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The Effects of Low-level Repetitive Blasts on Neuropsychological Functioning

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As a follow-up to this initial assessment, breacher instructors were repeatedly administered the neurocognitive test battery over the course of two years. Importantly, testing only occurred during the down time in the weeks between each breacher course. The results suggest that neurocognitive performance in breacher instructors remains relatively stable over time. Longitudinal cognitive performance among breacher instructors did not differ from a control group of breacher engineers (i.e., support staff who are not exposed to blasts) who were similarly assessed. The findings from the current study suggest that Marine breacher instructors do not suffer from long-term neurocognitive impairments due to repetitive low-level blast exposure.

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Introduction

Mild traumatic brain injury (mTBI), also commonly referred to as “concussion,” has become known as the signature injury suffered by U.S. Warfighters in Operation Iraqi Freedom and Operation Enduring Freedom (Hoge et al., 2008). Frequent use of improvised explosive devices (IEDs) and other blast-related weapons account for a significant proportion of mTBI incidents (Okie, 2005; Warden, 2006). Despite a recent push to develop refined prognostic, diagnostic, and intervention strategies that specifically address blast-related mTBI, surprisingly little empirical evidence exists from which to draw firm conclusions and choose the best approaches (Kochanek, Bauman, Long, Dixon, & Jenkins, 2009). As a result, relatively little is understood about its associated symptomatology.

Any injury to the brain has the potential to create both immediate and lasting impairments on psychological health and neurocognitive function. Unfortunately, the ability to carefully study the pathology of blast-related mTBI is hindered by the lack of access to populations that are frequently exposed to blast-related events in a controlled environment. Understanding the pathology of brain injury stemming from blast exposure in war zones is complicated by the multitude of mechanisms in which the injury can occur. Primary blast injury (resulting from the blast wave that alters air-fluid pressure within the brain) is often accompanied by secondary and tertiary forms of injury to the brain related to the blast, such as displaced fragments striking the skull and the impact of the head striking the ground or another solid object following blast propulsion. Therefore, the extent to which a resulting mTBI is due to shock wave exposure *per se* is difficult to determine.

Animal models are useful in demonstrating the consequences of exposure to blast from a mechanistic standpoint. A single exposure to a “low level” blast results in acute axonal damage and shrinking of cortical neurons, although recovery is usually observed within several days (Pun et al., 2011). Repetitive blast-induced mTBI leads to increased impairment severity on several neurological parameters including body weight regulation, righting reflex time, and neuromotor function (Wang et al., 2011). The combination of ionic disturbance, altered cerebral blood flow, and metabolic dysfunction that occurs following mTBI may leave the brain vulnerable to more serious damage if another concussion is experienced. However, animal research on blunt-induced mTBI (i.e., physical head trauma) suggests that this period of increased vulnerability is confined to a critical timeframe following the initial concussion, during which time the brain is more susceptible to cellular injury (Cantu, 1998; Kissick & Johnston, 2005; Longhi et al., 2007; Putukian, 2006; Vagnozzi et al., 2007). It stands to reason that repeated blast exposure following an initial blast may similarly decrease the threshold for experiencing and exacerbating the level of mTBI severity. However, a recent study examining biomarkers in military personnel exposed to multiple gun blasts and explosive detonations failed to provide evidence for blood-brain barrier damage or mTBI (Blennow et al., 2011), suggesting that repeated low-level blast exposure may not necessarily make the brain more sensitive to subsequent injury.

The evidence regarding the long-term consequences of mTBI on cognitive functioning is mixed. The majority of studies that have investigated the cognitive sequelae in the acute phase following mTBI suggest that subtle impairments exist in the domains of memory, processing

speed, and attention (Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005; Carroll et al., 2004; Frencham, Fox, & Maybery, 2005). Most of these individuals recover from mTBI-related neurocognitive deficits within days to weeks following the injury (Lovell et al., 2003; McCrea, Kelly, Randolph, Cisler, & Berger, 2002; Pellman, Lovell, Viano, & Casson, 2006), although a small minority continue to suffer from long-term cognitive difficulties (Belanger, Spiegel, & Vanderploeg, 2010; Ruff, 2011). Importantly, the source of mTBI injury (i.e., blast- vs. blunt-induced) does not appear to make a difference (Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009; Luethcke, Bryan, Morrow, & Isler, 2011). However, most of the research, to date, on the impact of mTBI on cognitive functioning has focused only on singular incidences of injury. Very little is known about the long-term neurocognitive consequences of multiple mTBIs.

Recently, a collaboration between Department of Defense researchers and The U.S. Marine Corps Methods of Entry School has provided the scientific community with a platform in which to study the impact that blast exposure has on both short-term and long-term neurocognitive functioning. Breacher instructors train Marines how to strategically build, place, and detonate explosive charges in order to gain access into enclosed and barricaded structures (e.g., rooms, buildings, gates). During training exercises, the Marine trainees stand in a “stack” (i.e., in a line, positioned belly-to-back) placed at the minimally safe distance from the structure to be breached in order to allow quick access into the structure following detonation. The breacher instructors stand either in or alongside the stack in order to observe operations. Throughout the 3-week training course, trainees and instructors are typically exposed to 50 to 60 repeated blasts that can exceed 183 dB peak sound pressure level (SPL). Instructors teach up to six of these courses each year and are typically stationed at the school for several years. Therefore, these instructors are potentially exposed to hundreds of blasts during their tenure. Anecdotal evidence provided by the instructors suggests that some of the cadre suffer from problems with sleep, mood, memory, concentration, and what has been referred to as a general “brain fog.” It remains to be determined whether these neuropsychological complaints are related to the controlled blasts or psychological stress associated with their occupation.

Although the breacher instructors may not be exposed to blast levels that reliably reach the threshold to induce a concussion, their neuropsychological complaints resemble those reported by athletes, accident victims, and Soldiers diagnosed with a concussion (Boake et al., 2005; Meehan & Bachur, 2009; Ruff, 2005). The cumulative effect of repeated exposure to blasts may therefore translate to the long-term effects of multiple mTBIs that are observed in war zones. Importantly, due to the safety standards and protective equipment employed in the controlled explosive environment, the breacher instructors are exposed to primary blast waves in the absence of serious secondary and tertiary blast-related injury threats that commonly accompany blast exposure in theater. Thus, the breacher instructors represent a unique case study opportunity to examine the isolated neurocognitive consequences of repeated (albeit week) primary blast wave exposure.

Previous pilot studies examining neurocognitive functioning in Marine breachers have reported mild impairments on attention and memory tasks (Carr et al., 2009; Parish et al., 2009). However, an important shortcoming in these studies is the time frame in which neurocognitive testing occurred. To this end, the “baseline” assessment took place during the first few days of a

breacher course and the post-exposure assessment took place shortly after the last blast exposure in the course. Therefore, alterations in stress and/or sleep patterns related to participation and facilitation of the course itself may have masked impairments that occur as a result of exposure to the controlled blasts. A more recent study examining New Zealand Defence Force breachers across multiple time points both before, during, and after a breacher course demonstrated that low-level blast exposure is associated with performance decrements on simple reaction time and delayed visual recognition memory, as well as increased symptom self-reports of fatigue and headache (Tate et al., 2013). Interestingly, performance deficits and symptom reporting returned to baseline levels two weeks after the course, suggesting the neurocognitive consequences of blast exposure may be transient. Collectively, these studies provide a snapshot of the neurocognitive issues related to a breacher training course, but fall short of providing a long-term picture of the potential consequences of cumulative blast-exposure for instructors. In addition, the majority of the participants in each of these breacher studies to date were students in the breacher course rather than instructors. The cumulative neurocognitive effects of repeated blast exposure over time among breacher instructors alone have not been assessed.

Current study

The primary objective of the current study was to determine whether repeated exposure to low-level controlled blasts produces observable changes in cognitive functioning and psychological health. To this end, two specific aims were explored. Our first aim was to conduct an initial assessment comparing the breacher course instructors to instructors from other training courses at the same Weapons Training Battalion (WTB). This served to provide us with a general picture of whether breacher instructors exhibit any inherent neuropsychological differences from other U.S. Marine instructors who are not regularly exposed to blasts. Our second aim was to administer serial assessments to the breacher instructors using a comprehensive neuropsychological battery of tests in order to track whether they display any changes in psychological health and cognitive functioning over time. To address limitations noted in the literature, all assessments occurred during the “down time” in the weeks between training courses in order to avoid the confounding influence of instruction-related stress and/or sleep changes, as well as transient effects that may be expressed immediately following a blast. Regular serial assessments preceding and then following each course throughout the year thus allowed us to examine whether there were any chronic neurocognitive deficits associated with repeated exposure to blast, and whether they changed over time.

Methods

Aim 1. Assessment

Participants

Participants were 40 male, active-duty U.S. Marines from the WTB at Quantico Marine Corps Base, Virginia. Of these 40 participants, 12 were from the breacher instructor cadre at the Methods of Entry School. These individuals serve as the target group (i.e., “Breachers”). The remaining 28 subjects were instructors recruited from the other school houses within the WTB,

including the Foreign Weapons Instructor Course, Reserve Combat Marksmanship Training Course, Scout Sniper Instructor School, Combat Marksmanship Course, and Combat Marksmanship Trainer. These participants collectively served as the control group (i.e., “Controls”). Background demographics for both groups are provided in Table 1. To be considered eligible for the study, participants could not have a previous or active diagnosis of a psychiatric disorder.

Table 1
Aim 1 Demographics

Variable	Breachers (<i>n</i> =12)	Controls (<i>n</i> =28)
Age	30.8 ± 1.2	28.3 ± 0.7
Education level in years	12.7 ± 0.4	12.5 ± 0.2
Number of deployments	3.6 ± 0.7	2.5 ± 0.2

Procedure

The school houses in the WTB conduct several training classes throughout the year. Each of these classes last 3 to 4 weeks and are followed by 3-week periods of “down time” in which classes are not taught. An important feature of this study is that all instructors were only administered the test battery during the period of “down time” at their assigned school house. Specifically, all attempts were made to test the instructors during the second week of down time (i.e., occurring approximately 1 week after their most recent course and thus approximately 1 week prior to their upcoming course).

Participants were consented individually prior to every testing session. After providing consent, a participant was taken to a quiet, empty classroom located in the Methods of Entry School building. The only person in the classroom with the participant during the test administration was the testing administrator.

The test battery had two main components. The first component included basic demographics, deployment history, health-related behaviors, psychological health questionnaires, and neurobehavioral symptoms. The second component included both traditional pencil-and-paper and automated cognitive tasks. The specifics of each of the subtests/questionnaires within these two main components are provided below. Total testing lasted approximately 90 minutes.

Dependent measures

Questionnaires

- a) *Demographics*: The following demographic variables were collected for each participant: age, gender, ethnicity, Military Occupational Specialty (MOS), rank, education level, mother's education level, current medications, language, and number of deployments.
- b) *TBI Short Questionnaire - Post-Deployment Health Assessment (PDHA)*, DD Form 2796: Three mTBI questions were extracted from the PDHA. The questions asked for type of injury, severity of injury, and symptoms from injury.
- c) *Zung Depression Scale (ZDS)* (Zung, 1965): The 20-item instrument has a split-half reliability of 0.73 and an alpha coefficient of 0.82. The ZDS when correlated with the physician's global rating received a correlation of 0.69. In addition, ZDS has a strong correlation with the Hamilton Rating Scale and the Beck Depression Inventory in assessing self-criticism, hysteria, hypochondriasis, and paranoia. This scale is used to quantify a participant's general level of depression by asking how much of the time a statement describes how the individual felt during the past 2 weeks. Answers can range from "a little of the time" to "most of the time." Example: "I feel down-hearted and blue."
- d) *Zung Anxiety Scale (ZAS)* (Zung, 1971, 1974): The 20-item instrument has an internal consistency reliability coefficient of 0.80 and Cronbach's alpha of 0.79. This scale is used to quantify a participant's general level of anxiety by asking how often the participant felt or acted a certain way over the past few days. Answers can range from "a little of the time" to "most of the time." Example: "I feel calm and can sit still easily."
- e) *Perceived Stress Scale (PSS)* (Cohen, Kamarck, & Mermelstein, 1983): A 14-item self-report instrument used to measure self-perceived stress level. This questionnaire has a good internal reliability of 0.78 and established validity at 0.85. The participant is asked to rate how often he or she has felt a particular statement over the past month. The responses range from "never" to "sometimes" to "very often." Example: "In the last month, how often have you felt nervous and 'stressed'?"
- f) *Pittsburgh Sleep Quality Index (PSQI)* (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989): The PSQI is composed of 19 self-rated sleep questions with good internal consistency (0.83). The scale has high sensitivity of 89.6% and a specificity of 86.5% for sleep disorders, and has strong retest reliability for the global sleep score (0.85) and for component scales (0.65 to 0.84). Example question: "During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 minutes?" The participant can select from "not at all during the past month," "less than once a week," "once or twice a week," or "three or more times a week."

- g) *Neurobehavioral Symptom Inventory (NSI)* (Cicerone & Kalmar, 1995): This instrument consists of 22 common physical, cognitive, and emotional complaints of mTBI and post-concussive syndrome. Participants are told to rate each symptom with regard to how much they were disturbed by the symptom. Ratings range from “None” to “Moderate” to “Very Severe.” Examples: Feeling dizzy, poor coordination, nausea, and sensitivity to light.
- h) *PTSD Checklist-Military Version (PCL-M)* (Weathers et al., 2013): The PCL-M is a 17-item questionnaire with a test-retest reliability of 0.96. The questionnaire presents a list of problems and complaints that veterans sometimes have in response to stressful life experiences. Participants are asked to indicate how often they have been bothered by each problem over the past month. Answers can range from “not at all” to “moderately” to “extremely.” Example: “Repeated, disturbing memories, thoughts, or images of a stressful military experience from the past.”

Cognitive assessments

Test of Everyday Attention (TEA) (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996): The TEA gives a broad-based measure of important clinical and theoretical aspects of attention. The TEA is ecologically plausible and acceptable to participants. It is sensitive enough to also show normal age effects in the normal population. It can be used analytically to identify different patterns of attentional breakdown. The TEA has a wide range of applications, from patients with Alzheimer’s disease to young, normal subjects. It is the only test of attention based largely on every day materials; the real-life scenario means that individuals enjoy the test and find it relevant to the problems faced in life. The TEA is considered a “pencil-and-paper” assessment given that the test administrator sits with the participant and directly administers the test. Three subtests of the TEA were used in the current study:

- a) **Map Search:** In this subtest, participants were asked to imagine that they were navigating a map during a trip to Philadelphia. They were shown a particular symbol that could be found on the map (e.g., a gas station pump) and were told to circle as many of those symbols they could find on the color map of the Philadelphia area in 2 minutes. The maximum possible score was 80 (i.e., 80 symbols exist on the map). This subtest loads on selective attention.
- b) **Elevator Counting:** In this subtest, participants were asked to imagine that they were on an elevator in which the visual floor indicator light that tells them what floor they are at is broken. However, as the elevator passes each floor, a tone can be heard, so by counting the tones they can determine which floor they were on. The participants were asked to count the tones during seven different trials. This task is meant to familiarize the participants with the sound of the tone in order to prepare them for the next task.
- c) **Elevator Counting with Distraction:** Participants were asked to imagine that they were still in the elevator with the broken floor indicator light. This time, in order to determine the floor they were on, they were asked to count on 10 different trials the

low tones (i.e., the tones that they heard in the previous subtest) while ignoring higher pitched tones that serve as distracters. This auditory selective attention task loads on auditory-verbal working memory processes.

Test of Memory Malinger (TOMM) (Tombaugh, 1996): The TOMM consists of two learning trials. On each learning trial, the participant is shown 50 pictures (line-drawings) on the laptop. The same 50 pictures were used on each trial. However, they were presented in a different order during the second learning trial. Each picture is shown for 3 seconds, with a 1-second interval between pictures. After the last picture was presented, the participant was shown 50 two-choice recognition panels on the laptop. Each panel contained one of the previously presented pictures and a distracter picture not previously shown. No distracter picture is used more than once throughout the three trials. The participant is required to select the correct picture (i.e., the one previously presented) from each panel. For each answer, the test administrator provides feedback on the correctness of the response. This test is used to primarily screen out individuals who are not making an effort and/or feigning illness. A score of less than 45 out of 50 on either learning trial suggests that the participant is malingering.

Central Nervous System - Vital Signs (CNS-VS) (Gualtieri & Johnson, 2006): This test battery is self-administered on a laptop, and includes five subtests (i.e., verbal memory, symbol digit coding, Stroop test, shifting attention test, and continuous performance) that are widely used by neuropsychologists and are known to be reliable and valid (Baker et al., 1985; Gualtieri & Johnson, 2006). These five subtests generate 13 primary scores, which are used to calculate cognitive domain scores for verbal memory, information processing speed, complex attention, cognitive flexibility, reaction time, and executive function. CNS-VS also contains two additional subtests (i.e., dual task test and digit span) that are known to be sensitive to most of the causes of mild cognitive dysfunction. Taken together, the subtests embedded within the CNS-VS platform embrace an appropriate span of cognitive domains and are sensitive to detecting small changes in neurocognitive ability (Gualtieri, Johnson, & Benedict, 2006). Because the presentation of stimuli is randomized, no two presentations of CNS-VS are ever the same; therefore, the battery is ideal for serial administration (see Aim 2). The individual subtests are explained in detail below (in chronological order in which they were administered to the participant).

- a) Verbal Memory: This test measures recognition memory for words. Fifteen words are presented, one by one, on the computer screen every 2 seconds. Immediately after this presentation, the participant is presented 30 words, 15 of which are the previous words that the participant was told to remember and 15 of which are new distracter words. Presentation of these 30 words is randomized and the participant is instructed to press the space bar when a word from the original list of 15 is recognized. This first portion of the test is referred to as initial verbal memory. Then, after the participant completes the remaining six cognitive tests, there is a delayed verbal memory trial in which the participant is again shown 30 words (15 that the participant was originally told to remember nested among 15 new distracter words) and told to press the space bar when a word is recognized.

- b) **Symbol Digit Coding:** A static display of digits 2 through 9 appears in a row at the top of the screen with a unique symbol (e.g., Ω , \geq , ∞ , \downarrow , \sum , $\sqrt{\quad}$, \pm , \div) above each digit. The test consists of serial presentations of tables below this static display, each of which contains a top row of 8 cells (each containing a symbol) and a bottom row of 8 empty cells. The participant is instructed to type the number in each empty cell that corresponds to the number/symbol pairing provided in the static display at the top of the screen. The participant is only allowed to use the numbers 2 through 9 at the top of a traditional keyboard (i.e., the computer program does not allow the participant to use the number pad). This prevents the potential for a distinct advantage for those who are skilled at using the numerical pad or for those who are right- versus left-handed.
- c) **Stroop Test:** This test has three parts. In the first part (Simple reaction time), the words RED, YELLOW, BLUE, or GREEN (printed in black) appear at random on the screen, and the participant presses the space bar as soon as the word is seen. In the second part (Complex reaction time), the words RED, YELLOW, BLUE, or GREEN appear on the screen displayed in color. The participant is told to press the space bar only when the font color of the word matches what the word says (e.g., the participant should press the space bar if the word is RED and it is the color red). In the third part (Stroop reaction time), the words RED, YELLOW, BLUE, or GREEN appear on the screen displayed in color. The participant is told to press the space bar when the font color of the word does not match what the word says (e.g., the participant should press the space bar if the word says RED but it is the color green).
- d) **Shifting Attention Test:** This test measures executive function in terms of how well the participant can shift from one instruction set to another quickly and accurately. It measures how well a participant can recognize set shifting (mental flexibility) and abstraction (rules, categories), while managing multiple tasks simultaneously. Participants are to match geometric objects either by shape or color. Three figures appear on the screen, one on top and two on the bottom (on the left and right sides of the screen). The top figure is either a square or a circle and is either red or blue. One of the bottom figures is a square and the other one is a circle, and these two figures are either red or blue, mixed randomly (they are never the same color). The participant is asked to match one of the bottom figures to the top figure either in terms of color or shape. The participant does this by pressing either the left or right shift key on the key pad, corresponding to the bottom figure on the left or right of the screen. The rules change at random (i.e., match the figure by shape, and then for another, match the figure by color). The rule is displayed at the top of the screen for each trial.
- e) **Continuous Performance:** This test is a measure of vigilance or sustained attention over time. Every 1.5 seconds (s), a single letter is presented in the middle of the computer screen. The participant is told that the target stimulus is the letter “B” and the space bar should be pressed every time the letter “B” appears on the screen. The participant is instructed to ignore all other letters and

not respond. In 5 minutes (min), the test presents 200 letters, 40 of which are the target (the letter B) and 160 of which are non-targets (other letters). The stimuli are presented at random, although the target stimulus is blocked so it appears eight times during each minute of the test.

- f) Dual Task Test: This test is a measure of divided attention. The participant is told to keep a mouse cursor within a box that moves randomly across the screen. Within the moving box there are numbers that randomly appear every 2.5 s. Along with keeping the cursor inside of this moving box, the participant is also told to press the space bar every time the number that appears in the box is greater than or equal to 56.
- g) Digit Span: This is a test of working memory ability. The task involves the presentation of a sequence of random numbers, one at a time, with the participant being told to remember each sequence and then type it out when prompted. The task involves two phases. The first phase is referred to as the forward digit span. The participant is told to type out each sequence in the order that it was presented. For example, if the participant was shown the sequence 4-2-3-6 (each number presented one at a time in that order), then the correct response would be for the participant to then type in 4-2-3-6 (in that order) when prompted. The second phase is referred to as the backward digit span. The participant is told to type out each sequence in the reverse order in which it was presented. For example, if the participant was shown the sequence 4-2-3-6 (each number presented one at a time in that order), then the correct response would be for the participant to then type in 6-3-2-4 (in that order) when prompted. The sequence length in both phases always started with two digits and then would progress by one digit until the participant commits an error (i.e., exceeds recall).

Data reduction and analysis

Frequencies and averages were calculated for each of the variables included in the demographics questionnaire. Each of the neuropsychological questionnaires was scored according to its conventional guidelines, resulting in a single composite score for each questionnaire. In addition, the TOMM was used solely as a screening tool in order to determine malingering. If an individual scored below the 45 out of 50 threshold on the TOMM, then the scores on the questionnaires/cognitive tasks were removed from the analyses.

The Map Search portion of the TEA was analyzed by measuring the total number of symbols correctly located within the 2-min time limit. The Elevator Counting with Distraction portion of the TEA was analyzed by measuring the total number of correct trials (i.e., trials in which the number of low tones were counted correctly).

The principle dependent variables for the neurocognitive tasks presented in CNS-VS are the six domain scores generated by differential combinations of the primary raw scores calculated from each subtest. Formulation of these six domain scores has previously been established and validated through a rigorous factor analysis of the raw data (Gualtieri & Johnson, 2006). The

Reaction Time domain score is calculated by summing the Stroop Test's "Complex reaction time" and "Stroop reaction time" and dividing that sum by two. The *Complex Attention* domain score is calculated by summing together the Stroop test commission error responses, shifting attention test error responses, continuous performance test error responses, and the continuous performance test omission error responses. The *Cognitive Flexibility* domain score is calculated by taking the number of correct responses on the shifting attention test and subtracting both the shifting attention test error responses and the Stroop test commission error responses. The *Processing Speed* domain score is calculated by subtracting symbol digit coding error responses from symbol digit coding correct responses. The *Executive Function* domain score is calculated by subtracting shifting attention test error responses from shifting attention test correct responses. Finally, the *Verbal Memory* domain score is calculated by summing all of the correct responses during both the initial and delayed trials of the verbal memory subtest. The domain scores are presented as standard scores as a way of presenting the scores relative to other people in a normative sample. The normative sample scores generated by CNS-VS are based on age-matched performance on the cognitive domains and are normalized to a scale with a mean of 100 and a standard deviation of 15. Higher scores on each of the domains are considered "better" than lower scores.

CNS-VS does not provide normative data for the digit span and dual task tests; therefore, standard scores were unable to be generated for these measures. The forward and backward digit span scores represent the highest sequence (i.e., string of numbers) that a participant was able to recall. The Dual Task Test score was calculated through the use of an algorithm that determines a "performance index" by taking into account average percentage of time that the cursor was kept inside the box and number of correct responses using the space bar. The maximum possible score is 100 (which would suggest that a participant was able to maintain the cursor inside of the box for the entire test time and correctly responded to the space bar task each trial).

Group differences (Breacher vs. Control) in the demographic variables (age, years of education, and number of deployments) and each of the neuropsychological questionnaires were compared using independent samples *t*-tests. In addition, separate *t*-tests were used to analyze performance on each of the CNS-VS domain scores, as well as on the TEA subtests, digit span test (forward and backward) and the dual task test. All group averages are presented in the results section in the form of mean \pm the standard error of the mean.

Aim 2. Tracking breacher instructors over time

Participants

Participants were 18 active-duty, male U.S. Marines from a WTB at Quantico Marine Corps Base, Virginia. All 18 participants worked at the Methods of Entry School. Twelve of these participants were instructors at the school house (i.e., breacher instructors) and the remaining six were engineers (i.e., breacher engineers) who assist with preparing and maintaining the breacher range for each course, but who are not regularly exposed to blasts. This group serves as a "control" for blast exposure. Two of the 12 breacher instructors had to drop out of the study due to a permanent change in station (PCS) and are not included in any of the analyses from the

longitudinal aim of this study; therefore, the final sample size for breacher instructors was 10. Background demographics for both groups are provided in Table 1.

Procedure

All testing sessions occurred during the weeks of “down time” in between courses at the Methods of Entry school house. Participants consented to volunteer during an informed consent meeting with one of the study investigators. All informed consent meetings were conducted individually. After providing consent, a participant was taken to a quiet, empty classroom located in the Methods of Entry School building. The only person in the classroom with the participant during the test administration was the testing administrator.

The same test battery of questionnaires and cognitive tasks described in Aim 1 (see above) was used to accomplish Aim 2. However, it is important to note that the demographics questionnaire and the TBI Short Questionnaire were only administered during a participant’s first session. In addition, use of the Elevator Counting Task portion of the Test of Everyday Attention was discontinued after the first session, and therefore longitudinal data on that measure is not available.

The participants were repeatedly administered the test battery over the course of 2 years. A participant’s first administration of the test battery was designated as “Session 1.” The next administration was designated as “Session 2” and subsequent administrations are designated as “Session 3,” “Session 4,” etc. The first testing session lasted approximately 90 min, with all subsequent testing sessions lasting approximately 80 min given the few questionnaires and lack of the Elevator Counting Task.

Dependent measures

Refer to the Dependent measures section for Aim 1.

Data analysis and reduction

Group differences (Breacher Instructor vs. Breacher Engineer) in the demographic variables (age, years of education, and number of deployments) were compared using independent samples *t*-tests. Separate mixed-factor analyses of variance (ANOVAs) were used to analyze each of the neuropsychological scores from the questionnaires using “Group” (Breacher Instructor vs. Breacher Engineer) as the between-subjects variable and “Session” (1 through 6) as the repeated measure. Separate mixed factor ANOVAs were also used to analyze performance on each of the CNS-VS domain scores, as well as on the Map Counting task, digit span test (forward and backward) and the dual task test. Again, “Group” was the between-subject factor and “Session” was the repeated variable. The data collected are presented in graphical form within the Results section. All group averages are presented in the form of mean \pm the standard error of the mean.

Results

Aim 1. Assessment

Demographics

The Breacher group consisted of 11 Caucasians and 1 Asian. The control group consisted of 26 Caucasians, 1 African American, and 1 individual of mixed ethnicity. All individuals in both groups indicated English as their primary spoken language. Military ranking in both groups ranged from E5 to E7. Table 1 provides group means for several additional demographic variables. Breachers and controls were not significantly different from each other in terms of age, education level, or number of deployments.

Neuropsychological questionnaires

Based on self-reports using the TBI Short Questionnaire, 6 of 12 Breachers (50%) and 11 of 28 Controls (39%) endorsed having previously experienced a combat-related mTBI.

The results from each of the remaining neuropsychological questionnaires are presented in Table 2. Note that for each of the measures, a higher score is “worse” (i.e., indicates more severity). Controls displayed significantly higher scores than Breachers on the depression, perceived stress, and Post Traumatic Stress Disorder (PTSD) Symptoms scales.

Table 2
Psychological Health Measures

Measure	Group	<i>n</i>	\bar{X}	SEM
Depression (ZDS) *	Breacher	12	31.42	2.60
	Control	28	39.64	1.65
Anxiety (ZAS)	Breacher	12	30.25	2.73
	Control	28	35.07	1.32
Perceived Stress (PSS) *	Breacher	12	31.50	2.12
	Control	28	38.67	1.41
Sleep Quality (PSQI)	Breacher	12	6.08	1.11
	Control	28	7.99	0.71
Neurobehavioral Symptoms (NSI)	Breacher	12	14.25	3.81
	Control	28	19.11	1.89
PTSD Symptoms (PCL-M) *	Breacher	12	27.17	2.87
	Control	28	37.32	2.37

(*) denotes significance at $p < 0.05$

Neurocognitive assessment

Results from the Map Search test and the Elevator Counting task from the Test of Everyday Attention are presented in Figures 1 and 2, respectively. No significant group differences were detected.

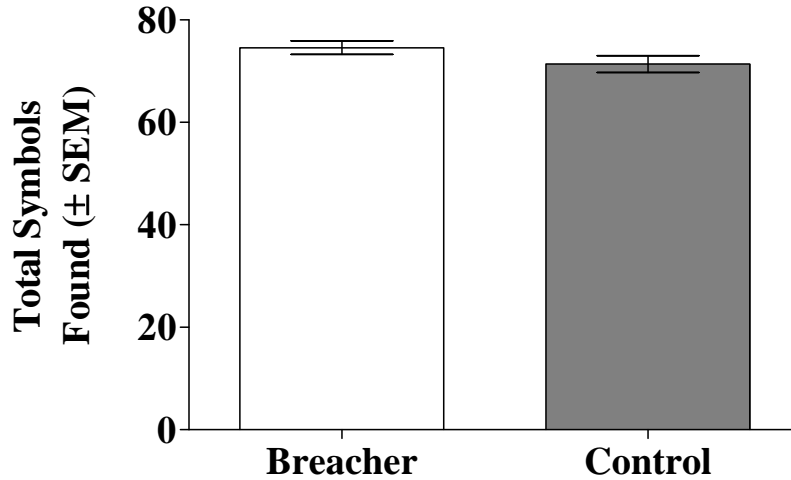


Figure 1. Total number of correct symbols (±SEM) found during the Map Search portion of the Test of Everyday Attention. Maximum number that could be found was 80. Total test time was 2 min.

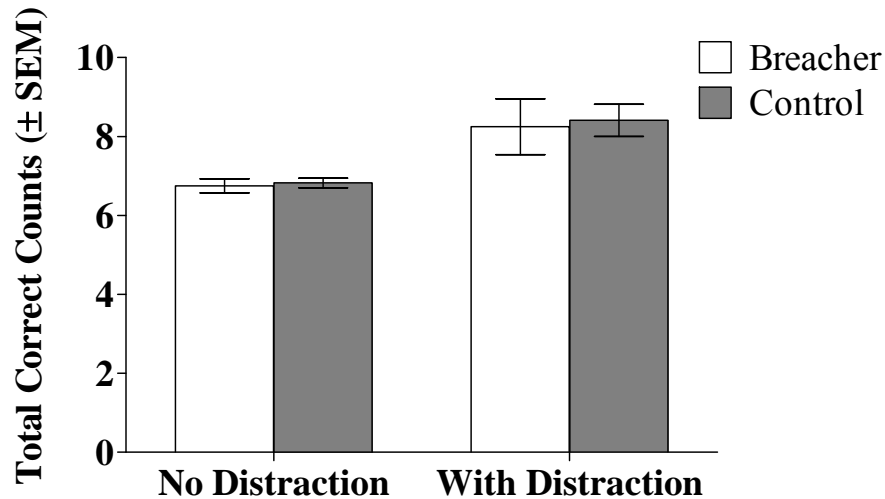


Figure 2. Correct Trials (±SEM) during both the Elevator Counting (without distraction) and Elevator Counting Task with Distraction portions of the Test of Everyday Attention. The maximum number of correct trials was 10. A trial was considered correct if the respondent could accurately count all of the low tones that were interspersed with high tones.

Results for each of the neurocognitive domain scores calculated by CNS-VS are presented in Figure 3. Note that a higher standardized score is “better.” Breachers did not differ significantly from Controls on any of the CNS-VS domains.

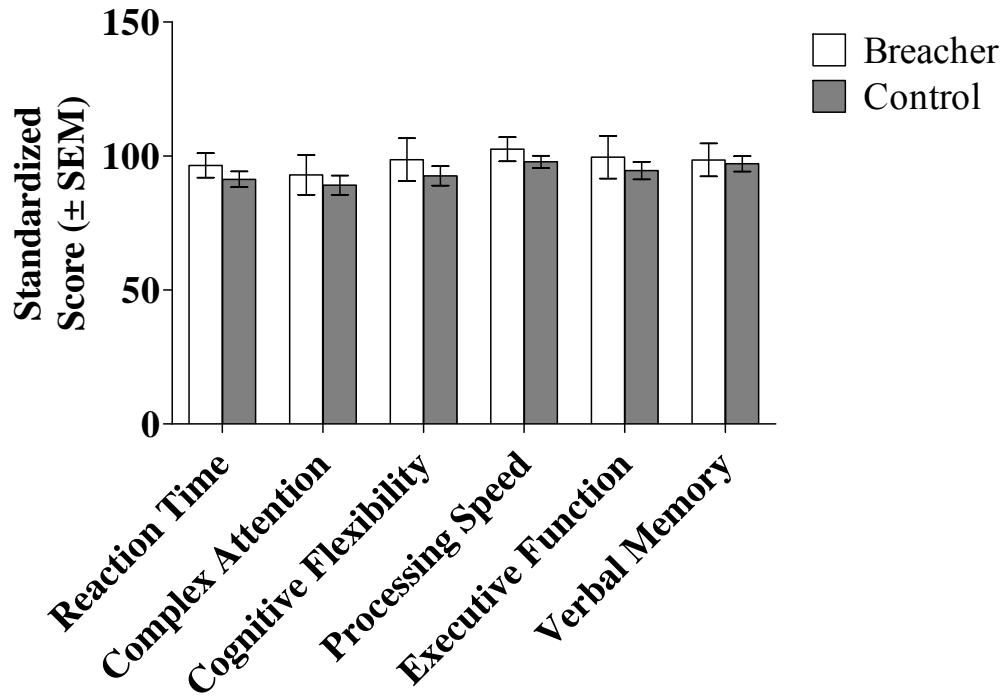


Figure 3. CNS-VS Neurocognitive Domain Scores. Performance is indicated by standard scores (\pm SEM).

Results for the forward digit span test and backward digit span test are presented in Figure 4. No significant group differences were detected.

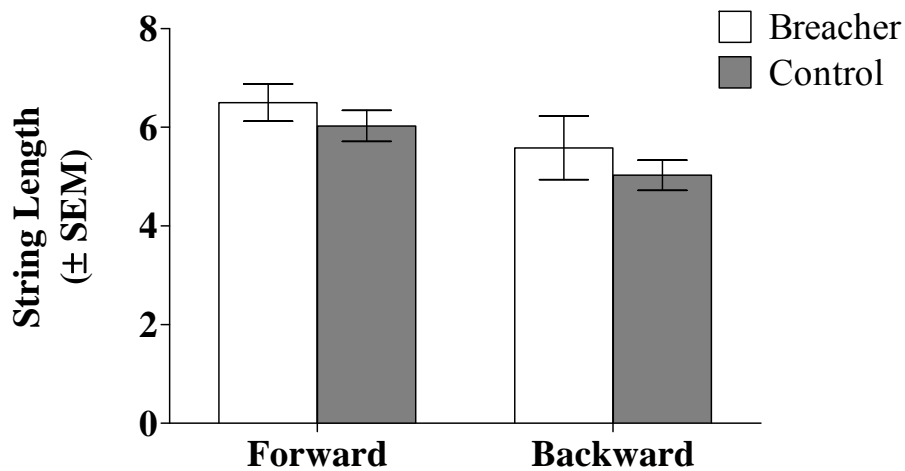


Figure 4. Forward and Backward Digit Span Test. Performance is indicated by highest string length of numbers (\pm SEM) able to be recalled.

Results for the Dual Task test are presented in Figure 5. No significant group differences were detected.

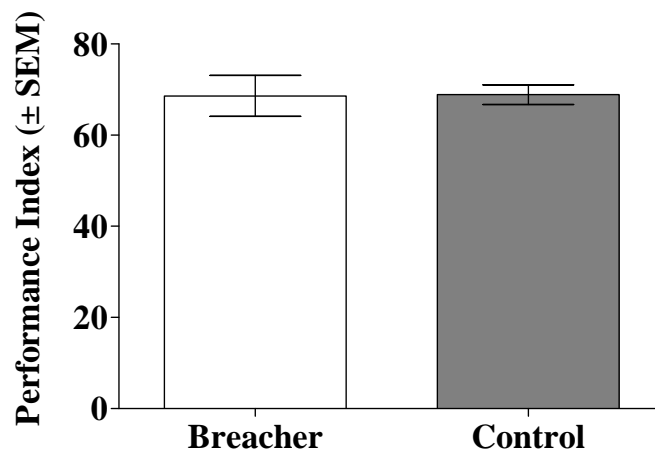


Figure 5. Dual Task Test. Performance Index (\pm SEM) indicates how well a participant was able to correctly respond to a flashing number (i.e., press the space bar when the number was ≥ 56) while simultaneously keeping a cursor inside of a box moving across the screen. Higher score indicates better ability to perform this task. A score of 100 would indicate perfect completion of the task.

Aim 2. Tracking breacher instructors over time

Demographics

All 10 of the breacher instructors were Caucasian. The breacher engineers consisted of five Caucasians and one Hispanic individual. All individuals in both groups indicated English as their primary spoken language. Military ranking in both groups ranged from E5 to E7. Table 3 provides group means for several additional demographic variables. The breacher instructors and breacher engineers were not significantly different from each other in terms of age, education level, or number of deployments.

Table 3
Aim 2 Demographics

Variable	Breacher Instructors (<i>n</i> =10)	Breacher Engineers (<i>n</i> =6)
Age	30.6 ± 1.4	29.8 ± 1.8
Education level in years	12.8 ± 0.5	13.5 ± 0.8
Number of deployments	3.9 ± 0.9	3.2 ± 0.6

Neuropsychological questionnaires

Based on self-reports using the TBI Short Questionnaire, 5 out of 10 Breachers (50%) and 2 out of 6 Controls (33%) endorsed having previously experienced a combat-related mTBI.

The results from each of the neuropsychological questionnaires are presented in Figure 6. For both groups, neuropsychological health remained relatively stable across time. No interactions were detected on any of the measures. The only notable finding was a significant main effect of group on the Perceived Stress Scale [$F(1,14) = 24.63, p < 0.001$], indicating that the breacher engineers displayed higher stress scores throughout the study.

Neurocognitive assessment

Results from the Map Search task are presented in Figure 7. There were no group differences observed at any time point and performance remained relatively stable.

Results for each of the neurocognitive domain scores calculated by CNS-VS are presented in Figure 8. Note that a higher standardized score is “better.” No significant interactions or group differences emerged on any of the CNS-VS cognitive domains. Cognitive performance for both groups remained relatively stable across time.

Results for the forward digit span test and backward digit span test are presented in Figures 9 and 10, respectively. Results for the dual task test are presented in Figure 11. For these

additional subtests within CNS-VS, there were no significant interactions or group differences across time, and performance remained relatively stable.

Discussion

Despite repetitive blast-wave exposure during the course of their tenure at the U.S. Marine Corps Methods of Entry School, the results of the present study fail to provide evidence that breacher instructors suffer from neurocognitive impairments. The initial assessment conducted in Aim 1 suggests that instructors from the control population (i.e., other school houses at the WTB) demonstrated significantly higher depression, perceived stress, and PTSD symptom scores compared to breacher instructors. However, despite these mood and psychological health differences, there were no significant differences in performance across any of the neurocognitive domains. The results of Aim 2 demonstrate that psychological health measures remain relatively stable over time for both the breacher instructors and the blast-naïve breacher engineers who work alongside them at the Methods of Entry School. Notably, the breacher engineers displayed higher perceived stress scores at each time point assessed, but this may be explained, in part, by the fact that the breacher engineers remained involved in maintaining the blast range even during the weeks of “down time” in which the assessments took place. Nevertheless, despite this higher stress profile observed in the breacher engineers compared to breacher instructors, performance across each of the neurocognitive domains remained stable and did not differ between groups at any time point.

In addition to providing occupational health hazard information related to breacher training, the goal of this study was to examine whether cumulative, low-level blast-wave exposure results in cognitive deficits and symptomatology similar to that which is commonly observed following a blast-related mTBI. Studying this particular population of Marines allows for a better understanding of the contribution of blast-wave exposure *per se* as the mechanism of blast-related brain injury given that the controlled nature of the breacher blast environment helps eliminate secondary and tertiary mechanisms of injury from contributing to cognitive sequelae. To our knowledge, this is the first study to examine neurocognitive performance in U.S. Marine breacher instructors from a longitudinal perspective (i.e., following several training courses over two years). Previous studies that were conducted within the timeframe of a single 2-week training course at the U.S. Marine Corps Methods of Entry School have provided evidence of mild deficits on domains such as auditory attention, verbal recall, and visual short-term memory following repeated blast exposure (Carr et al., 2009; Parish et al., 2009). However, neurocognitive domains such as processing speed, executive functioning, working memory, mathematical processing, and reaction time were not affected (Carr et al., 2009; Parish et al., 2009). Although the performance decrements noted in these acute studies suggest possible blast-related neurocognitive sequelae consistent with anecdotal reports of memory issues from breacher instructors, it is not clear how specific or persistent these decrements are given that assessments took place within the timeframe of the course itself. A recent New Zealand Defence Force breacher study reported that subtle memory and reaction time deficits observed following blast exposure recover after two weeks (Tate et al., 2013). Interestingly, this neurocognitive rebound is concomitant with a return to baseline of levels of several blood-based levels

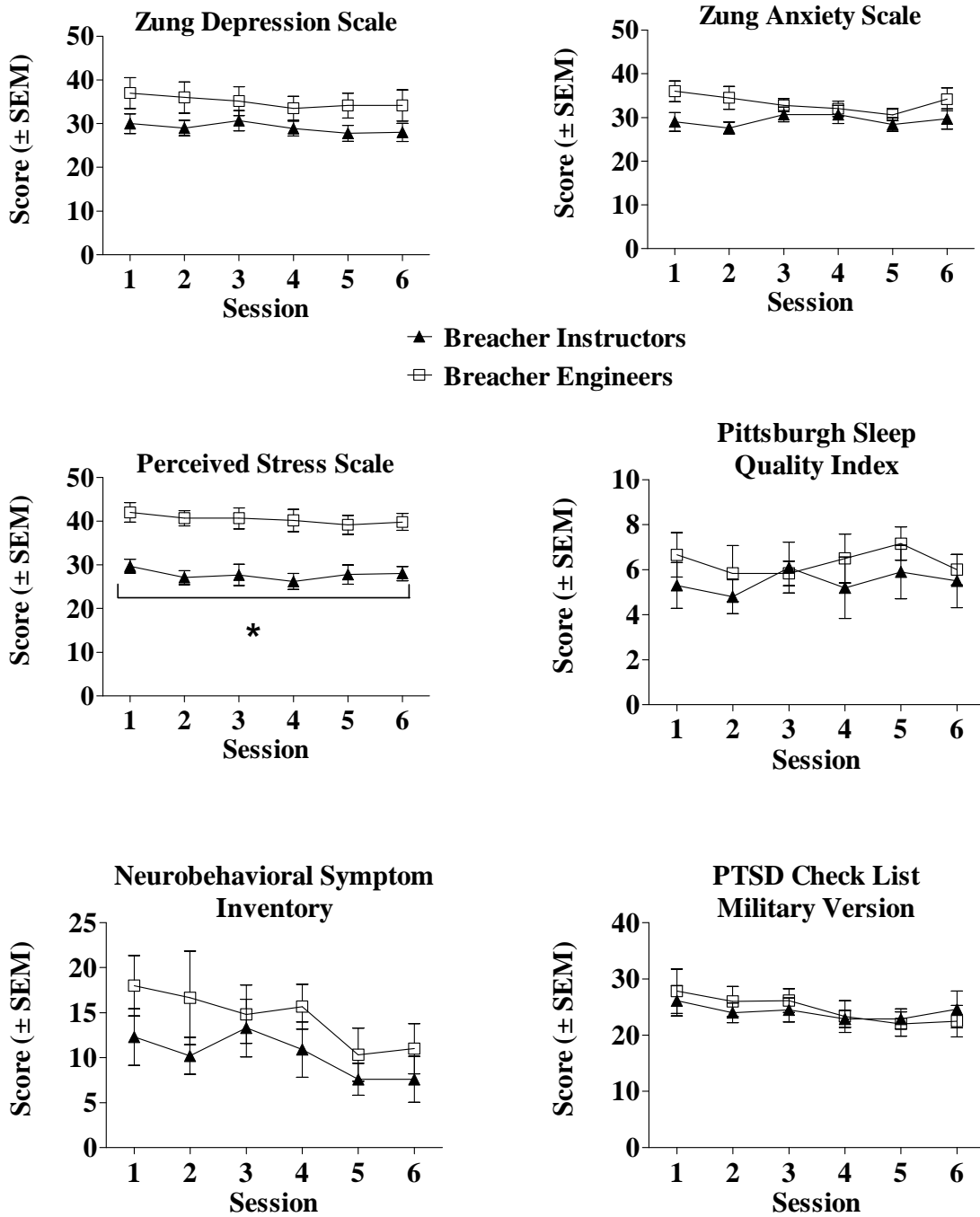


Figure 6. Mean scores (\pm SEM) on each of the neuropsychological questionnaires for Breacher Instructors (solid triangles) and Breacher Engineers (open squares). For each measure a higher score indicates greater severity (i.e., is considered “worse”). The asterisk (*) indicates significant main effect of group ($p < 0.05$).

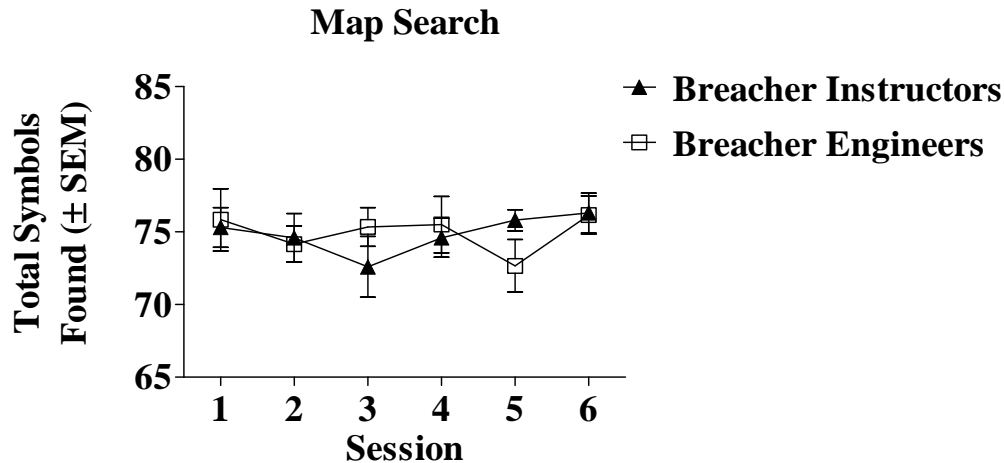


Figure 7. Total number of correct symbols (\pm SEM) found during the Map Search portion of the Test of Everyday Attention for Breacher Instructors (solid triangles) and Breacher Engineers (open squares). Maximum number that could be found was 80. Total test time was 2 m.

that are altered following blast exposure (Tate et al., 2013), suggesting that brain perturbations resulting from controlled blast overpressure may only be transient. The present study expands upon these findings by demonstrating steady neurocognitive performance and neuropsychological health over time when assessments occur during the weeks of “down time” in between training courses. Collectively, these results suggest that breacher instructors are able to recover from subtle blast-related neuropsychological alterations experienced during their training course and do not suffer from severe long-term deficits resulting from cumulative blast exposure.

The lack of practice effects (i.e., improvement over time) on each of the neurocognitive domains may be interpreted as evidence of mild impairment. In their original study of Marine Corps breachers, Parish et al. (2009) observed practice effects on single-trial measures of processing speed and executive function taken prior to and following the breacher training course. In contrast, practice effects were absent on single-trial measures of auditory attention and immediate verbal recall for the breachers but not the blast-naïve control group, which the authors interpreted as evidence of subtle neurocognitive impairment following blast exposure (Parish et al., 2009). However, the lack of practice effects in the breacher instructor group in the present study is mitigated by the lack of a practice effects in the breacher engineer “control” group as well. Furthermore, an important methodological difference between the study by Parish and colleagues and the present study is the time period between testing. The pre- and post-blast exposure testing sessions in (Parish et al., 2009) were separated by approximately 2 weeks and occurred just before and just after the training course, whereas testing sessions in the present study were separated by at least 5 to 6 weeks and occurred during the weeks in between training courses. This distinction is important given the evidence that practice effects on a cognitive test battery are reliably present when test administrations are separated by a day or a week, but not after a full month (Falletti, Maruff, Collie, & Darby, 2006). Therefore, it is not surprising that we failed to detect practice effects in the present study.

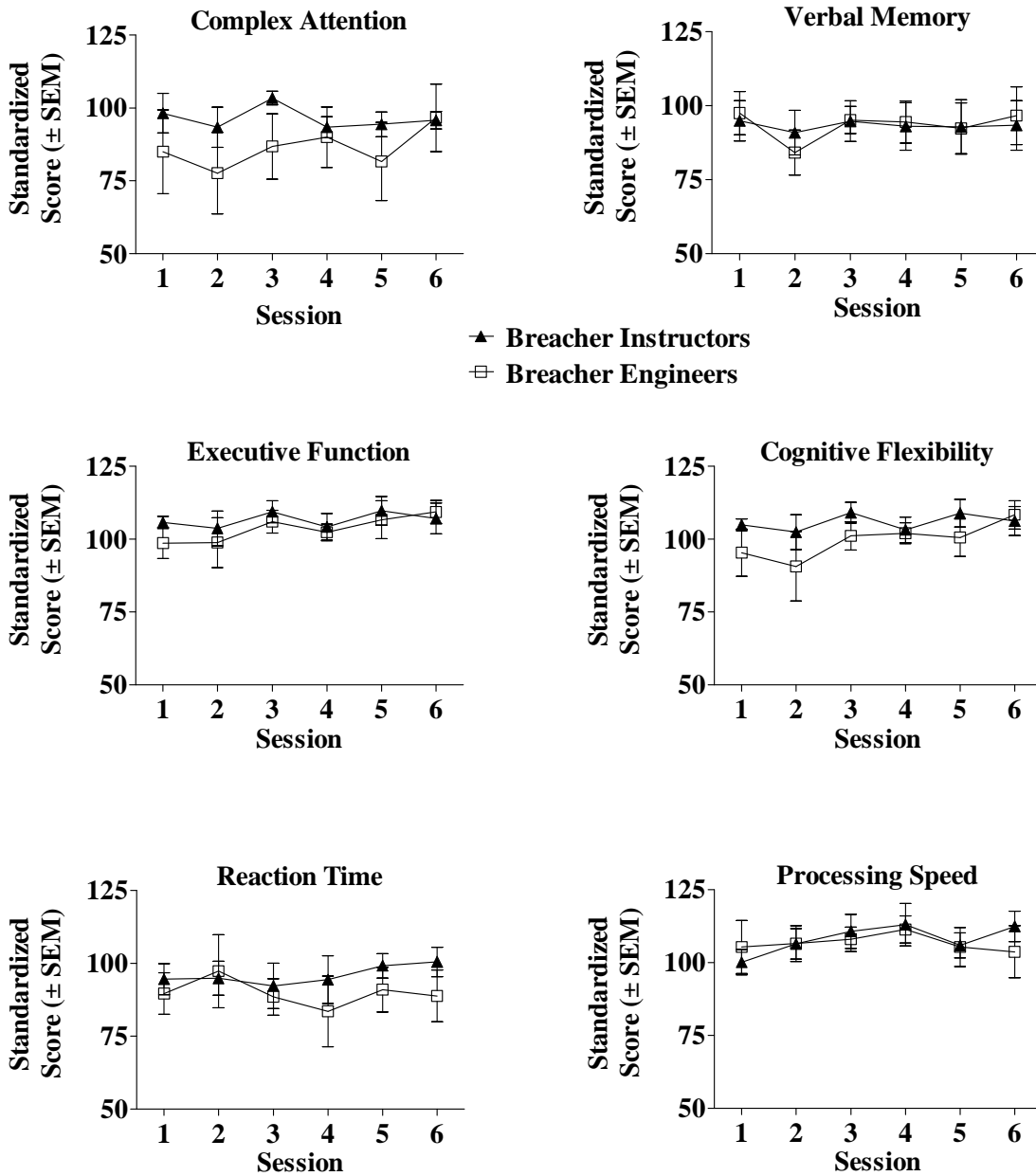


Figure 8. CNS-VS Cognitive Domain Scores for Breacher Instructors (solid triangles) and Breacher Engineers (open squares). Performance is indicated by standard scores (\pm SEM).

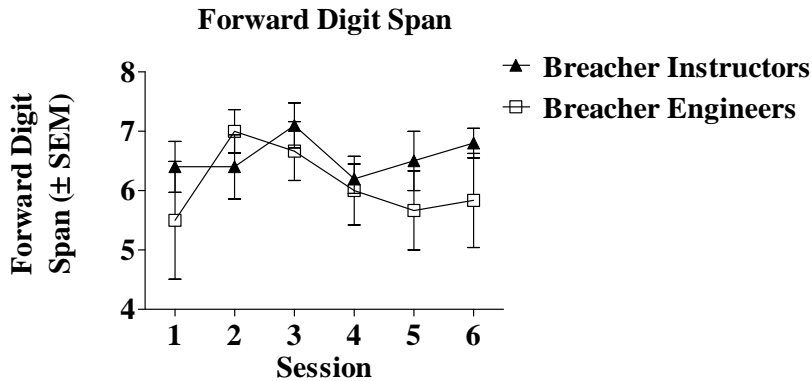


Figure 9. Forward Digit Span for Breacher Instructors (solid triangles) and Breacher Engineers (open squares). Performance is indicated by highest string length of numbers able to be recalled.

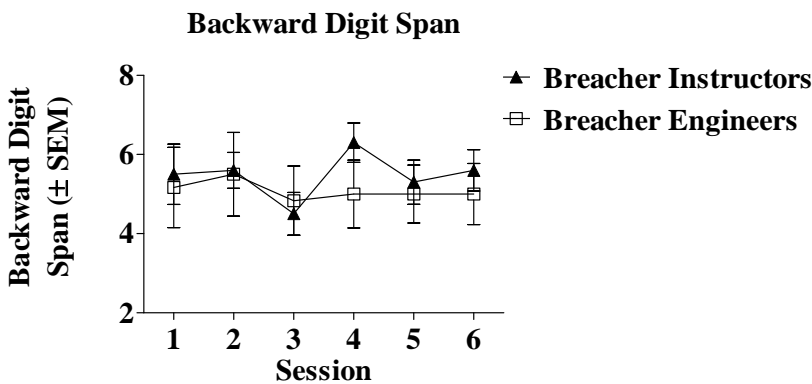


Figure 10. Backward Digit Span for Breacher Instructors (solid triangles) and Breacher Engineers (open squares). Performance is indicated by highest string length of numbers able to be recalled.

Although it is unlikely that isolated blast exposures during the training exercises reach the threshold for inducing mTBI in the breacher instructors, our hypothesis was that the cumulative nature of these exposures over time could lead to a detectable cognitive sequelae similar to that which might be observed in individuals with a diagnosed blast-related mTBI. This research effort is in line with the recent push within the military community to elucidate the specific neurocognitive consequences of blast wave exposure. Studying this phenomenon has been hampered by difficulties in identifying Soldiers who are exposed to significant blast wave overpressure levels in the absence of additional injury (e.g., being struck in the head by flying debris and/or falling and hitting their head against a solid object). For example, Mac Donald et al. (2011) used diffusion tensor imaging to identify axonal injury in the cerebellar peduncles, cingulum bundles, and right orbitalfrontal gray matter in the brains of Soldiers clinically diagnosed with blast-related mTBI. However, they were unable to demonstrate the extent to which axonal injury was specifically due to primary blast exposure because every participant had

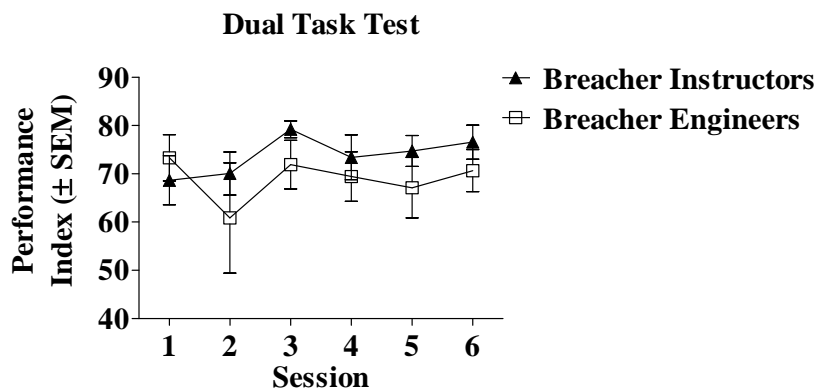


Figure 11. Dual Task Test for Breacher Instructors (solid triangles) and Breacher Engineers (open squares). Performance Index indicates how well a participant was able to correctly respond to a flashing number (i.e., press the space bar when the number was ≥ 56) while simultaneously keeping a cursor inside of a box moving across the screen. Higher score indicates better ability to perform this task. A score of 100 would indicate perfect completion of the task.

also experienced secondary and/or tertiary forms of head injury (Mac Donald et al., 2011). The evidence regarding the severity and persistence of neurocognitive impairments following mTBI, regardless of mechanism, are mixed. Although the majority of reports suggest little deficiency and rapid recovery (Dikmen et al., 2009; Ivins, Kane, & Schwab, 2009; McCrea et al., 2009; Waljas et al., 2014), while others demonstrate that at least a subset of individuals will continue to experience long-lasting cognitive decrements that can interfere with occupational duties (Drake, Gray, Yoder, Pramuka, & Llewellyn, 2000). In a comparison of blast- versus blunt-induced TBI, Belanger, Ketzmer, et al. (2009) suggest that severity of injury, rather than mechanism of injury, is more important in determining long-term neurocognitive functioning and symptom reporting. Luethcke et al. (2011) examined cognitive and psychological symptoms within the first 72 hours of a diagnosed mTBI and again found that mechanism of brain injury (i.e., blast- vs. non-blast-induced) was less important than severity of injury in predicting performance and symptomatology. However, there have still not been any reports in which the contribution of primary blast wave exposure in blast-induced mTBI has been teased apart from the additional sources of head injury that typically accompany mTBI in warzones. Researchers should continue to search for unique populations of individuals who are at high risk for primary blast-wave overexposure levels that are sufficient to result in mTBI, but who are at low risk to experience the frequently accompanying secondary and tertiary mechanisms of brain injury. Our results suggest that the breacher population may not be an optimal group from which to study this phenomenon.

It should be noted that the results of this study contradict anecdotal reports from past breacher instructors who have complained of persistent memory, concentration, and thought processing impairments that they felt might be associated with their job. Given that our assessments took place outside the context of blast exposure, it is possible that many of the symptom complaints reported by the breacher instructors are only present and/or being communicated during the breacher training exercises. Therefore, this study should not be taken

as evidence that the symptoms do not exist, but rather, that manifestation of the symptom complaints are transient and perhaps not cumulative. It is also important to note that not every breacher instructor has complained of cognitive impairments. It is only a subset of an already small group of individuals that has voiced concerns over their mental health integrity. In addition, we cannot rule out the possibility that the individuals from whom the anecdotal reports were obtained did not arrive to the Method of Entry School with pre-morbid brain injury conditions from prior training and/or military deployment. Perhaps most importantly, the safety standards at the Methods of Entry School have evolved since the inception of the current research initiative, in large part due to the concerns over instructor and student mental health stemming from anecdotal reports. The improved standards (e.g., minimum distance from charge detonation and better personal protective equipment) that have been in place with newer cohorts of breacher instructors may also explain why the breacher instructors are able to maintain relatively stable neuropsychological health throughout their tenure.

Limitations

One important factor potentially masking group differences in neurocognitive performance is the relatively high percentage of individuals in each of the groups who endorsed symptoms of having experienced a previous combat-related mTBI. Although the literature largely suggests that lasting cognitive impairments from a previous mTBI are unlikely, this pre-morbid condition certainly presents a potential confound in our data analysis. If there were sufficient sample sizes in each group then it would have been possible to create sub-groups consisting of individuals with a previous mTBI versus those without. However, an unavoidable limitation with this study is the small group sizes. This is due to the fact that the Methods of Forced Entry School employs only 10 to 12 personnel at any given time. This creates difficulty in being able to conduct statistical analyses with such low power. However, given that almost all of the personnel at the school house volunteered to participate in this study, we essentially captured the entire Marine breacher population that we aimed to investigate. Thus, although caution should be made in making generalizations beyond the breacher population, we feel confident that the results of this study can be used to assist in occupational hazard assessments for individuals who may be exposed to repeated blasts in a controlled environment. Nevertheless, additional studies using a more sizable population of individuals who are repeatedly exposed to controlled blasts over an extended period of time will be needed in order to more carefully control for the presence of brain injury conditions that may precede initial blast exposure.

Conclusion

Testing the breacher instructors during the weeks of down time between the Methods of Entry courses allowed us to investigate the potential impact of cumulative blast exposure on cognitive health and symptomatology. The findings from the current study suggest that Marine breacher instructors do not suffer from long-term neurocognitive impairments due to repetitive low-level blast exposure. Indeed, similar to blast-naïve support staff, the breacher instructors displayed stability on all measures of neurocognitive performance and neuropsychological health that were assessed. These findings contribute to an emerging body of literature suggesting that the acute neurocognitive decrements and biomarker fluctuations observed immediately following

low-level blast exposure may recover once blast-exposed individuals are allowed a period of down time [see Tate et al., (2013)]. Future studies aimed at characterizing the long-term sequelae stemming from blast overpressure exposure may need to identify and focus on individuals who are more regularly exposed to higher-level blast waves in a controlled environment.

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