

## Methodological Question

**Psychophysiological resiliency** is critical for individuals working in stressful environments where the ability to manage emotions, maintain situational awareness, and respond quickly and accurately for extended durations is required. Such occupations include law officers, paramedics, trauma physicians, athletes, military personnel, pilots, etc. The US Army seeks to enhance resiliency in soldiers, in particular, prior to deployment. **We are completing a double-blind RCT of phospholipid-bound omega-3 supplementation on resiliency in officers preparing for Ranger school.** This presentation outlines key design elements, including outcome measures, naturalistic stress condition, monitoring adherence, and data quality assurance.

## Introduction

The Ranger Resilience and Improved Performance on Phospholipid-Bound Omega-3s (RRIPP-3) study was crafted to evaluate effect of omega-3 fatty acid (n-3) supplementation on aspects of neuropsychological functioning relevant to battlefield performance. ClinicalTrials.gov: NCT02908932  
**Participants:** US Army Officers entering Infantry Basic Officer Leadership Course (IBOLC), an ~18-week intensive program combining classroom instruction, field training, and physical fitness. Nutrient intake from foods and dietary supplements (DS) was assessed at the beginning and end of the study. Study participants agreed to not consume DS that would interfere with the study design for the study duration. All volunteered, provided written informed consent, and agreed to follow study protocol for participants.

### Arms

- Treatment: 2.2 g/d n-3 HUFA (2:1 EPA:DHA) from 8 capsules of krill oil
- Placebo 2.2 g/d of macadamia nut oil.

**Study Duration:** IBOLC entry through Ranger entry (ca. 22-40 weeks).

## Study Design

**Outcome measures:** Cognitive functions identified by Army leadership as essential to battlefield performance, including **attention, vigilance, response inhibition, spatial working memory, verbal reasoning, and adaptive risk-reward decision-making** were measured by a computerized test battery using E-Prime 2.0 and G-Squared Software. Anxiety, mood, sleep, and resiliency were assessed with validated questionnaires using REDCap. All tests and questionnaires were administered via Dell 3570 Windows 10 17" Latitude laptops (i5).

**Power Analysis:** The study was powered based on prior research showing specific benefit of n-3 on response inhibition in healthy young adults<sup>1</sup>. At 80% power and alpha=0.025 with a repeated measures design with 3 time points, the total sample size needed to detect this difference is 352 (176 per group).

**Stressor: Leader Forge**, an intense 3-day competitive field maneuver exercise, is completed week 14 of IBOLC. Leader Forge simulates combat and involves significant stress, physical exertion, and sleep deprivation.

### Assessment schedule:

	Baseline Intake* Week 0	Safety Check Week 8	Pre-Leader Week 14	Post-Leader Week 16	Pre-Ranger Week 20-40	Post-Ranger Week 40-52
Demographics	X					
Biometrics	X		X	X	X	X
Dietary Assessment	X				X	
Lipid Profile	X	X	X	X	X	X
Cognitive Functioning	X		X	X		X
Psychological Well-Being	X		X	X		X

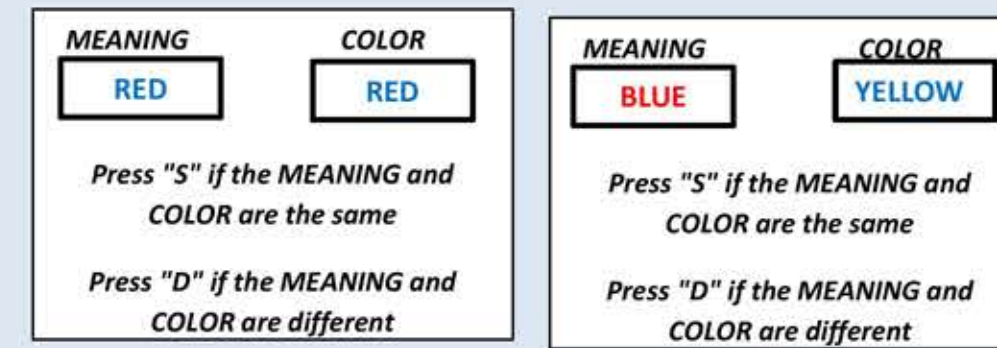
**Monitoring Adherence:** Erythrocyte lipid profiles were measured at baseline, 8 weeks, pre and post-Leader Forge, pre-Ranger entry, and post-Ranger. This ensured adherence and monitored response to both treatment and placebo.

**Quality Assurance:** Cognitive data were systematically screened for validity, including technical issues and insufficient effort.<sup>2</sup>

## Cognitive Outcome Measures

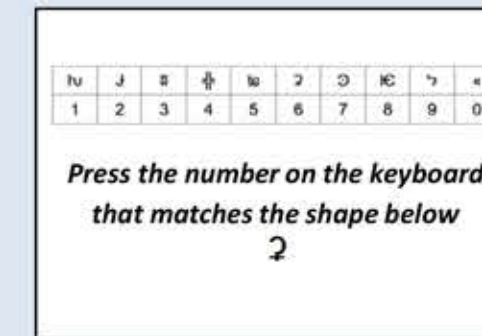
### Stroop

- Variant of classic task of psychomotor inhibition
- Stonehouse et al. showed sensitivity to effects of n-3 supplementation in healthy young adults<sup>1</sup>
- Relevant to mental control and accuracy of quick decision-making in combat situations
- Discriminability = Total Correct – Total Errors



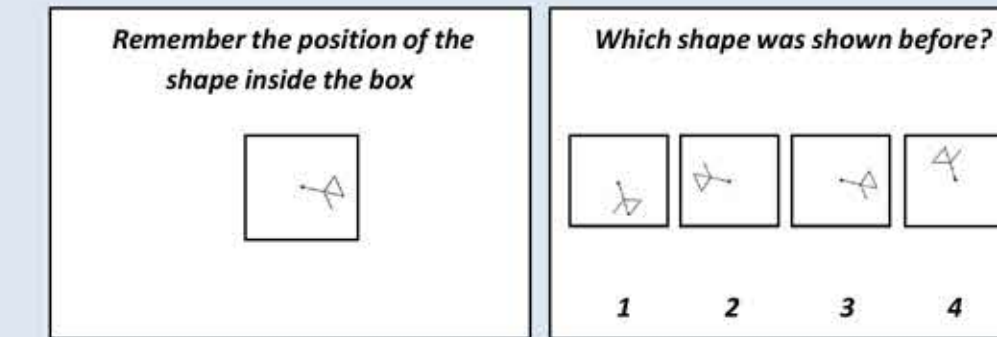
### Digit-Symbol Coding

- Measure of mental speed and visual learning
- Previous research by Marriott et al. showed this task to be most sensitive to effects of psychophysiological fatigue during Ranger<sup>3</sup>
- Relevant to focused attention and mental speed
- Primary outcome is total correct



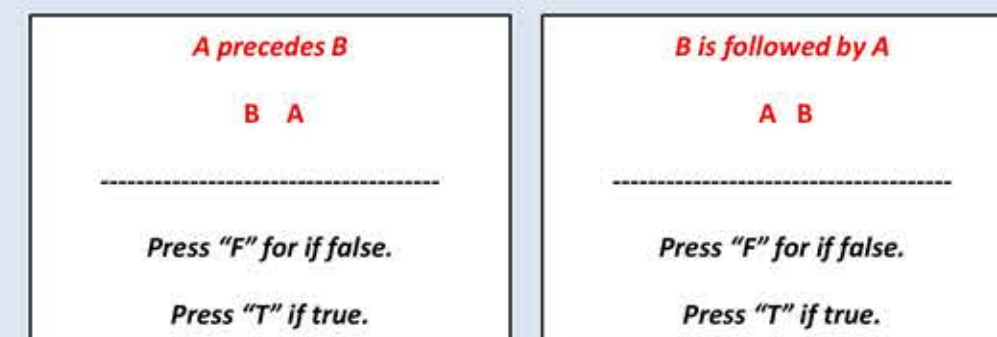
### Spatial N-Back

- Continuous spatial working memory task for the orientation of a shape within a box.
- Interval between study and test varies from 0 to 4
- Previous studies demonstrate sensitivity to sleep deprivation in healthy young adults<sup>4,5</sup>
- Primary outcome is total correct
- Computational modeling estimates parameters for Attention, Rehearsal span, & Episodic Encoding<sup>6,7</sup>



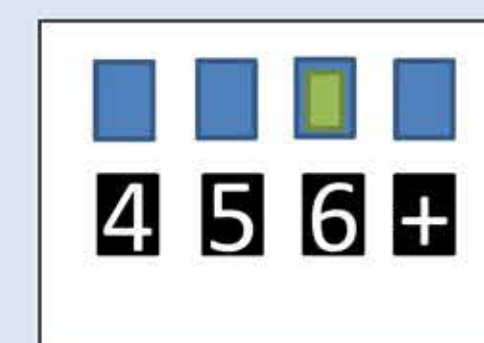
### Grammatical Reasoning

- Variant of classic test developed by Baddeley for assessing nitrogen narcosis in healthy adults, and sensitive to other environmental stressors
- 32 items, 5 second time limit per item
- Primary outcome is number correct



### 4 Choice Serial Reaction Time

- Measures sustained attention, vigilance, and psychomotor reaction time<sup>8</sup>
- 500 trials, 300ms ISI, 2000ms timeout
- Primary outcome is number correct



### BART (Balloon Analog Risk Task)

- Measures risk-reward balancing and impulsivity<sup>9</sup>
- Includes implicit learning component
- Participant inflates balloon, each puff adds \$.05 to value if collected before popping.
- 120 balloons – 40 small, 40 medium, 40 large
- Primary outcome is total cash collected



## Additional Measures

### Psychological

- Conner-Davidson Resiliency Scale
- PROMIS: Fatigue, Sleep-Related Impairment, and Applied Cognition
- Profiles of Mood State, bipolar form
- State-Trait Anxiety Inventory
- Narcissism Personality Inventory (baseline only)

### Dietary (baseline and pre-Ranger)

- Automated Multiple Pass Method (AMPM) 24-hour dietary recall
- Diet History Questionnaire (DHQ) Food Frequency Questionnaire– 30 day

### Erythrocyte n-3

- Finger prick to obtain lipid profiles reflecting changes associated with active treatment and placebo

## Sample

555 participants (546 male) enrolled from 12 IBOLC classes (Aug 2016 - Jan 2018). The blind will be broken Dec 2018 when final participants complete Ranger school.

Age Group	n	Race	n	Ethnicity	n	Education	n	Source	n	Destination	n
≤ 21	28	White	449	Hispanic or Latino	47	Bachelor's Degree	532	USMA	135	IBCT-ABN	268
22	234	African-American	42	Not Hispanic or Latino	508	Master's Degree	20	ROTC	337	IBCT-Light	169
23	138	Asian	26			Doctoral Degree	3	OCS	82	ABCT-Armored	31
24-28	119	Multi	27					DC	1	SCBT-Stryker	87
≥ 29	36	Other	11								

## Data Screening

### Invalid Performance Criteria

**Stroop:** Chance level accuracy (~55%) or Discriminability (Correct-Incorrect) < 10  
**Spatial N-back:** Less than 3/8 correct on 0-back condition or total correct at chance (<33%)  
**Grammatical Reasoning:** Chance level accuracy (<19 correct)  
**4 Choice RT:** "Extreme" cases (accuracy < 3 box lengths from 25<sup>th</sup> quartile)

Task	Valid	Invalid	Missing
Stroop	494 (89.0%)	39 (7.0%)	22 (4.0%)
Digit-Symbol	517 (93.2%)	0	38 (6.8%)
Spatial N-back	479 (86.3%)	48 (8.6%)	28 (5%)
Grammatical Reasoning	412 (74.2%)	110 (19.8%)	33 (5.9%)
4 Choice Reaction Time	516 (93.5%)	9 (1.6%)	30 (5.4%)
BART	539 (97.1%)	0	16 (2.9%)

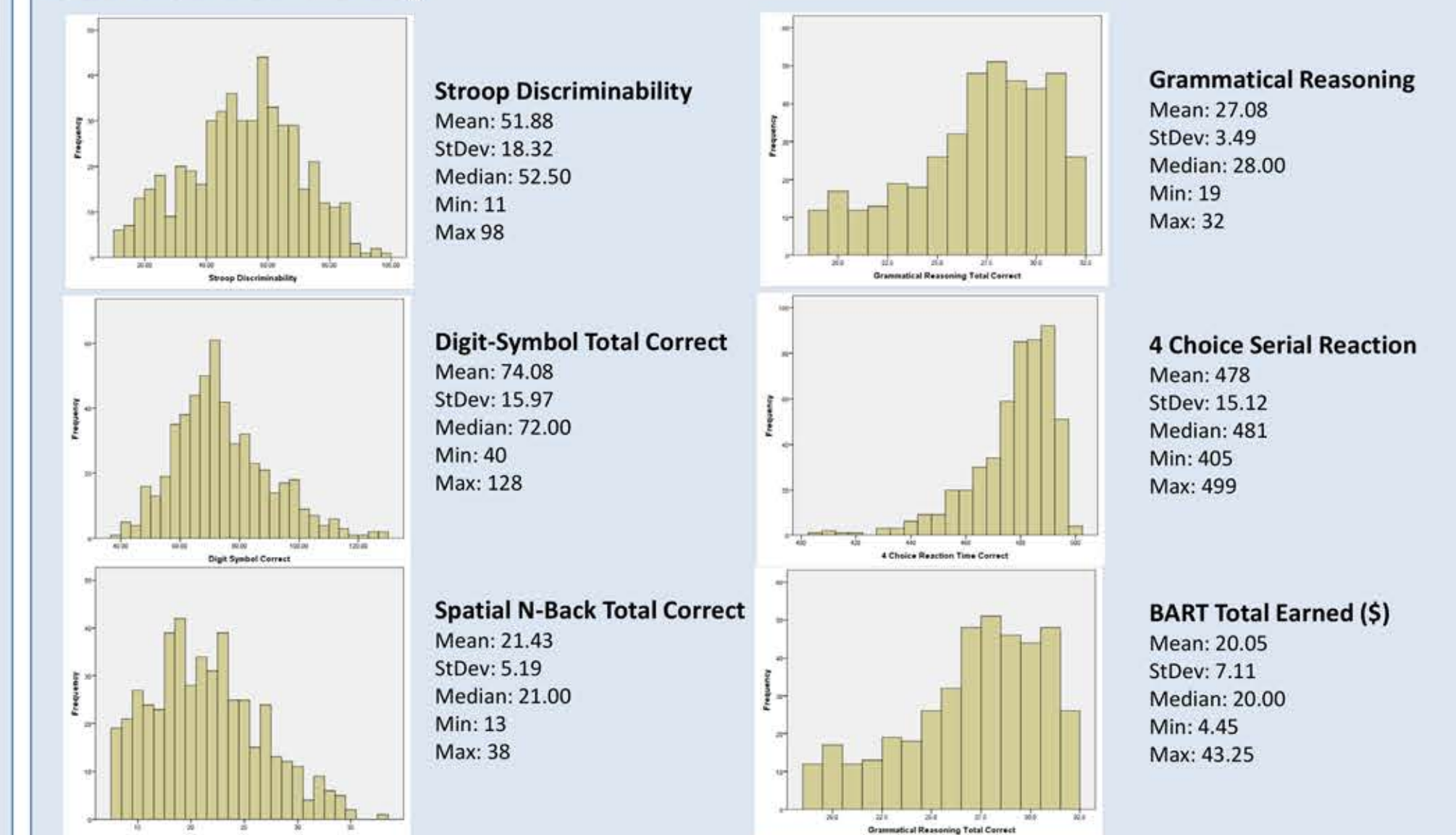
### Completeness of data by participants

All Tasks Complete = 328  
Missing data = 71  
1 invalid = 122  
2 invalid = 31  
3 invalid = 2  
4 invalid = 1

### Invalid Data Common Across Tasks (# cases)

	Stroop	Spatial	Grammatical Reasoning
Spatial	7		
Grammatical Reasoning	15	16	
4 Choice RT	1	0	0

## Central Tendency



## Intercorrelations

	Stroop Discriminability	Digit-Symbol Total Correct	Spatial N-back Total Correct	BART Total Earned	4 Choice RT Total Correct
Digit-Symbol	.298** (472)				
Spatial N-Back	.154** (441)	.335** (457)			
BART	.022 (481)	.094* (502)	.097* (467)		
4 Choice RT	.100* (462)	.029 (479)	.041 (447)	-.059 (516)	
Grammatical Reasoning	.199** (372)	.217** (381)	.151** (359)	.052 (412)	.097 (405)

\* p<.05 \*\*p<.01

## Conclusions

Evaluating an intervention to enhance resiliency in healthy adults presents unique challenges in RCT design. Baseline data collected in our study are promising, and aspects of our approach may have relevance for RCTs to boost resiliency or enhance neuropsychological functioning with other interventions and populations.

**Disclosure:** The project has been reviewed and approved by the Medical University of South Carolina Institutional Review Board for Human Research and the U.S. Army Center for Initial Military Training (USACMT) Research and Analysis Directorate (R&AD) RPAP. Department of the Army Headquarters, United States Army Training And Doctrine Command. This project is supported by contract no. 88422-01 between Aker BioMarine Antarctic AS and the Medical University of South Carolina. The authors Turner, Hibbeln, Newman, Pregulman and Marriott state that they have no additional financial or other conflicts of interest. The opinions expressed in this presentation are those of the authors and do not necessarily represent the position or policy of Aker BioMarine Antarctic AS.