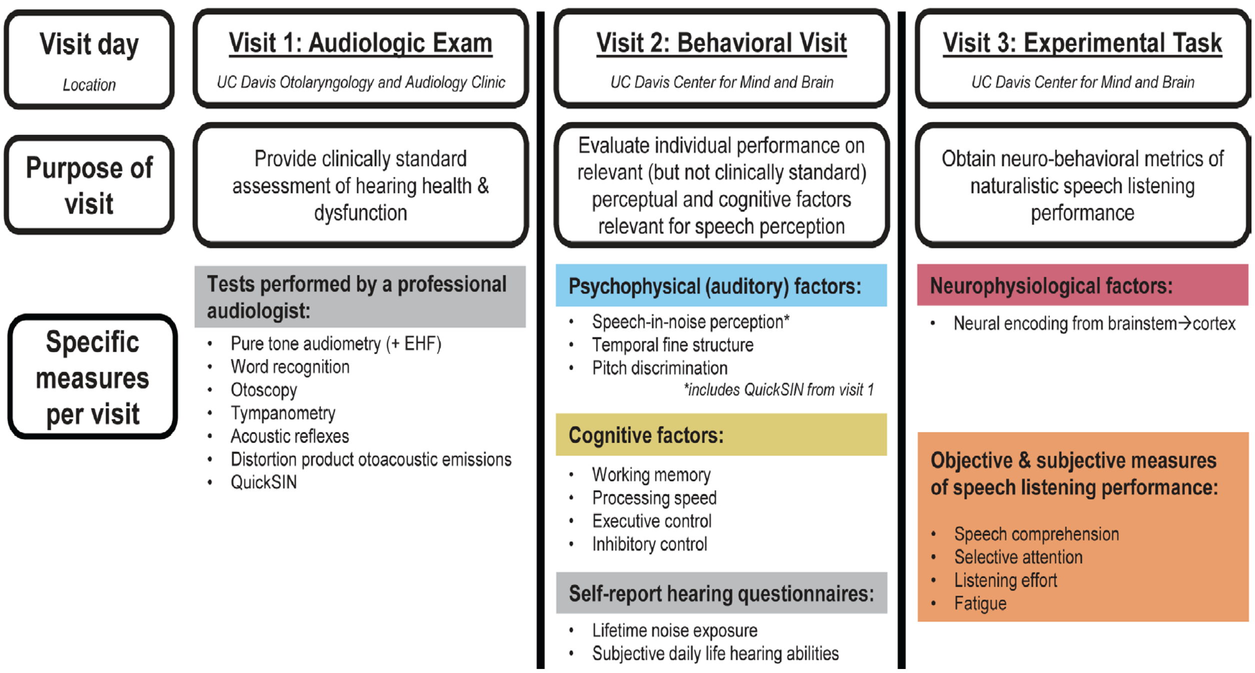
		shutdown allowed)	
Audiological Exams	6-24	Actively running	10%
Behavioral and EEG-task sessions	6-24	Actively running	5%
Specific AIM 2: Test-retest reliability and "Early Warning" profile			
Audiological Exams, sessions 2-4	2-30	(Anticipated to commence 9/15/2022)	0%
Behavior and EEG-tasks, sessions 2-4	2-30	(Anticipated to commence 9/15/2022)	0%

Despite the COVID-19 research shutdown, we continued to make substantial progress on the following goal well in advance of its proposed timeline.

Specific AIM 3: Non-specialist use in austere environment			
Software development: automated processing framework and intuitive GUI interface	25-27	6/30/2022	80%
Non-specialist testers administer fitness-for-duty classifier with durable, off-the-shelf hardware and minimal training, in austere environment	27-32	(Anticipated to commence 1/1/2023)	0%

- **What was accomplished under these goals?**
  Major activities and significant results
  In this award period, we achieved significant progress on all project goals including completion of the behavioral-EEG paradigm development, validation of the data processing pipeline, and establishing the core algorithms for the machine learning classifier. Following the normalization of Covid-related research protocols at UC Davis, we have also made substantial advances on our human subjects related aims since spring 2022. We have presented our preliminary data at the flagship conference for cognitive neuroscience and now have a manuscript in preparation describing our powerful methodological approach. Below is an overview of the experimental sessions we are currently running, a conceptual framework for our analysis pipeline as it is now implemented, and examples of neural (EEG) data from our core behavior-EEG paradigm showing multiple levels of speech processing in a challenging, dynamic task.

  We are now actively enrolling participants, all of whom complete the following three visits: 1) Audiological exam, 2) Behavioral visit, 3) Experimental (behavior-EEG) task. The audiological exam provides a clinically standard assessment of hearing health and dysfunction, in addition to several measures not always acquired clinically but that have particular relevance for "hidden" hearing loss, including extended high frequency (EHF) audiometry and otoacoustic emissions. Our clinical partners at the UC Davis Audiology Clinic have been extremely helpful in implementing our paradigm and scheduling participants. Visit 2 comprises a battery of perceptual and cognitive tests that are likely predictive of speech perception in realistic environments. Some of these are low level perceptual tests, as for temporal fine structure (fast changes in sound), while others are cognitive (working memory) or reflect hearing history (noise exposure). Finally Visit 3 consists of the EEG and pupillometry recordings while subjects perform the challenging, dynamic listening task. Subjects must switch their attention and gaze between two simultaneous talkers in two different spatial locations in order to understand a narrative and identify target words. This is where we use our patented engineered speech EEG approach to differentiate multiple levels of dysfunction from the auditory periphery to cognition.

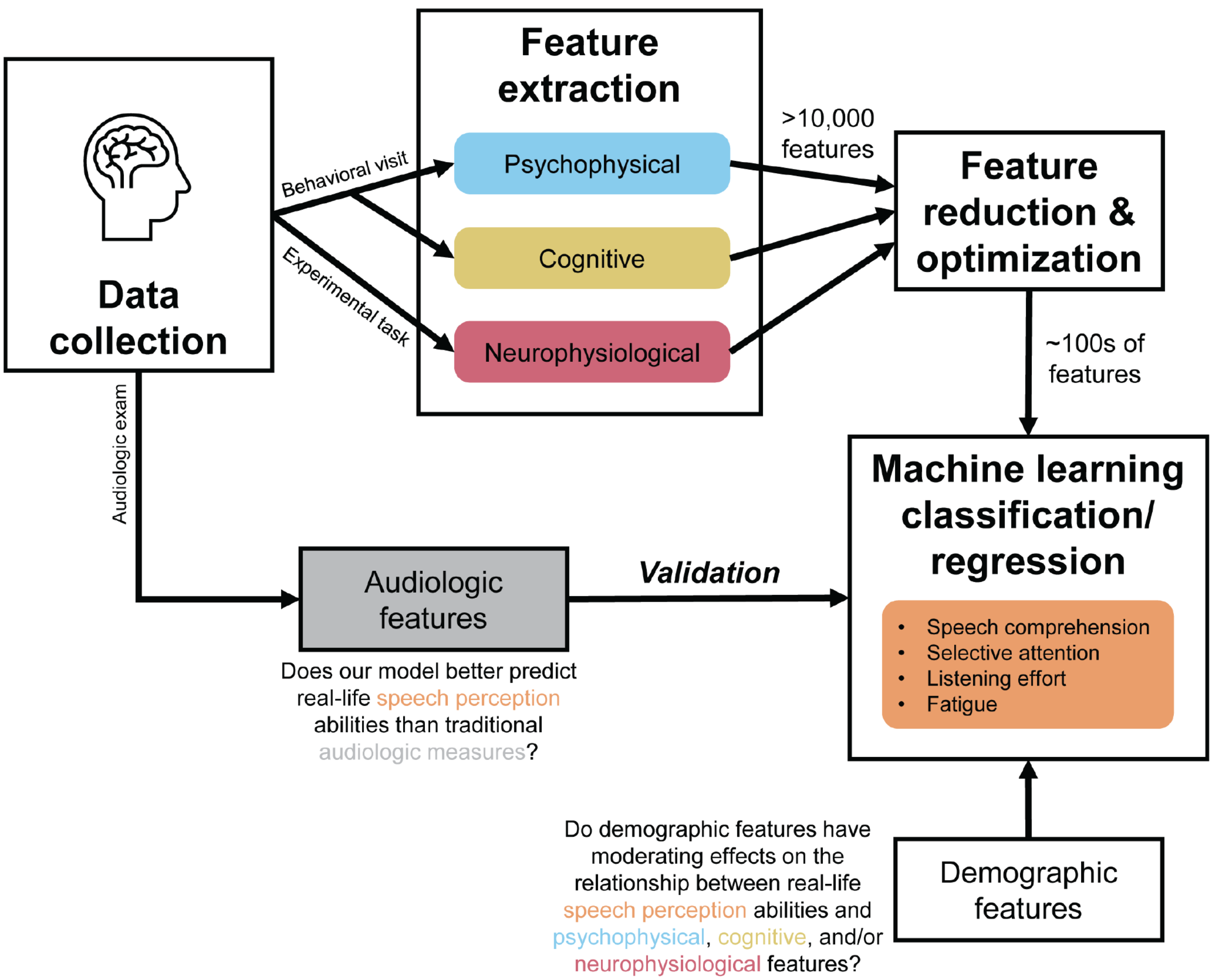


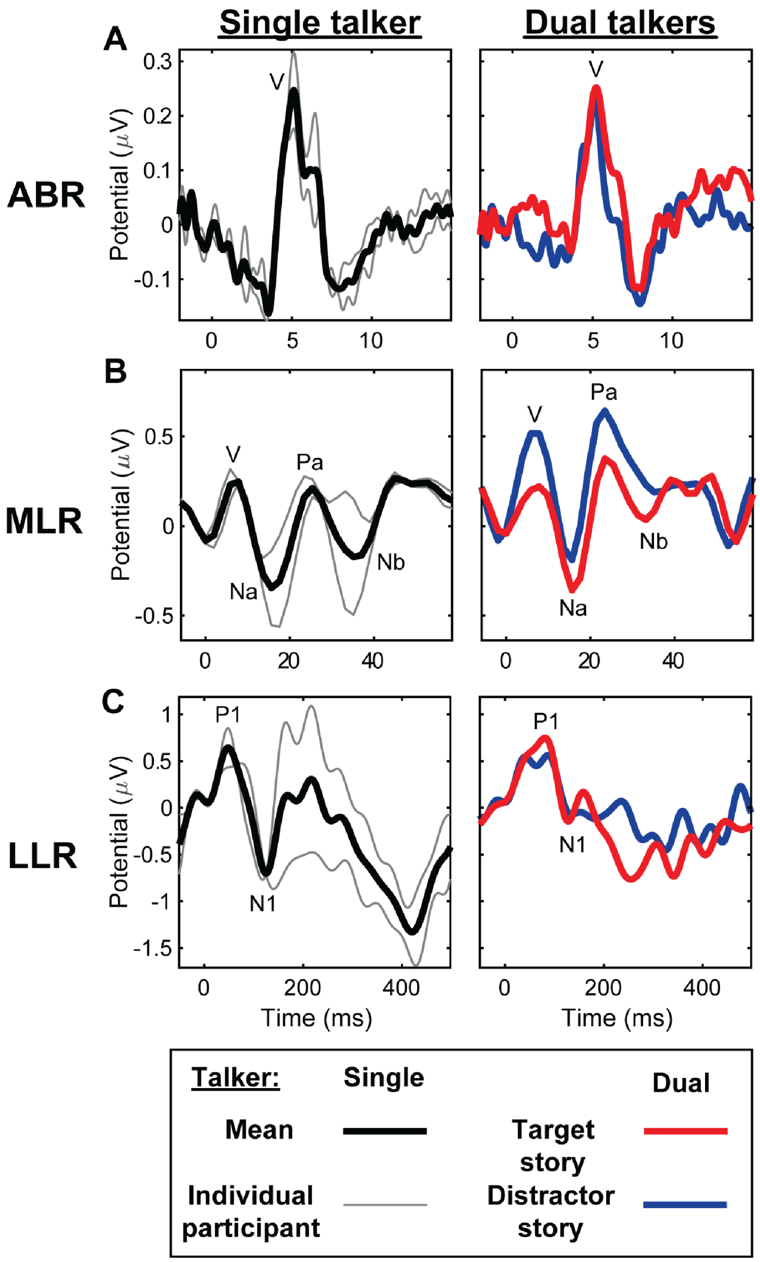
Specific measures from each of these visits – most importantly the neurobehavioral metrics from Visit 3 – will determine which tests or factors best predict objective and subjective naturalistic speech listening performance in Veterans (orange box, bottom right) and will drive the auditory fitness-for-duty classification. These performance measures include:

- Speech comprehension: accuracy on target narrative comprehension questions at the end of each block
- Selective attention: target word hit rate (identification accuracy) & gaze-shift accuracy to the cued target speech location
- Objective listening effort: pupil dilation responses
- Speech tracking fatigue: reaction times of target word identification & cued gaze-shift

• Subjective listening effort & general fatigue: self-report ratings

The three visits yield a large number of metrics or features (>10,000) – practically too many for a fitness-for-duty classifier to operate on. Features of interest will therefore be winnowed by a feature reduction/optimization process. In the prior funding period, we had proposed a Genetic Algorithm (GA) to accomplish this; we will now complement GA with a newer technique using deep neural networks that has recently shown great promise for this application, known as an **autoencoder**. Finally, a machine learning algorithm (e.g. Support Vector Machine) will then characterize neurobehavioral profiles on this reduced feature set to distinguish good versus poor speech listeners. Demographic features (e.g., age; SES) will be evaluated as potential moderating variables. These results will be validated against traditional audiologic measures to predict real-life speech perception performance.





Crucial for the classification is obtaining high-quality speech neurophysiological data, using our patented approach (red boxes in the figures above). As shown here, we are readily acquiring EEG data depicting neural processing at multiple levels of the auditory pathway, simultaneously during continuous, naturalistic speech listening: Auditory brainstem (ABR; A), middle latency (MLR; B), and late latency responses (LLR; C) to the engineered speech in a single-talker condition (left) and a dual-talker condition with simultaneous, competing voices (right). The ABR waves reflect how well speech sound is first encoded in the brain after it enters the ear. In older listeners with hearing loss, we expect the fidelity of this signal to degrade. The MLR waves reflect how well the speech is transmitted from low levels to higher levels in the auditory brain. The LLR reflects how the speech is processed in auditory cortex and further stages – those that determine speech meaning, attention, etc.

We are encouraged by these results, as they demonstrate high sensitivity to exactly the kinds of neural features that will distinguish good from poor listeners in our classifier.

Stated goals not met: Goals not met are enumerated in the SOW chart above and are strictly limited to those impacted by the COVID-19 research shutdown. Although the shutdown delayed our human subjects data acquisition significantly, we were able to accomplish goals from latter portions of the SOW in advance are now making rapid progress on all goals, <u>including all those</u>

involving human subjects. We are also bringing on additional staff to schedule and run subjects faster than originally planned. Thus we estimate our overall SOW delay from the COVID-19 shutdown will be greatly reduced in the coming months. We anticipate our milestones to align with SOW:Month-29 in late Y22-23, when we expect to request a one-time COVID-related extension (EWF) as per the CDMRP Award Guide Ch. 2 Sec. II-E to complete the work.

- **What opportunities for training and professional development has the project provided?**
  The project is not primarily framed as a training and professional development opportunity, however research of this kind inevitably serves that purpose – particularly for junior researchers. During this reporting period, both our postdoctoral scholars completed intensive training in deep neural networks through a graduate course in Spring 2022 (Neuroscience 211: "Advanced Topics in Neuroimaging") and in advanced EEG analysis through the UC Davis ERP Bootcamp organized by Prof. Steve Luck. Postdoc Kelsey Mankel also participated in a mentored career-development course through the Association for Research in Otolaryngology (ARO). Our lead Research Specialist participated in a training internship addressing big data and cloud computing infrastructure with Amazon.

- **How were the results disseminated to communities of interest?**
  Our research was very well received at the flagship cognitive neuroscience conference, the Cognitive Neuroscience Society Annual Meeting (4/2022), with a poster entitled *The role of auditory, neural, and cognitive factors in detecting hidden hearing loss on a novel speech comprehension task*. (Mankel K, Comstock DC, Abou Najm K, Bormann B, Sagiv D, Brodie H, Miller LM.)

  Professor Miller delivered Invited Presentations describing our ongoing work at several forums including the UC Davis Dept. Otolaryngology / Head & Neck Surgery Annual Research Symposium and the UC Davis Center for Neuroengineering and Medicine. These presentations were attended by local and regional researchers and clinicians, as well as university administrators and Office of Research staff.

- **What do you plan to do during the next reporting period to accomplish the goals?**
  In spring 2022 (following the winter Covid surge), our lab returned to operation under largely pre-COVID-shutdown protocols. Furthermore we have all necessary project personnel on board and working productively. All the logistics of subject recruitment, clinical assessment, and experimentation are complete. As a result, we will rapidly realign with the proposed SOW timeline, and plan to complete all behavioral and EEG-task sessions and classifier training in the next reporting period.

4. **IMPACT:**

- **What was the impact on the development of the principal discipline(s) of the project?**
  This research is likely to significantly advance toward clinical/field application the first and only auditory fitness-for-duty assessment that validates operational performance and readiness for active-duty Service members. This novel assessment tool will have immediate, profound impact on Service member team safety, communication, and effectiveness in dynamic and noisy environments.

Our listening diagnostic builds on years of careful research by our lab and many others, but real world impact depends as much on practical implementation as it does on the underlying science: if an auditory fitness-for-duty assessment can only be conducted in a large hospital or laboratory by highly trained personnel, its impact will be sorely limited. Our approach is uniquely designed from the outset for the broadest possible application, through its speed, portability, robustness in austere or adverse environments, and ease of use by non-specialists. Our proposed research will validate all these attributes, demonstrating that inexperienced individuals with only one hour of training can conduct the assessment rapidly and reliably.

The method is equally applicable in post-deployment Veterans, many of whom suffer from lasting service-related auditory injury. Here, the method's speed and ease of use will also impact its utility, bringing the tool within reach not only of large VA hospitals but also small private audiology practices and local, non-specialized clinics.

- **What was the impact on other disciplines?**
  Beyond the operational and post-deployment impact on military personnel and their families, in the long term our approach has the potential to transform restorative hearing health care globally, ultimately improving care for the half a billion people worldwide who have hearing loss. Every day these individuals struggle to understand speech, particularly in noisy conditions, leading to billions of dollars in lost productivity (in the US alone, hundreds of billions annually) and, too often, a tragic and costly cascade of social, psychological, and physical decline. The challenge is that a listener's difficulty understanding speech in real life stems not only from problems in the ear, but from how each individual's brain processes sounds. For decades, our capable audiology providers and hearing device manufacturers have struggled to enact effective, individualized hearing care because they lack the means to rapidly and reliably assess the integrated functioning of the auditory system in a life-relevant context. As a result, they are limited in how to guide treatment. For instance hearing aids and other devices are often poorly matched to an individual's impairment, and aids often fail in the situations where listeners need them most: e.g. restaurants, business meetings, family gatherings. Moreover, nascent cellular and molecular treatments for hearing loss (e.g. hair cell restorative drugs) also lack an objective, multileveled metric of therapeutic impact. For this profound global health problem and frank scientific-industrial need, no clinical assessment tool has ever existed. Our ongoing research will finally provide it.

- **What was the impact on technology transfer?**
  Granting of the core patent underlying our approach in the prior period (8/4/2020) represented a significant step toward technology transfer. We expect this technology to have a commercial impact, either through a startup and/or licensing agreements. As we obtain human subjects data in Y22-23, our Office of Research will prepare a regulatory approach with UC Davis Tech Transfer office, including any premarket applications to the FDA, will help apply for funding to conduct any anticipated trials necessary for classification and clearance, and will contact potential industry partners.

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

The work is likely to have a substantial impact on society and employment by improving the audiological treatment, social integration, and work productivity of those with hearing loss. Since hearing loss leads to a cascade of mental and physical impairments (social isolation, depression), the research promises to ameliorate many of these costly downstream effects as well.

5. **CHANGES/PROBLEMS:**

- **Changes in approach and reasons for change**
  Nothing to Report.

- **Actual or anticipated problems or delays and actions or plans to resolve them**
  As noted above, human subjects research at UC Davis was further curtailed for portions of the '21-22 period due to the COVID-19. Presently, our Office of Research is allowing operation under near-pre-Covid protocols and we are proceeding rapidly with human subjects research and all project goals.

- **Changes that had a significant impact on expenditures**
  Delays due to the COVID-19 research shutdown led to a temporary reduction in expenditures, in particular delays in hiring staff and human subjects costs (subject payments, audiological exams). Two postdocs onboarded in late summer / fall 2022. One graduate student assisted part time on the experimental paradigm.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**: None.
- **Significant changes in use or care of human subjects**: None
- **Significant changes in use or care of vertebrate animals:** N/A
- **Significant changes in use of biohazards and/or select agents**: N/A

6. **PRODUCTS: Publications, conference papers, and presentations**

- **Journal publications.**
  In preparation: Mankel K, Comstock DC, Abou Najm K, Bormann B, Sagiv D, Brodie H, Miller LM. *The role of auditory, neural, and cognitive factors in detecting hidden hearing loss on a novel speech comprehension task*.
  Acknowledgment of federal support: **Yes**

- **Books or other non-periodical, one-time publications.** Nothing to Report.
- **Other publications, conference papers, and presentations.**
  - *The role of auditory, neural, and cognitive factors in detecting hidden hearing loss on a novel speech comprehension task*. Mankel K, Comstock DC, Abou Najm K, Bormann B, Sagiv D, Brodie H, Miller LM. Poster presentation at the Cognitive Neuroscience Society Annual Meeting (4/2022)
  - Invited presentation at the UC Davis Center for Neuroengineering and Medicine (3 Nov, 2021)
  - Invited presentation at the UC Davis Humans, Robotics, Vehicles Integration & Performance Laboratory (HRVIP), a NASA funded lab (5 Nov, 2021)

- Invited presentation at the UC Davis Department of Otolaryngology / Head and Neck Surgery Research Symposium (17 June, 2022)

- **Website(s) or other Internet site(s)**
  At this stage we are not yet disseminating data and results to the scientific community. This will commence as we are rapidly acquiring human subjects data in Y22-23.

- **Technologies or techniques**
  We have begun developing the machine learning model that will serve as the core of our auditory fitness-for-duty classifier (see section *Accomplishments* for details). We will make all Research Resources publicly available in accordance with CDMRP expectations, as expressed in the General Application Instructions, Appendix 2, Section K.

- **Inventions, patent applications, and/or licenses**
  None in the present reporting period.

- **Other Products**
  Our novel behavioral-EEG paradigm and the EEG data analysis pipeline are complete, and our machine learning classifier is under active development.

7. **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

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

Name:	Lee M. Miller
Project Role, etc.:	PI (no change)

Name:	Hilary Brodie
Project Role, etc.:	co-PI (no change)

Name:	Kelsey Mankel
Project Role:	Postdoc
Researcher Identifier (ORCID ID):	0000-0002-6953-4778
Nearest person month worked:	10
Contribution to Project:	Dr. Mankel is lead postdoc on the audiological and auditory cognitive aspects of the project

Funding Support:	No funding outside this award.

Name:	Daniel Comstock
Project Role:	Postdoc
Researcher Identifier (ORCID ID):	0000-0001-5861-0838
Nearest person month worked:	11
Contribution to Project:	Dr. Comstock is lead postdoc on the EEG analysis and machine learning aspects of the project
Funding Support:	No funding outside this award.

Name:	Brett Bormann
Project Role:	graduate student
Researcher Identifier (ORCID ID):	none
Nearest person month worked:	4
Contribution to Project:	Mr. Bormann worked to develop the behavioral-EEG task.
Funding Support:	Remaining funding during the academic Y21-22 was provided through a Teaching Assistantship

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

  No

- **What other organizations were involved as partners?**
  Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

o QUAD CHART:

Rapid, Multileveled Assessment of Hearing Dysfunction in Operational and Post-deployment Environments

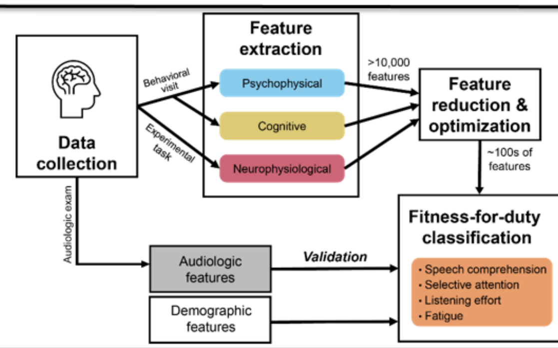
Log #: RH190061
Award # W81XWH2010485
PI: Miller, Lee M **Org:** University of California, Davis **Award Amount:** $1,530,179

Project Aims

1. Relate brain-based measures of hearing ability to operational performance (comprehension, ignoring distractions) and readiness (listening fatigue).
2. Establish test-retest reliability of the measures within individual listeners over time (months to years). This will enable an "Early Warning" system to detect any decline in listening ability.
3. Demonstrate that non-specialists can use the automated test to classify auditory fitness-for-duty with durable, off-the-shelf hardware and minimal training, in noisy or remote environments.

Approach

A rapid (5-10min) brain-behavior assessment of listening uses continuous, uniquely engineered speech and EEG to differentiate multiple levels of dysfunction from the auditory periphery to cognition (US Patent #10,729,387). This will enable quick screening of Service members in the field for auditory combat-readiness.



Accomplishments: Actively running subjects on three-visit paradigm combining audiological, cognitive, and neurobehavioral features that will inform the fitness-for-duty classifier.

Timeline and Cost

Activities Year	20-21	21-22	22-23	EWF**
Develop Machine Learning Classifier				
Behavior-EEG and Audiological Exams				
Test / Retest Reliability (sessions 2-4)				
Non-specialist testers administer fitness-for-duty classifier				
Estimated Budget ($K)	**$235k**	**$350k**	**$694k**	**$250**

Updated: 26 July, 2022

GOALS / MILESTONES

Y20-21 Milestones – Experimental and Software Development

☑ Awarded US Patent for approach (No. 10,729,387, 4 Aug., 2020)

☑ Published in high-profile journal (J Cognitive Neuroscience)

Y21-22 Milestones

☑ Began EEG-task and audiological sessions, designed machine learning classifier, and completed data pre-processing pipeline

Y22-23 Goals

☐ Complete all behavioral and EEG-task sessions and classifier training; substantially advance test-retest reliability and Aim 3

Comments/Challenges

- Human subjects research was curtailed due to COVID-19 through Winter 2022, however we made rapid progress on all period goals
- ** Budget and milestones anticipated to match SOW:Month-29 in late Y22-23, when we expect to request a one-time COVID-related extension (EWF) as per the CDMRP Award Guide Ch. 2 Sec. II-E.

Budget Expenditure to Date

- Projected Expenditure: $920,000. Actual Expenditure: $585,473

9. APPENDICES:

N/A