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Monica Vemulapalli April 6, 2020

PTSD Severity and Neurovascular Responses to Device Guided Slow Breathing: Acute and Long-term Effects

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Abstract

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Background: Posttraumatic stress disorder (PTSD) is associated with an increased risk for developing hypertension and cardiovascular disease (CVD). We previously showed that device-guided slow breathing (DGB) acutely lowers muscle sympathetic nerve activity (MSNA) and improves hemodynamics in patients with PTSD. However, it remains unclear whether the physiological responses to DGB depend on the severity of PTSD symptoms. **Hypothesis:** Study 1. Neural and cardiovascular responses to acute DGB will be heightened in severe PTSD. Study 2. Chronic use of DGB will decrease resting MSNA, blood pressure (BP) and heart rate (HR) in severe PTSD. **Methods:** The clinician-administered PTSD scale (CAPS) was used to confirm the diagnosis of PTSD (CAPS score ≥45) and the severity of PTSD symptoms. To test our hypothesis, we recruited 25 veterans with PTSD (age, 36±2 years). The CAPS scores in our sample ranged from 45 to 95 with a median score of 70 that was used to separate study participants into two groups: Moderate (CAPS ≤70, n=13) and Severe (CAPS >70, n=12). Within each group, participants were randomized to either breathing with the DGB device or with an identically looking Sham device. Beat-to-beat blood pressure (BP) via finger plethysmography, HR via EKG, HR variability (HRV) and MSNA using microneurography were measured for both studies. Study 1. Measurements were made at baseline and during 10 minutes of breathing with either the DGB or sham device in all 25 participants. Study 2. Resting measurements were taken before and after 8 weeks of daily DGB only in a subset of 12 participants with PTSD. **Results:** Study 1. As we hypothesized, HR (interaction, p=.049) and MSNA (interaction, p=0.025) significantly decreased more with DGB compared to Sham in the severe PTSD group compared to the moderate group. Changes in BP and HRV were not different between the groups. Study 2. Resting MSNA decreased (interaction, p = .011) after 8 weeks of DGB in severe PTSD, but other variables were comparable between severe and moderate PTSD. In summary, the acute and long-term effects of DGB depends on PTSD severity, suggesting that individuals with severe PTSD could benefit more from DGB.

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Monica Vemulapalli

Honors Thesis

INTRODUCTION

Post-Traumatic Stress Disorder (PTSD)

PTSD is a debilitating chronic illness that develops following a traumatic event and is associated with significant morbidity and mortality (McFarlane 2010). The traumatic event must involve experiencing or witnessing actual or threatened death, serious injury, sexual violence or extreme exposure to an adverse event (American Psychiatric Association 2013). A growing number of military service members have been deployed to Iraq and Afghanistan in the past decade since 9/11 and are returning with high rates of post-traumatic stress disorder (PTSD). These statistics are higher among veterans who have served in wars, because they are exposed to various potential trauma. 11% to 20% of post-9/11 veterans are estimated to experience PTSD (Veteran's Affairs 2018). This disorder is also prevalent in the general population, as about 7-8% will meet the diagnostic criteria for PTSD at some point in their lives (Bedi and Arora 2007), of which about 60% are men and 50% are women (Veteran's Affairs 2018. The American Psychiatric Association classifies PTSD under trauma and stress related disorders in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), a standard book classifying all mental disorders diagnosed by mental health professionals. PTSD is characterized by four clusters of symptoms: re-experiencing (e.g. flashbacks); avoidance (e.g., avoiding

trauma-related thoughts and feelings); negative changes in cognitions and mood (e.g. inability to recall key details of the trauma) and alterations in arousal or reactivity symptoms (e.g., irritability, hypervigilance). These symptoms must be present for more than one month in order to qualify for a diagnosis of PTSD, and must not be due to medications, substance use, or a medical condition (American Psychiatric Association 2013).

PTSD Diagnostics

The Clinician Administered PTSD Scale (CAPS) for Diagnostic, Statistical Manual of Mental Disorders (DSM) and/or PTSD Checklist (PCL) is used to confirm the diagnosis of PTSD (Weathers et al. 2014). CAPS is a 17-item (CAPS-IV, DSM-IV) or-20 item (CAPS-V, DSM-V) interview administered by a clinical psychologist and is currently the gold standard for the diagnostic of PTSD (Blake et al. 1995). A score ≥45 is needed to confirm the presence of PTSD using CAPS-IV or PCL-M (Weathers et al. 2014).

The diagnosis of PTSD with CAPS is based on several different categories, which include Criteria A-F. Each criterion is made of questions that are ranked with an item score from 0 (absent) to 4 (extreme/incapacitating) to evaluate the presence and severity of each particular symptom. Criterion A identifies the stressor or traumatic event, if one exists. Criterion B assesses symptoms of intrusion such as intrusive recollections, nightmares and flashbacks, cued distress and cued physiological arousal. Criterion C assesses symptoms of avoidance such as responses to fear and distressing memories. Criterion D includes symptoms surrounding arousal and reactivity such as reckless or self-destructive behavior, negative emotional state, hypervigilance, exaggerated startle, difficulty with concentration, and disturbance in sleep. The last two criteria, Criterion E and Criterion F, establish that symptoms have lasted for at least one month and that there is functional impairment or clinically significant distress present, respectively (Weathers et

al. 2014). The diagnosis of PTSD and the determination of its severity are made by the clinical psychologist, based on the cumulative score from all the criteria.

The PTSD checklist for the military (PCL-M), a self-reported assessment for 17 symptoms of PTSD, designed specifically for the military, is another widely used and validated PTSD questionnaire ((Weathers et al. 2014). Although they differ in how they are administered (clinician for CAPS and self-reported for PCL-M), CAPS-IV and PCL-M are both highly correlated and are reliable between each other (Blanchard et al. 1996). Currently, the fifth edition of CAPS and PCL are available and will be used in future studies.

PTSD is a growing public health concern that is expected to continue to rise given prolonged and ongoing military conflicts, increased natural disasters, societal violence and sexual assaults (Committee on the Assessment of Ongoing Efforts in the Treatment of Posttraumatic Stress, Board on the Health of Select, and Institute of 2014). Available literature suggest that Veterans with the greatest exposure to combat trauma are at the highest risk for PTSD, along with predisposing factors like genetic and other environmental influences (Wolf et al. 2014)

Environmental/genetic determinants of PTSD

Environmental determinants of PTSD include combat exposure among veterans, sexual abuse, and other external factors apart from genetic factors (Xue et al. 2015). A study found that veterans' exposure to traumatic events resulted in most of the psychiatric symptoms associated with PTSD (Gilbertson et al. 2010). Additionally, sexual assault has been shown to exacerbate PTSD symptoms. Within a study looking at women sexual assault survivors, researchers found that violent and alcohol-related assaults resulted in more PTSD symptoms than less severe assaults (Peter-Hagene and Ullman 2015). Apart from events that occur in the veteran

population, other groups of people are also at risk for developing PTSD. For example, there is a 24% to 46% risk of developing PTSD in volunteers who respond after natural disasters (Thormar et al. 2016). Understanding environmental factors that affect PTSD can help inform prevention and treatment approaches to limit the progression and complication of the disorder.

Moreover, research has also shown that there might be a genetic component, possibly heritable, that may predispose to developing PTSD. Adult children of Holocaust survivors with PTSD were found to have a higher risk of PTSD compared to children of survivors without PTSD (Yehuda, Halligan, and Bierer 2001). Others revealed that genetic risk factors can account for 30-40% heritability of PTSD (Almli et al. 2014). The discovery of a gene, Tac2, whose role is to mediate fear memory consolidation could suggest that certain genes play a role in developing PTSD (Andero, Dias, and Ressler 2014). Both these studies demonstrate heredity as an important non-modifiable risk factor for PTSD. When studying the brains of twins to distinguish a PTSD brain from a non-PTSD brain, Gilbertson et al found that the twin with chronic PTSD showed smaller hippocampal volume and abnormally large cavum septum pellucidum, the space between white and gray matter of the septum pellucidum studied in mental disorders, than in their non-combat exposed twin sibling (Gilbertson et al. 2002). Furthermore, another genetic study showed that intervening life traumas and stressors increased the heritability of PTSD (Wolf et al. 2014). These findings constitute a strong support to the possible genetic basis of PTSD in some individuals and highlight how genetics might also influence the severity of PTSD symptoms.

PTSD and Cardiovascular Disease Risk

Severe PTSD is characterized by more debilitating symptoms and high levels of negative habits like cigarette smoking, alcohol abuse and illicit drug use in the veteran

population (Veterans Affairs 2017). The severity of PTSD might impact the likelihood of developing comorbid health conditions, such as major depressive disorder (Post et al. 2011), hypertension and cardiovascular diseases (Boscarino 2008). One less recognized and understudied consequence of PTSD is a significantly greater risk of developing cardiovascular disease and hypertension (HTN) (Brudey et al. 2015; Kibler 2009). Multiple large epidemiological studies have shown that PTSD is independently associated with an increased risk of hypertension and cardiovascular disease (Brudey et al. 2015; Granado et al. 2009; Kibler 2009), but the mechanisms remain largely unknown. The link between PTSD and cardiovascular disease is likely the consequence of multiple mechanisms. 1) An important characteristic in those with PTSD is heightened sympathetic nervous system (SNS) activity (Park et al. 2017), which may be a key factor in the increased risk for hypertension and cardiovascular disease (Grassi 2009). One potential mechanism underlying heightened SNS activity could be a high allostatic load, which refers to exaggerated *in vivo* physiological adjustments in response to external stimuli, such as exposure to high levels of stress and trauma in war veterans (Bedi and Arora 2007). The high allostatic load could lead to chronic elevations in SNS activity. 2) Additionally, a meta-analysis reported that individuals with PTSD have an elevated resting heart rate, about 5 beats/ minute higher than those without PTSD (Buckley and Kaloupek 2001). Other studies have also demonstrated a correlation between higher resting heart rates and early mortality from cardiovascular disease (Greenland et al. 1999). Moreover, patients with more severe PTSD had the largest differences in basal heart rates, indicating that PTSD can lead to structural and functional changes in the body and the repeated responses to stress over time may increase incidence of cardiovascular disease (Buckley et al. 2004). 3) Besides higher sympathetic activity and elevated heart rate, another potential mechanism underlying cardiovascular disease risk in

PTSD is impaired baroreflex sensitivity (BRS). Blood pressure is tightly regulated by pressure sensitive afferent nerve endings called arterial baroreceptors, located in the wall of the carotid sinus and the aortic arch. Arterial baroreceptors control blood pressure by reducing fluctuations that occur during stress and help maintain blood pressure around a set point (homeostasis) or in a certain range (allostasis) (Sleight et al. 1977). BRS is the measure of the response of baroreceptors to increases or decreases in blood pressure. These increases or decreases in blood pressure can occur due to changes in sympathetic nervous system (SNS) activity or parasympathetic nervous system nervous system activity (PNS) (Figure 1). The SNS overactivation described in PTSD could be caused by decreased arterial BRS (Park et al. 2017) which is characteristic of conditions such as chronic heart failure (Grassi et al. 1995) and hypertension (Matsukawa et al. 1991). Under normal conditions, arterial baroreceptors reduce SNS activity if blood pressure is acutely heightened by external stressors; however, in PTSD, arterial BRS is decreased. Therefore, the impaired BRS found in veterans with PTSD could be a potential mechanism underlying SNS overactivation or decreased resting parasympathetic nervous system activation in this population. It has been recently reported in a sample of 70 veterans, that this autonomic dysfunction and sympathetic overactivity in PTSD is also a function of PTSD symptom severity; veterans with severe PTSD showed greater derangements in autonomic function, highlighting the importance of the impact

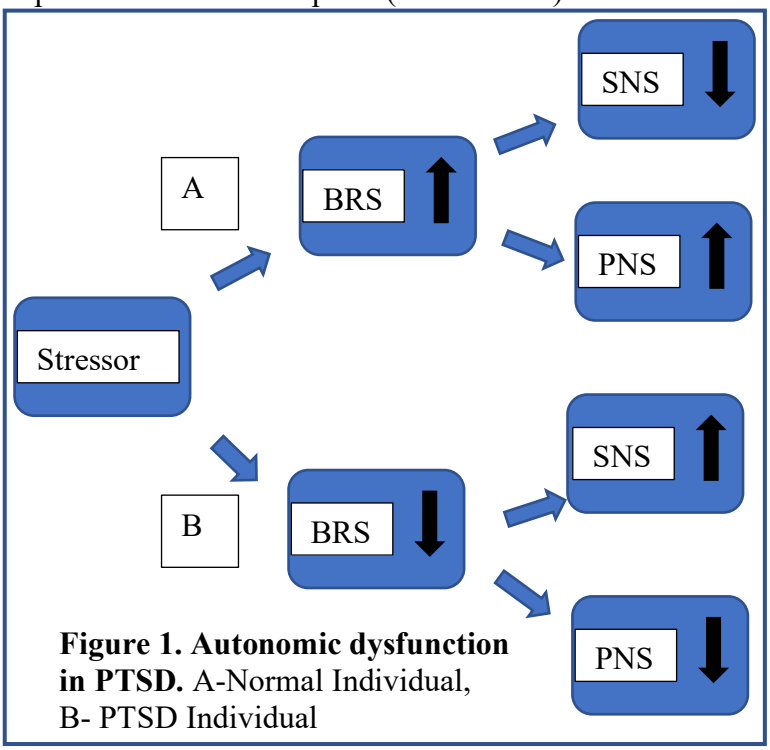


Figure 1. Autonomic dysfunction in PTSD. A-Normal Individual, B- PTSD Individual

of PTSD symptom severity on autonomic function and subsequent cardiovascular risk and morbidity (Fonkoue, Marvar, et al. 2019).

PTSD severity and mechanisms of increased CV risk in PTSD

Recent studies have shown that symptom severity of PTSD impacts risk and likelihood of developing cardiovascular disease (Howard et al. 2018). Howard et al. reported that in a retrospective study of 3846 US military personnel injured in the Iraq and Afghanistan conflicts between February 1, 2002, and February 1, 2011, the unadjusted risk of hypertension increased significantly with increased severity of PTSD symptoms. This increased risk in patients with PTSD could be due to the exaggerated autonomic dysfunction and low-grade inflammation present in patients with severe PTSD compared to those with milder symptoms (Fonkoue, Marvar, et al. 2019). Given the possible link between the physiological manifestations of PTSD and symptom severity, early intervention strategies in people suffering from a more severe form PSTD might yield significant cardiovascular benefits.

Interventional strategies to reduce cardiovascular disease risk in PTSD

While treatments targeting cardiovascular disease risk or autonomic dysfunction in PTSD are not currently the standard of care, the current mainstay for treatment options for PTSD itself include psychotherapy and medication. Many find different coping mechanisms to lessen the severity of the symptoms, such as smoking, alcohol abuse and illicit drugs use in this population that further contribute to increased cardiovascular disease risk (Veteran's Affairs 2017). Peripheral sympatholytic medications such as beta-blockers are often prescribed for PTSD symptoms; however, treatment is often complicated by adverse side effect including hypotension, orthostasis, fatigue, and erectile dysfunction. In addition, these agents cause a reflex increase in SNS activity (Grassi et al. 2000; Carella et al. 2010), and long-term beta-

blocker use is associated with development of hyperlipidemia and insulin resistance (Carella et al. 2010) and so is a particularly less desirable treatment option in young veterans already at a higher cardiovascular disease risk. Therefore, safe and effective alternative treatments targeting increased SNS activation are needed in this high-risk population. Slow breathing has been shown to reduce blood pressure in hypertension and to improve baroreflex sensitivity (Joseph et al. 2005). In addition, available literature also show that slow breathing could be helpful in people with stress-related disorders such as PTSD (Rosaura Polak et al. 2015).

Device-Guided Slow Breathing

The RESPeRATE device (InterCure, Inc), used for guided slow breathing, is currently an FDA approved device for the adjunctive treatment of hypertension (Elliott and Izzo 2006). This device monitors breathing movements and uses biofeedback along with musical tones to effortlessly guide and decrease breathing rates to 5-6 breaths/min (Fonkoue, Le, et al. 2019; Sharma, Frishman, and Gandhi 2011). This device-guided slow breathing (DGB) has recently been shown to acutely lower blood pressure and SNS activity in prehypertensive veterans with PTSD (Fonkoue et al. 2018). However, whether DGB has a greater beneficial effect on blood pressure and SNS activity in those with more severe PTSD symptoms was unknown.

The mechanisms underlying the cardiovascular beneficial effects of slow breathing can be understood by considering pulmonary physiology (Russo, Santarelli, and O'Rourke 2017). When breathing is slowed to about 6 breaths/ min, there is an increase in the tidal volume (the volume of air taken in each breath), in order to maintain the same degree of ventilation. The resulting increase in tidal volume causes an inhibition of the SNS because of the activation of pulmonary stretch receptors (Goso et al. 2001). Other have shown that slow breathing reduces sympathoexcitation and increases BRS in chronic obstructive pulmonary disease (Meles et al.

2004) and increases BRS in patients with chronic heart failure (Bernardi et al. 2002). Slow breathing also reduced blood pressure via increased BRS, that was related to reductions in sympathetic activity (Joseph et al. 2005).

Although it was previously shown that DGB reduces blood pressure and SNS activity in prehypertensive veterans with PTSD, the question of whether the **severity** of PTSD influences the **acute** and **long-term effects of DGB** on blood pressure, heart rate and SNS activity had not been explored. We hypothesized that Veterans with severe PTSD, compared to those with moderate PTSD, will show **1)** greater decreases in BP, HR, and MSNA during 10 min (acute) of DGB compared to an identically looking Sham device (Study 1), and **2)** greater reductions in resting BP, HR and MSNA (long-term) after 8 weeks of daily DGB (Study 2).

Study 1- PTSD Severity and Acute Neural and Cardiovascular Effects of Device-Guided Slow Breathing

METHODS 1

Participants

To test our hypothesis, we recruited 25 clinically diagnosed prehypertensive veterans with PTSD. The Joint National Committee (JNC) 7 (Chobanian et al. 2003), JNC 8 (James et al. 2014), and the newer American College of Cardiology/American Heart Association (ACC/AHA) guidelines (Whelton et al. 2018) all define normotension as blood pressure < 120/80 mmHg. A higher resting blood pressure of 120–139/80–89 mmHg is defined as prehypertension by the JNC 7, whereas the ACC/AHA guidelines divide this range of elevated resting blood pressure into elevated blood pressure (systolic blood pressure 120–129 mmHg), and Stage I hypertension (blood pressure 130–139/80–89 mmHg).

All participants had a diagnosis of PTSD in their medical record. Exclusion criteria included pregnancy, hypertension, diabetes, smoking, heart disease, illicit drug use, excessive alcohol use (>2 drinks/day), hyperlipidemia, autonomic dysfunction, medications known to affect SNS activity (clonidine, β-blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers), treatment with monoamine oxidase inhibitors, and any serious systemic disease. This study was approved by the Emory Institutional Review Board and the Atlanta Veterans Affairs Medical Center Research and Development Committee. All participants signed an approved informed consent document before study procedures.

Measurements

Blood Pressure. On the morning of each study visit, three seated blood pressures, separated by 5 min, were recorded using a standard blood pressure cuff placed on the arm. All blood pressure measurements were taken using the ACC/AHA guideline technique (Whelton et al. 2018) and an automated blood pressure device (Omron, HEM-907XL, Omron Healthcare, Kyoto, Japan). Following that, participants were placed in a supine position on a comfortable stretcher for instrumentation. Finger cuffs were placed on the fingers of the dominant arm for continuous beat-to-beat arterial blood pressure measurements continuously and noninvasively using digital pulse photoplethysmography (CNAP Monitor 500, CNSystems, Graz, Austria) (Fortin et al. 2006). Electrocardiogram (ECG) patch electrodes were placed on the chest for continuous heart rate recordings, as well as heart rate variability (HRV) which is the indirect measure of parasympathetic control of the heart. Next, the leg of the participant was positioned for microneurography.

Heart Rate. Electrocardiogram (ECG) patch electrodes were placed on the participant's chest in three positions (three leads ECG) for continuous heart rate recordings.

Muscle sympathetic nerve activity (MSNA). MSNA is obtained via microneurography, which is the most direct way of recording sympathetic activity in humans (Mano, Iwase, and Toma 2006). The technique requires the insertion of a tungsten microelectrode (tip diameter 5–15 μm; Bioengineering, University of Iowa, Iowa City, IA) into the peroneal nerve to directly record the activity of the sympathetic nerve innervating the blood vessels that supply the muscles of the lower leg (Wallin and Fagius 1988). Signals were amplified (total gain: 50,000–100,000), filtered (700–2000 Hz), rectified, and integrated (time constant: 0.1 s) to obtain a mean voltage display of sympathetic nerve activity (Nerve Traffic Analyzer, model 662C-4, Bioengineering,

University of Iowa). The neurogram was recorded using LabChart 7 (PowerLab 16sp, AD Instruments, Sydney, NSW, Australia) along with continuous ECG recordings using a bioamp. All MSNA recordings met previously established criteria (Delius et al. 1972a, 1972b; Mano, Iwase, and Toma 2006) and were analyzed by a single investigator who was blinded to the device used by the participant. MSNA was expressed as burst frequency (bursts/min) and burst incidence (bursts/100 heart beats).

Device-guided slow breathing (DGB). DGB was performed using the RESPeRATE (InterCure) device (DGB group) or an identical sham device (sham group) for 15 min during the testing procedure in the laboratory. The RESPeRATE device was used for DGB and an identical sham device was used for comparison. The device is composed of an elastic belt with a respiration sensor placed around the upper abdomen for biofeedback and earbuds used for auditory guidance (Sharma, Frishman, and Gandhi 2011). The device monitors respiratory rate, calculates inspiration and expiration times, and generates a personalized melody of two distinct ascending and descending tones for inhalation and exhalation. Participants effortlessly entrain their breathing pattern with the tones, and the device gradually guides the user to a prolonged expiration time and slower respiratory rate of around 5 breaths/min. The device automatically stores usage data, allowing for quantification of adherence and performance. The sham device was identical to the DGB device, using the same display, musical tones, and respiratory sensor belt. However, the sham device guided respiratory rates at a normal physiological rate of 14 breaths/min.

Respiratory rate (RR). RR was continuously monitored via a respiratory belt pressure transducer placed around the upper abdomen.

PTSD severity classification. We used the median CAPS score of 70 and/or PCL-M of 70 to separate our participants into moderate and severe groups. Participants with a CAPS score

of > 70 were placed into the severe group, while participants with a CAPS score of ≤ 70 were placed into the moderate group. Similarly, participants with a PCL-M score of > 70 were placed into the severe group, while participants with a PCL-M score of ≤ 70 were placed into the moderate group. Within each group, participants were randomized to either DGB or breathing with an identically looking Sham device.

Experimental Procedure

All participants presented for one or two screening visits before experimental procedures. During the screening visit(s), seated blood pressure measurements were taken a total of three times, separated by 5 min, and averaged to ensure the absence of hypertension and obtain baseline values. CAPS-IV was performed during the screening visit to confirm the diagnosis of PTSD. Participants were trained on the use of the breathing device during the screening visit. Female participants underwent a urine pregnancy test to rule out pregnancy. Participants were randomized to the DGB device (n = 11, 5 moderate and 6 severe) during which respiratory rate was slowed to subphysiological levels of ~5 breaths/min ,or to an identical sham device (n = 13, 8 moderate and 6 severe) during which respiratory rate was guided to 14 breaths/min using the same biofeedback mechanism.

On the day of the study, participants reported to the laboratory in the morning after abstaining from food, medications, caffeine, and alcohol for at least 12 h and exercise for at least 24 h. The study room was quiet, semi dark, and at a temperate of ~21°C. Participants were placed in a supine position on a comfortable stretcher. Finger cuffs were fitted and placed on the fingers of the dominant arm for continuous beat-to-beat arterial blood pressure measurements, and an upper arm cuff was placed for intermittent automatic calibrations with the finger cuffs. ECG patch electrodes were placed for continuous ECG recordings, and two belts with respiratory

rate sensors were placed around the upper abdomen for monitoring of continuous respiratory rates and for biofeedback as part of the breathing intervention. The leg was positioned for microneurography, and the tungsten microelectrode was inserted and manipulated to obtain a satisfactory nerve recording. After 10 min of rest, baseline blood pressure, heart rate, and MSNA were recorded continuously for 10 min. After baseline measurements, participants underwent 10 min of breathing intervention with either the DGB or sham device.

Data Analysis

blood pressure, MSNA and ECG data were exported from Labchart to WinCPRS (Absolute Aliens, Turku, Finland) for analysis. R waves were detected and marked from the continuous ECG recording. MSNA bursts were automatically detected by the program using the following criteria: 3:1 burst-to-noise ratio within a 0.5-s search window, with an average latency in burst occurrence of 1.2–1.4 s from the previous R wave. After automatic detection, the ECG and MSNA neurograms were visually inspected for accuracy of detection by a single investigator (Dr. Ida Fonkoue) without knowledge of the experimental status as DGB or sham. MSNA was expressed as burst frequency (bursts/min) and burst incidence (bursts/100 heart beats).

Heart Rate. After ECG data were exported from Labchart to WinCPRS (Absolute Aliens, Turku, Finland) for analysis, R waves were detected and marked using WinCPRS.

MSNA. MSNA data were exported from Labchart to WinCPRS (Absolute Aliens, Turku, Finland) for analysis. MSNA bursts were automatically detected by the program using the following criteria: 3:1 burst-to-noise ratio within a 0.5-s search window, with an average latency in burst occurrence of 1.2–1.4 s from the previous R wave. MSNA neurograms were visually marked for bursts by a single investigator without knowledge of PTSD or severity status.

HRV. Using R wave intervals, we obtained HRV, the indirect measure of parasympathetic activity (Malik et al. 1996). HRV is the fluctuation in time intervals between heartbeats. Most common measures include standard deviation between normal-to-normal R-R intervals (SDNN). SDNN reflects the variance in a normal EKG reading and depends on the length of the recording period (Malik et al. 1996). We used SDNN as a measure of HRV because it is an appropriate variable when used for short durations such as 10 minutes of breathing or 10 minutes of baseline. The root mean square of consecutive differences between normal heartbeats (RMSSD) is calculated by the successive time difference between heartbeats then squared and averaged before the square root can be taken. The RMSSD displays heart rate beat-to-beat variance and is considered to be the primary time domain measure to represent vagally mediated changes (Shaffer, McCraty, and Zerr 2014). HRV was quantified in the time domain as SDNN and RMSSD. These HRV measures have been validated as reflecting cardiac parasympathetic nervous system activity (Malik et al. 1996; Scheinin et al. 1999).

Statistical analysis

All baseline values (Table 1) were compared between moderate and severe PTSD groups using an independent T-test. Blood pressure, heart rate, MSNA, and HRV responses to 10 min of breathing were analyzed using a three-way repeated measure analysis of variance (ANOVA) to analyze change after breathing across devices and groups. The repeated measures ANOVA was the preferred statistical method in order to determine the effects of device (variable 1) between the severity groups (variable 2) over time (variable 3). Most repeated measures ANOVAs are used to assess the effect of the independent variable(s) over a time period in addition to

when there is more than one variable being assessed. Advantages to using an ANOVA include greater statistical power due to controlling for differences between participants across groups, lower sample sizes, and time-related effects (Park, Cho, and Ki 2009).

In this study, the change from baseline to last 2 min of breathing (time) was the within factor, while severity (severe vs moderate group) and device (DGB vs Sham group) were the two between factors. The ANOVA aimed to determine if there were statistically significant differences in the variables between severe and moderate groups in response to breathing with DGB or Sham. Our results were also confirmed using a linear mixed model, in order to account for missing points in the data set, as well as taking into account the starting point of the variable of interest for both groups. This analysis is also able to model nonlinear, individual characteristics in a longitudinal trial like our study 2 (Krueger and Tian 2004).

RESULTS 1

Baseline characteristics of the participants in Study 1 can be found in Table 1. Age, body mass index (BMI), blood pressure, heart rate and respiratory rate were comparable between the severe and moderate groups. As expected, CAPS score, which was the distinguishing factor between the two severity groups, was higher in the Severe group. Resting MSNA was found to be significantly higher ($p = .011$) in participants with severe PTSD compared to moderate PTSD (Table 2). There was no difference in HRV measures at rest between the Moderate and Severe PTSD groups.

Variables	Moderate PTSD (n=13)	Severe PTSD (n=12)	p value
Age (years)	36.5 ± 2.3	36.2 ± 2.6	0.933
BMI (kg m^2)	29.8 ± 1.8	28.7 ± 2.2	0.687
Sex (M/F)	11/2	11/1	0.531
Race (B/W)	9/4	11/1	0.186
CAPS score	54 ± 0.8	84 ± 0.9	<0.001
SAP (mmHg)	128.3 ± 5.0	121.8 ± 5.5	0.403
DAP (mmHg)	81.4 ± 3.3	78.5 ± 2.9	0.516
MAP (mmHg)	96.6 ± 2.8	92.9 ± 3.5	0.425
heart rate (beats/min)	69 ± 2.4	74.4 ± 3.4	0.223
RR (breaths/min)	17.8 ± 0.5	17.5 ± 0.7	0.698

Table 1. Baseline values for Study 1**.** Values are mean ± SE; BMI, body mass index; CAPS, clinician-administered PTSD scale, SAP, systolic arterial blood pressure, DAP, diastolic arterial blood pressure, MAP, mean arterial blood pressure; Heart Rate; RR, respiratory rate.

Variables	Moderate PTSD (n=13)	Severe PTSD (n=12)	p value
MSNA (bursts/min)	**12.5 ± 1.6**	**24.8 ± 4.0**	**0.011**
SDNN (ms)	**78 ± 14.3**	**87.3 ± 13.0**	**0.753**
RMSSD (ms)	**51.4 ± 6.9**	**44.7 ± 9.0**	**0.564**
HF (ms^2)	**625 ± 164**	**689 ± 228**	**0.828**

Table 2. Resting Autonomic Function. Values are mean ± SE; MSNA, muscle sympathetic nerve activity; SDNN, standard deviation of normal to normal R-R intervals; RMSSD, root mean square of the successive differences; and HF, high frequency power.

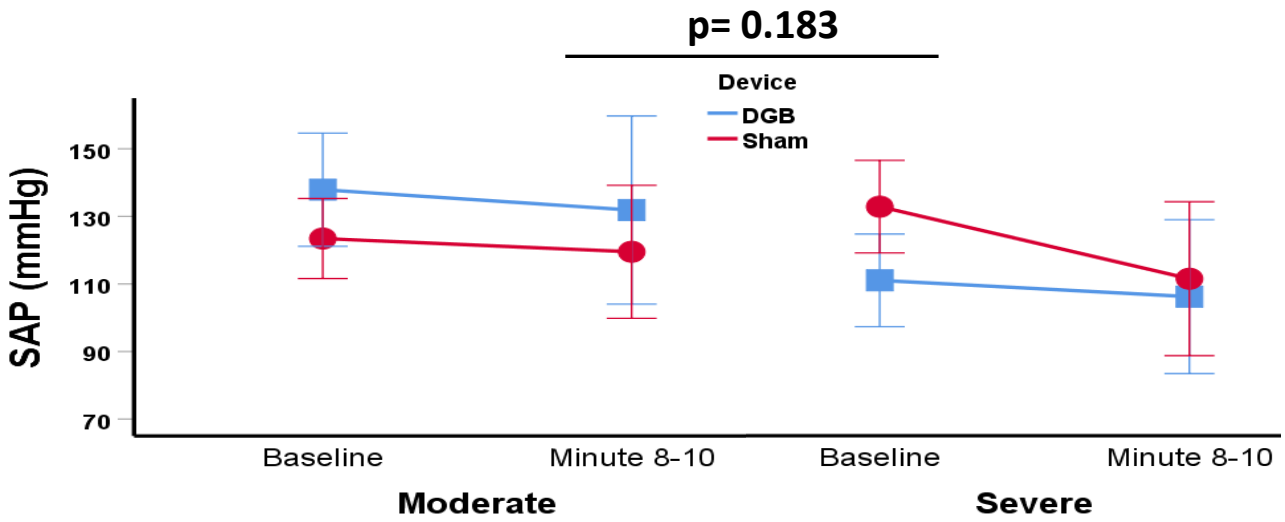
Blood Pressure: In response to the breathing intervention, the change in systolic blood pressure was comparable (time*group*device, p = 0.183) between the severe and the moderate group during DGB versus Sham (Figure 2). Likewise, the change in diastolic blood pressure (time*group*device, p = 0.276) was comparable between severe and moderate during DGB versus Sham (Figure 3). Mean arterial pressure (time*group*device, p = 0.438) was also comparable between severe and moderate during DGB versus Sham (Figure 4).

Heart Rate: There was a significant difference (time*group*device, p = 0.049*) in heart rate changes from baseline to minute 8-10 with DGB compared to Sham between the severe and moderate PTSD groups (Figure 5). Specifically, heart rate decreased significantly (time*device, p = 0.006**) in the severe PTSD group with DGB versus Sham but not in the moderate group (time*device, p = 0.233).

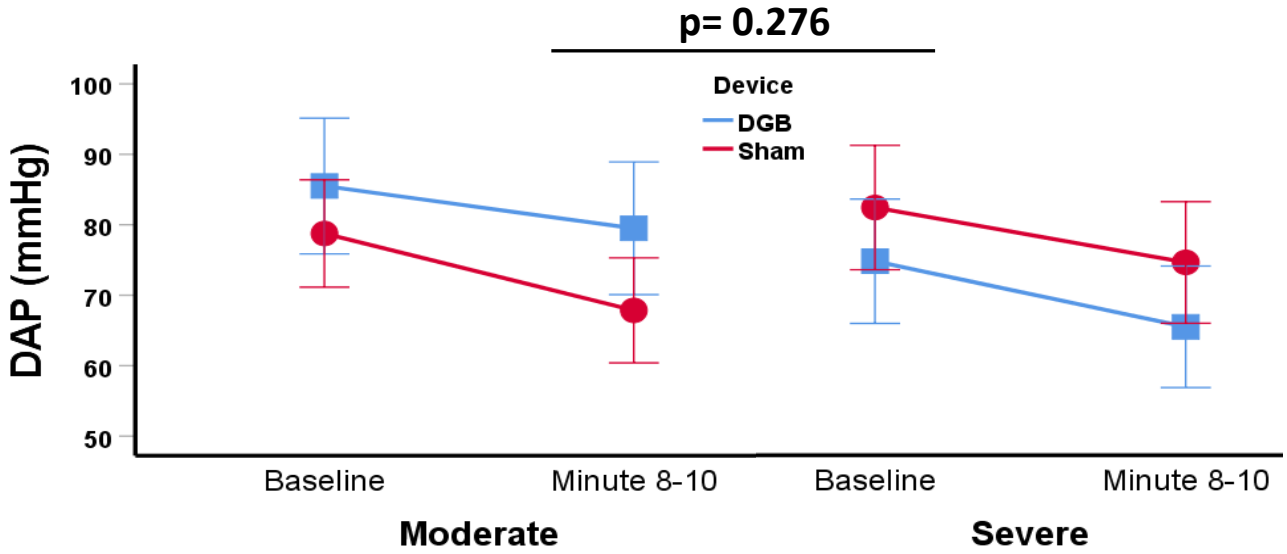
MSNA and HRV: There was a significant difference (time*group*device, p = 0.025*) in MSNA changes from baseline to minute 8-10 with DGB when compared to Sham between the Severe and Moderate PTSD groups (Figure 6). Specifically, MSNA decreased significantly (time*device p = 0.021**) in the Severe PTSD group with DGB versus Sham but not in the moderate group (time*device p = 0.271).

HRV was estimated with two-time domains variables: RMSSD and SDNN. Unlike MSNA, SDNN was comparable (time*group*device, p = 0.197) between the severe and moderate group using DGB versus Sham (Figure 7). RMSSD was also comparable

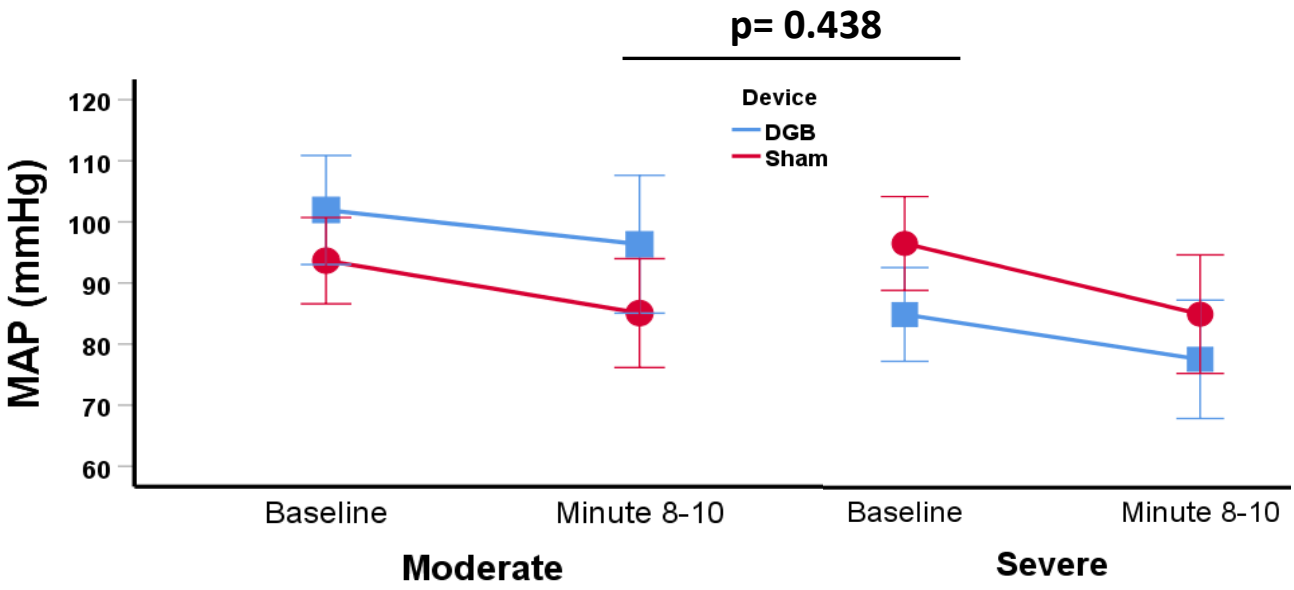
time*group*device, p = 0.433) between the severe and moderate group using DGB versus Sham (Figure 8).



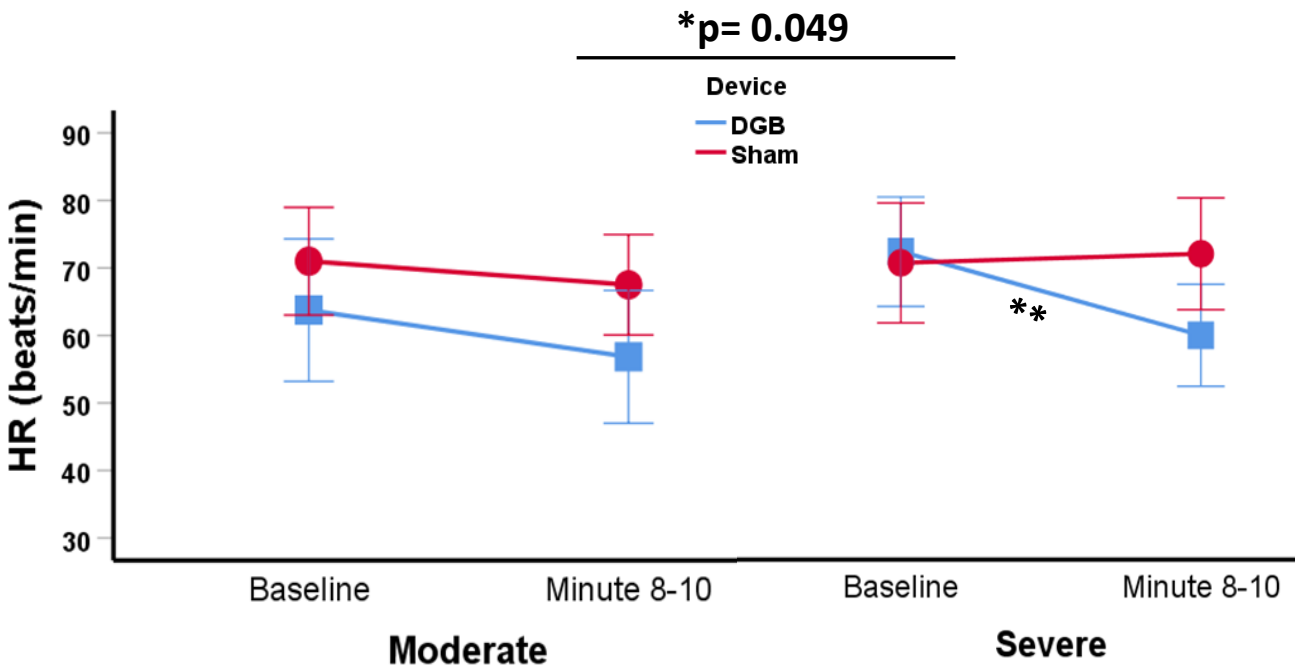
Figures 2. This figure represents systolic arterial pressure (SAP) at baseline before DGB and during minutes 8-10 of breathing with DGB and Sham in Moderate and Severe PTSD. Changes in SAP were comparable (time*group*device, p = 0.183) between severe and moderate groups across both the DGB and Sham device. Error bars represent the standard error of the mean.



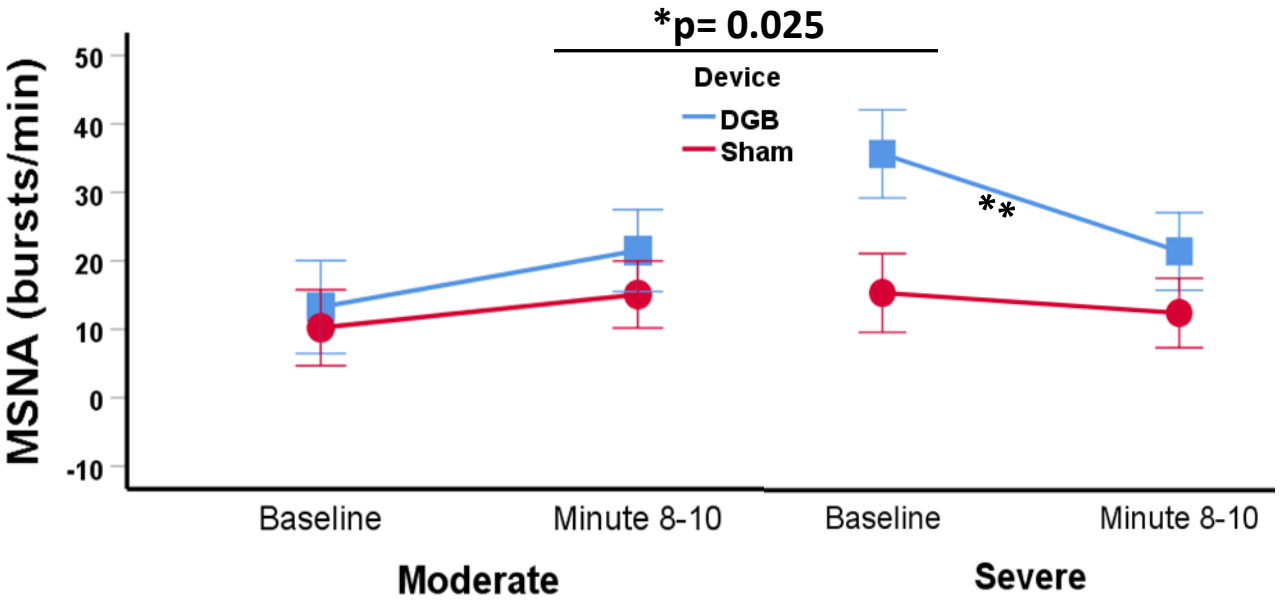
Figures 3. This figure represents diastolic arterial pressure (DAP) at baseline before DGB and during minutes 8-10 of breathing with DGB and Sham in Moderate and Severe PTSD. Changes in DAP were comparable ((time*group*device, p = 0.276) between severe and moderate groups across both the DGB and Sham device. Error bars represent the standard error of the mean.



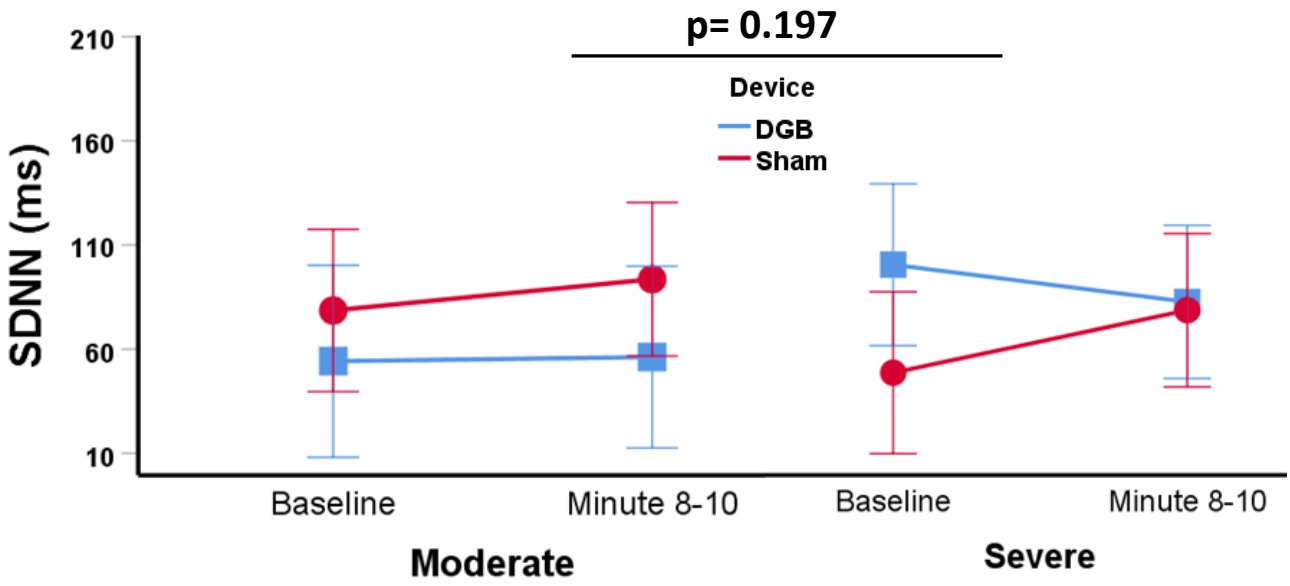
Figures 4. This figure represents mean arterial pressure (MAP) at baseline before DGB and during minutes 8-10 of breathing with DGB and Sham in moderate and severe PTSD. Changes in MAP were comparable (time*group*device, p = 0.438) between severe and moderate groups across both the DGB and Sham device. Error bars represent the standard error of the mean.



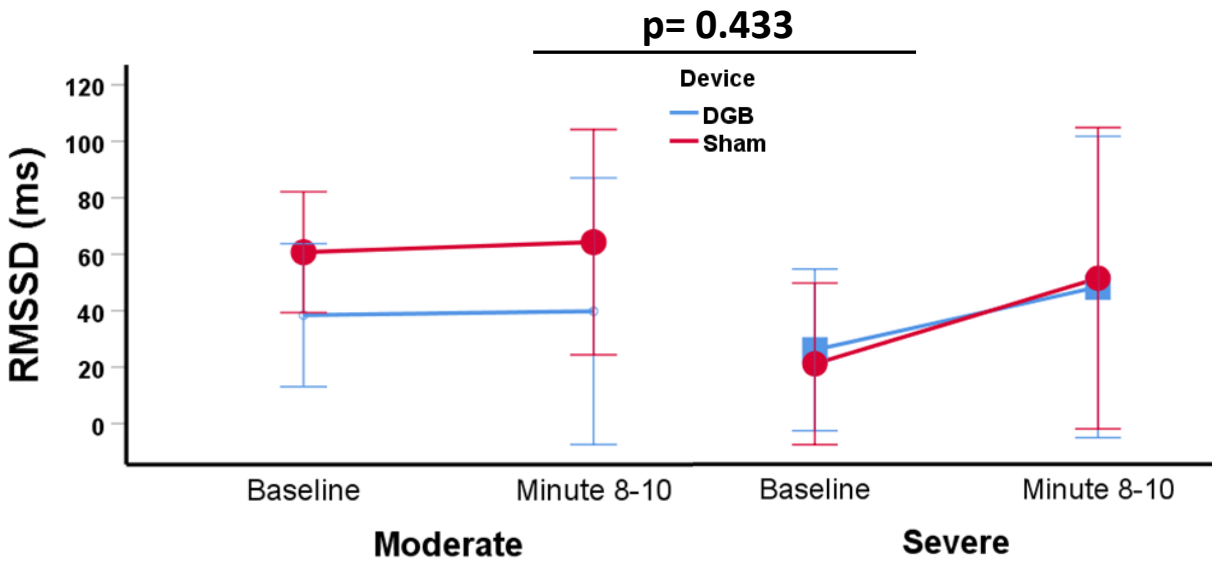
Figures 5. This figure represents heart rate (beats/min) at baseline before DGB and during minutes 8-10 of breathing with DGB and Sham in moderate and severe PTSD. heart rate decreased (time*group*device, p = 0.049*) after DGB only in the Severe group (baseline vs min8-10, p=0.006**), but not in the Moderate group (baseline vs min8-10, p=0.233). Error bars represent the standard error of the mean



Figures 6. This figure represents muscle sympathetic nerve activity (bursts/min) at baseline before DGB and during minutes 8-10 of breathing with DGB and Sham in moderate and severe PTSD. MSNA decreased (time*group*device, p = 0.025*) after DGB only in the Severe group (baseline vs min8-10, p=0.021**), but not in the Moderate group (baseline vs min8-10, p=0.271). Error bars represent the standard error of the mean.



Figures 7. This figure represents the standard deviation of normal to normal R-R intervals (SDNN) at baseline before DGB and Sham during minutes 8-10 of breathing with DGB in moderate and severe PTSD. The changes in SDNN were comparable (p = 0.197) between severe and moderate groups across both the DGB and Sham device. Error bars represent the standard error of the mean.



Figures 8. This figure represents the root mean square of the successive differences (RMSSD) at baseline before DGB and during minutes 8-10 of breathing with DGB and Sham in moderate and severe PTSD. Changes in RMSSD were comparable ($p = 0.433$) between severe and moderate groups across both the DGB and Sham device. Error bars represent the standard error of the mean.

Study 2- PTSD Severity and Long-Term Neural and Cardiovascular Effects of Device-Guided Breathing

METHODS 2

Participants:

12 participants from Study 1 continued into Study 2, of which 6 had severe PTSD and 6 had moderate PTSD. All 12 participants used DGB daily for 8 weeks.

Experimental Protocol (Figure 9):

A subset of participants who previously underwent the protocol described in Study 1 continued to use DGB daily over a period of 8 weeks. They were given the device to take home and instructed to use it daily for 15 minutes. After 8 weeks, the participants reported back to the laboratory for another testing visit similar to the study 1 visit. Briefly, participants reported to the laboratory in the morning after abstaining from food, medications, caffeine, and alcohol for at least 12 h and exercise for at least 24 h. The study was conducted under the same room conditions and participants were instrumented for beat-to-beat arterial blood pressure, continuous ECG recordings and breathing rate measurements in a supine position. The microneurography procedure was done, and after 10 min of rest, baseline blood pressure, heart rate, and MSNA were recorded continuously for 10 min.

Figure 9. Timeline for measurements recorded for Study 2. Baseline represents the resting values before the 8-week daily breathing period, while End-of-study represents the resting values after the 8-week daily breathing period.

Data Analysis

We analyzed and compared data from Baseline (pre-8 weeks) and End-of-study (post-8 weeks) to examine the effect of 8 weeks of DGB on physiologic measures (see Figure 8 for a schematic of the timeline). Same data analysis methods were used for blood pressure, heart rate, MSNA, and HRV variables as described for Study 1 (refer to pages 20-21).

Statistical Analysis:

All baseline values (Table 3) were analyzed using an independent T-test. blood pressure, heart rate, MSNA, and HRV variables were analyzed using a two-way repeated measure analysis of variance (ANOVA) to analyze change after breathing for 8 weeks between moderate and severe PTSD participants. Time was a within factor, while severity group (severe or moderate) was a between factors. The ANOVA aimed to determine if there were statistically significant differences in the variables from baseline to end-of study between severe and moderate group.

RESULTS 2

In study 2, we compared the change in resting blood pressure, heart rate, MSNA and HRV taken before and after 8 weeks of DGB in Severe versus Moderate PTSD groups. In

particular, we examined the long-term effect of DGB in both severe and moderate PTSD participants in order to determine if there was a greater improvement in physiologic measures with DGB in severe PTSD compared to moderate PTSD. Baseline characteristics of the participants in Study 2 can be found in Table 3. All baseline characteristics were comparable between the severe and moderate groups, except for CAPS score which was the distinguishing factor between the two groups.

Blood Pressure: The change in resting systolic blood pressure (p= 0.391, Figure 10) and resting diastolic blood pressure (p=0.383, Figure 11) before and after 8 weeks of using DGB were comparable between the severe and moderate groups. The change in resting Mean arterial pressure (MAP) was also comparable between the severe and moderate group (p=0.361, Figure 12) before and after 8 weeks of DGB.

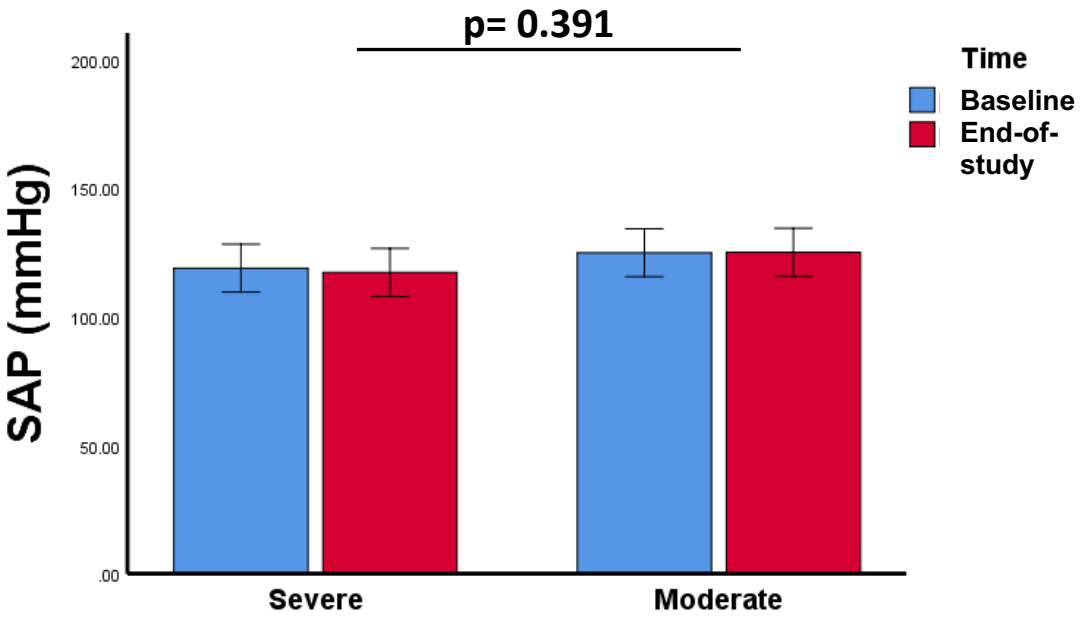
Heart Rate: Resting heart rate tended to decrease (p=0.07, Figure 13) more in the severe PTSD versus the moderate PTSD group after 8 weeks of DGB.

MSNA and HRV: Baseline values for resting MSNA showed that there was already a significant difference between resting MSNA for severe PTSD and moderate PTSD (Table 2). MSNA decreased significantly more (p = 0.011*, Figure 14) in the severe group versus the moderate group after 8 weeks of using DGB. Change in the resting HRV measures of SDNN (p=0.269, Figure 15) and RMSSD (p=0.173, Figure 16) before and after 8 weeks of DGB were comparable in the severe group compared to the moderate group.

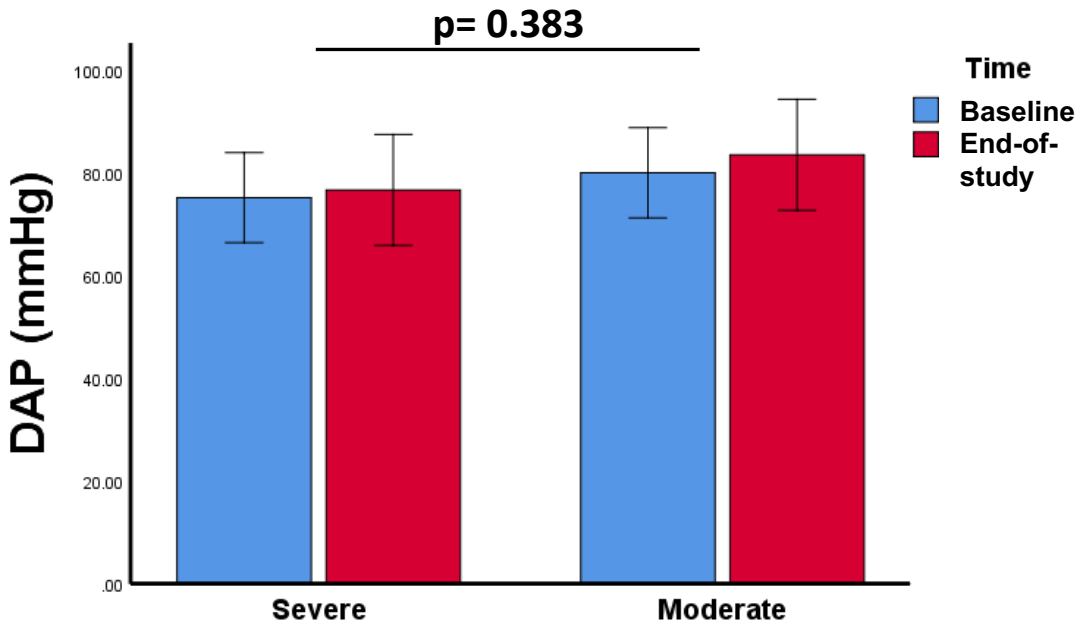
These results show that long-term use of DGB has a greater impact on resting sympathetic activity in individuals with severe PTSD.

Variables	Moderate PTSD (n=6)	Severe PTSD (n=6)	p value
Age (years)	35.7 ± 4.3	36.8 ± 1.9	0.408
BMI (kg m^2)	30.4 ± 3.0	31 ± 2.3	0.449
Sex (M/F)	5/1	5/1	0.5
Race (B/W)	4/2	2/4	0.182
CAPS score	57.3 ± 6.5	86.2 ± 2.8	<0.001
SAP (mmHg)	125 ± 3.7	119 ± 5.4	0.261
DAP (mmHg)	80 ± 5.2	75.1 ± 3.3	0.244
MAP (mmHg)	95 ± 4.4	89.8 ± 3.9	0.243
heart rate (beats/min)	66.5 ± 7.1	74.7 ± 3.9	0.161
RR (breaths/min)	16.8 ± 0.8	19.3 ± 1.3	0.114

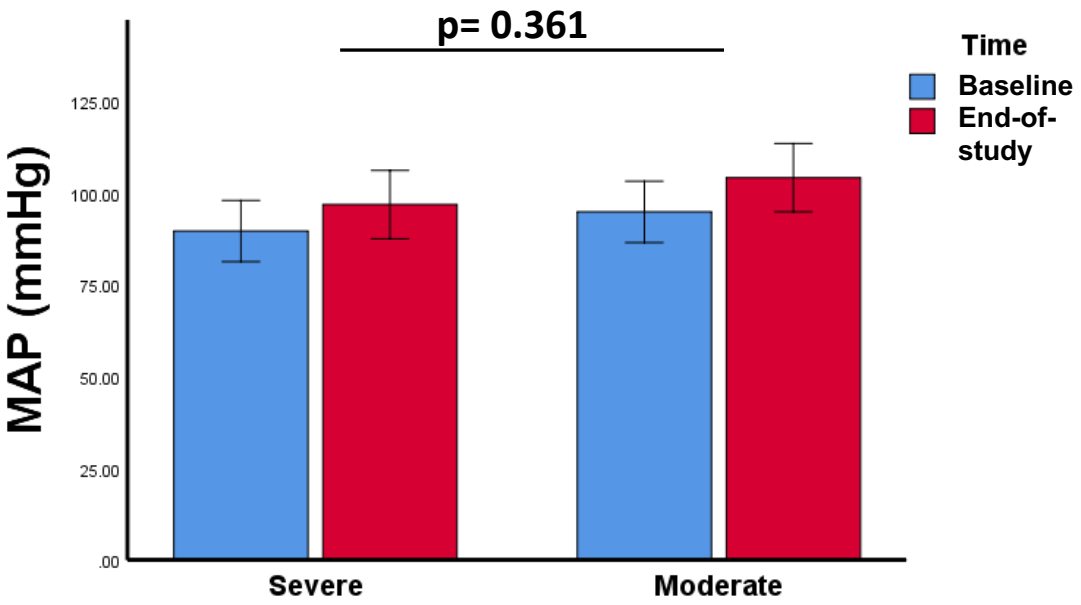
Table 3. The table above shows the baseline values for Study 2 for 12 prehypertensive veterans who were able to finish the study. Values are mean ± SE; BMI, body mass index; CAPS, clinician-administered PTSD scale, SAP, systolic arterial blood pressure, DAP, diastolic arterial blood pressure, MAP, mean arterial blood pressure; heart rate; RR, respiratory rate.



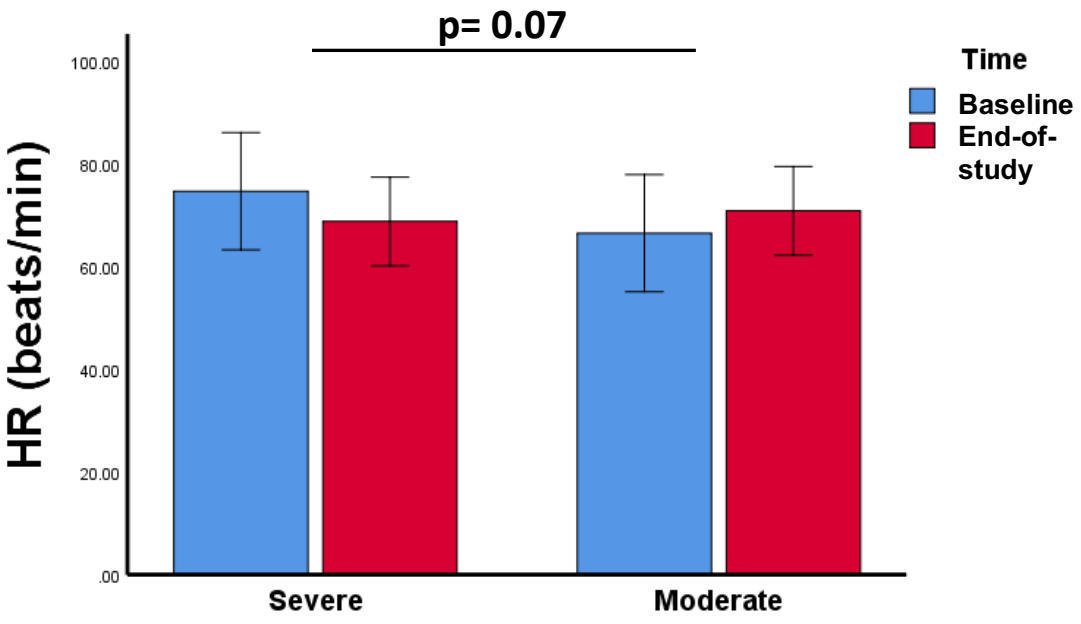
Figures 10. This figure represents the systolic arterial pressure (SAP) in moderate and severe PTSD at Baseline recorded before 8 weeks of breathing, and End-of-study recorded after 8 weeks of breathing. There was no statistical difference (p = 0.391) in DAP between severe and moderate groups when comparing Baseline to End-of-study.



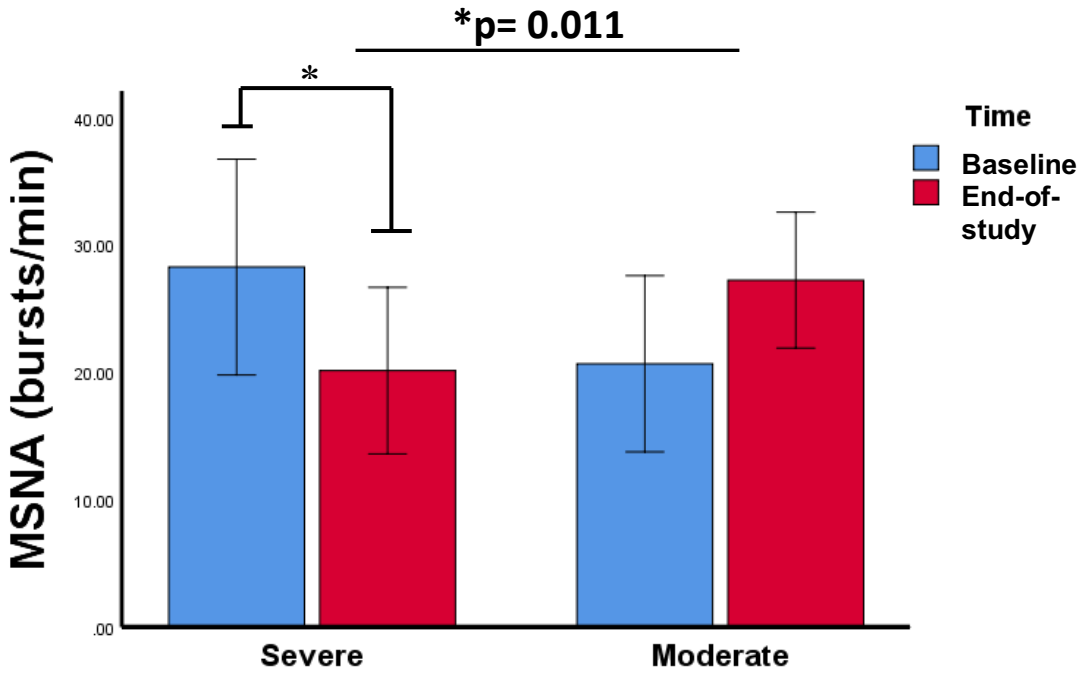
Figures 11. This figure represents the diastolic arterial pressure (DAP) in moderate and severe PTSD at Baseline recorded before 8 weeks of breathing, and at End-of-study recorded after 8 weeks breathing. There was no statistical difference (p = 0.383) in DAP between severe and moderate groups when comparing Baseline to End-of-study.



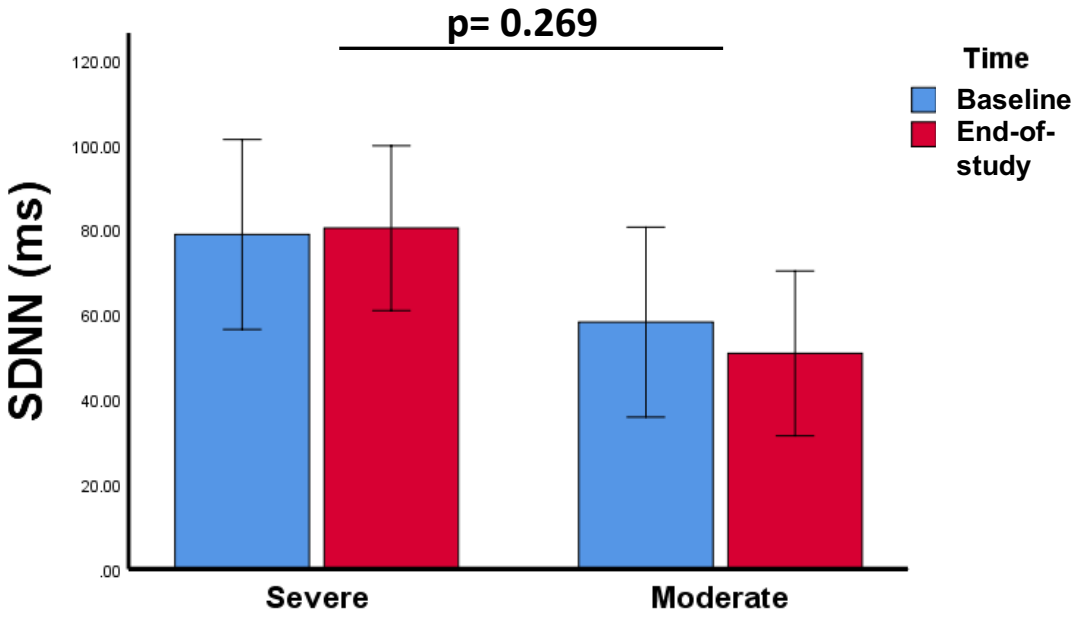
Figures 12. This figure represents the mean arterial pressure (MAP) in moderate and severe PTSD at Baseline recorded before 8 weeks of breathing, and End-of-study recorded after 8 weeks of breathing. There were no statistical differences (p = 0.361) in MAP between severe and moderate groups when comparing Baseline to End-of-study.



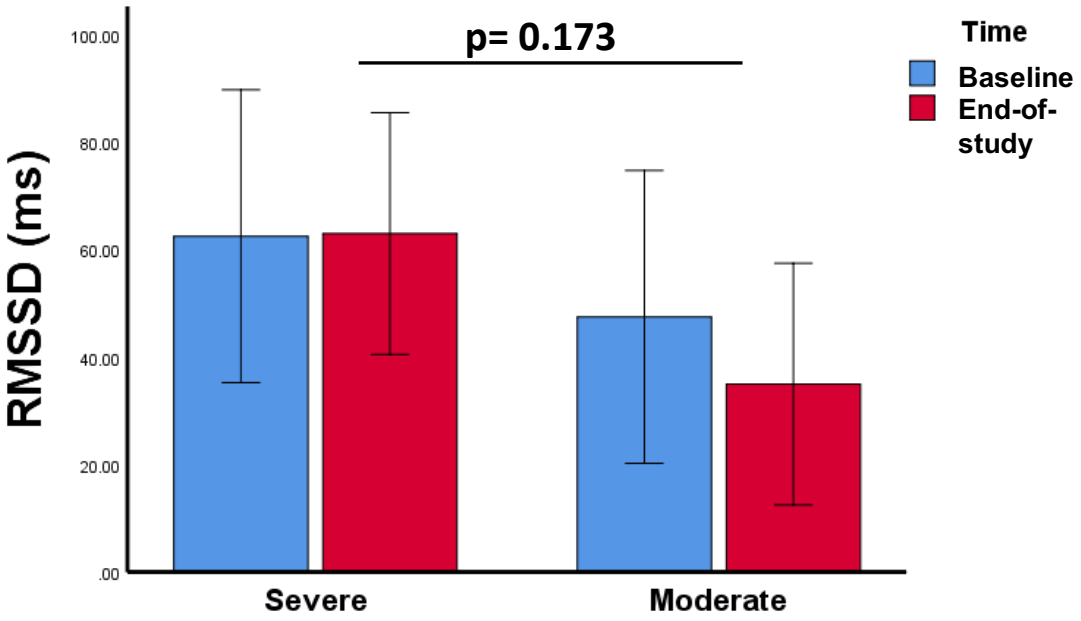
Figures 13. This figure represents the heart rate in moderate and severe PTSD at Baseline recorded before 8 weeks of breathing, and End-of-study recorded after 8 weeks of breathing. Resting heart rate tended to (**p = 0.07**) in heart rate between severe and moderate groups when comparing Baseline to End-of-study.



Figures 14. This figure represents the muscle sympathetic nerve activity (MSNA) in moderate and severe PTSD at Baseline recorded before 8 weeks breathing, and End-of-study, recorded after 8 weeks breathing. Resting MSNA significantly decreased (**p = 0.011)** after using DGB long-term in the severe group compared to the moderate group.



Figures 15. This figure represents the standard deviation of normal to normal R-R intervals (SDNN) in moderate and severe PTSD at Baseline recorded before 8 weeks breathing, and End-of-study, recorded after 8 weeks breathing. There were no statistical differences (p = 0.269) in SDNN between severe and moderate groups when comparing Baseline to End-of-study.



Figures 16. This figure represents the root mean square of the successive differences (RMSSD) in moderate and severe PTSD at Baseline recorded before 8 weeks breathing, and End-of-study, recorded after 8 weeks breathing. There were no statistical differences ($p = 0.173$) in RMSSD between severe and moderate groups when comparing Baseline to End-of-study.

DISCUSSION

These two studies, focused on relatively healthy young veterans with no hypertension or other cardiovascular disease, are the first studies to consider the severity of PTSD when evaluating the neural and cardiovascular effects of slow breathing in this population. The goal of study 1 was to examine if a one-time 10 min session of DGB compared to a sham device acutely decreases blood pressure, heart rate, SNS and increases parasympathetic activity more in individuals with severe PTSD than those with moderate PTSD. The goal of study 2 was to further examine if after using the DGB at home for 15 min each day for 8 weeks, veterans with severe PTSD have greater reductions in resting blood pressure, heart rate, SNS and greater increases in parasympathetic activity compared to those with moderate PTSD. The major findings of these studies are 1) DGB acutely lowers heart rate and MSNA more in veterans with severe PTSD compared to those with moderate PTSD; and 2) After 8 weeks of daily use, DGB decreased resting sympathetic activity more in veterans with severe PTSD than those with moderate PTSD. Together, these findings suggest that DGB could be an effective short and long-term intervention to mitigate the cardiovascular consequences of severe PTSD, specifically the sympathetic overexcitation that is associated with future hypertension and cardiovascular risk.

Prior studies showed that resting blood pressure and heart rate were higher in those with PTSD, while resting HRV was lower, demonstrating SNS overactivity and reduced PNS control of the heart (Buckley and Kaloupek 2001; Bedi and Arora 2007). Most of the baseline values in our study, except for CAPS which differentiated the groups, were comparable between severe and moderate PTSD groups, except for higher resting MSNA levels in severe PTSD compared to those with moderate PTSD. Our underlying rationale for taking into account the severity of PTSD is because the severe population has more debilitating symptoms associated with an even

higher risk for cardiovascular disease. Previous studies have shown that PTSD is associated with increased cardiovascular disease risk, and resting SNS overactivity can contribute to increased risk for cardiovascular disease(Grassi 2009; Grassi et al. 1995). Additionally, a recent study found that increased PTSD symptom severity was associated with increased resting heart rate and larger impairment of baroreflex sensitivity when exposed to mental stress (Fonkoue, Marvar, et al. 2019). These studies along with our baseline MSNA findings demonstrate that PTSD symptom severity is an important factor that impacts resting autonomic function in those with PTSD. This tells us that MSNA may be a key target to reducing future risk for cardiovascular disease in PTSD, and treating severity of PTSD symptoms may also have implications for future risk for cardiovascular disease and hypertension (Brudey et al. 2015; Granado et al. 2009; Kibler 2009). We studied whether device guided slow breathing might be a possible treatment option that the PTSD population could benefit from to reduce this cardiovascular disease and hypertension risk.

Although some studies of slow breathing resulted in inconclusive results (Joseph et al. 2005; Anderson, McNeely, and Windham 2009; Mahtani, Nunan, and Heneghan 2012), slow breathing in other studies has been shown to have beneficial effects. Previous studies have shown that DGB results in a decrease in SNS activity in people with chronic heart failure (Bernardi et al. 2002). Slow breathing has also been shown to decrease blood pressure and has been used as an adjunct treatment for hypertension (Elliott and Izzo 2006). In another study of hypertensive patients, slow breathing has been shown to be effective by increasing impaired baroreflex sensitivity and decreasing blood pressure (Joseph et al. 2005). DGB was also shown to acutely reduce blood pressure and MSNA in prehypertensive veterans with PTSD (Fonkoue et

al. 2018). However, this study did not look at how the severity of PTSD impacted the responses to DGB as we did in this study.

In our study, we investigated the effects of DGB in a group of veterans with severe PTSD compared to moderate PTSD to see whether the results were more profound in those with severe PTSD. We found that 10 minutes of DGB compared to sham breathing acutely decreased MSNA and heart rate more in veterans with severe PTSD compared to those with moderate PTSD. However, the effects of DGB on blood pressure and HRV were comparable between the severe and moderate PTSD groups. One explanation of the observed decrease in sympathetic activity, without change in parasympathetic activity can be the greater control of blood pressure by the sympathetic nervous system compared to the parasympathetic nervous system (Harada et al. 2014). The possible mechanism behind the beneficial effects of slow breathing on sympathetic activity is that the slow breathing rates lead to increased tidal volumes in order to maintain minute ventilation, which then activates the cardiopulmonary stretch receptors, leading to a reflex reduction in sympathetic activity. Slow breathing may also impact the vagal afferent nerve signals regulating sympathetic flow (Alabdulgader 2012). Our findings of DGB reducing heart rate and MSNA more in veterans with severe compared to moderate PTSD show that slow breathing may be more effective at improving autonomic function in those with more severe PTSD symptoms

Given these promising acute results, we additionally examined the long-term effects of daily slow breathing on resting cardiovascular and autonomic variables across the severe and moderate groups. We showed that resting blood pressure was comparable between the severe and moderate groups before and after the 8-week usage of DGB. However, while there were no differences in hemodynamic responses between groups, our results showed that baseline MSNA

decreased more after using DGB for 8 weeks in those with severe PTSD compared to moderate PTSD. Apart from MSNA, no changes in resting heart rate or HRV were found in both severe and moderate PTSD. The decrease in baseline MSNA after 8 weeks is interesting as in Study 1, we found that baseline MSNA values were higher in those with severe PTSD. This suggests that individuals with severe PTSD, who have greater sympathetic overactivity, may be more responsive to DGB than those with moderate PTSD. Although there was a reduction in resting MSNA in severe PTSD after 8 weeks of DGB, we did not observe a reduction in blood pressure. It could be that the degree of reduction in sympathetic activity was not enough to translate into a change in blood pressure, or other factors such as other vasoconstrictors or lack of vasodilators may have contributed to the overall blood pressure response (Stanfield et al., 2009).

In summary, the major findings of these studies are 1) DGB acutely lowers HR and MSNA more in veterans with severe PTSD compared to those with moderate PTSD; and 2) After 8 weeks of daily use, DGB decreased resting sympathetic activity more in veterans with severe PTSD than those with moderate PTSD. Together, these findings suggest that DGB could be an effective short and long-term intervention to mitigate the cardiovascular consequences of severe PTSD, specifically the sympathetic overexcitation that is associated with future hypertension and cardiovascular risk.

Limitations

We understand there are several limitations to this study which could have possibly affected the results and treatment outcomes. First, the adherence to the device during the 8-week daily breathing period of the study was not strictly monitored except for the use of a self-reported tracking sheet. We did not have a way to confirm whether and how often the participants adhered to the daily 15-minute breathing protocol. We might predict that some participants may have

been more compliant than others. In addition, we did not control the time of day that the participants used their DGB device at home.

Second, the sample sizes for Study 1 and Study 2 were small, limiting the accuracy and generalizability of the results. In addition, there are factors beyond our control such as a participant withdrawal of a study for various reasons or not being able to continue the long-term study.

Third, another limitation is that we were not aware of the tidal volume or the depth of each breath during slow breathing. This is important because the amount of tidal volume can explain part of why slow breathing is effective. Slow breathing has been shown to benefit those with heart failure because tidal volume was shown to increase more when breathing rate slowed (Anderson, McNeely, and Windham 2009). More specifically, end tidal carbon dioxide (etCO2) another way to monitor physiologically the degree of ventilation in a session was not done in this study. Using a device such as a Transcutaneous Monitor for p02 and pC02 (Radiometer, Copenhagen, Denmark) to measure transcutaneous P_{O2} and P_{CO2} might allow analysis of these values to determine the relationship between pulmonary, autonomic and cardiovascular variables.

Future Directions

One future direction might be to use a technological interface where the researchers can verify at-home usage of DGB and monitor important variables such as the respiratory rate and tidal volume. This would allow controlling for changes in tidal volume influencing the autonomic or cardiovascular variables. In addition, having a greater sample size with a more representative population can lead to stronger analysis and evidence to show the greater effects of DGB in a higher severity PTSD population.

Another possible future direction includes taking a more holistic approach to treating severity of PTSD symptoms. This includes personalizing the treatments for each individual based on physiologic parameters. For example, we can lower the respiratory rate (RR) to a set percentage rate lower than the participant's normal RR instead of decreasing everyone's RR to one standard rate. This will allow the experimental group to breathe at a rate that is a standard amount lower than their normal RR.

Conclusion

To our knowledge, this is the first study to demonstrate that DGB acutely lowers heart rate and MSNA to a greater extent in veterans with severe PTSD compared to moderate PTSD. In addition, when examining long-term effects of DGB, there was a significantly greater decrease in baseline MSNA after 8 weeks of slow breathing in the severe group compared to the moderate group. We would like to emphasize that this is a pilot study examining how the acute and long-term responses to DGB depend on PTSD severity, which can help us determine potential new treatments for improving autonomic function and decreasing future risk of cardiovascular disease and hypertension.

APPENDIX

1) **CAPS-IV QUESTIONNAIRE**
2) **PCL-M QUESTIONNAIRE**

National Center for PTSD

CLINICIAN-ADMINISTERED PTSD SCALE FOR DSM-IV

Name: _____ ID # : _____

Interviewer: _____ Date:_____

Study: _____

Dudley D. Blake, Frank W. Weathers, Linda M. Nagy,
Danny G. Kaloupek, Dennis S. Charney, & Terence M. Keane

National Center for Posttraumatic Stress Disorder

Behavioral Science Division -- Boston VA Medical Center
Neurosciences Division -- West Haven VA Medical Center

Revised July 1998

Criterion A. The person has been exposed to a traumatic event in which both of the following were present:
(1) the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
(2) the person's response involved intense fear, helplessness, or horror. Note: In children, this may be expressed instead by disorganized or agitated behavior

I'm going to be asking you about some difficult or stressful things that sometimes happen to people. Some examples of this are being in some type of serious accident; being in a fire, a hurricane, or an earthquake; being mugged or beaten up or attacked with a weapon; or being forced to have sex when you didn't want to. I'll start by asking you to look over a list of experiences like this and check any that apply to you. Then, if any of them do apply to you, I'll ask you to briefly describe what happened and how you felt at the time.

Some of these experiences may be hard to remember or may bring back uncomfortable memories or feelings. People often find that talking about them can be helpful, but it's up to you to decide how much you want to tell me. As we go along, if you find yourself becoming upset, let me know and we can slow down and talk about it. Also, if you have any questions or you don't understand something, please let me know. Do you have any questions before we start?

ADMINISTER CHECKLIST, THEN REVIEW AND INQUIRE UP TO THREE EVENTS. IF MORE THAN THREE EVENTS ENDORSED, DETERMINE WHICH THREE EVENTS TO INQUIRE (E.G., FIRST, WORST, AND MOST RECENT EVENTS; THREE WORST EVENTS; TRAUMA OF INTEREST PLUS TWO OTHER WORST EVENTS, ETC.)

IF NO EVENTS ENDORSED ON CHECKLIST: *(Has there ever been a time when your life was in danger or you were seriously injured or harmed?)*

IF NO: *(What about a time when you were threatened with death or serious injury, even if you weren't actually injured or harmed?)*

IF NO: *(What about witnessing something like this happen to someone else or finding out that it happened to someone close to you?)*

IF NO: *(What would you say are some of the most stressful experiences you have had over your life?)*

EVENT #1

What happened? *(How old were you? Who else was involved? How many times did this happen? Life threat? Serious injury?)*	*Describe (e.g., event type, victim, perpetrator, age, frequency):*
How did you respond emotionally? *(Were you very anxious or frightened? Horrified? Helpless? How so? Were you stunned or in shock so that you didn't feel anything at all? What was that like? What did other people notice about your emotional response? What about after the event -- how did you respond emotionally?)*	*A. (1)* *Life threat? NO YES [self ___ other ___]* *Serious injury? NO YES [self ___ other ___]* *Threat to physical integrity? NO YES [self ___ other ___]* *A. (2)* *Intense fear/help/horror? NO YES [during ___ after ___]* *Criterion A met? NO PROBABLE YES*

EVENT #2

What happened? *(How old were you? Who else was involved? How many times did this happen? Life threat? Serious injury?)*	*Describe (e.g., event type, victim, perpetrator, age, frequency):*
How did you respond emotionally? *(Were you very anxious or frightened? Horrified? Helpless? How so? Were you stunned or in shock so that you didn't feel anything at all? What was that like? What did other people notice about your emotional response? What about after the event -- how did you respond emotionally?)*	*A. (1)* *Life threat? NO YES [self ___ other ___]* *Serious injury? NO YES [self ___ other ___]* *Threat to physical integrity? NO YES [self ___ other ___]* *A. (2)* *Intense fear/help/horror? NO YES [during ___ after ___]* *Criterion A met? NO PROBABLE YES*

EVENT #3

What happened? *(How old were you? Who else was involved? How many times did this happen? Life threat? Serious injury?)*	*Describe (e.g., event type, victim, perpetrator, age, frequency):*
How did you respond emotionally? *(Were you very anxious or frightened? Horrified? Helpless? How so? Were you stunned or in shock so that you didn't feel anything at all? What was that like? What did other people notice about your emotional response? What about after the event -- how did you respond emotionally?)*	*A. (1)* *Life threat? NO YES [self ___ other ___]* *Serious injury? NO YES [self ___ other ___]* *Threat to physical integrity? NO YES [self ___ other ___]* *A. (2)* *Intense fear/help/horror? NO YES [during ___ after ___]* *Criterion A met? NO PROBABLE YES*

For the rest of the interview, I want you to keep (EVENTS) in mind as I ask you some questions about how they may have affected you.

I'm going to ask you about twenty-five questions altogether. Most of them have two parts. First, I'll ask if you've ever had a particular problem, and if so, about how often in the past month *(week)*. Then I'll ask you how much distress or discomfort that problem may have caused you.

Criterion B. The traumatic event is persistently reexperienced in one (or more) of the following ways:

1. (B-1) recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions. **Note:** In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.

Frequency	***Intensity***	***Past week***
Have you ever had unwanted memories of (EVENT)? What were they like? *(What did you remember?)* [IF NOT CLEAR:] *(Did they ever occur while you were awake, or only in dreams?)* [EXCLUDE IF MEMORIES OCCURRED ONLY DURING DREAMS] **How often have you had these memories in the past month *(week)*?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much distress or discomfort did these memories cause you? Were you able to put them out of your mind and think about something else?** *(How hard did you have to try?)* **How much did they interfere with your life?** 0 None 1 Mild, minimal distress or disruption of activities 2 Moderate, distress clearly present but still manageable, some disruption of activities 3 Severe, considerable distress, difficulty dismissing memories, marked disruption of activities 4 Extreme, incapacitating distress, cannot dismiss memories, unable to continue activities ***QV (specify)*** _____	***F*** _____ ***I*** _____ ***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N*** ***Lifetime*** ***F*** _____ ***I*** _____ ***Sx: Y N***

2. (B-2) recurrent distressing dreams of the event. **Note:** In children, there may be frightening dreams without recognizable content.

Frequency	***Intensity***	***Past week***
Have you ever had unpleasant dreams about (EVENT)? Describe a typical dream. *(What happens in them?)* **How often have you had these dreams in the past month *(week)*?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much distress or discomfort did these dreams cause you? Did they ever wake you up?** [IF YES:] *(What happened when you woke up? How long did it take you to get back to sleep?)* [LISTEN FOR REPORT OF ANXIOUS AROUSAL, YELLING, ACTING OUT THE NIGHTMARE] *(Did your dreams ever affect anyone else? How so?)* 0 None 1 Mild, minimal distress, may not have awoken 2 Moderate, awoke in distress but readily returned to sleep 3 Severe, considerable distress, difficulty returning to sleep 4 Extreme, incapacitating distress, did not return to sleep ***QV (specify)*** _____	***F*** _____ ***I*** _____ ***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N*** ***Lifetime*** ***F*** _____ ***I*** _____ ***Sx: Y N***

3. (B-3) acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated). **Note:** In young children, trauma-specific reenactment may occur.

Frequency	***Intensity***	***Past week***
Have you ever suddenly acted or felt as if (EVENT) were happening again? *(Have you ever had flashbacks about [EVENT]?)* [IF NOT CLEAR:] *(Did this ever occur while you were awake, or only in dreams?)* [EXCLUDE IF OCCURRED ONLY DURING DREAMS] **Tell me more about that. How often has that happened in the past month *(week)*?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much did it seem as if (EVENT) were happening again?** *(Were you confused about where you actually were or what you were doing at the time?)* **How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No reliving 1 Mild, somewhat more realistic than just thinking about event 2 Moderate, definite but transient dissociative quality, still very aware of surroundings, daydreaming quality 3 Severe, strongly dissociative (reports images, sounds, or smells) but retained some awareness of surroundings 4 Extreme, complete dissociation (flashback), no awareness of surroundings, may be unresponsive, possible amnesia for the episode (blackout) ***QV (specify)*** _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

4. (B-4) intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

Frequency	***Intensity***	***Past week***
Have you ever gotten emotionally upset when something reminded you of (EVENT)? *(Has anything ever triggered bad feelings related to [EVENT]?)* **What kinds of reminders made you upset? How often in the past month *(week)*?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much distress or discomfort did (REMINDERS) cause you? How long did it last? How much did it interfere with your life?** 0 None 1 Mild, minimal distress or disruption of activities 2 Moderate, distress clearly present but still manageable, some disruption of activities 3 Severe, considerable distress, marked disruption of activities 4 Extreme, incapacitating distress, unable to continue activities ***QV (specify)*** _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

5. (B-5) physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

Frequency	***Intensity***	***Past week***
Have you ever had any physical reactions when something reminded you of (EVENT)? *(Did your body ever react in some way when something reminded you of [EVENT]?)* **Can you give me some examples?** *(Did your heart race or did your breathing change? What about sweating or feeling really tense or shaky?)* **What kinds of reminders triggered these reactions? How often in the past month *(week)*?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong were (PHYSICAL REACTIONS)? How long did they last?** *(Did they last even after you were out of the situation?)* 0 No physical reactivity 1 Mild, minimal reactivity 2 Moderate, physical reactivity clearly present, may be sustained if exposure continues 3 Severe, marked physical reactivity, sustained throughout exposure 4 Extreme, dramatic physical reactivity, sustained arousal even after exposure has ended ***QV (specify)*** _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ *Sx: Y N* ***Lifetime*** *F* _____ *I* _____ *Sx: Y N*

Criterion C. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:

6. (C-1) efforts to avoid thoughts, feelings, or conversations associated with the trauma

Frequency	***Intensity***	***Past week***
Have you ever tried to avoid thoughts or feelings about (EVENT)? *(What kinds of thoughts or feelings did you try to avoid?)* **What about trying to avoid talking with other people about it?** *(Why is that?)* **How often in the past month *(week)*?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much effort did you make to avoid (THOUGHTS/FEELINGS/CONVERSATIONS)?** *(What kinds of things did you do? What about drinking or using medication or street drugs?)* [CONSIDER ALL ATTEMPTS AT AVOIDANCE, INCLUDING DISTRACTION, SUPPRESSION, AND USE OF ALCOHOL/DRUGS] **How much did that interfere with your life?** 0 None 1 Mild, minimal effort, little or no disruption of activities 2 Moderate, some effort, avoidance definitely present, some disruption of activities 3 Severe, considerable effort, marked avoidance, marked disruption of activities, or involvement in certain activities as avoidant strategy 4 Extreme, drastic attempts at avoidance, unable to continue activities, or excessive involvement in certain activities as avoidant strategy ***QV (specify)*** _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ *Sx: Y N* ***Lifetime*** *F* _____ *I* _____ *Sx: Y N*

7. (C-2) efforts to avoid activities, places, or people that arouse recollections of the trauma

Frequency	***Intensity***	***Past week***
Have you ever tried to avoid certain activities, places, or people that reminded you of (EVENT)? *(What kinds of things did you avoid? Why is that?)* **How often in the past month *(week)*?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much effort did you make to avoid (ACTIVITIES/PLACES/PEOPLE)?** *(What did you do instead?)* **How much did that interfere with your life?** 0 None 1 Mild, minimal effort, little or no disruption of activities 2 Moderate, some effort, avoidance definitely present, some disruption of activities 3 Severe, considerable effort, marked avoidance, marked disruption of activities or involvement in certain activities as avoidant strategy 4 Extreme, drastic attempts at avoidance, unable to continue activities, or excessive involvement in certain activities as avoidant strategy ***QV (specify)*** _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

8. (C-3) inability to recall an important aspect of the trauma

Frequency	***Intensity***	***Past week***
Have you had difficulty remembering some important parts of (EVENT)? Tell me more about that. *(Do you feel you should be able to remember these things? Why do you think you can't?)* **In the past month *(week)*, how much of the important parts of (EVENT) have you had difficulty remembering?** *(What parts do you still remember?)* 0 None, clear memory 1 Few aspects not remembered (less than 10%) 2 Some aspects not remembered (approx 20-30%) 3 Many aspects not remembered (approx 50-60%) 4 Most or all aspects not remembered (more than 80%) ***Description/Examples***	**How much difficulty did you have recalling important parts of (EVENT)?** *(Were you able to recall more if you tried?)* 0 None 1 Mild, minimal difficulty 2 Moderate, some difficulty, could recall with effort 3 Severe, considerable difficulty, even with effort 4 Extreme, completely unable to recall important aspects of event ***QV (specify)*** _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

9. (C-4) markedly diminished interest or participation in significant activities

Frequency	***Intensity***	***Past week***
Have you been less interested in activities that you used to enjoy? *(What kinds of things have you lost interest in? Are there some things you don't do at all anymore? Why is that?)* [EXCLUDE IF NO OPPORTUNITY, IF PHYSICALLY UNABLE, OR IF DEVELOPMENTALLY APPROPRIATE CHANGE IN PREFERRED ACTIVITIES] **In the past month *(week)*, how many activities have you been less interested in?** *(What kinds of things do you still enjoy doing?)* **When did you first start to feel that way?** *(After the [EVENT]?)* 0 None 1 Few activities (less than 10%) 2 Some activities (approx 20-30%) 3 Many activities (approx 50-60%) 4 Most or all activities (more than 80%) ***Description/Examples***	**How strong was your loss of interest?** *(Would you enjoy [ACTIVITIES] once you got started?)* 0 No loss of interest 1 Mild, slight loss of interest, probably would enjoy after starting activities 2 Moderate, definite loss of interest, but still has some enjoyment of activities 3 Severe, marked loss of interest in activities 4 Extreme, complete loss of interest, no longer participates in any activities ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***F*** _____ ***I*** _____ ***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N*** ***Lifetime*** ***F*** _____ ***I*** _____ ***Sx: Y N***

10. (C-5) feeling of detachment or estrangement from others

Frequency	***Intensity***	***Past week***
Have you felt distant or cut off from other people? What was that like? How much of the time in the past month *(week)* have you felt that way? When did you first start to feel that way? *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How strong were your feelings of being distant or cut off from others?** *(Who do you feel closest to? How many people do you feel comfortable talking with about personal things?)* 0 No feelings of detachment or estrangement 1 Mild, may feel "out of synch" with others 2 Moderate, feelings of detachment clearly present, but still feels some interpersonal connection 3 Severe, marked feelings of detachment or estrangement from most people, may feel close to only one or two people 4 Extreme, feels completely detached or estranged from others, not close with anyone ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***F*** _____ ***I*** _____ ***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N*** ***Lifetime*** ***F*** _____ ***I*** _____ ***Sx: Y N***

11. (C-6) restricted range of affect (e.g., unable to have loving feelings)

Frequency	***Intensity***	***Past week***
Have there been times when you felt emotionally numb or had trouble experiencing feelings like love or happiness? What was that like? *(What feelings did you have trouble experiencing?)* **How much of the time in the past month *(week)* have you felt that way? When did you first start having trouble experiencing (EMOTIONS)?** *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How much trouble did you have experiencing (EMOTIONS)?** *(What kinds of feelings were you still able to experience?)* [INCLUDE OBSERVATIONS OF RANGE OF AFFECT DURING INTERVIEW] 0 No reduction of emotional experience 1 Mild, slight reduction of emotional experience 2 Moderate, definite reduction of emotional experience, but still able to experience most emotions 3 Severe, marked reduction of experience of at least two primary emotions (e.g., love, happiness) 4 Extreme, completely lacking emotional experience ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

12. (C-7) sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)

Frequency	***Intensity***	***Past week***
Have there been times when you felt there is no need to plan for the future, that somehow your future will be cut short? Why is that? [RULE OUT REALISTIC RISKS SUCH AS LIFE-THREATENING MEDICAL CONDITIONS] **How much of the time in the past month *(week)* have you felt that way? When did you first start to feel that way?** *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How strong was this feeling that your future will be cut short?** *(How long do you think you will live? How convinced are you that you will die prematurely?)* 0 No sense of a foreshortened future 1 Mild, slight sense of a foreshortened future 2 Moderate, sense of a foreshortened future definitely present, but no specific prediction about longevity 3 Severe, marked sense of a foreshortened future, may make specific prediction about longevity 4 Extreme, overwhelming sense of a foreshortened future, completely convinced of premature death ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

Criterion D. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:

13. (D-1) difficulty falling or staying asleep

Frequency	***Intensity***	***Past week***
Have you had any problems falling or staying asleep? How often in the past month *(week)*? When did you first start having problems sleeping? *(After the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day Sleep onset problems? Y N Mid-sleep awakening? Y N Early a.m. awakening? Y N Total # hrs sleep/night _____ Desired # hrs sleep/night _____	**How much of a problem did you have with your sleep?** *(How long did it take you to fall asleep? How often did you wake up in the night? Did you often wake up earlier than you wanted to? How many total hours did you sleep each night?)* 0 No sleep problems 1 Mild, slightly longer latency, or minimal difficulty staying asleep (up to 30 minutes loss of sleep) 2 Moderate, definite sleep disturbance, clearly longer latency, or clear difficulty staying asleep (30-90 minutes loss of sleep) 3 Severe, much longer latency, or marked difficulty staying asleep (90 min to 3 hrs loss of sleep) 4 Extreme, very long latency, or profound difficulty staying asleep (> 3 hrs loss of sleep) ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F _____ I _____ ***Past month*** F _____ I _____ Sx: Y N ***Lifetime*** F _____ I _____ Sx: Y N

14. (D-2) irritability or outbursts of anger

Frequency	***Intensity***	***Past week***
Have there been times when you felt especially irritable or showed strong feelings of anger? Can you give me some examples? How often in the past month *(week)*? When did you first start feeling that way? *(After the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong was your anger?** *(How did you show it?)* [IF REPORTS SUPPRESSION:] *(How hard was it for you to keep from showing your anger?)* **How long did it take you to calm down? Did your anger cause you any problems?** 0 No irritability or anger 1 Mild, minimal irritability, may raise voice when angry 2 Moderate, definite irritability or attempts to suppress anger, but can recover quickly 3 Severe, marked irritability or marked attempts to suppress anger, may become verbally or physically aggressive when angry 4 Extreme, pervasive anger or drastic attempts to suppress anger, may have episodes of physical violence ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F _____ I _____ ***Past month*** F _____ I _____ Sx: Y N ***Lifetime*** F _____ I _____ Sx: Y N

15. (D-3) difficulty concentrating

Frequency	***Intensity***	***Past week***
Have you found it difficult to concentrate on what you were doing or on things going on around you? What was that like? How much of the time in the past month *(week)*? When did you first start having trouble concentrating? *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How difficult was it for you to concentrate?** [INCLUDE OBSERVATIONS OF CONCENTRATION AND ATTENTION IN INTERVIEW] **How much did that interfere with your life?** 0 No difficulty with concentration 1 Mild, only slight effort needed to concentrate, little or no disruption of activities 2 Moderate, definite loss of concentration but could concentrate with effort, some disruption of activities 3 Severe, marked loss of concentration even with effort, marked disruption of activities 4 Extreme, complete inability to concentrate, unable to engage in activities ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

16. (D-4) hypervigilance

Frequency	***Intensity***	***Past week***
Have you been especially alert or watchful, even when there was no real need to be? *(Have you felt as if you were constantly on guard?)* **Why is that? How much of the time in the past month *(week)*? When did you first start acting that way?** *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How hard did you try to be watchful of things going on around you?** [INCLUDE OBSERVATIONS OF HYPERVIGILANCE IN INTERVIEW] **Did your (HYPERVIGILANCE) cause you any problems?** 0 No hypervigilance 1 Mild, minimal hypervigilance, slight heightening of awareness 2 Moderate, hypervigilance clearly present, watchful in public (e.g., chooses safe place to sit in a restaurant or movie theater) 3 Severe, marked hypervigilance, very alert, scans environment for danger, exaggerated concern for safety of self/family/home 4 Extreme, excessive hypervigilance, efforts to ensure safety consume significant time and energy and may involve extensive safety/checking behaviors, marked watchfulness during interview ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

17. (D-5) exaggerated startle response

Frequency	***Intensity***	***Past week***
Have you had any strong startle reactions? When did that happen? *(What kinds of things made you startle?)* **How often in the past month (week)? When did you first have these reactions?** *(After the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong were these startle reactions?** *(How strong were they compared to how most people would respond?)* **How long did they last?** 0 No startle reaction 1 Mild, minimal reaction 2 Moderate, definite startle reaction, feels "jumpy" 3 Severe, marked startle reaction, sustained arousal following initial reaction 4 Extreme, excessive startle reaction, overt coping behavior (e.g., combat veteran who "hits the dirt") ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

Criterion E. Duration of the disturbance (symptoms in Criteria B, C, and D) is more than 1 month.

18. onset of symptoms

[IF NOT ALREADY CLEAR:] **When did you first start having (PTSD SYMPTOMS) you've told me about?** *(How long after the trauma did they start? More than six months?)*	_____ ***total # months delay in onset*** ***With delayed onset (≥ 6 months)? NO YES***

19. duration of symptoms

		Current	***Lifetime***
[CURRENT] **How long have these (PTSD SYMPTOMS) lasted altogether?** [LIFETIME] **How long did these (PTSD SYMPTOMS) last altogether?**	*Duration more than 1 month?* *Total # months duration* *Acute (< 3 months) or chronic (≥ 3 months)?*	***NO YES*** _____ ***acute chronic***	***NO YES*** _____ ***acute chronic***

Criterion F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

20. subjective distress

		Past week
[CURRENT] **Overall, how much have you been bothered by these (PTSD SYMPTOMS) you've told me about?** [CONSIDER DISTRESS REPORTED ON EARLIER ITEMS] [LIFETIME] **Overall, how much were you bothered by these (PTSD SYMPTOMS) you've told me about?** [CONSIDER DISTRESS REPORTED ON EARLIER ITEMS]	0 None 1 Mild, minimal distress 2 Moderate, distress clearly present but still manageable 3 Severe, considerable distress 4 Extreme, incapacitating distress	_____ ***Past month*** _____ ***Lifetime***

21. impairment in social functioning

[CURRENT] **Have these (PTSD SYMPTOMS) affected your relationships with other people? How so?** [CONSIDER IMPAIRMENT IN SOCIAL FUNCTIONING REPORTED ON EARLIER ITEMS] [LIFETIME] **Did these (PTSD SYMPTOMS) affect your social life? How so?** [CONSIDER IMPAIRMENT IN SOCIAL FUNCTIONING REPORTED ON EARLIER ITEMS]	0 No adverse impact 1 Mild impact, minimal impairment in social functioning 2 Moderate impact, definite impairment, but many aspects of social functioning still intact 3 Severe impact, marked impairment, few aspects of social functioning still intact 4 Extreme impact, little or no social functioning	***Past week*** _____ ***Past month*** _____ ***Lifetime*** _____

22. impairment in occupational or other important area of functioning

[CURRENT – IF NOT ALREADY CLEAR] **Are you working now?** IF YES: **Have these (PTSD SYMPTOMS) affected your work or your ability to work? How so?** [CONSIDER REPORTED WORK HISTORY, INCLUDING NUMBER AND DURATION OF JOBS, AS WELL AS THE QUALITY OF WORK RELATIONSHIPS. IF PREMORBID FUNCTIONING IS UNCLEAR, INQUIRE ABOUT WORK EXPERIENCES BEFORE THE TRAUMA. FOR CHILD/ADOLESCENT TRAUMAS, ASSESS PRE-TRAUMA SCHOOL PERFORMANCE AND POSSIBLE PRESENCE OF BEHAVIOR PROBLEMS] IF NO: **Have these (PTSD SYMPTOMS) affected any other important part of your life?** [AS APPROPRIATE, SUGGEST EXAMPLES SUCH AS PARENTING, HOUSEWORK, SCHOOLWORK, VOLUNTEER WORK, ETC.] **How so?** [LIFETIME – IF NOT ALREADY CLEAR] **Were you working then?** IF YES: **Did these (PTSD SYMPTOMS) affect your work or your ability to work? How so?** [CONSIDER REPORTED WORK HISTORY, INCLUDING NUMBER AND DURATION OF JOBS, AS WELL AS THE QUALITY OF WORK RELATIONSHIPS. IF PREMORBID FUNCTIONING IS UNCLEAR, INQUIRE ABOUT WORK EXPERIENCES BEFORE THE TRAUMA. FOR CHILD/ADOLESCENT TRAUMAS, ASSESS PRE-TRAUMA SCHOOL PERFORMANCE AND POSSIBLE PRESENCE OF BEHAVIOR PROBLEMS] IF NO: **Did these (PTSD SYMPTOMS) affect any other important part of your life?** [AS APPROPRIATE, SUGGEST EXAMPLES SUCH AS PARENTING, HOUSEWORK,	0 No adverse impact 1 Mild impact, minimal impairment in occupational/other important functioning 2 Moderate impact, definite impairment, but many aspects of occupational/other important functioning still intact 3 Severe impact, marked impairment, few aspects of occupational/other important functioning still intact 4 Extreme impact, little or no occupational/other important functioning	***Past week*** _____ ***Past month*** _____ ***Lifetime*** _____

SCHOOLWORK, VOLUNTEER WORK, ETC.] **How so?**		

Global Ratings

23. global validity

ESTIMATE THE OVERALL VALIDITY OF RESPONSES. CONSIDER FACTORS SUCH AS COMPLIANCE WITH THE INTERVIEW, MENTAL STATUS (E.G., PROBLEMS WITH CONCENTRATION, COMPREHENSION OF ITEMS, DISSOCIATION), AND EVIDENCE OF EFFORTS TO EXAGGERATE OR MINIMIZE SYMPTOMS.	0 Excellent, no reason to suspect invalid responses 1 Good, factors present that may adversely affect validity 2 Fair, factors present that definitely reduce validity 3 Poor, substantially reduced validity 4 Invalid responses, severely impaired mental status or possible deliberate "faking bad" or "faking good"

24. global severity

ESTIMATE THE OVERALL SEVERITY OF PTSD SYMPTOMS. CONSIDER DEGREE OF SUBJECTIVE DISTRESS, DEGREE OF FUNCTIONAL IMPAIRMENT, OBSERVATIONS OF BEHAVIORS IN INTERVIEW, AND JUDGMENT REGARDING REPORTING STYLE.	0 No clinically significant symptoms, no distress and no functional impairment 1 Mild, minimal distress or functional impairment 2 Moderate, definite distress or functional impairment but functions satisfactorily with effort 3 Severe, considerable distress or functional impairment, limited functioning even with effort 4 Extreme, marked distress or marked impairment in two or more major areas of functioning	***Past week*** _____ ***Past month*** _____ ***Lifetime*** _____

25. global improvement

RATE TOTAL OVERALL IMPROVEMENT PRESENT SINCE THE INITIAL RATING. IF NO EARLIER RATING, ASK HOW THE SYMPTOMS ENDORSED HAVE CHANGED OVER THE PAST 6 MONTHS. RATE THE DEGREE OF CHANGE, WHETHER OR NOT, IN YOUR JUDGMENT, IT IS DUE TO TREATMENT.	0 Asymptomatic 1 Considerable improvement 2 Moderate improvement 3 Slight improvement 4 No improvement 5 Insufficient information

Current PTSD Symptoms

Criterion A met (traumatic event)?	*NO*	*YES*
_____ *# Criterion B sx (≥ 1)?*	*NO*	*YES*
_____ *# Criterion C sx (≥ 3)?*	*NO*	*YES*
_____ *# Criterion D sx (≥ 2)?*	*NO*	*YES*
Criterion E met (duration ≥ 1 month)?	*NO*	*YES*
Criterion F met (distress/impairment)?	*NO*	*YES*

_____

CURRENT PTSD (Criteria A-F met)?	*NO*	*YES*

IF CURRENT PTSD CRITERIA ARE MET, SKIP TO ASSOCIATED FEATURES.

IF CURRENT CRITERIA ARE NOT MET, ASSESS FOR LIFETIME PTSD. IDENTIFY A PERIOD OF AT LEAST A MONTH SINCE THE TRAUMATIC EVENT IN WHICH SYMPTOMS WERE WORSE.

Since the (EVENT), has there been a time when these (PTSD SYMPTOMS) were a lot worse than they have been in the past month? When was that? How long did it last? *(At least a month?)*

IF MULTIPLE PERIODS IN THE PAST: **When were you bothered the most by these (PTSD SYMPTOMS)?**

IF AT LEAST ONE PERIOD, INQUIRE ITEMS 1-17, CHANGING FREQUENCY PROMPTS TO REFER TO WORST PERIOD: **During that time, did you (EXPERIENCE SYMPTOM)? How often?**

Lifetime PTSD Symptoms

Criterion A met (traumatic event)?	*NO*	*YES*
_____ *# Criterion B sx (≥ 1)?*	*NO*	*YES*
_____ *# Criterion C sx (≥ 3)?*	*NO*	*YES*
_____ *# Criterion D sx (≥ 2)?*	*NO*	*YES*
Criterion E met (duration ≥ 1 month)?	*NO*	*YES*
Criterion F met (distress/impairment)?	*NO*	*YES*

_____

LIFETIME PTSD (Criteria A-F met)?	*NO*	*YES*

Associated Features

26. guilt over acts of commission or omission

Frequency	***Intensity***	***Past week***
Have you felt guilty about anything you did or didn't do during (EVENT)? Tell me more about that. *(What do you feel guilty about?)* **How much of the time have you felt that way in the past month *(week)*?** 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How strong were these feelings of guilt? How much distress or discomfort did they cause?** 0 No feelings of guilt 1 Mild, slight feelings of guilt 2 Moderate, guilt feelings definitely present, some distress but still manageable 3 Severe, marked feelings of guilt, considerable distress 4 Extreme, pervasive feelings of guilt, self-condemnation regarding behavior, incapacitating distress ***QV (specify)*** _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

27. survivor guilt [APPLICABLE ONLY IF MULTIPLE VICTIMS]

Frequency	***Intensity***	***Past week***
Have you felt guilty about surviving (EVENT) when others did not? Tell me more about that. *(What do you feel guilty about?)* **How much of the time have you felt that way in the past month *(week)*?** 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) 8 N/A ***Description/Examples***	**How strong were these feelings of guilt? How much distress or discomfort did they cause?** 0 No feelings of guilt 1 Mild, slight feelings of guilt 2 Moderate, guilt feelings definitely present, some distress but still manageable 3 Severe, marked feelings of guilt, considerable distress 4 Extreme, pervasive feelings of guilt, self-condemnation regarding survival, incapacitating distress ***QV (specify)*** _____	*F* _____ *I* _____ ***Past month*** *F* _____ *I* _____ ***Sx: Y N*** ***Lifetime*** *F* _____ *I* _____ ***Sx: Y N***

28. a reduction in awareness of his or her surroundings (e.g., "being in a daze")

Frequency	***Intensity***	***Past week***
Have there been times when you felt out of touch with things going on around you, like you were in a daze? What was that like? [DISTINGUISH FROM FLASHBACK EPISODES] **How often has that happened in the past month *(week)*?** [IF NOT CLEAR:] *(Was it due to an illness or the effects of drugs or alcohol?)* **When did you first start feeling that way?** *(After the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong was this feeling of being out of touch or in a daze?** *(Were you confused about where you actually were or what you were doing at the time?)* **How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No reduction in awareness 1 Mild, slight reduction in awareness 2 Moderate, definite but transient reduction in awareness, may report feeling "spacy" 3 Severe, marked reduction in awareness, may persist for several hours 4 Extreme, complete loss of awareness of surroundings, may be unresponsive, possible amnesia for the episode (blackout) ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F _____ I _____ ***Past month*** F _____ I _____ Sx: Y N ***Lifetime*** F _____ I _____ Sx: Y N

29. derealization

Frequency	***Intensity***	***Past week***
Have there been times when things going on around you seemed unreal or very strange and unfamiliar? [IF NO:] *(What about times when people you knew suddenly seemed unfamiliar?)* **What was that like? How often has that happened in the past month *(week)*?** [IF NOT CLEAR:] *(Was it due to an illness or the effects of drugs or alcohol?)* **When did you first start feeling that way?** *(After the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong was (DEREALIZATION)? How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No derealization 1 Mild, slight derealization 2 Moderate, definite but transient derealization 3 Severe, considerable derealization, marked confusion about what is real, may persist for several hours 4 Extreme, profound derealization, dramatic loss of sense of reality or familiarity ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F _____ I _____ ***Past month*** F _____ I _____ Sx: Y N ***Lifetime*** F _____ I _____ Sx: Y N

30. depersonalization

Frequency	***Intensity***	***Past week***
Have there been times when you felt as if you were outside of your body, watching yourself as if you were another person? [IF NO:] *(What about times when your body felt strange or unfamiliar to you, as if it had changed in some way?)* **What was that like? How often has that happened in the past month *(week)*?** [IF NOT CLEAR:] *(Was it due to an illness or the effects of drugs or alcohol?)* **When did you first start feeling that way?** *(After the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong was (DEPERSONALIZATION)? How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No depersonalization 1 Mild, slight depersonalization 2 Moderate, definite but transient depersonalization 3 Severe, considerable depersonalization, marked sense of detachment from self, may persist for several hours 4 Extreme, profound depersonalization, dramatic sense of detachment from self ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***F*** _____ ***I*** _____ ***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N*** ***Lifetime*** ***F*** _____ ***I*** _____ ***Sx: Y N***

CAPS SUMMARY SHEET

Name:_____ ID#:_____ Interviewer:_____ Study:_____ Date:_____

A. Traumatic event:

B. Reexperiencing symptoms	*PAST WEEK*			*PAST MONTH*			*LIFETIME*		
	Freq	*Int*	*F+I*	*Freq*	*Int*	*F+I*	*Freq*	*Int*	*F+I*
(1) intrusive recollections									
(2) distressing dreams									
(3) acting or feeling as if event were recurring									
(4) psychological distress at exposure to cues									
(5) physiological reactivity on exposure to cues									
B subtotals									
Number of Criterion B symptoms (need 1)									

C. Avoidance and numbing symptoms	*PAST WEEK*			*PAST MONTH*			*LIFETIME*		
	Freq	*Int*	*F+I*	*Freq*	*Int*	*F+I*	*Freq*	*Int*	*F+I*
(6) avoidance of thoughts or feelings									
(7) avoidance of activities, places, or people									
(8) inability to recall important aspect of trauma									
(9) diminished interest in activities									
(10) detachment or estrangement									
(11) restricted range of affect									
(12) sense of a foreshortened future									
C subtotals									
Number of Criterion C symptoms (need 3)									

D. Hyperarousal symptoms	*PAST WEEK*			*PAST MONTH*			*LIFETIME*		
	Freq	*Int*	*F+I*	*Freq*	*Int*	*F+I*	*Freq*	*Int*	*F+I*
(13) difficulty falling or staying asleep									
(14) irritability or outbursts of anger									
(15) difficulty concentrating									
(16) hypervigilance									
(17) exaggerated startle response									
D subtotals									
Number of Criterion D symptoms (need 2)									

Total Freq, Int, and Severity (F+I)	*PAST WEEK*			*PAST MONTH*			*LIFETIME*		
	Freq	*Int*	*F+I*	*Freq*	*Int*	*F+I*	*Freq*	*Int*	*F+I*
Sum of subtotals (B+C+D)									

E. Duration of disturbance	*CURRENT*	*LIFETIME*
(19) duration of disturbance at least one month	*NO YES*	*NO YES*

F. Significant distress or impairment in functioning	*PAST WEEK*	*PAST MONTH*	*LIFETIME*
(20) subjective distress			
(21) impairment in social functioning			
(22) impairment in occupational functioning			
AT LEAST ONE ≥ 2?	*NO YES*	*NO YES*	*NO YES*

PTSD diagnosis	*CURRENT*	*LIFETIME*
PTSD PRESENT -- ALL CRITERIA (A-F) MET?	*NO YES*	*NO YES*
Specify: (18) with delayed onset (≥ 6 months delay)	*NO YES*	*NO YES*
(19) acute (< 3 months) or chronic (≥ 3 months)	*acute chronic*	*acute chronic*

Global ratings	*PAST WEEK*	*PAST MONTH*	*LIFETIME*
(23) global validity			
(24) global severity			
(25) global improvement			

Associated features	*PAST WEEK*			*PAST MONTH*			*LIFETIME*		
	Freq	*Int*	*F+I*	*Freq*	*Int*	*F+I*	*Freq*	*Int*	*F+I*
(26) guilt over acts of commission or omission									
(27) survivor guilt									
(28) reduction in awareness of surroundings									
(29) derealization									
(30) depersonalization									

PCL-M

INSTRUCTIONS: Below is a list of problems and complaints that veterans sometimes have in response to stressful military experiences. Please read each one carefully, then circle one of the numbers to the right to indicate how much you have been bothered by that problem in the past month.

		Not at all	A little bit	Moderately	Quite a bit	Extremely
1.	Repeated, disturbing *memories, thoughts,* or *images* of a stressful military experience?	1	2	3	4	5
2.	Repeated, disturbing *dreams* of a stressful military experience?	1	2	3	4	5
3.	Suddenly *acting* or *feeling* as if a stressful military experience *were happening again* (as if you were reliving it)?	1	2	3	4	5
4.	Feeling *very upset* when *something reminded you* of a stressful military experience?	1	2	3	4	5
5.	Having *physical reactions* (e.g., heart pounding, trouble breathing, sweating) when *something reminded you* of a stressful military experience?	1	2	3	4	5
6.	Avoiding *thinking about* or *talking about* a stressful military experience or avoiding *having feelings* related to it?	1	2	3	4	5
7.	Avoiding *activities* or *situations* because *they reminded you* of a stressful military experience?	1	2	3	4	5
8.	Trouble *remembering important parts* of a stressful military experience?	1	2	3	4	5
9.	*Loss of interest* in activities that you used to enjoy?	1	2	3	4	5
10.	Feeling *distant* or *cut off* from other people?	1	2	3	4	5
11.	Feeling *emotionally numb* or being unable to have loving feelings for those close to you?	1	2	3	4	5
12.	Feeling as if your *future* will somehow be *cut short*?	1	2	3	4	5
13.	Trouble *falling* or *staying asleep*?	1	2	3	4	5
14.	Feeling *irritable* or having *angry outbursts*?	1	2	3	4	5
15.	Having *difficulty concentrating*?	1	2	3	4	5
16.	Being "*super-alert*" or watchful or on guard?	1	2	3	4	5
17.	Feeling *jumpy* or easily startled?	1	2	3	4	5

PCL-M for DSM-IV (11/1/94) Weathers, Litz, Huska, & Keane National Center for PTSD - Behavioral Science Division

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