AWARD NUMBER: W81XWH-16-2-0001

TITLE: Evaluation of the Effects of High Level Overpressure (8+psi) on Cognitive Performance, Brain Blood Biomarkers and Symptom Reporting

PRINCIPAL INVESTIGATOR: Dr. Walter S. Carr

RECIPIENT: The Geneva Foundation
917 Pacific Ave, Suite 600
Tacoma, WA 98402

REPORT DATE: January 2021

TYPE OF REPORT: Annual

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

REPORT DOCUMENTATION PAGE

Form Approved

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
JANUARY 2021	ANNUAL REPORT	30 Dec 2019 – 29 Dec 2020

4. TITLE AND SUBTITLE

Evaluation of the Effects of High Level Overpressure (8+ psi) on Cognitive Performance, Brain Blood Biomarkers and Symptom Reporting

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-16-2-0001

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Walter Carr, PhD
Email: walter.s.carr.civ@mail.mil

5d. PROJECT NUMBER
10445

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The Geneva Foundation
917 Pacific Ave, Suite 600
Tacoma, WA 98402

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)
USAMRMC

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

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This is a multi-site observational study of military and law enforcement personnel who are exposed to overpressure (OP) where data is collected in conjunction with occupational training exercises. The study's primary purpose is to characterize a variety of weapon systems/environments (OP, impulse, acoustics) and measure effects (neurocognitive, biomarkers, symptom reporting, etc.) immediately after OP exposure (< 5 min)and/or at end of training day (i.e., acute effects). 2 data collections took place (n_1 = 15, n_2 = 15 at 2 different sites. Sensor orientation, position, and distance from the blast source are necessary details for sufficiently interpreting occupational blast exposure. Blast exposure levels are affected by a variety of factors; tactical methods and weapon suppressors may mitigate overpressure and acoustic exposures, whereas helmet shape may increase exposure due to an under-wash effect. Overpressure and acoustic exposure levels measured in a low overpressure blast environment were associated with neurocognitive deficits. Changes were identified in blood-based biomarkers (targeted proteins, DNA methylation) after repeated blast overpressure exposure.

15. SUBJECT TERMS
mTBI, neurotrauma, blast, blast exposure, immediate effects, military, breacher, explosive entry, blast injury, brain injury, blood based biomarker, injury threshold

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
					USAMRMC
a. REPORT	b. ABSTRACT	c. THIS PAGE	Unclassified	20	19b. TELEPHONE NUMBER *(include area code)*
Unclassified	Unclassified	Unclassified			

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

Page No.

1. INTRODUCTION:

Military and law enforcement personnel are repeatedly exposed to overpressure (OP) during training and operations. This multi-site observational study will collect individual OP exposure data (including impulse and acoustics data when possible) and measure neurocognitive and physiological (blood based biomarkers, genetic markers, eye-tracking, tactile sensory perception, balance, symptom reporting) effects immediately after OP exposure and/or at end of day. The study will occur in conjunction with training exercises from a variety of weapon systems/environments where operators are exposed to OP ranging from safe (< 4 psi) to high exposure (> 8 psi) levels at local and national military and law enforcement training facilities. A parallel effort will collect biomechanical data using surrogate head forms that are embedded with sensors for obtaining pressures and accelerations. The surrogate head forms will be developed and customized for this project as a collaborative effort by the Naval Research Laboratory (NRL). Data collection efforts from this study will be used to quantify blast and its effects (neurocognitive and physiological) on the operator and identify variable(s) and/or test(s) which will serve to inform medical research with regards to increased risk and/or the effects of OP exposure. In addition, data derived from this study will be available for pertinent medical research in terms of OP exposure and neurotrauma modeling efforts. The Initiating Principal Investigator (PI) for the overall award and effort was Dr. Gary Kamimori at the Walter Reed Army Institute of Research (WRAIR); role of the PI was changed to and assumed by Dr. Walter Carr. The Collaborating/Partnering PI for the sub-award to develop surrogate head models is Dr. Amit Bagchi at the Naval Research Laboratory (NRL); annual progress is not applicable under this report as sub-award funding for NRL ended Dec 2019.

2. KEYWORDS:

mTBI, neurotrauma, blast, blast exposure, immediate effects, military, breacher, explosive entry, blast injury, brain injury, blood based biomarker, injury threshold

3. ACCOMPLISHMENTS:

The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Goal 1) Collect high overpressure exposure (8-12 psi) data on human operators during operational training and secondly to collect possible injury data using extensively instrumented human surrogates.

Goal 2) Identify and quantify acute, transient decrements in cognitive performance resulting from overpressure exposure within a variety of environments. This portion of the project will

encompass as many different exposure environments as possible in order to characterize overpressure within these specific environments as well as individual operator exposure.

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

1) Major Activities
   a. (WRAIR) Protocol was amended two times which involved adding collaborators, increasing sample size to 1200, data sharing with Defense Health Agency, and PI change.
   b. (WRAIR) Two human subjects data collections took place at 2 different sites, 1 x site #7 (Camp Pendleton, CA, Jan – Mar 2020); 1 x site #4 (Tacflow Academy, Feb 2020).
   c. (WRAIR) Blood based biomarker assay/analyses blood based protein quantification and biological specimens transfer continues with collaborating investigators for genetic analyses continues.
   d. (WRAIR) Nine peer reviewed manuscripts were published; an additional 5 publications have been submitted and are currently under review.
   e. (WRAIR) Three abstracts were presented at the Military Health Research Symposium, Congressional National Defense Authorization Act (NDAA), Section 734, Working Group (12 AUG 2020).
   f. (WRAIR) Symptom, demographics, and neurocognitive data from 4 data collections were submitted to the Federal Interagency Traumatic Brain Injury Research (FITBIR) Informatics System 5 OCT 2020. Blast exposure data (psi/impulse) to be submitted, but pending FITBIR consult and guidance.
2) Specific Objectives
   a. (WRAIR) Site #7, CY20 data collection #1, Camp Pendleton, CA
      i. Date(s): JAN 2020- MAR 2020
      ii. Environment: expeditionary operational training
      iii. Data measures: overpressure exposure, acoustics, neurocognitive performance, symptoms, stress, demographics/occupational history, cheek swab, blood sampling
      iv. Number of subjects (complete data collection): 15
   b. (WRAIR) Site #4, CY20 data collection #2, Tacflow Academy
      i. Date(s): FEB 2020
      ii. Environment: 50 caliber rifle training
      iii. Data measures: overpressure exposure, acoustics, neurocognitive performance, symptoms, demographics/occupational history, cheek swab, blood sampling
      iv. Number of subjects (complete data collection): 15
   c. (WRAIR) Data analysis in progress.

i. Analyses of cognitive performance, symptoms, exposure, demographics continues.
ii. Analyses of blood samples continues.
a. TBI or brain-related protein concentrations were measured; quantitation of a seven biomarker panel (GFAP, UCH-L1, NF-L, Tau, Aβ-40 and Aβ-42). Biomarkers were assessed in a control dataset (non-overpressure exposed persons, commercially purchased) to build a protein data repository for biomarker comparisons.
b. Mass spectrometry and human genome databases used to identify and measure relative protein levels.
c. Determine if biomarkers are physiological responders of overpressure exposure, alone, or in concert with observed operational decrement (from neurocognitive assessment/s) and/or self-reported concussion-like symptoms within individuals and groups.
d. DNA methylation was used to compare responses before and after exposure time points.
e. DNA samples and genome-scale DNA methylation assays were analyzed using demographics data, specifically, quantification of career blast exposures to investigate what factors contribute to a response.

3) Key outcomes
a. (WRAIR) Thorough investigation of environmental characterization from multiple weapon systems/configurations/materials resulted in critical findings that affect quantifying exposures such that knowing the orientation, position, and distance of the sensors is critical to sufficiently interpreting occupational blast exposure.
b. (WRAIR) There are multiple factors that contribute to blast exposure levels experienced in training ranging from tactical methods/accessories that possibly mitigate overpressure and acoustic exposures, such as tamping methods and weapon suppressors, but also include unfavorable factors such as helmet shapes that may increase exposure due to an under-wash effect.
c. (WRAIR) It continues that both overpressure and acoustics measures are exposure targets of interest to determine the presence of associated performance deficits or physiological changes. The resulting data and analyses of blast exposure measurements contribute to an improved understanding of effects and risk mitigation in military training environments.
d. (WRAIR) Serum protein levels varied across studies site and among study participants. However, serum GFAP suppression and Aβ elevation were frequently observed within hours or days of breaching exercises or heavy caliber rifle usage. Biomarker levels in GFAP, UCH-L1, NF-L, Tau, Aβ-40 and Aβ-42 are lower in controls compared to participants who are sampled before and after overpressure exposure. Findings may be used to develop blood tests capable of monitoring health-related effects with hours or days of overpressure exposure.
e. (WRAIR) DNA methylation was altered by chronic exposure to blast overpressure quantified as a high number of accumulative blast overpressure across a military career. Thus, DNA methylation is a highly stable, long-lasting marker, and capable of capturing lifetime accumulative exposures to repeated blast events.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

(WRAIR) Nothing to report.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

(WRAIR) Study progress and/or results were presented at the following meetings and conferences,
Military Health Research Symposium, Congressional National Defense Authorization Act (NDAA), Section 734, Working Group Topic, 12 AUG 202, Virtual
In-progress review to CDMRP, 20-22 OCT 2020, Virtual

(WRAIR) Preliminary brief back on site-specific blast exposure data (overpressure, impulse, acoustics) were presented to the following sites,
-Ft Benning, GA
-Camp Pendleton, CA

(WRAIR) Study collaborators:
Dr. Haghighi (James J Peters VA Medical Center Collaborating Investigator) facilitated a U.S. Department of Veteran Affairs Health Services Research & Development Cyberseminars on 15 MAY 2020.

(WRAIR) WRAIR press release:
https://www.wrair.army.mil/node/593#:~:text=Brain%20Injury%20Signatures%20Found%20among%20Healthy%20Persons%20Link%20to%20Occupational%20Blast%20Exposure,-Contact%20us%20for&text=Scientists%20at%20the%20Walter%20Reed,and%20explosives%20used%20in%20training.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

(WRAIR) Data analyses and final report preparations will continue; an effort to combine data across study sites and blast environments is underway. Both overpressure and acoustic measurements will be analyzed to characterize the blast environments and quantify individual blast exposures. Statistical analyses looking at pre/post blast exposure will continue, in addition to incorporating individual blast exposures, demographic information, behavioral, cognitive, and physical outcome metrics in analyses.

(WRAIR) The seven-biomarker panel in serum blood samples testing and comparisons from multiple sites will continue. Blood proteome, genome, transcriptome, bioinformatics development and testing will also continue. Novel biomarker (undisclosed) testing and evaluation and ability to classify the effects of blast exposure will continue. Genome scale DNA methylation profiling on blood samples will continue and analyses that will incorporate demographics/cognitive response/behavioral/physical outcomes data collected during training will also continue.

(WRAIR) Submit abstracts to the following conferences,
-Military Health Systems Research Symposium (abstracts due 31 MAR 2021)
-National Neurotrauma Symposium, (abstracts due 15 April 2021)
-Military Aspects of Shock and Blast (abstracts due TBD)

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

(WRAIR) Blast environmental characterization and quantifying individual exposure inform safety and occupational health groups on possible occupational training hazards. Outcomes and associated effects will be used by the operational community for their risk/benefit assessment.

(WRAIR) This work has provided evidence that protein associated with diagnosed neurological trauma or disease have utility as peripheral biomarkers of subconcussive overpressure exposure.

The overarching concepts are poised for further validation in military, as well as pertinent civilian settings.

(WRAIR) DNA methylation and gene expression patterns change through both acute blast exposure (before and after blast) and in cumulative (lifetime) exposure to blast throughout a career in the military. This data and these findings will make an impact on the field of blast exposure research, mild TBI research, and research conducted in the context of the military.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

(WRAIR) This work is likely to impact policies, research protocols, and laws related to military personnel, the Department of Defense, and blast exposure. Notably, a recent 2020 National Defense Authorization Act (NDAA) ordered the history of blast exposure and blast duration from both combat exposure and trainings to be included in Service Members' medical histories.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:
- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

(WRAIR) Blood based biomarker results may be used for development of rapid, field deployable blood tests performed using near-term and far-forward technology.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:
- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

(WRAIR) Results from environmental characterization impact military and law enforcement groups by increasing knowledge of blast pressure leading to possible modifications in training practices, aiding in mission planning, and improving safety. This work also identifies biological

responses to blast exposure and has the potential to impact blast-related policies and training/exposure protocols.

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

(WRAIR) Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

(WRAIR) Travel restrictions related to COVID-19 canceled data collections, efforts were diverted to data analysis which resulted in 9 published articles in peer reviewed journals. Travel restrictions also interfered with opportunities to present findings/disseminate results. This resulted in 14 of 17 abstracts submitted and accepted to various conferences that were not presented [2 x International Neurotrauma Symposium (Melbourne, AU), 1 x National Capital Area Traumatic Brain Injury Research Symposium (Bethesda, MD), 3 x 26th International Symposium on Military Aspects of Blast and Shock (Wollongong, AU), 7 of 10 x Military Health System Research Symposium (Kissimmee, FL)]. These abstracts will be resubmitted and presented at postponed/rescheduled events, but may have to undergo the submission process again.
Minor delays occurred in sample collection, processing, assaying, and analyzing biospecimens as staff adjusted to COVID-19 based closures and implemented stringent safety protocols.
Data submission to FITBIR was delayed due to WRAIR's internet security measures blocking the FITBIR data submission tool from running. A ticket was placed with WRAIR IT and the issue was resolved with data being submitted 5 OCT 2020. Currently, guidance has been sought for several CDEs in FITBIR blast data due to data complexities and submission of this data is delayed.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

(WRAIR) No cost extension was requested to complete reporting/disseminating study outcomes. The Initiating PI retired and the study underwent a PI change.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

(WRAIR) Core protocol Amendment #12 received limited WRAIR Commander Authorization was on 06 JAN 2020. This amendment added and approved collaborations/data sharing with New Jersey Institute of Technology, Penn State University, and Walter Reed National Military Medical Center. The authorization is limited by pending support letters for sites #8 and #9.

(WRAIR) Core protocol Amendment #13 was submitted to WRAIR HSPB/IRB on 7 JAN 2020, with updated submission on 6 FEB 2020. WRAIR IRB approval was received 20 FEB 2020 and limited WRAIR Commander Authorization was received 08 MAR 2020; HRPO will be notified during annual reporting. The amendment added data sharing language to the protocol for sharing identified and de-identified data with the Defense Health Agency. The authorization is limited by pending support letters for sites #8 and #9.

(WRAIR) Core protocol Amendment #14 was submitted to WRAIR HSPB/IRB on 20 MAY 2020 with updated submission on 29 MAY 2020, and 01 JUL 2020. WRAIR IRB approval was received on 24 AUG 2020, limited HRPO approval on 31 AUG 2020, full HRPO approval on 23 SEPT 2020, and limited WRAIR Commander Authorization on 24 SEPT 2020. The amendment was used to change and update the PI, add 1 associate investigator, revise site information, and sample size (from 800 to 1200). This amendment also included approval to collaborate with US Naval Hospital Okinawa (collaboration initiated in Amendment #12). The authorization is limited by pending support letters for sites #8 and #9.

Significant changes in use or care of vertebrate animals.

(WRAIR) Nothing to Report, not applicable

Significant changes in use of biohazards and/or select agents

(WRAIR) Nothing to Report, not applicable

6. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Chen, Y., O'Shaughnessy, T. J., Kamimori, G. H., Horner, D. M., Egnoto, M. J., & Bagchi, A. Role of Interfacial Conditions on Blast Overpressure Propagation into the Brain. Frontiers in Neurology-Neurotrauma, 11, 2020, p. 323, published, yes. https://www.frontiersin.org/articles/10.3389/fneur.2020.00323/full?report=reader

Kamimori, G. H., Egnoto, M. J., & McQuiggan, W. An Expansion on Suppressor Usage for Weapon Systems: Combining Evaluations of Auditory Insult to Blast Overpressure Assessment. Journal of the National Tactical Officers Association, Summer 2020, 2020, p. 54, published, yes.

Medda, A., Funk, R., Ahuja, K., & Kamimori, G. Measurements of Infrasound Signatures From Grenade Blast During Training. Military Medicine, 186(Supplement_1), p. 523-528, published, no.
https://academic.oup.com/milmed/article/186/Supplement_1/523/6119507?login=true

Misistia, A., Skotak, M., Cardenas, A., Alay, E., Chandra, N., & Kamimori, G. H. Sensor orientation and other factors which increase the blast overpressure reporting errors. Plos One, 15(10), 2020, e0240262, published, yes.
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0240262

Skotak, M., Salib, J., Misistia, A., Cardenas, A., Alay, E., Chandra, N., & Kamimori, G. H. Factors contributing to increased blast overpressure inside modern ballistic helmets. Applied Sciences, 10(20), 2020, p. 7193, published, yes.
https://www.mdpi.com/2076-3417/10/20/7193

Thangavelu, B., LaValle, C. R., Egnoto, M. J., Nemes, J., Boutté, A. M., & Kamimori, G. H. Overpressure exposure from. 50-caliber rifle training is associated with increased amyloid beta peptides in serum. Frontiers in neurology, 11, 2020, p. 620, published, yes.
https://www.frontiersin.org/articles/10.3389/fneur.2020.00620/full?report=reader

Thangavelu, B., Kamimori, G. H., Gilsdorf, J. S., Shear, D. A., & Boutté, A M. Dataset of Rat and Human Serum Proteomes Derived from Differential Depletion Strategies prior to Mass Spectrometry. Data In Brief, 30, 2020, p. 105657, published, yes.
https://www.sciencedirect.com/science/article/pii/S2352340920305515

Wang, Z., Wilson, C. M., Ge, Y., Nemes, J., LaValle, C., Boutte, A., Carr. W., Kamimori, G. H., & Haghighi, F. (2020). DNA methylation patterns of chronic explosive breaching in US Military Warfighters. Frontiers in neurology, 11, 2020, published, yes.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7645105/

Wang, Z., Wilson, C.M., Mendelev, N., Ge, Y., Galfalvy, H., Elder, G., Ahlers, S., Yarnell, A.M., LoPresti, M.L., Kamimori, G.H. and Carr, W. (2020). Acute and chronic molecular signatures and associated symptoms of blast exposure in military breachers. Journal of neurotrauma, 37(10), pp.1221-1232. https://www.liebertpub.com/doi/full/10.1089/neu.2019.6742

Przekwas, A., Garimella, H. T., Chen, Z. J., Zehnbauer, T., Gupta, R. K., Skotak, M., Carr, W., & Kamimori, G. H. Fast-running tools for personalized monitoring of blast exposure in military training and operations. Military medicine, accepted/awaiting publication, yes.

Boutté, A. M., Thangavelu, B., Nemes, J., LaValle, C. R., Egnoto, M., Carr, W., & Kamimori, G. H. Elevation of Neurotrauma Biomarkers and Adverse Symptomology among Personnel Exposed to Occupational Overpressure without Clinically Diagnosed Traumatic Brain Injury. JAMA Network Open, submitted/in review, yes.

Kamimori, G.H, McQuiggan, W., Ramos, A.N., LaValle, C.R., Misistia, A., Salib, J., & Egnoto, M. J. A Comparison of Water Tamped and Untamped Explosive Breaches: Practical Applications for the Tactical Community. Journal of Special Operations Medicine, submitted/in review, yes.

Salib, J., Egnoto, M.J., Skotak, M., LaValle, C.R., Misistia, A., & Kamimori, G.H. A Comparison of the Internal and External Overpressure for various Ballistic Helmets. Journal of Military Medicine, submitted/in review, yes.

Wiri, S., Brisby, J., Rule, G. T., Needhm, C. E., Carr, W., & Kamimori, G. H. Field Data Comparisons with High Fidelity Simulations of Blast Exposure to Breachers during Training. Shock Waves, submitted/in review, yes.

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Boutté, A. M., Thangavelu, B., Nathan, D., LaValle, C. R., Egnoto, M. J., Nemes, J., Carr, W., Shear, D. A., & Kamimori, G. H. Measurement of Blood Derived Biomarkers for Neurotrauma and Acute Repeated Low Level Overpressure Exposure using Targeted Quantitation and Unbiased Proteomics. Military Health Research Symposium, Congressional National Defense Authorization Act (NDAA), Section 734, Working Group, 12 AUG 2020, virtual presentation, yes.

Brungart, D., Sheffield, B., Kulinski, D., Carr, W., Vause, N., Hecht, Q., & Kamimori, G. H. Field Assessment of Acute Auditory Responses to Noise and Blast Exposure. Military Health Research Symposium, Congressional National Defense Authorization Act (NDAA), Section 734, Working Group, 12 AUG 2020, virtual presentation, no.

Carr, W., LaValle, C., Boutté, A., Salib, J., Nemes, J., Misistia, A., Thangavelu, B., & Kamimori, G. Breacher's Brain Association with Peak Overpressure and Impulse Exposures in Military Training. Military Health Research Symposium, Congressional National Defense Authorization Act (NDAA), Section 734, Working Group, 12 AUG 2020, virtual presentation, yes.

Haghighi, F. Acute and Chronic Molecular Signatures and Associated Symptoms of Blast Exposure in Military Breachers. U.S. Department of Veteran Affairs Health Services Research & Development Cyberseminars, 15 MAY 2020, virtual presentation, no.
https://www.hsrd.research.va.gov/for_researchers/cyber_seminars/archives/video_archive.cfm?SessionID=3811

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

(WRAIR) Nothing to Report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

(WRAIR) Nothing to Report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

(WRAIR) Nothing to Report

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *biospecimen collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

- (WRAIR) Data: Overpressure, acoustics, neurocognitive, symptom, demographic/occupational history data were collected at Camp Pendleton, CA and Tacflow Academy (sites #7 and #4, respectively); in addition, stress inventory data were collected at site #7.
- (WRAIR) Biospecimen collections: cheek swab and blood samples were collected at sites #7 and #4.
- (WRAIR) Symptom, neurocognitive, demographics data from sites #2 (x 2), #6, #7 were submitted to FITBIR Informatics System on 5 OCT 2020.
- (WRAIR) Biospecimens were transferred to James J. Peters VA Medical Center, Icahn School of Medicine at Mount Sinai (New York, NY) for additional biomarker (genetic) analyses.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Example:

Name: *Mary Smith*
Project Role: *Graduate Student*
Researcher Identifier (e.g. ORCID ID): *1234567*

Nearest person month worked: *5*

Contribution to Project: *Ms. Smith has performed work in the area of combined error-control and constrained coding.*

Funding Support: *The Ford Foundation (Complete only if the funding support is provided from other than this award).*

Name: Gary Kamimori
Project Role: WRAIR PI
Research Identifier (ORCID ID): 0000-0001-7899-9553
Nearest person month worked: 9
Contribution to project: no change.

Name: Angela Boutté
Project Role: WRAIR Laboratory Investigator
Research Identifier (ORCID ID): 0000-0003-3542-8122
Nearest person month worked: 6
Contribution to project: no change.
Funding Support: The Combat Casualty Care Research Program

Name: Bharani Thangavelu
Project Role: WRAIR Research Fellow; National Research Council
Nearest person month worked: 6
Contribution to project: Conducted blood based biomarker assays and analytics.

Name: Fatemeh Haghighi
Project Role: WRAIR Collaborating Laboratory Investigator, James J. Peters VA Medical Center, Icahn School of Medicine at Mount Sinai
Research Identifier (ORCID ID): 0000-0003-0920-6956
Nearest person month worked: 1
Contribution to project: no change.
Funding Support: Research Career Scientist Award (#1IK6CX002074) from the Department of Veterans Affairs. RR&D: RX001705

Name: Caroline Wilson
Project Role: Research Associate, James J. Peters VA Medical Center, Icahn School of Medicine at Mount Sinai
Research Identifier (ORCID ID): 0000-0002-2553-4151
Nearest person month worked: 6
Contribution to project: DNA sample processing and preparation for sequencing. Conducted blood based biomarker assays involving ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) analyses.
Funding Support: RR&D: RX001705

Name: Zhaoyu Wang

Project Role: Data Scientist, James J. Peters VA Medical Center, Icahn School of Medicine at Mount Sinai
Nearest person month worked: 6
Contribution to project: Quality control and data analysis of methylation and sequencing data. Creating and running pipelines for analyzing data; figure generation.
Funding Support: RR&D: RX001705

Name: Yongchao Ge
Project Role: Senior Biostatistician, James J. Peters VA Medical Center, Icahn School of Medicine at Mount Sinai
Nearest person month worked: 1
Contribution to project: Senior statistician on DNA methylation pipelines and analyses.
Funding Support: RR&D: RX001705

Name: Christina LaValle
Project Role: WRAIR Data Manager/Statistician, Study Coordinator
Research Identifier (ORCID ID): 0000-0003-1529-4761
Nearest person month worked: 12
Contribution to project: no change

Name: Walter Carr
Project Role: Research Psychologist, WRAIR PI,
Research Identifier (ORCID ID):
Nearest person month worked: 2
Contribution to project: oversight of all study-related aspects, protocol preparation, data collection, data analyses, dissemination of results

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

(WRAIR) Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Military

Organization Name: I & III Marine Expeditionary Force (MEF)
Location of Organization: Camp Pendleton, CA (I MEF) & Camp Hansen, Okinawa, Japan (III MEF)
Partner's contribution to the project

- Facilities – project staff used partner's facilities for project activities
- Collaboration – technical discussions between partner and project staff
- Other – partner organization permitted subject recruitment to enroll study volunteers

Organization Name: US Army Research Laboratory (ARL)
Location of Organization: Adelphi, MD
Partner's contribution to the project

- Facilities – project staff used partner's facilities for project activities
- Collaboration – technical discussions between partner and project staff

Organization Name: US Army Asymmetric Warfare Group (AWG)
Location of Organization: Ft A.P. Hill, VA
Partner's contribution to the project

- Facilities – project staff used partner's facilities for project activities
- Collaboration – technical discussions between partner and project staff

Organization Name: Engineer Research and Development Center
Location of Organization: Champaign, IL
Partner's contribution to the project

- Facilities – project staff used partner's facilities for project activities
- Collaboration – technical discussions between partner and project staff

Organization Name: US Army Aeromedical Research Laboratory (USAARL)
Location of Organization: Ft Rucker, AL
Partner's contribution to the project

- Facilities – project staff used partner's facilities for project activities
- Collaboration – technical discussions between partner and project staff

Private Tactical Training Groups
Organization Name: Forced Entry Tactical Training (FETT)/Global Assets Integrated
Location of Organization: multiple sites/locations
Partner's contribution to the project

- Facilities – project staff use partner's facilities for project activities
- Collaboration – partner staff work with project staff on project

Organization Name: Tacflow Academy
Location of Organization: multiple sites/locations
Partner's contribution to the project

- Facilities – project staff used partner's facilities for project activities
- Collaboration – technical discussions between partner and project staff
- Other – partner organization will permit subject recruitment to enroll study volunteers

Academic
Organization Name: Georgia Tech Research Institute (GTRI)
Location of Organization: Atlanta, GA
Partner's contribution to the project

- Facilities – project staff use partner's facilities for project activities
- Collaboration – partner staff work with project staff on project

Organization Name: Johns Hopkins University Applied Physics Laboratory
Location of Organization: Laurel, MD
Partner's contribution to the project

- Facilities – project staff use partner's facilities for project activities
- Collaboration – partner staff work with project staff on project

Organization Name: New Jersey Institute of Technology
Location of Organization: Newark, NJ
Partner's contribution to the project

- Facilities – project staff used partner's facilities for project activities
- Collaboration – partner staff work with project staff on project

Organization Name: James J. Peters VA Medical Center, Icahn School of Medicine at Mount Sinai
Location of Organization: New York, NY
Partner's contribution to the project

- Facilities – project staff use partner's facilities for project activities
- Collaboration – partner staff work with project staff on project

Organization Name: Penn State University
Location of Organization: State College, PA
Partner's contribution to the project
- Collaboration – technical discussions between partner and project staff

Organization Name: New York Genome Center (NYGC)
Location of Organization: New York, NY
Partner's contribution to the project:
- In-kind support - NYGC completed DNA methylation assays on Infinium MethylationEPIC chips as a service to James J. Peters VA Medical Center, Icahn School of Medicine at Mount Sinai.

Private Technology
Organization Name: Applied Research Associates
Location of Organization: San Antonio, TX
Partner's contribution to the project
- Collaboration – partner staff work with project staff on project

Organization Name: CFD Research Corporation
Location of Organization: Huntsville, AL
Partner's contribution to the project
- Collaboration – technical discussions between partner and project staff

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES: