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TITLE: Neurocognitive and Biomarker Evaluation of Combination mTBI from Blast Overpressure and Traumatic Stress

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14. ABSTRACT

Mild traumatic brain injury (mTBI) and post-traumatic stress disorder (PTSD) are major medical issues for the warfighter. The current project is designed to evaluate the impact of mild traumatic brain injury (using blast over pressure) and traumatic stress (using a predator exposure procedure and conditioned fear procedure) in a rodent model. The studies evaluate these insults alone and in combination to specifically address the question of whether mTBI can exacerbate the effects of psychological stress. Additionally, following the insults, a molecular biological evaluation is performed based upon the discovery of biomarkers that have been shown to be correlated with other forms of TBI. Thus, the project aims to systematically assess the combined effects of blast overpressure, traumatic stress and learned stress responses in rodents with the aim of understanding how these forces may interact to impact behavior as well as evaluating their outcome on known biomarkers involved in TBI and stress response system activation. This project is a new start and while progressing, results are too incomplete to provide conclusions at this point.

15. SUBJECT TERMS

Traumatic brain injury, post-traumatic stress disorder, blast over pressure

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INTRODUCTION:

There is a high co-morbidity of mild traumatic brain injury (mTBI) and post traumatic stress disorder (PTSD) in Warfighters. Co-morbid mTBI and PTSD appears to be more prevalent than mTBI cases in isolation. Mild TBI and PTSD are statistically ranked the highest of battlefield injuries in OIF and OEF. It is generally assumed that the manifestation of mTBI symptoms result from one or more exposures to improvised explosive devices (IEDs) and that PTSD symptoms result from exposure to prolonged battlefield stress. The high incidence and comorbidity of PTSD and mTBI underscore an imperative for the DoD research community to gain an understanding of the underlying mechanisms that precipitate these conditions together with the often associated post-concussive syndrome (PCS) which appears to share many of the same cognitive and emotive symptoms associated with TBI and PTSD. The purpose of the proposed experiments is to determine the relative contributions of repeated exposure to blast overpressure (BOP) and exposure to stressful (predatory) events, when presented alone and in combination, in a rodent model. The level of BOP used in the proposed experiments has been demonstrated by the PI (Ahlers) to be associated with mild outcomes where there is evidence of cognitive impairment in the absence of demonstrable pathology. The proposed experiments take advantage of years of extensive experience from the primary investigators (Ahlers & Genovese) in studies of the effects of BOP and stressful events and their effects on behavior. The assessment behavioral outcomes resulting from exposure to BOP and stress will be complemented by the assessment of the potential protein biomarkers by Dr. Dave and his group who have considerable experience identifying protein biomarkers for brain injury.

BODY:

The objective of this research proposal is to systematically assess the combined effects of BOP and exposure to traumatic stress in rodents with the aim of understanding how these forces may interact with the manifestation of cognitive and emotive dysfunction, as well as evaluating their outcome on known biomarkers involved in TBI and stress response system activation.

Specific Aims

- Specific Aim 1: Assess the effects of repeated exposure to BOP and stress on cognitive and emotional performance.

- Specific Aim 2: To characterize the extent to which BOP will specifically modify the process of conditioned fear in rats.

- Specific Aim 3: Evaluate the combined effects of repeated exposure to BOP and stress on established biomarkers of traumatic brain injury (TBI).

Task 1: Generation of approved IACUC protocols. We have generated one protocol and gained WRAIR/NMRC approval. The ACURO oversight body has also approved the

protocol. A second protocol is still being prepared.

KEY RESEARCH ACCOMPLISHMENTS: (Ahlers portion) None significant, owing to the fact that the effort is in the early stages. We have exposed rats to BOP as prescribed in the proposal.

REPORTABLE OUTCOMES:

Presentations- This effort (as well as the companion effort from Dr. Genovese) was presented/reviewed at a recent In Progress Review (IPR) held in conjunction with the ATACCC meeting in Ft. Lauderdale, FL.

CONCLUSION: The project is on pace to complete the milestones provided in the proposal.

APPENDICES: None, work is in early stages.

SUPPORTING DATA: None, work is in early stages.