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**TITLE:** Characterization of Psychological Resilience and Readiness: Cross-Validation of Cognitive and Behavioral Metrics During Acute Military Operational Stress

**PRINCIPAL INVESTIGATOR:** Dr. Bradley C. Nindl

**CONTRACTING ORGANIZATION:** The University of Pittsburgh, Pittsburgh, PA

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<b>14. ABSTRACT:</b> Military operational stress can come in many forms via physical exertion, cognitive overload, sleep restriction, energy insufficiency, and emotional or psychological stress. In 2013, a DoD Human Performance Optimization Metrics Conference was held and identified the lack of a consensus for operationally relevant and standardized metrics that meet military requirements as the single most important issue related to the translation of cognitive readiness to operational and military leader utility. For metrics to be of benefit to the military, their relationship to Service member health and performance must be established under acute and chronic military operational stress scenarios. Our objective is to validate a comprehensive series of neurocognitive, psychological, psychomotor, sensorimotor, physiological, and sleep metrics within military operational stress paradigms to assess military-relevant and tactical cognitive readiness and resiliency. Our study proposes to use an ecologically valid model of simulated military operational stress (sleep restriction, caloric deficit, and physical work). This model will provide a biomedical framework to quantify temporal changes in metrics across the neurocognitive, psychological, psychomotor, sensorimotor, physiological, and sleep domains. Machine learning will be used to provide a dashboard and predictive algorithm for dependent variables centered on military-relevant and tactical cognitive readiness and resiliency					
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## **Characterization of Psychological Resilience and Readiness: Cross-Validation of Cognitive Behavioral Metrics During Acute Military Operational Stress**

Dr. Bradley C. Nindl (Co-PI), Fabio Ferrarelli (Co-PI), Chris Connaboy, Shawn Flanagan, Qi Mi, Mita Lovalekar, Nicole Sekel, Meaghan Beckner, Aaron Sinnott, William Conkright, Felix Proessl, Maria Canino, Maggie Sphar, Alice Lagoy, Amy Haufler, Peter Roma, Brian Martin, Amy Haufler, Hassen Khan, Mackenzie Osborn, Jenna Parrish

The McGowan Institute for Regenerative Medicine, Pittsburgh, PA

University of Pennsylvania, Philadelphia, Pennsylvania

National Aeronautics and Space Administration, Houston, TX

Johns Hopkins University, Baltimore, MD

### **Corresponding Author**

Bradley C. Nindl  
Neuromuscular Research Laboratory  
Warrior Human Performance Research Center  
School of Health and Rehabilitation Sciences  
University of Pittsburgh  
3860 South Water Street  
Pittsburgh, PA 15203  
Email: [bnindl@pitt.edu](mailto:bnindl@pitt.edu)  
Phone: 412-246-0466

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## 1. INTRODUCTION

### IMPORTANCE OF COGNITIVE RESILIENCE AND READINESS TO ARMY STRATEGIC OBJECTIVES

Cognitive resilience can be operationally defined as “*the capacity to overcome the negative effects of setbacks and associated stress on cognitive function or performance*”.<sup>1</sup> Military operational stress can come in many forms via the singular or combined effects of physical exertion, cognitive overload, sleep restriction, energy insufficiency, and emotional and psychological stress<sup>2-6</sup>. In the volatile, uncertain, complex, and ambiguous (VUCA) contemporary operating national security environment, both current and future operations demand and place a higher priority on enhancing and sustaining the cognitive readiness and resiliency of our military service members (SMs).<sup>8,9</sup>

Cognitive neuroscience has highlighted the role and importance of various cognitive processes for optimal functioning. Attention, short-term working memory, generalized intelligence, reasoning, judgement, decision making, problem solving, adaptability, creativity, emotional bias, emotional intelligence, social intelligence, and metacognition all contribute to different, but often complementary aspects of cognition.<sup>4-6,12,13</sup> While there are studies in the literature that have reported on metrics of these varied cognitive dimensions, these studies are replete with limitations in their ability to predict real-world performance or capacity for performance, particularly regarding high-stress military training and occupational environments.<sup>14</sup>

Progressive neuroscience efforts are necessary for understanding and developing cognitive resilience and readiness. Neuroscience efforts have elucidated the transient and long-term, deprecating effects of a range of operational stressors on brain functioning and, ultimately, performance. The application of non-invasive approaches such as using biochemical, electrophysiological, and psychophysiological indices during neurobehavioral tasks, provides validation as objective measures of the effects of both stress and stress-mitigation practices. These approaches are also sensitive to individual differences, related to both experiential and trait-like factors, which can predict performance during stress or challenge conditions<sup>12,13</sup>. As such, the application of diverse and progressive neuroscience approaches which includes electrophysiological, psychophysiological, neurobehavioral, neurophysiological, and biochemical measurements is necessary for identifying and validating the biopsychosocial correlates and predictors of cognitive resilience and readiness.

For the military to achieve objectives related to providing a validated neurocognitive toolkit for assessing performance within military paradigms, cognitive readiness metrics and tools are required in order to translate cognitive resilience to military operational performance. Our study included an innovative test designed specifically to assess adaptive decision making during realistic military scenarios: a Soldier Performance and Effective Authentic Response (SPEAR) test developed by the Asymmetric Warfare Group (AWG) and the Johns Hopkins University Applied Physics Laboratory. Using this test as a one of our dependent variable outcome measures allows a unique opportunity to monitor and assess selected metrics and mediating domains as indices/correlates and predictors across neurocognitive, psychological, psychomotor, sensorimotor, physiological, and sleep domains regarding military relevant cognitive-centric outcome measures.

## OBJECTIVE

The overall objective of this project was to validate a comprehensive series of neurocognitive, psychological, psychomotor, sensorimotor, physiological, and sleep metrics within military operational stress paradigms to assess military-relevant and tactical cognitive readiness and resiliency.

## RESEARCH STRATEGY

*Simulated Stress Scenario:* The laboratory-based simulated military operational stress scenario that we will conduct for Specific Aim 1 will be a modification based upon the US Army Research Institute of Environmental Medicine (USARIEM) Sustained Operations Model (SUSOPS) developed by Dr. Scott Montain in 2000. The ARIEM/Montain model has been published and characterized the effects of 72 hrs of combined (sleep restriction, caloric deficit, and physical work) operational stress on physical, cognitive, and military performance.<sup>2,4,30-32</sup> The simulated military operational stress scenario will emphasize those military skills deemed most vital to operational effectiveness: shooting, moving, and communicating.

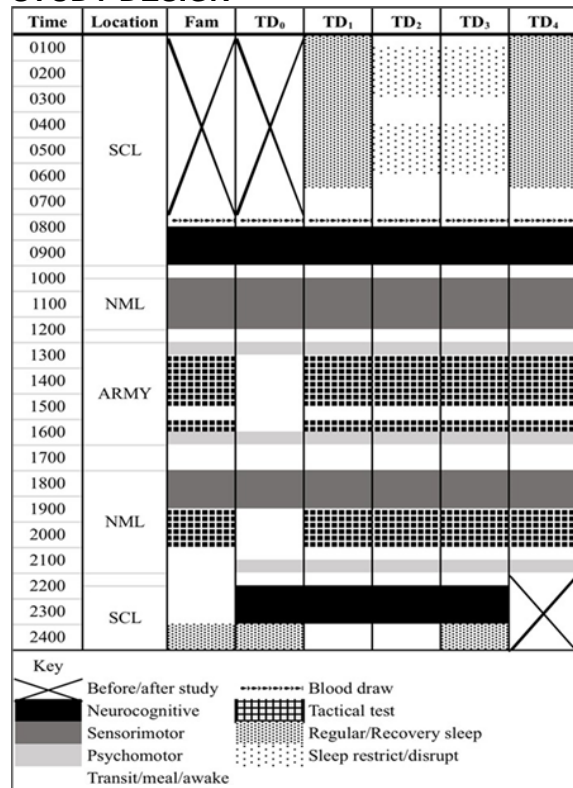
*Recruitment:* This study targeted men and women with military experience, including currently serving or have served within the last 5 yrs on either Active or Reserve component.

## DEPENDENT AND MEDIATING VARIABLES

*Dependent Variables:* Marksmanship (assessed via an EST 3000); individual movement techniques (assessed via a THOR3 operator readiness assessment); military communication and decision making (assessed by the Soldier Performance and Effective Authentic Response (SPEAR) Adaptability test, and Code-substitution tests). The SPEAR test was selected due to its high face validity, reliability and high military applicability. Nevertheless, in recognition of the developmental stage of the SPEAR test, we also selected well established higher cognitive function assessments: The Matching to Sample<sup>4-6,17</sup>, the Grammatical Reasoning test<sup>4-6,17,34</sup>, and the Reading the Mind in the Eyes Test<sup>35,36</sup> and spatial navigation test to enable a comparison between novel and military relevant assessments and established metrics.

*Mediating Variables:* Neurocognitive (attention, short-term memory, decision making/reasoning, adaptability/creativity); Psychomotor (Psychomotor Vigilance Test, Multiple Object Tracking, Reaction Time, Perception Span, Go/No Go, Depth Perception, Dynamic Visual Acuity); Sensorimotor/neuromuscular (perception-action coupling task, action boundary coordinated interceptive jumping task, obstacle course); Physiological (aerobic fitness, maximal loaded broad jump, maximal vertical jump height, maximal voluntary contractile force, heart rate variability, stress biomarkers).

## STUDY DESIGN



The overall study design is depicted in the Figure to the left. After completing screening procedures to ascertain eligibility, eligible individuals were invited to complete the 96- hour protocol. Specifically, participants will be invited to spend 4 consecutive nights in the UPMC Sleep and Chronobiology laboratory. Night 1 served as a baseline and adaptation night to the sleep environment. Sleep was monitored with high-density EEG to identify baseline EEG characteristics that may predict cognitive vulnerability of resilience to SR, fatigue, and caloric deficit and was obtained on Night 1. Sleep restriction was accomplished by allowing participants to sleep only 50% of their habitual sleep time (as determined by sleep diary and actigraphy) by postponing their habitual bedtime and advancing their habitual rise time for 2 consecutive nights (Night 2 and 3). The daytime fatigue protocol consisted of a series of physically and mentally demanding, tactically oriented military tasks that service members would be required to do largely related to battlefield mobility. More specifically, prolonged endurance-based load

carriage interspersed by a series of assessments via the USASOC operator readiness assessment. A similar simulated model of military operational stress has been successfully used in the past and is known to result in cognitive degradation.<sup>2,4</sup> Neuromuscular force production, sensorimotor perception-action coupling, heart-rate variability, and fatigue hormonal biomarkers measures were also periodically assessed to quantify physiological and neurocognitive fatigue. On Night 4, all participants were allowed to sleep undisturbed at their habitual bedtime, and ad libidum in the morning, and post-recovery testing will follow the same schedule as determined on prior testing days.

After the initial screening and informed consent process, subjects reported to the UPITT NMRL for baseline testing and test familiarization approximately 1 week before the simulated military operational stress scenario. At baseline, participants completed measures of individual traits and baseline characteristics, as well as baseline performance on primary tasks of interest. At pre-set intervals during the experimental protocol, they completed tasks and measures that allowed for the capture of changes in performance across different primary dependent and mediating domains of interest. Volunteers returned to the UPITT NMRL on another day (test day 0 [TD0]) for a control period testing block. TD0 started at 0800 with a morning-fasted blood draw followed by a neurocognitive, sensorimotor, and psychomotor test batteries (3.75 hrs) occurring during the morning. Following a short break for lunch, the sensorimotor and psychomotor test batteries (3 hrs) occurred again in the afternoon. TD0 concluded with sleeping in the sleep laboratory, as mentioned above. The military operational stress scenario took place from test day 1 (TD1) through test day 3 (TD3). All of the testing conducted on TD0 also occurred on TD1-TD3. A list of all of the outcome measures is provided below.

The military operational stress occurring on TD1 through TD3 consisted of the following daily tasks and events: 1) a 1 hr tactical road march with a load of 20.4 kg at a pace of 4 mph, 2) a 30 min marksmanship realistic operational exercise emphasizing marksmanship accuracy and Shoot/Don't Shoot (threat discrimination) scenarios conducted on the EST 3000, 3) individual movement technique conducted by the THOR3 Operator Readiness Test (ORT) lasting approximately 30 minutes, 4) manual materials and wall building tasks<sup>2</sup> lasting 30 min, and 5) military communication and decision-making exercise via the Soldier Performance and Effective Authentic Response [SPEAR] adaptive decision-making task lasting 1 hr. Caloric restriction was accomplished by only providing half of their estimated caloric requirements based upon resting metabolic rate (measured upon waking on TD1), age, and activity level.<sup>37,38</sup> The study concluded with a recovery sleep night following TD3 and a recovery test day on TD4.

TEST BATTERY DOMAIN	MEASURE	T	B/F	D0	E1	D1	E2	D2	E3	D3	E4	D4
<b>INDEPENDENT VARIABLES:</b>												
<b>NEUROCOGNITIVE (1.5 hours)</b>	<i>Motor Praxis Test</i>	5 min	F	X		X		X		X		X
	<i>Visual Object Learning Test</i>	< 5 min	F	X		X		X		X		X
	<i>Fractal 2-Back</i>	5 min	F	X		X		X		X		X
	<i>Abstract Matching</i>	10 min	F	X		X		X		X		X
	<i>Line Orientation Test</i>	2 min	F	X		X		X		X		X
	<i>Emotion Recognition Test</i>	10 min	F	X		X		X		X		X
	<i>Matrix Reasoning Test</i>	15 min	F	X		X		X		X		X
	<i>Digit-Symbol Substitution Task</i>	5 mins	F	X		X		X		X		X
	<i>Balloon Analog Risk Test</i>	15 mins	F	X		X		X		X		X
	<i>Psychomotor Vigilance Test</i>	10 mins	F	X		X		X		X		X
	<i>Objective Cooperation/Dominance Test</i>	10 min	F	X		X		X		X		X
	<i>Affective Dot-Probe</i>	10 mins	F	X		X		X		X		X
	<b>PSYCHOLOGICAL (1.25 hours)</b>	<i>NEO Personality Test</i>	30 min	B								
<i>Connor Davidson Resilience Scale</i>		5 mi	B									
<i>Deployment Risk and Resilience Inventory- II</i>		20 mins	B									
<i>Coping Styles and Strategies</i>		< 5 mins	B									
<i>Patient Health Questionnaire</i>		5 mins	B									
<b>PSYCHOMOTOR (0.75 hour)</b>	<i>Psychomotor Vigilance Test</i>	10 mins	F	X		X		X		X		X
	<i>Multiple Object Tracking</i>	5 mins	F	X		X		X		X		X
	<i>Reaction Time</i>	5 mins	F	X		X		X		X		X
	<i>Perception Span</i>	5 mins	F	X		X		X		X		X
	<i>Go/No Go</i>	5 mins	F	X		X		X		X		X
	<i>Depth Perception</i>	5 mins	F	X		X		X		X		X
	<i>Dynamic Visual Acuity</i>	5 mins	F	X		X		X		X		X
	<i>Perception-Action Coupling Task</i>	15 mins	F	X		X		X		X		X
<b>SENSORIMOTOR (1.5 hours)</b>	<i>Action Boundary Coordinated Interceptive Jumping Task</i>	30 mins	F	X		X		X		X		X
	<i>Obstacle Cross</i>	15 mins	F	X		X		X		X		X
	<i>Contralateral/ ipsilateral cortical silent periods</i>	10 mins	F	X		X		X		X		X
	<i>Motor evoked potential recruitment curve</i>	10 mins	F	X		X		X		X		X
	<i>Resting motor thresholds</i>	10 mins										
<b>PHYSIOLOGICAL (4 hours)</b>	<i>Aerobic Capacity</i>	15 mins	B									
	<i>Maximal Loaded Broad Jump</i>	2 mins	B									
	<i>Maximal Vertical Jump Height</i>	5 mins	B									
	<i>Maximal Voluntary Contractile Force</i>	5mins	B									
	<i>Heart Rate Variability</i>	ALL DAY	B	X		X		X		X		X
	<i>Stress Biomarkers</i>	5 mins	B	X		X		X		X		X
<b>SLEEP (4-8 hours)</b>	<i>Polysomnography</i>	ALL NIGHT	F		X		X		X		X	
	<i>Actigraphy</i>	ALL DAY	F		X		X		X		X	
	<i>Breathing Rate</i>	ALL NIGHT	F		X		X		X		X	
	<i>Electrocardiogram</i>	ALL NIGHT	F		X		X		X		X	
<b>DEPENDENT VARIABLES:</b>												
<b>TACTICAL (4 hours)</b>	<b>SHOOTING:</b>											
	<i>Engagement Skills Trainer 3000</i>	30 mins	F			X		X		X		X
	<b>MOVEMENT:</b>											
	<i>modified Operator Readiness Assessment</i>	30 mins	F			X		X		X		X
	<i>Spatial Navigation Task</i>	30 mins	F			X		X		X		X
	<b>COMMUNICATION/DECISION MAKING:</b>											
	<i>Manual Materials Handling/Wall Building Task</i>	20 mins	F			X		X		X		X
<b>Higher Order Cognitive Tests (0.3 hours)</b>	<i>Soldier Performance and Effect Authentic Response</i>	2 hours	F			X		X		X		X
	<i>Code Substitution Task</i>	5 mins	F			X		X		X		X
	<i>Matching to Sample</i>	5 mins	F			X		X		X		X
	<i>Grammatical Reasoning</i>	5 mins	F			X		X		X		X
	<i>Reading the Mind in the Eyes Test</i>	10 mins	F			X		X		X		X
KEY:												
B= BASELINE TESTING F= FAMILIARIZATION, D= Day, E= Evening												

## 2. KEYWORDS

Resilience, readiness, sleep, health, performance

### 3. ACCOMPLISHMENTS

#### PHYSICAL PERFORMANCE AND TACTICAL MOBILITY

- **LaGoy et al., *Sleep Health* 2022** found that  $\dot{V}O_{2peak}$  ( $\beta = -1.849$ ), ESS ( $\beta = 0.038$ ) and frontal NREM SWA ( $\beta = 0.415$ ) were identified as informative predictors of baseline performance. Higher  $\dot{V}O_{2peak}$  (better aerobic fitness), lower Epworth Sleepiness Scale scores (lower daytime sleepiness) and lower frontal SWA collectively predicted better baseline physical performance. Collectively, this model predicted 66.1% of the variance in baseline physical performance. Of the explained variance,  $\dot{V}O_{2peak}$  explained 66.4% (43.9% of total variance), ESS explained 10.1% (6.7% of total variance) and frontal SWA explained 23.4% (15.5% of total variance).
- **Conkright et al., 2021** found that tactical mobility (TMT) was affected similarly in men and women with speed and anaerobic capacity (i.e., 300US) being most negatively impacted while other performance metrics were maintained over the course of five days. As hypothesized, men achieved higher values than women across the protocol in most events including the VJ, WCC, FM, CD and 300US.

**Table 2.** Tactical Mobility Test (TMT) events during five days of simulated military operational stress.

Event	Group	Day 1	Day 2	Day 3	Day 4	Main effect of day	Main effect of sex
						p-value (partial $\eta^2$ )	p-value (partial $\eta^2$ )
		Baseline	Stress Onset	Peak Stress	Recovery		
WCC ( $m \cdot s^{-1}$ )	Men	1.53 $\pm$ 0.38	1.56 $\pm$ 0.32	1.50 $\pm$ 0.39	1.50 $\pm$ 0.33	0.173 (0.027)	<0.001 (0.327)
	Women	0.98 $\pm$ 0.35	1.07 $\pm$ 0.42	0.96 $\pm$ 0.31	1.00 $\pm$ 0.37		
FM (s)	Men	145.6 $\pm$ 13.1	148.8 $\pm$ 16.1	146.5 $\pm$ 16.0	148.8 $\pm$ 16.6	0.119 (0.032)	0.020 (0.083)
	Women	152.5 $\pm$ 13.3	157.4 $\pm$ 19.2	150.7 $\pm$ 17.0	145.7 $\pm$ 15.2		
CD (s)	Men	41.5 $\pm$ 23.5	40.0 $\pm$ 13.7	39.8 $\pm$ 14.2	43.6 $\pm$ 11.3	0.129 (0.030)	<0.001 (0.374)
	Women	82.0 $\pm$ 32.2	72.7 $\pm$ 23.1	67.5 $\pm$ 11.0	67.1 $\pm$ 15.3		
300US (s)	Men	95.5 $\pm$ 18.5	98.3 $\pm$ 19.1	102.0 $\pm$ 21.7*	102.5 $\pm$ 18.4*	0.001 (0.084)	0.017 (0.087)
	Women	109.1 $\pm$ 14.8	109.8 $\pm$ 15.7	113.3 $\pm$ 16.7*	113.5 $\pm$ 17.9*		

300LS (s)	Men	117.5 ±	117.1 ±	117.7 ±	119.5 ±	0.440 (0.015)	0.130 (0.038)
	Women	25.8	28.5	28.5	25.8		
		128.9 ±	128.9 ±	133.5 ±	130.3 ±		
		19.8	21.4	23.7	18.8		
RM (s)	Men	1661.4 ±	1617.2 ±	1631.0 ±	1545.2 ±	0.127 (0.036)	0.881 (<0.001)
	Women	385.2	313.5	322.3	323.5		
		1659.9 ±	1599.4 ±	1645.8 ±	1604.7 ±		
		149.8	138.6	252.5	146.5		

WCC = water can carry. FM = fire and movement. CD = casualty drag. 300US = 300-m unloaded shuttle run. 300LS = 300-m loaded shuttle run. RM = ruck march. \*Significantly different than baseline. Data are presented as mean ± standard deviation. Significance was set at  $p < 0.05$ .

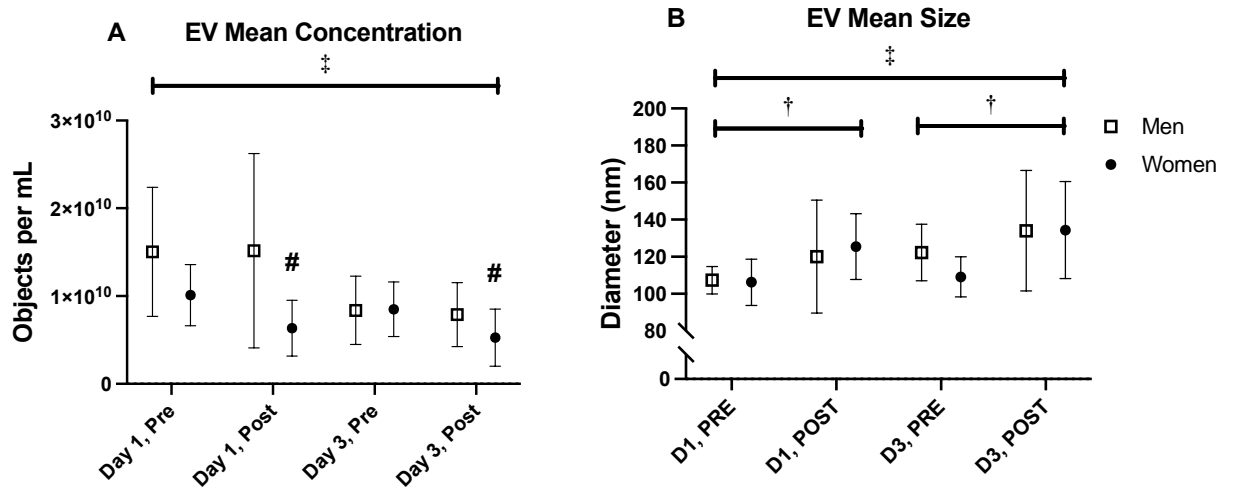
### CORTICOSPINAL EXCITABILITY

- Modeling studies have shed light on the off-target effects of double-cone coil (D-CONE) transcranial magnetic stimulation (TMS), but the physiological extent was largely undetermined. **Proessl et al., 2021** exhibited that off-target responses to TMS were evident in all muscles studied which included the vastus lateralis (VL) and first dorsal interosseous (FDI). Similar maximal motor-evoked potential (MEP<sub>MAX</sub>) were seen in the target contralateral VL (cVL) and off-target ipsilateral VL (iVL) leg ( $p=0.99$ ) and contralateral FDI (cFDI) compared with the positive control (CON) ( $p=0.99$ ). cFDI and CON MEP<sub>MAX</sub> were greater than iFDI ( $p<0.01$ ). A main effect of target ( $p<0.001$ ) indicated that latencies were shortest in CON, but similar for all targets during D-CONE.
- Proessl et al., 2020** compared the test retest-reliability of CSE and neuromuscular activity during isometric squats (SQT) and knee extensions (KE). KE produced more reliable and less variable corticospinal responses, but force and muscle activity were similarly reliable between tasks. Accordingly, compared to SQT, MEP<sub>MAX</sub> and V50 during KE displayed better absolute agreement between visits. Further, he investigated differences in CSE and neuromuscular activity between tasks and found greater maximal force and increased MEP<sub>MAX</sub> during KE despite an equated relative contraction intensity and similar submaximal muscle activity. These findings suggest that corticospinal responses are more variable during SQT compared to KE, particularly at higher intensities, and that improvements in ecological validity may occur at the expense of reliability.

### EXTRACELLULAR VESICLES AND NEUROENDOCRINE BIOMARKERS

- Sex is understudied in EV research, and most studies limit EV analysis to single stress conditions such as exercise. Multi-stress conditions consisting of physical exertion and sleep and caloric restriction are common in real-world settings. **Conkright et al., 2022** demonstrates that physical exertion results in sex-specific EV signatures and that EV profiles vary according to single versus multi-stress conditions and highlights important biological and ecological characteristics that should be considered in EV research.
- Conkright et al., 2022** observed a decline in EV concentration following exertion in women only as well as an increase in SGCA+ and CD63+ EVs (peak stress only) following exertion, whereas there were no differences in VAMP3+ or THSD1+ EVs. Contrary to their hypothesis, they observed an increase in mean EV size following exertion and from baseline to peak stress. Novel findings in this study were that the proportion of SGCA+ EVs was higher in women compared with men regardless of stress

condition, and that SGCA+ EVs increased following 48 h of restricted sleep and caloric intake compared with baseline independent of sex. Collectively, these results suggest that sex and stress condition have an impact on EV profiles and should be taken into consideration during experimental design of EV studies.



**Figure 2.** Extracellular vesicle (EV) mean concentration (objects per mL) (A) and size (B) before and after physical exertion (time) on day 1 (single stress) and day 3 (multi-stress; day) in men and women (sex). EV concentration data were natural log transformed for analysis; raw data were used for EV size analysis. All data are presented as raw mean  $\pm$  standard deviation. nm = nanometer. †Main effect of time where (B) EV mean size was greater following exertion. ‡Main effect of day where (A) EV mean concentration was greater on day 1 and (B) EV mean size was greater on day 3. #Sex by time interaction where (A) EV mean concentration declined after exertion in women only. Significance was set at  $p < 0.05$ .

- **Conkright et al., 2021** determined differential response patterns between men and women over time (GH and BDNF) and day (IGF-I) with no differences in patterns in cortisol but rather a significant increase in men and women following intense physical activity (TMT).
- **Beckner et al., 2022** found that none of the neuroendocrine biomarkers--including cortisol, neuropeptide-Y (NPY), brain-derived neurotropic factor (BDNF)-- or EV features (i.e., total EV size and average concentration) were able to discriminate high vs. low resilience at baseline. However, the results supported our hypothesis that EVs were a more sensitive indicator of high resilience compared to neuroendocrine biomarkers in response to a controlled stress scenario. While changes in neuroendocrine biomarkers were unable to differentiate resilience, we observed changes within EV features following 48 h of sleep and caloric restriction that were significantly different between high and low resilient individuals.

**Table 2.** Baseline Neuroendocrine Concentrations

		Low Resilience (n = 10)	High Resilience (n = 10)
$\alpha$ -Klotho (pg/mL)	Mean $\pm$ SD	1013.69 $\pm$ 332.89	956.37 $\pm$ 341.04

	Median [IQR]	852.02 [527.03]	871.19 [542.84]
BDNF (pg/mL)	Mean ± SD	5,595.60 ± 6,548.55	6,273.00 ± 4,592.35
	Median [IQR]	2,638.00 [5,778.75]	4,917.50 [6,567.75]
NPY (pg/mL)	Mean ± SD	2,210.53 ± 993.55	3,594.32 ± 2,496.45
	Median [IQR]	1,782.01 [1,751.00]	2,684.44 [4,718.89]
IGF-I (ng/mL)	Mean ± SD	273.57 ± 64.37	293.05 ± 91.62
	Median [IQR]	278.49 [112.41]	276.77 [98.44]
Cortisol (µg.dL)	Mean ± SD	26.15 ± 11.63	28.21 ± 9.57
	Median [IQR]	22.23 [20.40]	23.84 [12.99]

Independent samples t-test or Mann-Whitney U test (as appropriate) indicated there were no significant differences between high and low resilient individuals at baseline. BDNF = brain-derived neurotrophic factor, NPY = neuropeptide-Y, IGF-I = insulin-like growth factor I.

- **Beckner et al., 2021** determined that SMOS significantly reduced circulating concentrations of IGF-I (-8.4%), NPY (-6.4%), and α-klotho (-7.2%) from baseline through the recovery day, whereas BDNF declined after the onset of sleep restriction (-17.3%) with subsequent recovery by peak stress, while oxytocin remained stable. The rigors of military training have been shown to decrease somatotrophic hormones, such as IGF-I, suggesting that the simulated military protocol used in this study was adequate to elicit a similar IGF-I response.

**Table 3.** Basal neurocognitive biomarker concentrations during SMOS.

	N		Day 0	Day 1	Day 2	Day 3	Day 4
IGF-1 (ng/mL)	50	Mean ±	288.03 ±	292.94 ±	281.75 ±	263.71 ±	264.67 ±
		SD	80.84	90.51	90.35	83.64 <sup>a,b,c</sup>	86.17 <sup>a,b,c</sup>
		Median	272.87	260.59	261.72	250.15	255.36
Klotho (pg/mL)	50	Mean ±	1,010.77 ±	971.19 ±	964.93 ±	939.43 ±	937.58 ±
		SD	322.22	309.15 <sup>a</sup>	286.19	312.27 <sup>a</sup>	329.46 <sup>a,b</sup>
		Median	937.93	882.03	897.43	918.85	891.90
BDNF (pg/mL)	50	Mean ±	5,355.46 ±	4,325.92 ±	4,428.52 ±	5,395.47 ±	5,542.30 ±
		SD	4,167.12	4,559.52 <sup>a</sup>	4,464.11 <sup>a</sup>	6,879.34	5,587.21
		Median	4,366.50	3,416.00	2,965.50	3,127.00	3,553.50
NPY (pg/mL)	41	Mean ±	2,534.54 ±	2,445.62 ±	2,365.48 ±	2,215.18 ±	2,371.54 ±
		SD	1,495.83	1,469.21	1,445.16 <sup>a</sup>	1,285.13 <sup>a</sup>	1,514.49 <sup>a</sup>
		Median	2,077.999	2,106.852	2,061.788	1,903.475	1,852.343

Oxytocin (pg/mL)	50	Mean ± SD	5.93 ± 1.97	5.76 ± 1.65	5.49 ± 1.47	5.78 ± 2.10	5.56 ± 1.48
		Median	5.16	5.30	5.21	5.18	5.02

BDNF, Klotho, NPY and IGF-I data log transformed, raw values reported for ease of interpretation. Oxytocin not normally distributed even after log transformation, used Friedman ( $\alpha=0.005$ ). <sup>a</sup> Significantly lower than Day 0. <sup>b</sup> Significantly lower than Day 1. <sup>c</sup> Significantly lower than Day 3.

## SLEEP

- **LaGoy et al., *Sleep Health 2022*** found that higher aerobic fitness ( $\dot{V}O_{2peak}$ ), lower habitual daytime sleepiness (ESS) and lower frontal NREM SWA at baseline predicted better physical performance both at baseline and throughout SMOS

**Table 4.** Summary of primary results. Baseline characteristics and sleep predicted baseline physical performance and overall physical performance throughout simulated military operational stress (SMOS) but not changes in physical performance across SMOS

Predictors	Outcomes				
	Baseline TMT Performance	TMT Performance Throughout SMOS	Change in TMT Performance from Baseline to Peak Stress	Change in TMT Performance from Baseline to Recovery	Change in TMT Performance Across SMOS Restriction Days
Baseline Characteristics	ü	ü	—	—	—
Habitual Sleep	ü	ü	—	—	—
Baseline Sleep	ü	ü	—	—	—
Change in Sleep from Baseline to Recovery				—	
Change in Sleep Across SMOS Restriction Days					—

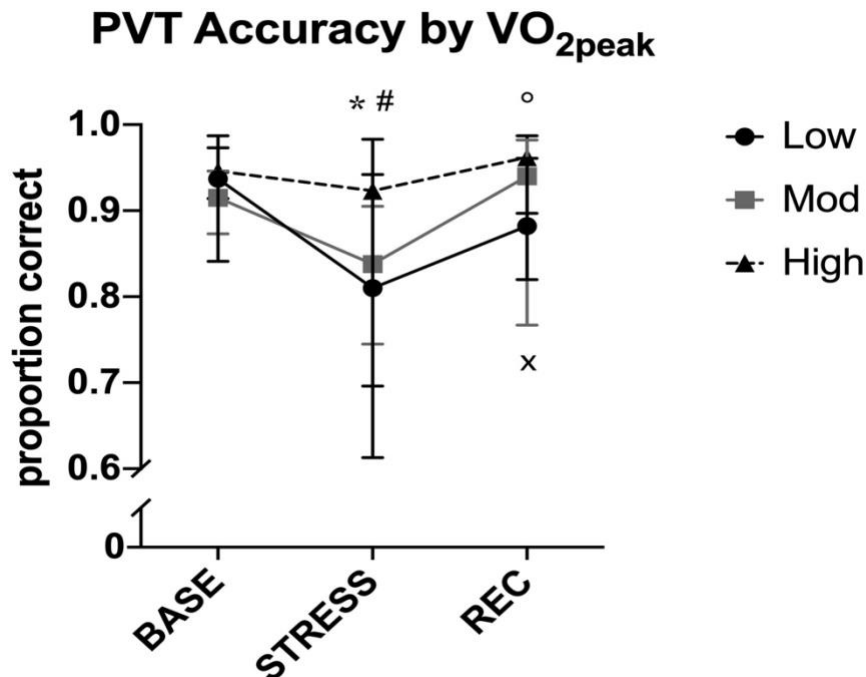
Abbreviations: SMOS, simulated military operational stress; TMT, tactical mobility test

- **LaGoy et al., *SLEEP 2022*** determined that sleep architecture parameters were less stable and robust than absolute and relative spectral activity parameters. Further, relative spectral activity parameters were less robust than absolute spectral activity. Absolute

alpha and sigma activity demonstrated the highest levels of stability that were also robust across sleep opportunities of varying duration and timing. Specific features of sleep, including non-rapid eye movement spectral activity (NREM), have demonstrated high stability within individuals across multiple nights. This high stability of sleep has been characterized as trait-like; however, the robustness of this stability across sleep opportunities of different timings and durations has not been well-described. NREM alpha (8 – 12 Hz) and sigma (12 – 16 Hz) demonstrated robust stability across variable sleep opportunities during a simulated military operational stress protocol, highlighting the trait-like behavior of these sleep features. Other sleep measures, including sleep architecture, may be more sensitive to state manipulations. Additionally, stability of sleep features was influenced by prior trauma exposure and resilience, such that less resilient individuals had less stable sleep.

## COGNITIVE PERFORMANCE AND MILITARY ADAPTIVE DECISION-MAKING

- Beckner et al., 2021** found that overall, PVT<sub>S</sub> slowed +6.6% from baseline to peak stress accompanied by a -11.3% decrease in accuracy, and both measures returned to near baseline values after 8 h of uninterrupted recovery sleep. Similar to previous military operational studies, our findings demonstrate that vigilance is compromised with limited sleep opportunity when combined with other stress factors (i.e. calorie restriction and physical exertion). However, Individuals categorized as H-RES (CD-RISC score > 90) or H-FIT ( $\dot{V}O_{2peak} > 51.53 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) demonstrated stable PVT<sub>A</sub> during the 48 hour sleep and caloric restriction, whereas L- and M-RES or FIT did exhibit reduced accuracy at peak stress compared to baseline. Further, the scenario revealed risk propensity increased 9.5% from baseline to peak stress and 14.5% from baseline to recovery, despite stable average reaction time. Differences in risk propensity based on grouping variables were inconclusive at large, but generally supported that risk propensity increased across the 5 day protocol regardless of level of trait-resilience or aerobic fitness.



**Figure 4.** Psychomotor Vigilance Test (PVT) accuracy based on aerobic fitness as determined by  $\dot{V}O_{2peak}$ . Data are presented as median  $\pm$  interquartile range with Bonferroni-corrected pairwise comparisons ( $p < 0.017$ ). BASE (Baseline, Day 1), STRESS (Peak Stress, Day 3), and REC (Recovery, Day 4). \* Significant decrease in PVT accuracy from BASE to STRESS in moderately fit individuals (Mod). # Significantly lower than REC in Mod group.  $\times$  Significant decline in PVT accuracy from BASE to REC in low-fit individuals (Low).  $^{\circ}$  Significant increase in PVT accuracy from STRESS to REC in high-fit individuals (High).

- In currently under review data, **Sekei et al., 2022** found that High adaptors—those with ability to improve in military relevant adaptive-decision making following 48-hrs of SMOS including decreased sleep opportunity, caloric restriction and physical work exhibited greater positive personality traits (i.e., significantly less neuroticism, and greater conscientiousness and extroversion), self-report resilience (i.e., CD-RISC test) and aerobic fitness compared to low adaptors. However, and contrary to our hypothesis, neurocognitive performance declined similarly in low and high adaptors following 48-hrs of SMOS, though grammatical reasoning speed improved in both groups. Similarly, neuroendocrine biomarkers were minimally impacted, with the exception of modest declines in IGF-I. Collectively, the present findings suggest that trait resilience, positive personality traits, and aerobic capacity were higher at baseline in subjects whose adaptive decision-making improved during SMOS (i.e., high adaptors).

**Table 5.** Cognition test batteries stratified by low and high adaptability at baseline and peak stress.

Variable	Group	Day 1: Baseline	Day 3: Peak Stress	Interaction Effect, $p$ (partial $\eta^2$ )	Main Effect of Group, $p$ (partial $\eta^2$ )	Main Effect of Day, $p$ (partial $\eta^2$ )
PVT Slowness (10-[1/RT])	High	2.4 $\pm$ 0.1	2.43 $\pm$ 0.1	0.332 (0.020)	0.336 (0.020)	<b>&lt; 0.001 (0.311)</b>
	Low	2.4 $\pm$ 0.1	2.49 $\pm$ 0.2			
PVT Accuracy (%)	High	91 $\pm$ 15%	83 $\pm$ 21%	0.200 (0.035)	0.104 (0.056)	<b>&lt; 0.001 (0.308)</b>
	Low	86 $\pm$ 13%	72 $\pm$ 22%			
BART Speed (ms)	High	7.3 $\pm$ 0.4	7.3 $\pm$ 0.5	0.645 (0.005)	0.273 (0.027)	0.881 (0.001)
	Low	7.5 $\pm$ 0.7	7.5 $\pm$ 0.5			
BART Accuracy (%)	High	59 $\pm$ 15%	60 $\pm$ 22%	0.280 (0.025)	0.370 (0.018)	0.177 (0.039)
	Low	51 $\pm$ 18%	59 $\pm$ 19%			
ERT Speed (ms)	High	45.0 $\pm$ 6.1	42.5 $\pm$ 7.2	0.996 (0.000)	0.071 (0.069)	0.197 (0.036)
	Low	48.8 $\pm$ 8.6	46.3 $\pm$ 15.5			
ERT Accuracy (%)	High	74.1 $\pm$ 8.5%	68.4 $\pm$ 11.2%	0.826 (0.001)	0.096 (0.059)	<b>0.026 (0.103)</b>
	Low	68.1 $\pm$ 12.7%	63.4 $\pm$ 21.3%			

Data presented as mean $\pm$  SD across baseline and peak stress and presented as  $p$  (partial  $\eta^2$ ) for group comparisons. Significance was set at  $p < 0.05$ . PVT= Psychomotor Vigilance Test, BART= The Balloon Analogue Risk Task, ERT= Emotion Recognition Test

#### 4. IMPACT

*Impact of Military Operational Stressors on Cognitive Performance:* Military occupational and field settings (i.e., deployment and combat) expose military personnel to operational stress and negatively impact cognitive readiness and resiliency abilities such as vigilance, reaction time, learning, memory, and reasoning<sup>2-6,10,11,17</sup>. Due to obvious operational, security, and institutional review board-related issues, it has proven challenging to conduct cognitive research during real-life military scenarios. However, as a surrogate, efforts have been successful in modeling sustained operational stress in laboratory conditions. For example, Lieberman and colleagues have extensively published cognitive decrements during actual and laboratory-based military operational scenarios and has concluded that simulated models are appropriate and sensitive to assess adverse effects of multi-stressor environments.<sup>4-6,17,18</sup>

*Sleep Behavior:* Sleep restriction, deprivation, and disruption are all well-known and robust degraders of cognitive performance. Members of the research team have extensive experience with sleep restriction protocol, polysomnography, HRV, and sensorimotor performance. The completed study comprehensively characterizes the interrelationships between sleep behavior, physical performance and cognitive function. A unique aspect of the current study was the ability to measure sensorimotor outcomes that can specifically address the link between cognitive decisions and subsequent military tactical performance. The detrimental effects of sleep deprivation on simple motor tasks such as reaction time tests have routinely been studied, indicating reduced alertness and cognitive fatigue with extended sleep loss<sup>14-21</sup>.

*Innovative Aspects of Research:* Several aspects of the research project were unique and innovative. First, we combined novel and established neurocognitive and performance measures to identify individual characteristics, including response to stress, that can be translated into actionable training and/or mitigation strategies. Second, the inclusion of the majority of relevant domains and the extensive test battery assembled for this project was an ambitious undertaking that is nevertheless critical for rapid impact and developing empirically driven tactical plans to promote, enhance, and sustain resilience and cognitive readiness. Third, the use of a military relevant challenge that combines sleep loss, caloric restriction, and physical fatigue under well controlled laboratory conditions will contextualize the study findings and interpretations in ways that support rapid translation and applications in a variety of operational settings. Fourth, our interdisciplinary team of investigators has extensive experience in collaborative research and brought together a unique set of conceptual, content, methodological, military, and statistical expertise.

#### 5. CHANGES/PROBLEMS

Due to the COVID-19 pandemic circumstances and the University of Pittsburgh and Neuromuscular Research Lab policies in order to maintain the health and well-being of all employees and subjects, all research activities were temporarily paused and work was moved remotely. The study team terminated data collection as of 27 May 2020 with written

correspondence from Claudio Ortiz approving to cease data collection at 69 participants instead of the originally planned 80 due to the COVID-19 pandemic.

The study team for Specific Aim 2 had faced a delay beginning data collection due to the pandemic but after modifying their spit collection protocol to accommodate COVID-19 safety measures, they were able to complete data collection. Finally, The study team faced difficulty recruiting women as the original subject recruitment target was 40 men and 40 women. It was agreed that while the study team would continue recruiting women, it was most important to reach the final target of 80 participants. The study team received written correspondence from Claudio Ortiz on 27 May 2020 confirming that it was appropriate to cease data collection at 69 participants instead of completing the originally planned 80 participants due to the COVID-19 pandemic.

## 6. PRODUCTS

### JOURNAL PUBLICATIONS

Conkright WR, Beckner ME, Sinnott AM, Eagle SE, Martin BJ, LaGoy AD, Proessl F, Lovalekar M, Doyle T, Agostinelli P, Sekel NM, Flanagan SD, Germain A, Connaboy C, Nindl BC. "Neuromuscular Performance and Hormonal Responses to Military Operational Stress In Men and Women" *JSCR*; Accepted; Yes

Proessl F, Canino MC, Beckner ME, Sinnott AM, Eagle SR, LaGoy AD, Conkright WR, Sterczala AJ, Connaboy C, Ferrarelli F, Germain A, Nindl BC, Flanagan SD. "Characterizing the spatial extent of off-target corticospinal responses to double-cone transcranial magnetic stimulation." *Experimental Brain Research*; Accepted; Yes

Beckner ME, Conkright WR, Eagle SR, Martin BJ, Sinnot AM, Lagoy AD, Proessl F, Lovalekar M, Jabloner LR, Roma PG, Basner M, Ferrarelli F, Germain A, Flanagan SD, Connaboy C, Nindl BC. "Impact of Simulated Military Operational Stress on Executive Function Relative to Trait Resilience, Aerobic Fitness, Sustained Vigilance, and Neuroendocrine Biomarkers" *Physiology and Behavior*; Accepted; Yes

Proessl F, Beckner ME, Conkright WR, LaGoy AD, Canino MC, Sinnott AM, Eagle SR, Sterczala AJ, Connaboy C, Ferrarelli F, Germain A, Nindl BC, Flanagan SD. "Corticospinal excitability moderates exercise-induced neuroplasticity during military operational stress." *Brain Research*; Accepted; Yes

LaGoy AD, Cashmere D, Beckner ME, Eagle SR, Sinnott AM, Conkright WR, Miller E, Derrow C, Dretsch MN, Flanagan SD, Nindl BC, Connaboy C, Germain A, Ferrarelli F. A trait of mind: stability and robustness of sleep across sleep opportunity manipulations during simulated military operational stress. *SLEEP*; Accepted; Yes

LaGoy AD, Sinnott AM, Eagle SR, Beckner ME, Conkright WR, Proessl F, Williams J, Dretsch MN, Flanagan SD, Nindl BC, Lovalekar M, Germain A, Ferrarelli F, Connaboy C. Combined effects of time-of-day and simulated military operational stress on perception-action coupling. *Chronobiology International*; Accepted; Yes

Proessl F, Canino MC, Beckner ME, Conkright WR, LaGoy AD, Sinnott AM, Eagle SR, Martin BJ, Sterczala AJ, Roma PG, Dretsch MN. Use-dependent corticospinal excitability is associated with

resilience and physical performance during simulated military operational stress. *Journal of Applied Physiology*. 2022 Jan 1;132(1):187-98; Accepted; Yes

AD LaGoy et al., Less daytime sleepiness and slow wave activity during sleep predict better physical readiness in military personnel, *Sleep Health* (2022), <https://doi.org/10.1016/j.sleh.2022.10.013>; Accepted; Yes

Sekel NM, Beckner ME, Conkright WR, LaGoy AD, Proessl F, Lovalekar M, Martin BJ, Jabloner LR, Beck AL, Eagle SR, Dretsch M, Roma PG, Ferrarelli F, Germain A, Flanagan SD, Connaboy C, Haufler AJ and Nindl BC (2023) Military tactical adaptive decision making during simulated military operational stress is influenced by personality, resilience, aerobic fitness, and neurocognitive function. *Front. Psychol.* 14:1102425. doi: 10.3389/fpsyg.2023.1102425

## **OTHER PUBLICATIONS, CONFERENCE PAPERS AND PRESENTATIONS.**

### **ABSTRACTS (ALPHABETICALLY ORDERED BY LAST NAME)**

Agostinelli, Philip. (2019, November 1-2) *Differences in Performance Decline Between Sex Under Simulated Military Operational Stress* [Conference presentation abstract]. Mid-Atlantic American College of Sports Medicine Conference; Harrisburg, PA.

Ambarian, Mikayla. (2019, November 19) *Impact of sleep quality and deployment history on resilience in a military population* [Conference presentation abstract]. Center for Sleep and Circadian Science Research Day; Pittsburgh, PA.

Beck, Alaska. (2020, November 6) *Similar Corticospinal Excitability in Military Men and Women During Simulated Operational Stress* [Conference presentation abstract]. Mid-Atlantic American College of Sports Medicine Regional Meeting; Virtual.

Beckner, Meaghan. (2019, November 1-2) *Simulated Military Operational Stress Negatively Impacts Psychomotor Vigilance and Neurocognitive Biomarkers in Men and Women* [Conference presentation abstract]. Mid-Atlantic American College of Sports Medicine Conference; Harrisburg, PA.

Beckner, Meaghan. (2020, February 11-14) *Emotion Recognition and Vigilance is Compromised During Military Operational Stress* [Conference presentation abstract]. The International Congress on Soldier's Physical Performance (ICSPP); Quebec City, CA.

Beckner, Meaghan. (2020, February 11-14) *High Grit Scores Associated with Elevated BDNF During Military Operational Stress* [Conference presentation abstract]. The International Congress on Soldier's Physical Performance (ICSPP); Quebec City, CA.

Beckner, Meaghan. (2020, June 17) *Simulated Military Operational Stress Negatively Impacts Psychomotor Vigilance and Neurocognitive Biomarkers in Men and Women* [Conference presentation abstract]. American College of Sports Medicine National Meeting; Virtual.

Beckner, Meaghan. (2021, June 1-5) *Impact of Simulated Operational Stress on Cognition Relative to Resilience, Fitness, Vigilance, and Neuroendocrine Biomarkers* [Conference presentation abstract]. American College of Sports Medicine National Meeting; Virtual.

Bird, Matthew. (2021, June 1-5) *Higher Baseline Aerobic Fitness Influences Jumping Performance During Military Operational Stress* [Conference presented abstract]. American College of Sports Medicine National Meeting; Virtual.

Canino, Maria. (2020, February 11-14) *Impact of Operational Stress on Motor Evoked Potentials in Military Personnel* [Conference presented abstract]. The International Congress on Soldier's Physical Performance (ICSPP); Quebec City, CA.

Canino, Maria. (2020, June 17) *Impact of operational stress on motor evoked potentials in military personnel* [Conference presented abstract]. American College of Sports Medicine National Meeting; Virtual.

Conkright, Will. (2019, November 1-2) *Implications on Estimated Susceptibility to Enemy Fire Following 5-Days of Simulated Military Operational Stress* [Conference presented abstract]. Mid-Atlantic American College of Sports Medicine Conference; Harrisburg, PA.

Conkright, William. (2020, February 11-14) *Implications on Estimated Susceptibility to Enemy Fire Following 5-Days of Simulated Military Operational Stress* [Conference presented abstract]. The International Congress on Soldier's Physical Performance (ICSPP); Quebec City, CA.

Conkright, William. (2020, June 17) *Differential Responses of Resting Vs. Post-exertion Hormone Concentrations During Simulated Military Operational Stress* [Conference presented abstract]. American College of Sports Medicine National Meeting; Virtual.

Conkright, William. (2020, November 6) *Extracellular Vesicle Concentration but Not Size Differs Between Men and Women During Military Operational Stress* [Conference presented abstract]. Mid-Atlantic American College of Sports Medicine Regional Meeting; Virtual.

Eagle, Shawn. (2020, February 11-14) *Simulated Military Operational Stress Impairs Action Boundary Perception* [Conference presented abstract]. The International Congress on Soldier's Physical Performance (ICSPP); Quebec City, CA.

Haufler, Amy. (2020, February 11-14) *Adaptability, Emotion, Perception and Attention: Tactical Cognitive Resilience in Response to Operational Stress* [Conference presented abstract]. The International Congress on Soldier's Physical Performance (ICSPP); Quebec City, CA.

Jablonek, Leslie. (2021, June 1-5) *Impact of Higher Aerobic Fitness on Neurocognitive Function During Simulated Military Operational Stress* [Conference presented abstract]. American College of Sports Medicine National Meeting; Virtual.

Lagoy, Alice. (2019, August 19-22) *Changes in affordance perception behaviors during exposure to acute military operational stress* [Conference presented abstract]. Military Health System Research Symposium; Kissimmee, FL.

Lagoy, Alice. (2019, November 1-2) *Increased deep sleep may relate to compromised perception-action coupling performance in military personnel* [Conference presented abstract]. Mid-Atlantic American College of Sports Medicine Conference; Harrisburg, PA.

LaGoy, Alice. (2020, February 11-14) *Visuomotor performance is maintained under conditions of military operational stress* [Conference presented abstract]. The International Congress on Soldier's Physical Performance (ICSPP); Quebec City, CA.

LaGoy, Alice. (2020, August 27-30) *Efficient perception-action coupling relates to more slow wave sleep in military personnel* [Conference presented abstract]. Associated Professional Sleep Societies (Sleep) Meeting; Virtual.

LaGoy, Alice. (2021, June 10-13) *Exposure to simulated military operational stress decreases alertness in the morning but not the evening* [Conference presented abstract]. Associated Professional Sleep Societies (Sleep) Meeting; Virtual

Proessl, Felix. (2019, November 1-2) *Normalization Removes Differences in Contractile Properties and Corticospinal Excitability Between Single- and Multi-Joint Exercises* [Conference presented abstract]. Mid-Atlantic American College of Sports Medicine Conference; Harrisburg, PA.

Proessl, Felix. (2021, June 1-5) *Corticospinal Excitability and Resilience during Simulated Military Operational Stress* [Conference presented abstract]. American College of Sports Medicine National Meeting; Virtual.

Nindl, Bradley. (2020) *Physiological, Behavioral, Neurocognitive and Tactical Performance Response Trajectories in Male and Female Soldiers During Military Operational Stress* [Conference presented abstract]. Military Health System Research Symposium; Cancelled due to COVID-19.

Sekel, N M.; Conkright, W R.; Beckner, M E.; LaGoy, A D.; Proessl, F; Jabloner, L R.; Beck, A L.; Eagle, S; Lovalekar, M; Haufler, A; Ferrerelli, F; Germain, A; Dretsch, M; Flanagan, S D.; Connaboy, C; and Nindl FACSM, B C. (2022) "Slow Wave Activity Sleep is Significantly Associated with Decision-Making During Simulated Military Operational Stress." *International Journal of Exercise Science: Conference Proceedings*: Vol. 9: Iss. 10, Article 17.  
Available at: <https://digitalcommons.wku.edu/ijesab/vol9/iss10/17>

Sinnott, Aaron. (2019, November 1-2) *Association between Affordance-Detection Accuracy and Marksmanship Performance during Sleep and Caloric Restriction among Active Duty Soldiers* [Conference presented abstract]. Mid-Atlantic American College of Sports Medicine Conference; Harrisburg, PA.

Sinnott, Aaron. (2020) *Association between Affordance-Detection Accuracy and Marksmanship Performance during Sleep and Caloric Restriction among Active Duty Soldiers* [Conference presented abstract]. Military Health System Research Symposium; Cancelled due to COVID-19.

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

Two students successfully defended their dissertations in July of 2021:

Dr. William R. Conkright. *Sex Differences in Hormonal and Extra Cellular Vesicles Responses to Military-Based Physiological Stress and Exercise.*

Dr. Meaghan Beckner. *Effect of Military Operational Stress on Neuroendocrine and Extracellular Vesicle Profiles Related to Cognitive and Physiological Resilience.*

One student successfully defended their dissertation in November of 2021:

Dr. Alice LaGoy. *Cruisin' for a Snoozin': The Role of Sleep in Resilience to Simulated Military Operational Stress*

## **7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

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

Name: Bradley C. Nindl

Project Role: co-PI

Nearest person month worked: 1

Contribution to project: Dr. Nindl has provided oversight of NMRL study preparations, coordinated collaborator efforts and recruitment procedures.

Name: Fabio Ferrarelli

Project Role: co-PI

Nearest person month worked: 1

Contribution to project: Dr. Ferrarelli has provided oversight of M-STARRT study preparations, coordinated collaborator efforts and recruitment procedures.

Name: Chris Connaboy

Project Role: PhD

Nearest person month worked: 1

Contribution to project: Dr. Connaboy has provided oversight over the sensorimotor and psychomotor task batteries, including study procedures, relevant metrics, and training of necessary personnel.

Name: Shawn Flanagan

Project Role: PhD

Nearest person month worked: 1

Contribution to project: Dr. Flanagan has provided oversight over neurophysiological task batteries, including study procedures, relevant metrics, and training of necessary personnel.

Name: Qi Mi

Project Role: PhD

Nearest person month worked: 1

Contribution to project: Dr. Mi has provided oversight over statistical modeling, as well as database management.

Name: Mita Lovalekar

Project Role: PhD

Nearest person month worked: 1

Contribution to project: Dr. Lovalekar has provided oversight over statistical analysis as it relates to changes in study design and protocol management.

Name: Nicole Sekel

Project Role: Research Assistant and Project Manager

Nearest person month worked: 0.5

Contribution to project: Ms. Sekel joined the project as a Research Assistant and Project Manager assisting primarily in data collection as well as regulatory processes.

Name: Meaghan Beckner

Project Role: Graduate Student

Nearest person month worked: 1

Contribution to project: Ms. Beckner has provided oversight over NMRL study procedures, relevant metrics, and training of necessary personnel. She also submitted the local IRB protocol to HRPO.

Name: Aaron Sinnott

Project Role: Graduate Student

Nearest person month worked: 1

Contribution to project: Mr. Sinnott has provided oversight over NMRL study procedures, primarily EST 3000, and training of necessary personnel.

Name: William Conkright

Project Role: Graduate student

Nearest person month worked: 1

Contribution to project: Recruitment, phone screening, and scheduling participants

Name: Felix Proessl

Project Role: Graduate Student

Nearest person month worked:1

Contribution to project: Felix will be involved with data collection, analysis and interpretation of TMS.

Name: Maria Canino

Project Role: Graduate Student

Nearest person month worked:1

Contribution to project: Maria will be involved with data collection, analysis and interpretation of TMS.

Name: Maggie Sphar

Project Role: Lab technician

Nearest person month worked: 1

Contribution to project: Recruitment, phone screening, and scheduling participants

Name: Alice Lagoy

Project Role: Graduate student

Nearest person month worked: 1

Contribution to project: Lab procedures for heart rate variability, psychological measures and sleep

Name: Brian Martin

Project Role: PhD

Nearest person month worked: 1

Contribution to project: Dr. Martin has provided oversight over blood analysis, including study procedures, relevant metrics, and training of necessary personnel.

Name: Amy Haufler

Project Role: PhD

Nearest person month worked: 1

Contribution to project: Dr. Haufler has provided oversight over SPEAR test, including study procedures, relevant metrics, and training of necessary personnel.

Name: Peter Roma

Project Role: PhD

Nearest person month worked: 1

Contribution to project: Dr. Roma has provided oversight over Cognition test battery, including study procedures, relevant metrics, and training of necessary personnel.

Name: Hassen Khan

Project Role: Database Manager

Nearest person month worked: 1

Contribution to project: Mr. Khan has provided oversight over database development and management procedures.

Name: Mackenzie Osborn

Project Role: Lab technician

Nearest person month worked: 1

Contribution to project: Recruitment, phone screening, and scheduling participants

Name: Jenna Parrish

Project Role: PhD

Nearest person month worked: 1

Contribution to project: Dr. Parrish has provided oversight over M-STARRT sleep study procedures, relevant metrics, and training of necessary personnel.

Nearest person month worked: 1

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

Organization Name: The McGowan Institute for Regenerative Medicine

Location of Organization: Pittsburgh, PA

Partner's Contribution to the project: Dr. Fabrisia Ambrosio at The McGowan Institute for Regenerative Medicine has provided in-kind support, allowing PhD students William Conkright and Meaghan Beckner to use their facilities and train them on techniques to isolate and characterize extracellular vesicles as part their respective Freddie Fu student grant projects.

Organization Name: University of Pennsylvania

Location of Organization: Philadelphia, Pennsylvania

Partner's contribution to the project: Dr. Mathias Basner from the Division of Sleep and Chronobiology at the University of Pennsylvania has provided both in-kind support by providing the Cognition software to perform the test battery and collaboration on this project, meeting with study staff to discuss the dataset.

Organization Name: National Aeronautics and Space Administration

Location of Organization: Houston, TX

Partner's contribution to the project: Dr. Peter Roma, who was previously at the Behavior Health and Performance Laboratory at NASA, has collaborated on this project in respect to the Cognition test battery providing valuable insight on our dataset.

Organization Name: Johns Hopkins University

Location of Organization: Baltimore, MD

Partner's contribution to the project: Dr. Amy Haufler from the Applied Physics Laboratory at the Johns Hopkins University provided in-kind support by providing the SPEAR testing software to the NMRL study team and providing the necessary training to grade the assessment. Dr. Haufler has also provided collaborative support throughout the project, discussing the dataset and providing insight on the results.

## 8. APPENDICES

### PUBLICATIONS

Proessl F, Canino MC, Beckner ME, Sinnott AM, Eagle SR, LaGoy AD, Conkright WR, Sterczala AJ, Connaboy C, Ferrarelli F, Germain A, Nindl BC, Flanagan SD. Characterizing off-target corticospinal responses to double-cone transcranial magnetic stimulation. *Experimental Brain Research*, 239(4), 1099-1110. doi: 10.1007/s00221-021-06044-5

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Proessl F, Canino MC, Beckner ME, Conkright WR, LaGoy AD, Sinnott AM, Eagle SR, Martin BJ, Sterczala AJ, Roma PG, Dretsch MN. Use-dependent corticospinal excitability is associated with resilience and physical performance during simulated military operational stress. *Journal of Applied Physiology*. 2022 Jan 1;132(1):187-98.

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