CAMPBELL, ALLISON ANN, Ph.D. Cardiovascular reactivity and the role of anxiety sensitivity in posttraumatic stress disorder. (2021)
Directed by Dr. Blair E. Wisco. 82 pp.

Posttraumatic stress disorder (PTSD) has long been characterized by its heightened stress response across a variety of cardiovascular measures. The current literature suggests this exaggerated response may be driven by either sympathetic over-activation, heightened parasympathetic withdrawal, or both. However, there has yet to be a study utilizing strong methodology incorporating cardiovascular reactivity measures of both the sympathetic nervous system (i.e., pre-ejection period) and parasympathetic nervous system (i.e., respiratory sinus arrhythmia). Additionally, anxiety sensitivity, or the fear of anxiety-related bodily sensations, is thought to influence the stress response by further heightening physiological reactivity. Research has yet to examine whether anxiety sensitivity accounts for changes in cardiovascular reactivity while controlling for PTSD. The current study sought to understand how the autonomic nervous system and its two branches (i.e., parasympathetic and sympathetic) influence cardiovascular reactivity during the stress response in PTSD and whether anxiety sensitivity influences that reactivity. The current study used a modified trauma-script imagery task to examine changes in cardiovascular measures across participants with PTSD (n = 53) and trauma-exposed controls (n = 68). Results indicated heightened heart rate reactivity in PTSD compared to controls. The current study found marginal evidence of heightened reactivity in PTSD for pre-ejection period and no evidence of heightened respiratory sinus arrhythmia reactivity, suggesting that heart rate reactivity is driven more by sympathetic activity. There was no evidence to suggest that anxiety sensitivity influences

cardiovascular changes. Further research is needed to better understand sympathetic influences on heart rate reactivity in PTSD. Future implications for treatment targeting the cardiovascular stress response to improve PTSD symptoms and the association between PTSD and poor cardiovascular health are considered.

CARDIOVASCULAR REACTIVITY AND THE ROLE OF ANXIETY SENSITIVITY IN POSTTRAUMATIC STRESS DISORDER

by

Allison Ann Campbell

A Dissertation Submitted to
the Faculty of The Graduate School at
The University of North Carolina at Greensboro
in Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy

Greensboro
2021

Approved by

Blair E. Wisco
Committee Chair

APPROVAL PAGE

This dissertation written by Allison Ann Campbell has been approved by the following committee of the Faculty of The Graduate School at The University of North Carolina at Greensboro.

Committee Chair Dr. Blair E. Wisco

Committee Members Dr. Rosemery Nelson-Gray

Dr. Suzanne Vrshek-Schallhorn

Dr. Mike Kane

May 19, 2020
Date of Acceptance by Committee

May 19, 2020
Date of Final Oral Examination

ACKNOWLEDGEMENTS

I would like to thank Dr. Blair Wisco, my committee chair, for her endless support and guidance throughout my graduate career. She has been an exceptional model for scientific inquiry and professional mentorship. I would also like to thank my family and friends for their unwavering encouragement and always believing in me.

"As we work to create light for others, we naturally light our own way."

-Mary Anne Radmacher

TABLE OF CONTENTS

Page

LIST OF TABLES

Page

LIST OF FIGURES

Page

CHAPTER I

INTRODUCTION

Posttraumatic stress disorder (PTSD) has long been defined by its psychophysiological abnormalities. Although the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for PTSD have evolved over the years, physiological symptoms have been an essential feature of symptom presentation since PTSD was first added to the DSM in its third edition (3rd ed.; DSM–III; American Psychological Association, 1980). DSM-5 includes the following psychophysiological symptom (American Psychological Association, 2013): Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s). This autonomic arousal response (i.e., physiological reactions) is often a focus of psychological research. The literature has sought to understand how and why stress reactivity presents differently in those with PTSD to best develop treatments to target the stress response.

Autonomic arousal may be driven by sympathetic over-activation, parasympathetic withdrawal, or both (i.e., the two branches of the autonomic nervous system). Traditionally, sympathetic nervous system over-activation was thought to be the driving factor in a maladaptive stress response in PTSD. In recent years there has been more research among individuals with PTSD to suggest that parasympathetic nervous system withdrawal may also influence the stress response, or potentially even drive this

response. Studies have measured this stress response by examining psychophysiological reactivity to stressful stimuli. Psychophysiological reactivity is the change in physiology from a resting state (i.e., baseline measure) to a stress response state (i.e., change that takes place in the presence of an environmental stressor). This is distinct from baseline measures which are collected at rest or in the presence of a neutral stimuli. There has yet to be an empirical study utilizing strong methodology to examine cardiovascular autonomic reactivity incorporating sympathetic, parasympathetic, and general autonomic nervous system measures in PTSD. Without a complete understanding of what cardiovascular autonomic reactivity looks like in individuals with PTSD, research cannot progress in evaluating to what extent the autonomic nervous system and its two branches (i.e., sympathetic nervous system and parasympathetic nervous system) influence stress reactivity. Thus, the current study examined differences in cardiovascular reactivity between individuals with PTSD and trauma-exposed controls across a general autonomic nervous system measure (i.e., heart rate), a sympathetic nervous system measure (i.e., pre-ejection period), and a parasympathetic system measure (i.e., respiratory sinus arrhythmia). Secondly, this study examined the role of anxiety sensitivity and whether anxiety sensitivity accounts for changes in cardiovascular reactivity in PTSD.

Stress Response in PTSD

Understanding all psychophysiological components of the autonomic nervous system during the stress response is critical in operationalizing what a maladaptive stress response looks like in PTSD. Brown, Chorpita, and Barlow (1998) posed a model indicating a common latent factor of autonomic arousal across DSM-IV anxiety

disorders, of which PTSD was included. This model emphasized the importance of integrating psychophysiological measures of autonomic activity with more traditional methods (i.e., clinical interview and self-report measures). Some research uses psychophysiological measures as a converging measure of symptom severity. Research suggests that psychophysiological assessment of PTSD, while still in development, is needed to best understand symptom presentations and develop effective interventions (Turpin, 1991). Psychophysiological measures can help expand upon what is addressed by clinical interviews and self-report measures. Psychophysiological measures are also less vulnerable than self-report or clinical interview measures to threats to internal validity. Specifically, psychophysiological measures can be more objective than self-report measures or clinical interviews, in that they are not as vulnerable to demand characteristics or general mood states (Gotlib & Cane, 1989). However, it is likely the case that not all psychophysiological measures are created equal. Some measures may be more sensitive to stress than others. The field has yet to explore within cardiovascular reactivity in PTSD which psychophysiological measures may be best for use in clinical practice. Similar to how research has developed "gold-standard" measures for self-report and clinical interviews to assess PTSD symptoms, research should also work toward developing "gold-standard" psychophysiological measures. The first step in this process is to compare different psychophysiological measures to each other.

Research has also sought to examine how well psychophysiological measures correlate with self-report and clinical interview measures and has found significant associations between measures of PTSD symptom severity and psychophysiological

reactivity measures (Arditi-Babchuk et al., 2009; Blanchard et al., 1996). Other studies have used psychophysiological reactivity constructs as outcome measures following treatment, finding that individuals have a more adaptive stress responses (i.e., less reactivity) at post-treatment (D'Andrea & Pole, 2012; Sack, Lempa, & Lamprecht, 2007). Psychophysiological reactivity measures may be particularly useful as concurrent markers of treatment outcome alongside self-report and clinical interview. Psychophysiological measures could be utilized as more objective means of assessing symptom improvement, specific to maladaptive physiology (i.e., marked physiological reactions). Clients may also benefit by seeing numeric changes in their physiological reactions.

The first step to utilizing psychophysiological measures in treatment outcome research is to conduct an empirical study to best operationalize what constitutes a maladaptive response (i.e., changes in psychophysiological measures) and understand which measures are most sensitive to stress. The information could then be implemented in future treatment outcome research as a potential symptom tracking or outcome measure. The current study sought to better understand the stress response in PTSD by evaluating cardiovascular reactivity through quantifying the relative role of the sympathetic nervous system versus the parasympathetic nervous system in PTSD.

General Measures of Cardiovascular Reactivity in PTSD

While there are several organ systems activated during the stress response, the cardiovascular system is of interest in PTSD research due to the association between PTSD and cardiovascular outcomes including hypertension and cardiovascular disease

(Coughlin, 2011; Boscarino & Chang, 1999). Research suggests this association can be partially explained by health behavior factors including smoking, physical inactivity, and obesity (Kibler, 2009). However, the "reactivity hypothesis" suggests consistent exaggerated reactivity to stress in the laboratory mimics the chronic hyperreactivity in natural settings (Blascovich & Katkin, 1993; Krantz & Manuck, 1984). These chronic elevations of the autonomic nervous system can lead to blood vessel damage, increasing risk for hypertension which has been tied to cardiovascular disease (Burker, Fredrikson, Rifai, & Siegel, 1994). So, although we cannot ignore health behaviors' influence on cardiovascular outcomes in PTSD, it appears the stress response also plays in important role.

The literature is not clear as to what mechanisms drive the association between stress and cardiovascular health in PTSD. It is beyond the scope of this study to investigate these possible mechanisms. However, a necessary step in understanding this association is to first better understand the contribution of the sympathetic nervous system or parasympathetic nervous system in the stress response in PTSD, which will be the focus of this dissertation.

Heart rate is a general measure of reactivity that is not categorized as a specific measure of the sympathetic nervous system or the parasympathetic nervous system. Instead, heart rate is influenced by both systems as found in pharmaceutical blockade studies (Harris, Schoenfeld, & Weissler, 1967) and foundational theoretical work (Berntson, Cacioppo & Quigley, 1993). Heart rate has long been a popular psychophysiological measure due to its ease of measurement and observed sensitivity to

influences by the sympathetic nervous system or parasympathetic nervous system (Lang, Bradley & Cuthbert, 1998).

Research has found that PTSD is associated with a larger increase in heart rate to startle sounds compared to control groups (Metzger et al., 1999). This finding has been consistently replicated. A meta-analysis conducted by Pole (2007) and a literature review conducted by Craske et al. (2011) examined stress reactivity in PTSD. Both reviews found that compared to control groups, those with PTSD display a greater increase in heart rate during generic threat (i.e., shock threat, startle paradigms) and disorder-specific threat (i.e. standardized trauma cues, and idiographic trauma cues). There were significant small-to-moderate effects for heart rate reactivity in PTSD across all types of stressors (Pole, 2007). As mentioned heart rate is influenced by both the sympathetic and parasympathetic nervous systems. A theoretical review by Pitman, Shalev, and Orr (2000) has suggested the increase in heart rate reactivity in PTSD is due to an over activation of the sympathetic branch of the autonomic nervous system (Pitman, Shalev, & Orr, 2000). However, there has been little empirical work to verify this theoretical claim. This suggests a need to specifically examine sympathetic nervous system measures when studying cardiovascular reactivity in PTSD.

Sympathetic Nervous System Reactivity in PTSD

A primary focus of research investigating the stress response in PTSD has been to examine sympathetic over-activation. The sympathetic nervous system is the system associated with our "fight or flight" response. As an example, imagine that a woman is crossing the street. Suddenly she sees a car coming straight toward her. Her sympathetic

nervous system would become activated to trigger the "fight or flight" response. Typically, this response includes increased heart rate, increased respiration, increased blood pressure, dilation of pupils, and increased sweating (McCorry, 2007). These physiological changes occur in order for her to respond in a manner that increases her chances of survival (i.e., dodging the car). Research suggests that in PTSD this "fight or flight" response is heightened, meaning an even greater increase in heart rate, respiration, etc. compared to healthy individuals (Craske et al., 2011). To understand what this heightened response looks like, the PTSD literature has traditionally examined measures specifically connected to the sympathetic nervous system (i.e., skin conductance). However, Pole's comprehensive meta-analysis (2007) found a larger effect in heart rate reactivity compared to skin conductance, suggesting examining cardiovascular responses may be an advantageous psychophysiological measure in PTSD samples.

More recently in the PTSD literature, pre-ejection period has been a cardiovascular measure of interest in examining sympathetic changes during the stress response. Pre-ejection period is a systolic time interval representing the period from onset of ventricle depolarization to the ejection of blood from the left ventricle (i.e., opening of aortic valve; Newlin & Levenson, 1979). Pre-ejection period is representative of the electrical-mechanical delay before ejection. Empirical studies have found that pre-ejection period is a valid measure of beta-adrenergic (i.e., sympathetic) influences on the heart. These studies utilized pharmacological blockade methods to conclude changes in pre-ejection period are specifically sensitive to beta-adrenergic influences as opposed to

both sympathetic and parasympathetic influences (Harris et al., 1967; Lewis, Leighton, Forester, & Weissler, 1974).

Studies have found those with PTSD have a decrease in pre-ejection period from rest to stressor (Sack, Lempa, Steinmetz, Lamprecht, & Hofmann, 2008). This suggests a heightened stress response, due to a shorter time between ventricle depolarization and ejection of blood. In other words, when pre-ejection period value is lower, this means there is a shorter time interval and the sympathetic nervous system is more activated. However, the generalizability of Sack et al. (2008) is limited due to the small sample size (i.e., $n = 10$). Another study found that pre-ejection period reactivity during a parent child discussion task was associated with post-traumatic symptoms in children when the child had been exposed to elevated trauma. This study did not find a direct association with pre-ejection period reactivity and post-traumatic stress symptoms (Cohen et al., 2019).

Another study found the opposite response when examining pre-ejection period reactivity in PTSD (Meyer et al., 2016). In this study participants were exposed to a mental arithmetic stressor and standardized emotional stressor (i.e., audio of a baby crying). Results found that participants with PTSD had increased pre-ejection period (i.e. less sympathetic activation). This study had several methodological weaknesses. First, Meyer et al (2016) used an inappropriate diagnostic interview for assessing PTSD (i.e., Structured Interview for Disorders of Extreme Stress [SIDES]; Boroske-Leiner et al. 2008). This measure assesses responses to trauma that are not specifically addressed in DSM-IV (Pelcovitz et al., 1997). In other words, this measure, while helpful in assessing symptoms of extreme stress, is not a diagnostic interview. Therefore, it is likely that the

participants in the PTSD group did not actually meet diagnostic criteria for PTSD. Second, this study utilized standard stressors (i.e. the same stressor for each participant). The stressors used were also not trauma-related (i.e., mental arithmetic, audio of a baby crying). These stressors may have not been salient enough to induce psychophysiological responses.

The literature on pre-ejection period in PTSD is limited, as studies more often use skin conductance as a measure of sympathetic activity during the stress response. To date, the literature on pre-ejection period in PTSD has not utilized strong methodology. Based on the literature, there is preliminary support for lower pre-ejection period in PTSD, but there is a need to replicate this finding and further examine pre-ejection period reactivity in PTSD with stronger methods.

Parasympathetic Nervous System Reactivity in PTSD

In conjunction with changes in the sympathetic nervous system during the stress response in PTSD, it is also crucial to consider changes in the parasympathetic nervous system. The parasympathetic nervous system is the second half of understanding the autonomic nervous system's response to stress. Without examining parasympathetic influences alongside sympathetic influences, research can only see half of the whole picture. It is important to understand to what extent the sympathetic, parasympathetic or both branches of the autonomic nervous system influence heart rate. This work could inform future research in understanding specific mechanisms involved in the association between PTSD and cardiovascular health outcomes and better understanding what cardiovascular indices may best predict these outcomes. This work could also better

inform treatment approaches by selecting specific biofeedback indices most applicable to individuals with PTSD.

The literature is currently too premature to suggest specific biofeedback indices tapping the sympathetic or parasympathetic nervous system. However, there has been progress to understand the parasympathetic nervous system and the concept of parasympathetic withdrawal during stress in PTSD. The parasympathetic nervous system is specifically in charge of relaxing or slowing body processes and is often referred to as the "rest and digest" system. The parasympathetic nervous system's main job is to promote physiological homeostasis through its regulatory ability. One way the parasympathetic nervous system promotes this homeostasis is through cardiac vagal control, or the contribution of the vagus nerve to the sinoatrial node, which serves as the heart's natural pacemaker (Berntson et al., 1993). The vagus nerve is the longest cranial nerve that connects the brain to the body. It has fibers that run from the brain to several major organs, including the heart (specifically the sinoatrial node). The activity that occurs through the vagus nerve fibers slows the heart rate by decreasing sinoatrial node firing (Levy & Warner, 1994). More simply, the vagus nerve influences the beat-to-beat fluctuations in heart rate by slowing heart rate (i.e., attempting to return the body to homeostasis following an environmental stressor).

The purpose of the vagus nerve slowing heart rate is to conserve energy (Levy & Warner, 1994). When the body is in a resting state it would be inefficient for the heart to beat faster than necessary. In these situations, the "vagal brake" is applied, meaning that the vagus nerve is heavily influencing heart rate and keeping it slow. However, when

presented with a stressor the body must prepare itself for that stressor. In these situations, the vagus nerve does not influence heart rate as much and the "vagal brake" is released (i.e., vagal withdrawal). This allows for an increase in heart rate, facilitating the body to best prepare for the stressor. In sum, the "vagal brake" is the parasympathetic nervous system's way to regulate the stress response.

Changes in vagal activity also occur during respiration. During respiration, there is rapid "vagal brake" withdrawal during inhalation and application during exhalation, leading to changes in heart rate (Rottenberg, 2007). This beat-to-beat variability in heart rate associated with respiration is known as respiratory sinus arrhythmia (Grossman & Taylor, 2007).

Respiratory sinus arrhythmia is a measure used to estimate cardiac vagal control (Berntson et al., 1997), and has become increasingly popular in PTSD research over several years. Prominent theories suggest that when humans are presented with stress, the "vagal brake" is released (i.e., vagal withdrawal), indicating a decrease in parasympathetic activity, and an increase in heart rate to facilitate an adaptive response to stress (Porges, 1995). In PTSD, there is evidence to suggest a heightened level of vagal withdrawal during the stress response. Heightened respiratory sinus arrhythmia withdrawal is considered maladaptive because the "vagal brake" is released too much, leading to disinhibition of the sympathetic nervous system. This causes the body to produce a heart rate faster than what is needed to respond to the stressor (i.e. over expenditure of resources; Thayer & Lane, 2000).

Empirical studies examining respiratory sinus arrhythmia reactivity in the presence of a stressor have found heightened respiratory sinus arrhythmia withdrawal in PTSD compared to control groups (Rabellino et al., 2017; Hauschildt et al., 2011; Tucker et al., 2012; Jovanovic et al., 2009; Norte et al., 2013). However, a few studies have found evidence of blunted respiratory sinus arrhythmia withdrawal in PTSD (i.e., no change in respiratory sinus arrhythmia level from baseline to stressor task in PTSD compared to respiratory sinus arrhythmia withdrawal in controls; Sahar et al., 2001) or no difference between PTSD and control groups (i.e., both groups showed a similar decrease in respiratory sinus arrhythmia from baseline to stressor task; Johnsen et al., 2017; Roberts et al., 2012).

In summary, the literature suggests evidence for increased heart rate and decreased pre-ejection period and respiratory sinus arrhythmia during stress in those with PTSD compared to controls. There has not yet been a study examining all three of these measures during a lab-based stressor. Meyer et al (2016), mentioned previously, conducted a similar study examining heart rate, pre-ejection period, and baroreflex sensitivity (another parasympathetic nervous system measure that estimates vagal control; La Rovere, Pinna, & Raczak, 2008) reactivity in PTSD compared to controls. Results found that participants with PTSD had increased pre-ejection period (i.e. less sympathetic activation) during the mental arithmetic stressor, and lower baroreflex sensitivity (i.e., less parasympathetic activation) during the emotional stressor than controls (Meyer, Albrecht, Bornschein, Sachsse, & Herman-Lingen, 2016). This finding of both sympathetic and parasympathetic blunting contrasts with the existing literature

suggesting greater reactivity in PTSD. However, as discussed earlier, this study had several methodological weaknesses.

Cardiovascular Reactivity in Anxiety Disorders

It is important to note that PTSD is not the only disorder to display heightened cardiovascular reactivity to stress. Anxiety disorders have also been associated with this same psychophysiological response (Craske et al., 2011). PTSD has long been a specific diagnosis within the category of anxiety disorders. The current version of the DSM-5 (APA, 2013) associates anxiety disorders with excessive fear displayed as "a surge of autonomic arousal necessary for fight or flight" (p. 189). The DSM-5 now distinguishes anxiety disorders from PTSD, with a separate category for trauma and stressor related disorders. However, like the development of anxiety disorders, much of the field still considers the classical conditioning of fear to be central to the development of PTSD (Zoellner, Rothbaum, & Feeny, 2011). For this reason, understanding more about cardiovascular reactivity in anxiety disorders is relevant in understand reactivity in PTSD.

A comprehensive literature review conducted by Craske et al. (2011) examined stress reactivity across anxiety disorders and PTSD. This review found that compared to control groups, those with anxiety disorders or PTSD displayed a heightened stress response as measured through heart rate. This finding suggests PTSD and anxiety disorders all display heightened heart rate reactivity; however, this review did not calculate effect sizes for direct comparison of the size of these effects across disorders.

Respiratory sinus arrhythmia reactivity appears to have more mixed findings in the anxiety disorder literature. Generalized anxiety disorder has little support for heightened respiratory sinus arrhythmia reactivity with only two of eight studies (Levine et al., 2016; Shinba, 2017; Kircanski et al., 2016; Fisher & Newman, 2013; Llera & Newman, 2010; Hammel et al., 2011; Meeten et al., 2016; Ottaviani et al., 2016) finding heightened reactivity compared to control groups (Llera & Newman, 2010; Levine et al., 2016). Social anxiety has similarly weak support, with only one of three studies (Gaebler et al., 2013; Grossman, Wilhelm, Kawachi, & Sparrow, 2001; Asmundson & Stein, 1994) finding heightened reactivity (Grossman et al., 2001). Specific phobia has similar null findings with only one of four studies (Simon, Meuret, & Ritz, 2017; Bornas et al., 2005; Friedman & Thayer, 1998; Sarlo et al., 2008) finding heightened reactivity (Friedman & Thayer, 1998). Finally, the literature on panic disorder and agoraphobia found significant results for heightened respiratory sinus arrhythmia reactivity in two of the six studies (Asmundson & Stein, 1994; Friedman & Thayer, 1998; Petrowski et al., 2017; Breuninger et al., 2017; Kotianova et al., 2018; Kikuchi et al., 2009), with Friedman and Thayer (1998) and Kotianova and colleagues (2018) finding greater respiratory sinus arrhythmia withdrawal during stress compared to controls.

The literature examining pre-ejection period reactivity to stress in anxiety disorders is small. Diamond and Fisher (2017) found no difference in pre-ejection period in individuals with generalized anxiety and social anxiety compared to healthy controls during a diagnostic interview. Another study found the pre-ejection period increased in individuals with a flying phobia following a stressor (Busscher, B., Spinhoven, P., van

Gerwen, L. J., & de Geus, E. J., 2013). This literature is too novel to draw any conclusions from. However, future research should seek to directly compare anxiety disorders to PTSD in regards to pre-ejection period reactivity.

In sum, the literature has found evidence of greater heart rate reactivity in those with anxiety disorders, but there is not yet evidence to suggest this reactivity is driven more by the sympathetic or parasympathetic nervous system. This ambiguity further supports the need to better understand which branch of the autonomic nervous system might be influencing changes in heart rate. Given the similarities in the stress response across PTSD and anxiety disorders, examining sympathetic and parasympathetic influences in PTSD could be generalized to anxiety disorders more broadly.

Cardiovascular Reactivity Measurement and Best Practices

Psychological research has operationalized best practices for measuring cardiovascular reactivity (i.e., heart rate, respiratory sinus arrhythmia, pre-ejection period) in lab settings. Heart rate is a simple frequency count of beats per minute. Each RR interval represents one heart beat in calculating heart rate. Heart rate was included in this study in order to assess general cardiovascular reactivity. Although heart rate is unable to distinguish between sympathetic activation and parasympathetic withdrawal, it does offer a physiological measurement that displays a general autonomic response. For this study, heart rate served as a general check of cardiovascular reactivity under stress.

Respiratory sinus arrhythmia is measured using two different methods, frequency-domain and time-domain. Time-domain measures are based on RR intervals. Some of the more common measures include the proportion of RR intervals that differ by more than

50 milliseconds (pNN50), the standard deviation of beat-to-beat intervals (SDNN), and the root mean square of successive differences (RMSSD), which appears to be the most popular time-domain measure. RMSSD is different from SDNN as it is looking at differences between adjacent intervals. Instead of subtracting each RR interval from the mean, it subtracts from the last RR interval.

Frequency domain measures divide the heart rate signal into frequency bands and quantify the spectral energy in these bands into very low (< 0.04 Hz), low (0.04-0.15 Hz), or high frequency (0.15-0.50 Hz). High-frequency heart rate variability (HF-HRV) is driven by the parasympathetic nervous system, whereas low frequency heart rate variability is influenced by both the sympathetic and parasympathetic nervous system (Heathers, 2007). The current literature appears to utilize HF-HRV as the most popular method for measuring respiratory sinus arrhythmia. Therefore, the current study used HF-HRV to estimate respiratory sinus arrhythmia and relatedly parasympathetic activity.

It is also important to note the influence of respiration on measuring respiratory sinus arrhythmia. Research has found that hyperventilation decreases respiratory sinus arrhythmia amplitude, whereas deep breathing increases respiratory sinus arrhythmia amplitude (Hirsch & Bishop, 1981). It is recommended to control for respiration (i.e., both respiratory rate and amplitude) when estimating respiratory sinus arrhythmia (Grossman & Taylor, 2007). When best practices are utilized, respiratory sinus arrhythmia has been shown to be a reliable and valid measure of cardiac vagal control (Cacioppo et al., 1994; Malik et al., 1996; Grossman & Taylor, 2007; Bernston et al., 1997).

Pre-ejection period is measured examining both the ECG waveform and cardiac impedance waveform. As previously mentioned, pre-ejection period is the time interval in milliseconds between the onset of depolarization (the Q point on the ECG waveform) and the onset of ejection, (the dZ/dt B point on the cardiac impedance waveform).

Medication and health-related variables are critical to consider when examining autonomic nervous system measures. A wide-variety of medications including psychotropic and blood pressure medications affect the cardiovascular system (Licht, de Geus, van Dyck, & Penninx, 2010; Burckhardt, Raeder, Muller, Imhof & Neubauer, 1978) and should be considered when assessing for changes in cardiovascular measures during lab-based stressors. Best practices indicate participants should be excluded for any of these medications known to change cardiovascular physiology.

As discussed, research suggests an association between autonomic nervous system reactivity in PTSD both through sympathetic nervous system over-activation and parasympathetic nervous system withdrawal. Berntson, Cacioppo, and Quigley (1991) found that the sympathetic and parasympathetic nervous system can act reciprocally, independently, or nonreciprocally. This finding has led to ambiguity in determining the autonomic origins of changes in psychophysiology. To begin to uncover this ambiguity and have a complete conceptualization of changes in the autonomic nervous system in PTSD, the literature needs an empirical study that measures cardiovascular reactivity for both the sympathetic and parasympathetic nervous system. However, to date only Meyer et al. (2016) looked at changes of both the sympathetic and parasympathetic nervous system on cardiovascular reactivity in PTSD compared to controls. As previously

discussed, this study had several methodological weaknesses the current study has better addressed.

Anxiety Sensitivity and Cardiovascular Reactivity

This study also addressed a second aim to consider how anxiety sensitivity may influence cardiovascular reactivity. Anxiety sensitivity is a transdiagnostic, trait-like construct, defined as the fear of anxiety-related bodily sensations (Reiss & McNally, 1985). Reiss and McNally (1985) theorized that those with greater autonomic reactivity would develop greater anxiety sensitivity. Specifically, those with heightened reactivity would have a greater opportunity to perceive these sensations as dangerous, leading to the development of fear of these bodily sensations. This "reactivity" hypothesis has been tested empirically with mixed results. Studies examining reactivity in nonclinical samples have tended to not find an association between anxiety sensitivity and physiological reactivity. Asmundson, Norton, Wilson, and Sandler (1994) did not find difference in heart rate reactivity between nonclinical participants high and low in anxiety sensitivity during a hyperventilation task. Stewart and colleagues found a similar null effect of heart rate reactivity to a loud tone task (Stewart & Pihl, 1994), and mental arithmetic/spelling task (Stewart, Buffett-Jerrott, & Kokaram, 2001). Conversely, Sturges and Goetsch (1996) found marginally greater ($p < .06$) heart rate reactivity in nonclinical high anxiety sensitivity women compared to low anxiety sensitivity women during a mental arithmetic stressor. These studies have been critiqued for methodological weaknesses, including no consideration of psychotropic or cardiovascular medications known to influence heart rate reactivity.

Schmidt, Santiago and Wernicke (2001), accounted for some of these methodological weaknesses and did find that higher anxiety sensitivity was related to greater heart rate and diastolic blood pressure reactivity to a hyperventilation task. The literature examining anxiety sensitivity and cardiovascular reactivity is sparse and often does not utilize adequate methodology. In addition, there is very little work examining the role of anxiety sensitivity on cardiovascular reactivity in clinical samples.

Anxiety Sensitivity and PTSD

When examining the association between anxiety sensitivity and cardiovascular reactivity it is also crucial to consider psychopathology. The literature has found higher anxiety sensitivity to be a risk factor for the development of anxiety disorders, most notably panic disorder (Olatunji & Wolizky-Taylor, 2009). There have also been a few studies to suggest anxiety sensitivity is associated with PTSD. Berenz et al. (2012) found anxiety sensitivity to be associated with PTSD symptom severity and specifically hypervigilance symptoms in a trauma-exposed sample. Olatunji and colleagues found that veterans with PTSD had significantly higher anxiety sensitivity than trauma-exposed veterans or healthy controls (Olatunji, Armstrong, Fan, & Zhao, 2014). Other work has suggested the relationship between anxiety sensitivity and PTSD is bidirectional. Marshall, Miles, and Stewart (2010) found that anxiety sensitivity predicted later PTSD symptoms in physical assault trauma survivors. They also found a reciprocal relationship, in that PTSD symptoms also predict later anxiety sensitivity, suggesting the two constructs may reinforce each other.

These studies administered the Anxiety Sensitivity Index (ASI-3; Taylor et al., 2007) to assess for anxiety sensitivity. The ASI-3 provides a both a full scale and three subscales (i.e., social concerns, cognitive concerns, and physical concerns). Although studies have found PTSD is related to the full scale of the ASI-3, some studies have found the strongest association with the physical concerns subscale (Asmundson & Stapleton, 2008; Fetzner, Collimore, Carelton, & Asmundson, 2012). This subscale assesses anxiety related to physical sensations (i.e., When I notice my heart skipping a beat, I worry that there is something seriously wrong with me). As discussed, a hallmark symptom of PTSD is marked physical reactions to trauma reminders. Based on the reactivity hypothesis (Reiss & McNally, 1985), individuals with PTSD would theoretically have greater autonomic reactivity, and therefore a greater opportunity to perceive autonomic reactivity as dangerous. This perception of physical concerns, as measured by the ASI-3 physical subscale, may play a role in further influencing cardiovascular reactivity in PTSD.

The literature has found evidence to support anxiety sensitivity being associated with cardiovascular reactivity in lab-based stressors. There is also a large body of work to suggest PTSD is associated with cardiovascular reactivity. Thirdly, empirical work suggests a bidirectional relationship between PTSD and anxiety sensitivity. However, to my knowledge, there here has yet to be a study examining whether anxiety sensitivity accounts for changes in cardiovascular reactivity, after controlling for PTSD. Examining this question could better inform clinical treatment. If anxiety sensitivity does account for

cardiovascular reactivity over and above PTSD diagnosis, there may be a need to assess for anxiety sensitivity prior to initiating treatment in PTSD populations.

Trauma-focused treatment typically involves imaginal and in vivo exposures in which clients are asked to sit with their distress to anxiety-provoking stimuli. During these exposures, many clients display an increase in autonomic arousal followed by a decrease as habituation occurs. Trauma-focused treatment helps the client to learn corrective information that these stimuli are not harmful (Foa & Rothbaum, 1998). However, trauma-focused cognitive behavioral therapy has a non-response rate of between 25 to 50 percent (Bisson et al., 2013; Bradley et al., 2005; Schottenbauer et al., 2008). More work is needed to understand what client factors may influence non-response.

It is possible that clients with high anxiety sensitivity may have even greater distress when experiencing autonomic arousal, making it more challenging to engage in and complete trauma-focused treatment. Wald and Taylor (2008) found that some clients could not receive full benefit of trauma-focused treatment due to an inability to tolerate physical arousal during exposures. This suggests a need to assess client sensitivity to physiological arousal prior to trauma-focused treatment. Past research has found that implementing dialectical behavior therapy (DBT) skills prior to trauma-focused treatment improves treatment tolerance (Becker & Zayfert, 2001). The DBT skills allow clients to improve their distress tolerance and emotion regulation prior to initiating trauma-focused treatment, which elicits strong negative emotions. In a similar vein, clients who have high anxiety sensitivity in conjunction with PTSD may tolerate trauma-focused treatment

better if the anxiety sensitivity is treated first. Interoceptive exposure is a main form of treatment used to reduce anxiety sensitivity in panic disorder (Taylor, 2003). This technique involves deliberately inducing anxiety-provoking physical sensations (e.g., hyperventilation, dizziness, etc.) so clients learn these sensations are not harmful. In case studies, Wald and Taylor (2008) found that interoceptive exposure sessions reduced PTSD symptoms. This finding further suggests there is clinical benefit to better understanding the association between anxiety sensitivity and cardiovascular reactivity in PTSD.

Goals and Hypotheses

The primary goal of this dissertation was to examine psychophysiological differences in PTSD across distinct cardiovascular measures at both baseline and stressor that assess general autonomic (i.e., heart rate), primarily sympathetic (i.e., pre-ejection period), and primarily parasympathetic (i.e., respiratory sinus arrhythmia) activity. To address this goal, the current study used a quasi-experimental design comparing the effect of PTSD (PTSD group vs trauma-exposed control group) on cardiovascular activity at baseline (i.e., time of rest with no stimulus present) and on cardiovascular reactivity (i.e., change in physiological measure from baseline to stressor stimulus present). Based on the literature regarding PTSD and psychophysiology, it was hypothesized that, at baseline, the PTSD group would display higher resting heart rate and lower pre-ejection period and respiratory sinus arrhythmia compared to controls. It was also hypothesized there would be larger reactivity in the PTSD group compared to controls across heart rate, pre-ejection period, and respiratory sinus arrhythmia. Specifically, I predicted the PTSD

group would display a larger increase in heart rate from baseline to stressor, and a larger decrease in pre-ejection period and respiratory sinus arrhythmia from baseline to stressor compared to controls.

The secondary goal of this dissertation was to examine whether anxiety sensitivity significantly contributes to cardiovascular reactivity in PTSD. I hypothesized greater physical concerns, as measured by the ASI-3 subscale, would account for more pronounced cardiovascular reactivity across all psychophysiological measures (i.e., heart rate, pre-ejection period, respiratory sinus arrhythmia) over and above PTSD diagnosis.

The current study implements best practices and addresses methodological limitations of prior studies in several ways. First, the Clinician Administered PTSD Scale-5 (CAPS-5; Weathers et al., 2013) was administered to all participants. This clinical interview is the current gold-standard assessment in diagnosing PTSD. Second, the current study incorporated an idiographic trauma script stressor (i.e., individualized trauma script for each participant's criterion A event). Pole's (2007) meta-analysis found larger effect sizes in sympathetic physiological reactivity (i.e., skin conductance, blood pressure) for trauma-focused cues compared to more generic paradigms (i.e., startle) in PTSD. Pole (2007) also found larger heart rate responses to idiographic trauma cues (e.g., script driven imagery) compared to standardized trauma cues (e.g., combat sounds, video tape of car crash). This suggests cardiovascular reactivity is the most pronounced when the stressor task is trauma related and individualized. Third, the current study also considered appropriate measurement and best practices for all cardiovascular measures. Respiration rate was specifically accounted for by conducting post-hoc ANOVAs,

controlling for respiration rate, for respiratory sinus arrhythmia analyses. Finally, the current study excluded participants taking medications known to change cardiovascular functioning. These medications included any medication for blood pressure or cholesterol, any antidepressant, any medication for attention deficit hyperactive disorder, any over-the-counter allergy or antihistamine medication, and the following medications: Atropine, Dramamine, Cogentin, Somenix.

CHAPTER II

METHOD

Participants

Participants were recruited as part of a larger study examining rumination and PTSD. The sample was made up of community members from the Greensboro area. Participants were recruited using electronic listservs, email advertisements, and public flyers. Participants were also recruited through the UNCG Psychology Clinic. To participate, subjects had to be at least 18 years old and report a Criterion A index trauma (as defined by DSM-5; APA, 2013) that occurred at least one month ago. Additionally, participants were excluded for the following reasons: (1) a traumatic event that occurred within the past month; (2) dissociative symptoms on the PTSD Checklist for DSM-5 (PCL-5; score of "2" or higher on either of the dissociative symptom items); or (3) a history of cardiovascular disease or medications known to affect cardiovascular functioning (i.e., antidepressant use in the past eight weeks, current use of any medications that treat a heart or a cardiovascular condition).

Measures

The Life Events Checklist for DSM-5 (Weathers et al., 2013) is a 17-item self-report measure used to screen for traumatic events. The LEC-5 assesses exposure to 16 events known to potentially result in PTSD. The measure also has one item assessing any traumatic events not captured in the first 16 items. Participants who reported directly or

indirectly experiencing more than one trauma event were asked to indicate which event was most traumatic and distressing.

The PTSD Checklist for DSM-5 (PCL-5; Weathers et al., 2013) is a 20-item self-report measure that assesses *DSM-5* symptoms of PTSD. The PCL-5 was administered during the prescreening process to oversample individuals with probable PTSD diagnoses. PCL-5 items are rated on a 5-point Likert scale from 0 (*Not at all*) to 4 (*Extremely*). The PCL-5 total severity index is a sum of all scores ranging from 0 to 80. Scores exceeding 33 on the PCL-5 have been suggested as the cut-off indicative of a probable PTSD diagnosis in clinical populations (Bovin et al., 2016). The PCL-5 has strong psychometric properties as a self-report measure for assessing PTSD symptoms (Blevins, Weathers, Davis, Witte, & Domino, 2015; Bovin et al., 2016).

The Clinician Administered PTSD Scale-5 (CAPS-5; Weathers et al., 2013) is a structured clinical interview used to diagnose PTSD and assess PTSD symptom levels over the past month as defined by DSM-5 (APA, 2013). The CAPS-5 consists of 20 items rated on a 5-point Likert scale ranging from 0 (*Absent*) to 4 (*Extreme/Incapacitating*), with higher scores reflecting greater overall severity. These items directly correspond to DSM-5 diagnostic criteria for PTSD. To meet diagnostic criteria, participants must report a Criterion A traumatic event. Participants must also report sufficient symptoms across symptom clusters B-E (intrusions, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity clusters respectively). DSM-5 states that, to meet diagnostic criteria for PTSD, individuals must report the following symptoms: at least one symptom of intrusion, at least one symptom of avoidance, at least two

symptoms of negative alterations in cognitions and mood, and at least two symptoms of alterations in arousal and reactivity. The CAPS-5 has strong psychometric properties and is accepted by the field as the gold standard in PTSD assessment (Weathers, Keane, & Davidson, 2001). All CAPS-5 interviews were audio recorded and underwent interrater reliability ratings by a second trained graduate research assistant. Discrepancies were resolved by consensus in consultation with the principal investigator. Inter-rater reliability on the CAPS-5 as measured by the intraclass correlation coefficient for total severity score was excellent (.99).

The Anxiety Sensitivity Index-3 (ASI-3; Taylor et al., 2007) is an 18-item self-report questionnaire that measures fear of anxiety-related symptoms within three subscales: physical, social, and cognitive. Given the primary focus of the current study was to examine physical changes under stress, I was interested specifically in how anxiety related to physical reactions is related to physical changes under stress. For this reason, I used the physical concerns subscale of the ASI-3. Conversely the social items (e.g., It is important for me not to appear nervous) and cognitive items (e.g., When I have trouble thinking clearly, I worry there is something seriously wrong with me) do not measure sensitivity to changes in physiology and were deemed less relevant to the current study's aims. The physical subscale is six items, and specifically assesses fear of anxiety-related bodily sensations. Items are rated on a Likert scale from 0 (very little) to 4 (very much). The ASI-3 total severity index is a sum of all items ranging from 0 to 72 for the total scale and 0 to 24 for the physical subscale. The ASI-3 has been well validated and displays good psychometric properties in both non-clinical and clinical samples (Taylor

et al., 2007). Internal consistency of ASI physical concerns subscale was high (Cronbach's α = .80).

Cardiovascular Assessment was collected using the Mindware Hardware system and Biopac software for Windows (Biopac Systems, Inc., Aero Camino, CA). For heart rate and respiratory sinus arrhythmia recordings, three disposable electrodes filled with electrolyte paste were placed on the right clavicle, lower left rib, and lower right rib, in a Lead-II configuration. For pre-ejection period recordings, four paired impedance electrodes were placed bilaterally on the neck and torso. Heart rate was collected in beats per minute. Respiratory sinus arrhythmia was collected using HF-HRV, with the frequency band set to 0.12-0.40 Hz. Pre-ejection period was calculated as the time interval between the Q-peak and B-point on the ECG and cardiac impedance waveforms respectively. Baseline values were computed across an eight-minute baseline epoch. This epoch was divided into eight, 60 second segments. The MindWare suite of software (MindWare Technologies, Inc., Gahanna, OH) computed one average value for heart rate, respiratory sinus arrhythmia, and pre-ejection period for each 60 second segment of data collected for a total eight segments (i.e., baseline epoch). These eight values were then averaged using IBM SPSS Statistics version 23 (IBM, 2016) to create one baseline value for each cardiovascular measure. Internal consistency of baseline epochs across heart rate, respiratory sinus arrhythmia and pre-ejection period were excellent (Cronbach's αs = .99, .98, .98 respectively). Trauma script values were computed across the 60 second trauma script epoch, which consisted of only one segment; thus, Cronbach's alphas were not able to be computed for those epochs.

All data was saved to both the hard drive of a Windows computer and to a shared lab drive. The data was then cleaned using MindWare software. All data was first filtered through MindWare's artifact detection algorithms (i.e., MAD/MED and IBI check). Data were then manually checked by trained research assistants and further cleaned for any algorithm errors.

Procedures

Eligible participants completed informed consent and data collection procedures in two lab sessions across two days, usually occurring within one week of each other. A portion of these participants completed a third session at a later date for an unrelated study aim, but those data are not considered here. Prior to informed consent, participants first completed an online pre-screening questionnaire on Qualtrics to determine study eligibility. Probable PTSD diagnosis was assessed using the PCL-5. A PCL-5 cutoff was used to recruit approximately half of the sample likely to meet diagnosis for PTSD, and the other half likely to be trauma-exposed controls. Participants above the suggested cutoff for the PCL were also matched with participants below this cutoff by trauma type, to have an even distribution of trauma type across groups. Eligible participants then completed a brief phone screening interview with trained research assistants to verify that their most distressing trauma met DSM-5 Criterion A for PTSD. If the event did not qualify (e.g., a romantic breakup endorsed as an "other stressful event" on the LEC-5), then the participant was not recruited into the study.

On the first day, following informed consent, participants completed the CAPS-5 interview to determine PTSD diagnosis. This was administered by a trained graduate

research assistant. Participants then completed script writing tasks for a neutral event, that occurred around the same time as the trauma, and for their index trauma. Participants were given the following instructions for writing about their neutral event: "Describe the neutral situation. Please include such details as who was there, what you were doing, where you were, how things looked, what you heard, people's names, dates, etc. Please write things in the order they happened and include bodily experiences from the next page at the appropriate times." Participants were provided with a list of various bodily experiences (e.g., heart races, feel warm, stomach is in a knot, feel relaxed all over, etc.). Once the participant finished writing about the neutral event a graduate research assistant would review the script to ask any necessary clarifying questions or gather more detail.

Participants were then given the following instructions for writing about their trauma:

"Please write a description of your personal traumatic event. You will use the same event that we talked about previously, in the interview. Include in your description the bodily sensations you were aware of at the time. Include details such as where you were; what you were doing; what other people were involved; and what they did or what happened to them; and how you felt." Participants were provided with the same list of various bodily experiences. Once the participant finished writing about the trauma event a graduate research assistant would again review the script to ask any necessary clarifying questions or gather more detail.

Participants then completed several self-report forms, for purposes unrelated to the current study. The first study session concluded with a grounding exercise and check-

out interview to manage and assess for any study-related distress. Following the first session, graduate research assistants edited and recorded the scripts of the neutral and trauma event. All scripts were edited to be 60 seconds long and include at least three bodily experiences. Trauma events were occasionally edited down to focus on the most distressing part of the trauma.

Prior to the second appointment participants were provided the following instructions: “Twenty-four hours prior to your appointment times, please avoid medication for attention deficit hyperactive disorder (ADHD; such as Adderall or Ritalin), over-the-counter allergy or antihistamine medication (such as Benadryl), and the following medications: Atropine, Dramamine, Sominex, and Cogentin.” These medications were prohibited due to their influence on cardiovascular functioning. On the second day, participants first completed psychophysiological data collection. Trained research assistants connected participants to psychophysiological equipment. Once all sensors were placed, research assistants then checked sensor signals to ensure adequate signal. Participants were then provided instructions about the study procedures and asked to keep as still as possible throughout procedures.

Physiological data acquisition then began. Participants first completed baseline data collection for eight minutes (i.e., baseline epoch). Participants were instructed to sit quietly with their eyes closed. No audio stimuli were presented during this phase. Participants then completed a modified script-driven imagery task. Participants first completed 60 seconds of a neutral baseline epoch. A neutral script was included in the paradigm to see if participants had changes in cardiovascular reactivity in the presence of

any stimuli compared to the baseline epoch, in which no stimuli was presented. Participants listened to their neutral event for 60 seconds, played over an audio speaker. Participants then were asked to continue thinking about the event for 60 seconds, and finally were asked to stop thinking about the event and sit quietly for another 60 seconds. Participants then completed 60 seconds of trauma baseline epoch where no stimuli were presented. They then listened to their trauma event for 60 seconds (i.e., trauma script epoch) They then completed an eight-minute induction for purposes unrelated to the current study, in which they were instructed to think about the trauma or other topics. Participants were then asked to stop thinking about the induction prompts and sit quietly for another 60 seconds. Participants finally completed an eight-minute recovery epoch where they were again instructed to sit quietly with their eyes closed. No audio stimuli were presented during this final recovery phase. The current study only used the initial eight-minute baseline epoch and the 60 second trauma script epoch for analyses.

Participants then completed several self-report measures, including the ASI-3. The session concluded with participants again completing a grounding exercise and checkout interview with the experimenter to assess for study-related distress. Participants then received compensation for their time and were provided with referral information for mental health resources. The university's Institutional Review Board approved all study procedures.

Proposed Analyses

All analyses were completed in IBM SPSS Statistics version 23 (IBM, 2016). To test my hypotheses regarding psychophysiological differences in PTSD across distinct

cardiovascular measures at both baseline and trauma, I conducted separate repeated measures ANOVAs with "Group" (PTSD or non-PTSD) entered as a between-subjects variable and "Time" (baseline- or trauma-script) entered as within-subjects variables, for each cardiovascular measure (i.e., heart rate, pre-ejection period, respiratory sinus arrhythmia). I anticipated a significant two-way interaction between Group and Time. I then conducted follow-up independent and paired samples *t*-tests to decompose significant interaction effects. These analyses were used to test my hypotheses that at baseline the PTSD group would display higher resting heart rate, and lower pre-ejection period and respiratory sinus arrhythmia compared to controls. I hypothesized at stressor the PTSD group would display a greater increase in heart rate and greater decrease in pre-ejection period and respiratory sinus arrhythmia compared to controls.

The neutral script epoch was not evaluated as a secondary baseline measure due to the nature of some participants' neutral scripts. Neutral scripts were required to be events that happened around the same time as the trauma. On average, participants completed the study five years after trauma. Approximately 14 percent of participants completed the study 10 years or more after trauma. This extended time since trauma resulted in several participants having difficulty identifying a neutral event, and instead wrote about events more positive or humorous in nature (e.g., spending time with friends, high school graduation) or events mildly stressful in nature (e.g., school presentation, work presentation). Due to this variability in neutral events, I decided secondary analyses measuring changes from neutral script to trauma script was not warranted.

To test my hypothesis as to whether heightened physical anxiety sensitivity explains cardiovascular reactivity in PTSD, I again conducted separate repeated measures ANOVAs with "Group" (PTSD or non-PTSD) entered as a between-subjects variable and "Time" (baseline- or trauma-script) entered as within-subjects variables, for each cardiovascular measure (i.e., heart rate, pre-ejection period, respiratory sinus arrhythmia). With these ANOVAs I entered physical concerns ASI-3 subscale scores as a covariate to determine if anxiety sensitivity was related to cardiovascular reactivity while accounting for PTSD diagnosis.

Power Analysis

A power analysis was conducted prior to data analyses using G*Power 3.1 software. Preliminary data available in July 2019 was used to set the expected bivariate correlation from baseline to stressor among cardiovascular measures ($r = 0.75$). Power analysis was calculated conservatively estimating effect size $F = 0.10$, indicating a small effect. Power was set to the recommended 0.80, with $r = 0.75$, and the nonspherecity correction $\varepsilon = 1$ (i.e., assumes sphericity assumption is met). Output parameters indicated that a total sample of $n = 102$ was needed for power of 0.81. Given this power analysis, and the conservative estimate of a small effect size, our final sample size was adequately powered to detect the small to medium effects hypothesized in this project.

CHAPTER III

RESULTS

The full sample consisted of 121 participants (with $n = 53$ for PTSD and $n = 68$ for trauma-exposed controls). No specific segments or epochs of heart rate or respiratory sinus arrhythmia data were dropped due to messy data (i.e., no segments with >10% artifact correction). Analyses with pre-ejection period data consisted of a slightly smaller sample of 112 participants (with $n = 50$ for PTSD and $n = 62$ for trauma-exposed controls). This was due to several participants' pre-ejection period data being unusable due to poor dZ/dt wave signal or cardiovascular physiology differences. These participants were removed from pre-ejection period analyses.

Demographics

Table A1 displays more detailed demographic and health behavior information on this sample. The sample was predominantly female ($n = 99$, 82% of sample), and reflected a younger age demographic (M (SD) = 25.03(9.19)). The sample also most frequently reported their index trauma as a sexual assault ($n = 56$, 46.3% of sample). Chi-square tests and independent samples t-test indicated that there were no significant differences between the groups on demographic variables including gender, race/ethnicity, or age (χ^2's < 3, t's < 1, p's > .05). Group differences were also assessed on health behaviors known to influence cardiovascular functioning including caffeine use, cigarette/other nicotine use, exercise level. Chi-square tests and independent samples

t-test indicated that there were no significant differences between the groups on these health variables (χ^2*'s* < 1, *t*'s < 1, *p*'s > .05). There was a significant group difference on CAPS-5 sum scores ($t(119) = 14.93$, $p < .001$), with individuals in the PTSD group reporting more severe PTSD symptoms than trauma-exposed controls. Groups also differed on mean ASI-3 physical subscale scores, with PTSD having a greater mean score on the ASI-3 physical subscale compared to controls ($t(119) = 3.58$, $p = .001$), indicative of more severe anxiety sensitivity physical symptoms.

Medications and Substance Use

Table A2 displays current medication use both one week and 24 hours prior to physiological data collection. Two participants reported use of medications that were not part of study exclusion criteria but interfere with cardiovascular functioning (i.e., analgesic, benzodiazepine). These participants were still included in data analyses. To ensure this did not compromise study results, all analyses were re-run excluding these two participants. All results remained the same, barring one follow-up independent samples t-test measuring heart rate at trauma script.[1] Approximately seven percent of the sample reported alcohol or marijuana use 24 hours prior to physiological data collection (see Table A2). Participants were coded dichotomously based on their report of any substance use 24 hours prior to physiological data collection. Point biserial correlations were then run correlating substance use and cardiovascular measures (both at rest and

35

[1]Independent samples t-tests found that heart rate was marginally higher in the PTSD group compared to the control group during the trauma script ($t(119) = 1.91$, $p = .059$). This finding became significant ($t(117) = 2.01$, $p = .047$) after removing the two participants who had taken an analgesic and benzodiazepine 24 hours prior to psychophysiological data collection (see p. 35).

during stressor) to assess for any association between the variables. No correlations were significant (-.10 < *r*'s < .06, *p*'s > .05).

Cardiovascular Outcomes Repeated Measure ANOVAs

The primary goal of this dissertation was to examine psychophysiological differences in PTSD across distinct cardiovascular measures at both baseline and stress that assess general autonomic (i.e., heart rate), primarily sympathetic (i.e., pre-ejection period), and primarily parasympathetic (i.e., respiratory sinus arrhythmia) activity. It was predicted the PTSD group would display higher resting heart rate and lower pre-ejection period and respiratory sinus arrhythmia compared to controls. It was also predicted there would be larger reactivity in the PTSD group compared to controls across heart rate, pre-ejection period, and respiratory sinus arrhythmia. To test these hypotheses, separate repeated measures ANOVAs were conducted for each cardiovascular measure. Results demonstrated a significant interaction for heart rate, Group x Time ($F = 6.03$, $p = .015$, $\eta_p^2 = .05$; Table A4; Figure B1), with a significant main effect of Time ($F = 34.27$, $p = <.001$, $\eta_p^2 = .22$; Table A4). There was no interaction for respiratory sinus arrhythmia, Group x Time ($F = .86$, $p = .355$, $\eta_p^2 = .01$; Table A4; Figure B3), but was a main effect of Time ($F = 24.07$, $p = <.001$, $\eta_p^2 = .17$; Table A4), such that respiratory sinus arrhythmia decreased across both groups from baseline to trauma script. There was a marginally significant interaction for pre-ejection period, Group x Time ($F = 3.04$, $p = .084$, $\eta_p^2 = .03$; Table A4; Figure B2), and a main effect of Group ($F = 7.16$, $p = .009$, $\eta_p^2 = .06$; Table A4).

Cardiovascular Outcomes Follow-Up Tests

Pertaining to heart rate, follow-up paired sample *t*-tests found that heart rate significantly increased from baseline to trauma script for both PTSD ($t(52) = 4.65$, $p < .001$, $d = .64$) and trauma-exposed controls ($t(67) = 3.13$, $p = .003$, $d = .38$). Independent samples *t*-tests found that heart rate was not significantly different across groups at baseline ($t(119) = .64$, $p = .521$, $d = .12$) but was marginally higher in the PTSD group compared to the control group during the trauma script ($t(119) = 1.91$, $p = .059$, $d = .34$). This finding became significant ($t(117) = 2.01$, $p = .047$, $d = .36$) after removing the two participants who had taken an analgesic and benzodiazepine 24 hours prior to psychophysiological data collection. Follow-up independent samples *t*-test found pre-ejection period was lower in the PTSD group compared to trauma-exposed controls at both baseline ($t(110) = 2.13$, $p = .035$, $d = .40$) and trauma script ($t(110) = 2.10$, $p = .004$, $d = .54$). Paired samples *t*-tests found that change in pre-ejection period from baseline to trauma script was not significant in trauma-exposed controls ($t(61) = .57$, $p = .572$, $d = .07$), and was marginally significant in the PTSD group ($t(49) = 1.80$, $p = .079$, $d = .25$). A post-hoc repeated measures ANOVA was conducted examining respiratory sinus arrhythmia with baseline respiration rate entered as a covariate. There was a significant effect of respiration rate by time ($F = 4.80$, $p = .029$). The interaction between respiratory sinus arrhythmia and PTSD remained not significant with respiration rate entered as a covariate ($F = .98$, $p = .323$). Baseline respiration rate was significantly correlated with baseline respiratory sinus arrhythmia ($r = -.24$) but was not significantly correlated with trauma script respiratory sinus arrhythmia ($r = -.09$).

Baseline to Neutral Script Cardiovascular Outcomes

Post-hoc repeated measures ANOVA analyses were conducted examining changes in cardiovascular measures from baseline to neutral script to assess cardiovascular reactivity in the presence of any stimuli. There was no interaction for heart rate ($F = 1.44$, $p = .233$). There was also no interaction for respiratory sinus arrhythmia ($F = 0.02$, $p = .881$). However, there was a main effect on Time for respiratory sinus arrhythmia ($F = 7.16$, $p = .009$), with respiratory sinus arrhythmia decreasing significantly from baseline to neutral script across all participants. There was a marginal interaction found for pre-ejection period ($F = 3.32$, $p = .071$), and also a main effect of Group for pre-ejection period ($F = 7.10$, $p = .009$). Follow-up independent samples *t*-test found pre-ejection period was lower in the PTSD group compared to trauma-exposed controls at both baseline ($t(110) = 2.13$, $p = .035$, $d = .40$) at the neutral script ($t(110) = 2.95$, $p = .004$, $d = .55$).[2] Paired samples *t*-tests found that change in pre-ejection period from baseline to neutral script was marginal in trauma-exposed controls ($t(60) = 1.93$, $p = .058$, $d = .25$)[2], with pre-ejection period increasing from baseline to neutral script. Pre-ejection period did not change for the PTSD group from baseline to neutral script ($t(49) = .55$, $p = .585$, $d = .08$).

Anxiety Sensitivity Outcomes

The secondary goal of this dissertation was to examine whether anxiety sensitivity significantly contributes to cardiovascular reactivity in PTSD. It was predicted that greater physical concerns, as measured by the ASI-3 subscale, will account for more

38

[2] These results had one less trauma-exposed control included in analysis, as data was missing for neutral script.

pronounced cardiovascular reactivity across all psychophysiological measures (i.e., heart rate, pre-ejection period, respiratory sinus arrhythmia) over and above PTSD diagnosis. To test this hypothesis similar repeated measure ANOVAs were conducted for each cardiovascular measure, with time entered as the within-subjects variable, PTSD diagnosis entered as the between-subjects variable, and the physical concerns ASI-3 subscale scores entered as a covariate. Results were not significant across respiratory sinus arrhythmia ($F = 3.21$, $p = .076$), heart rate ($F = .32$, $p = .571$), and pre-ejection period ($F = .53$, $p = .470$; Table A5).

CHAPTER IV

DISCUSSION

The present study examined psychophysiological differences in PTSD across distinct cardiovascular measures at both baseline and stress that assess general autonomic (i.e., heart rate), primarily sympathetic (i.e., pre-ejection period), and primarily parasympathetic (i.e., respiratory sinus arrhythmia) activity. This study also examined whether anxiety sensitivity contributes to cardiovascular reactivity in PTSD. Heart rate was first examined to confirm a general cardiovascular response to stress. Contrary to my prediction, the PTSD group had a comparable resting heart rate at baseline compared to controls. PTSD and trauma-exposed control groups both displayed a significant increase in heart rate from baseline to stressor. There was also a significant interaction for heart rate, finding the PTSD group had a larger increase in heart rate compared to controls. This finding supported my hypothesis that the PTSD group would display greater heart rate reactivity under stress, suggesting heightened autonomic activity in PTSD. This finding also confirmed the experimental manipulation was effective in increasing cardiovascular activity.

Pre-ejection period results found a marginally significant interaction. As predicted, PTSD displayed a lower pre-ejection period at baseline compared to control groups. This suggests those with PTSD are experiencing greater sympathetic activation at rest compared to controls. There was a marginally significant interaction for pre-ejection

period reactivity. Pre-ejection period did not significantly change from baseline to stressor for trauma-exposed controls, suggesting no evidence of sympathetic nervous system activation in this group. The PTSD group displayed a marginally significant decrease in pre-ejection period from baseline to stress, suggesting possible evidence of even further sympathetic nervous system activation compared to baseline levels. This finding supports the hypothesis that the PTSD group would have lower baseline pre-ejection period. However, there is only marginal evidence to support the hypothesis that those with PTSD display a larger decrease in pre-ejection period during stress compared to controls.

Respiratory sinus arrhythmia results did not support hypotheses. There was no significant difference in baseline respiratory sinus arrhythmia between PTSD and control groups. Both groups displayed similar decreases in respiratory sinus arrhythmia during stress, suggesting similar parasympathetic responses. This finding suggests both groups are showing comparable parasympathetic withdrawal under stress, meaning sympathetic influences are more likely to have driven heightened heart rate reactivity in the PTSD group compared to controls.

Follow-up analyses found that baseline respiration rate is a significant covariate for change in respiratory sinus arrhythmia from baseline to stress across both groups. Specifically, respiration sinus arrhythmia reactivity is significantly different when accounting for baseline respiration rate. The bivariate correlation between baseline respiratory sinus arrhythmia and baseline respiration rate found that as respiration rate increases respiratory sinus arrhythmia decreases. This finding is consistent with past

literature (Hirsch & Bishop, 1981; Grossman & Taylor, 2007) and further suggests respiration rate significantly contributes to changes in respiratory sinus arrhythmia. The association emphasizes the importance in accounting for respiration rate when examining respiratory sinus arrhythmia.

In sum, the current study found evidence to support heightened heart rate reactivity in PTSD during stress. This study also found that individuals with PTSD have lower pre-ejection period than controls at baseline. There was no evidence to suggest respiratory sinus arrhythmia presented differently at either baseline or stress, suggesting the parasympathetic nervous system responds similarly in individuals with PTSD and controls. The marginal effect of pre-ejection period reactivity, paired with the null finding of similar respiratory sinus arrhythmia withdrawal across groups, suggests this difference in heart rate is more likely to be influenced by a heightened sympathetic nervous system response in PTSD. However, this interpretation of findings is reliant on significantly heightened reactivity for pre-ejection period for PTSD compared to controls, which was a marginal finding. Across baseline measures, only pre-ejection period was significantly different between groups, with the PTSD group displaying a lower pre-ejection period. This finding suggests pre-ejection period may be the best measure of baseline cardiovascular psychophysiology in PTSD, as the other measures of heart rate and respiratory sinus arrhythmia display similar psychophysiology across groups at baseline.

Anxiety sensitivity results found that the PTSD group did report higher levels of anxiety sensitivity compared to controls as measured from the physical concerns subscale of the ASI-3. However, there was no evidence to support that anxiety sensitivity

influences cardiovascular reactivity during stress. This finding suggests that levels of anxiety sensitivity are not likely to influence cardiovascular responses to stress in those with PTSD.

Limitations

There are a few limitations to note for this study. As required in the informed consent process, participants were aware they would be listening to scripts about their personal traumatic experience. It is reasonable to assume participants experienced some anticipatory anxiety during baseline data collection. This may have resulted in higher baseline cardiovascular recordings than what is reflective of the larger PTSD population. In this same vein, the trauma script paradigm was intended to induce anxiety in participants, and the ASI-3 was completed following the trauma script. It is possible that responses on the ASI-3 may have been higher than normal due to anxiety from the experimental paradigm.

Another limitation of this study's analytic approach is that the results do not directly compare the cardiovascular measures to each other. In other words, this study is not able to make conclusions as to whether the effect of respiratory sinus arrhythmia reactivity in PTSD is larger than effect of pre-ejection period in PTSD. Future research should seek to directly compare these measures in hopes of examining whether one has a significantly larger effect. We also could not make any causal conclusions pertaining to the role of anxiety sensitivity on cardiovascular reactivity in PTSD. Even though this study had null findings, we were unable to draw conclusions as to whether anxiety sensitivity is or is not a risk factor or result of heightened cardiovascular reactivity in

PTSD. Future longitudinal work should seek to understand potential causality in the relationship between anxiety sensitivity and cardiovascular reactivity.

Implications

The primary goal of this study was to better understand cardiovascular reactivity in PTSD by further understanding the influences of the sympathetic and parasympathetic nervous system during stress. This study found that general autonomic reactivity (i.e., heart rate) is heightened in PTSD compared to trauma-exposed controls. This study's null findings related to respiratory sinus arrhythmia suggests that parasympathetic withdrawal is not contributing differentially to changes in heart rate in those with PTSD compared to controls. With parasympathetic withdrawal acting similarly across groups, the difference in heart rate reactivity across groups would then be driven by sympathetic activation. The marginal finding for pre-ejection period decreasing in the PTSD group and not the control group, further suggests that heart rate reactivity is influenced more by the sympathetic nervous system in individuals with PTSD than in trauma-exposed controls. However, this should be interpreted cautiously because the effect for pre-ejection period was only marginally significant and was a small effect.

Clinical application of these findings are two-fold. First, the study adds to the literature demonstrating that heart rate reactivity is heightened in those with PTSD (Orr & Roth, 2000; Pole, 2007; Castro-Chapman et al., 2018). This suggests heart rate may be the most sensitive cardiovascular measure to stress in PTSD. This further suggests there may be clinical utility in recording heart rate during psychotherapy exposures to best measure levels of reactivity throughout treatment in those with PTSD. Clinicians could

track heart rate reactivity over the course of treatment and utilize heart rate as an additional treatment outcome measure alongside self-report and clinical interviews. Past studies have included heart rate markers for exposure therapy and have found these markers beneficial in tracking treatment progress, with heart rate reactivity decreasing alongside PTSD symptom self-report measures (Sack et al., 2007; Nishith, Griffen, & Weaver, 2002). Heart rate reactivity data could also be provided directly to clients as biofeedback of treatment progress. Other studies have found preliminary evidence to suggest biofeedback in addition to treatment as usual is effective in decreasing PTSD symptoms as compared to only treatment as usual (Tan, Dao, Farmer, Sutherland & Gevirtz, 2011).

Second, the finding that pre-ejection period is lower in PTSD compared to controls at rest suggests this measure may have the most clinical utility for baseline cardiovascular measures. Pre-ejection period was the only measure in this study that displayed a group difference at baseline. This study did not find baseline differences for heart rate or respiratory sinus arrhythmia. This contradicts some past literature that has found baseline differences for these measures in those with PTSD compared to control groups (Jovanovic et al., 2009; Hopper, Spinazzola, Simpson, & van der Kolk, 2006; Blechert, Michael, Grossman, Lajtman, & Wilhelm, 2007). However, this literature has been mixed with other studies finding no difference in heart rate (Rothbaum, Kozak, Foa, & Whitaker, 2001; Barkay et al., 2012) or respiratory sinus arrhythmia (Bertram et al., 2014; Kamkwalala et al., 2012) at baseline.

In order to suggest with more certainty that pre-ejection period is the best measure for resting cardiovascular psychophysiology in PTSD there needs to be replications of this finding. If future studies find the same baseline difference for pre-ejection period in PTSD, this measure could then be applied to treatment outcome research. Future treatment outcome research is needed to measure pre-ejection period at rest over time to see if pre-ejection period increases with improvement of PTSD symptoms. If future research finds this, clinicians could implement measuring pre-ejection period at rest over the course of treatment as a treatment outcome measure. It is important to note that these psychophysiological measures are not intended to replace clinical interview or self-report measures, as findings are too preliminary at this stage. However, study findings do support clinical implementation for measuring heart rate reactivity during stress and pre-ejection period at rest alongside more traditional PTSD symptom measures (i.e., clinical interviews, self-reports).

Future research should attempt to replicate this study's design to further confirm or refute cardiovascular reactivity differences between PTSD and control groups. Studies should specifically examine pre-ejection period reactivity. This study's finding was marginal; however, that result could become significant with increased statistical power. The preliminary power analyses indicated the current study was adequately powered to detect small effects, but replication to confirm or refute heightened pre-ejection period reactivity is still warranted due to the novel state of the literature examining pre-ejection period in PTSD.

The observed effect sizes for heart rate and pre-ejection period are also worth noting in regards to clinical implications. Heightened heart rate reactivity in PTSD had a medium effect ($\eta_p^2 = .05$), while marginal heightened pre-ejection period reactivity had a small to medium effect ($\eta_p^2 = .03$). This suggests heart rate may be more clinically useful given the larger effect size and the increased sensitivity of the measure during stress. However, as mentioned previously heart rate does not tease apart sympathetic versus parasympathetic influences on cardiovascular reactivity. For this reason, heart rate will not be a valuable measure for research studies attempting to isolate and understand specific branches of the autonomic nervous system. Instead heart rate may be better for research examining general cardiovascular reactivity in group differences. On the other hand, pre-ejection period can better allow for this isolation, but the evidence of heightened pre-ejection period reactivity is marginal, and the effect may be so small that only studies with large samples see group differences.

The question the field needs to consider is whether a small effect is still clinically valuable? Meta-analyses examining cardiovascular psychophysiology in PTSD are consistent in their findings of small effects (Pole, 2007; Morris, Hellman, Abelson, & Rao, 2016; Campbell, Wisco, Silvia, & Gay, 2019). Small effects are common when studying psychophysiology because there are numerous factors that can account for variance in any research design. The current study improved internal validity by accounting for some of these factors (e.g., medications, history of cardiovascular problems, etc.). However, it is impossible to account for all possible means of variance when working with human subjects. Despite small effects, there is still clinical value in

studying cardiovascular psychophysiology in PTSD. This work can help facilitate implementation of cardiovascular measures to track stress reactivity and treatment outcomes. These cardiovascular psychophysiological measures can offer more objective and concrete measurements for clients to track their own progress. Incorporating cardiovascular psychophysiological measures alongside clinical interviews and self-report measures may also help clients better understand mind-body connections and techniques incorporated into cognitive behavioral treatments (i.e., psychoeducation around how thoughts andfeelings influence psychophysiological response, reappraisal of stress reactivity).

This work also allows for a more nuanced understanding in sympathetic and parasympathetic influences on heart rate. This is valuable in further examining how sympathetic influences could account for increases in heart rate and their association with poor cardiovascular health in PTSD. Teasing apart sympathetic versus parasympathetic influences could also inform pharmacological interventions intended to block or influence sympathetic activity. Clinicians could also utilize relaxation strategies or biofeedback that have been found to improve sympathetic overactivation (Stone & DeLeo, 1976; Tan et al., 2011).

Given the limited number of studies incorporating both sympathetic and parasympathetic measures, future research is needed to further understand the relationship between the sympathetic and parasympathetic nervous system during stress in those with PTSD. Cohen and colleagues (2019) examined cardiovascular responses in children with PTSD and found that their measure of cardiac autonomic balance (i.e., the

reciprocal relationship between respiratory sinus arrhythmia and pre-ejection period) was associated with post-traumatic stress symptoms and distinguished children with PTSD from those without. The cardiac autonomic balance measure used was sympathetically-oriented (i.e., heightened pre-ejection period reactivity), but pre-ejection period reactivity on its own did not distinguish children with and without PTSD. The findings of this study suggests it may be beneficial to examine cardiac autonomic balance which incorporates both sympathetic and parasympathetic influences simultaneously as opposed to measuring each separately. Heightened sympathetic activation in PTSD could then be further explored to understand how the cardiovascular stress response may be tied to problems like hypertension and cardiovascular disease. This work could ultimately inform psychotherapy and medical treatment to improve cardiovascular health in people with PTSD.

The current study did find that physical concerns, as measured through the ASI-3 subscale, were higher in those with PTSD. However, anxiety sensitivity did not contribute to any cardiovascular reactivity measure. This finding suggests it may be worthwhile for clinicians to measure anxiety sensitivity in clients with PTSD. Given the previous literature suggesting the bidirectional relationship between PTSD and anxiety sensitivity (Marshall et al., 2010), it may also be beneficial for treatment to target anxiety sensitivity in order to improve PTSD symptoms. However, it is unlikely that anxiety sensitivity is contributing to cardiovascular reactivity. Therefore, improving anxiety sensitivity in clients with PTSD is unlikely to facilitate improved cardiovascular reactivity. This this is not to say anxiety sensitivity does not influence client's subjective

distress levels during treatment. Clinicians should still measure anxiety sensitivity levels and determine whether techniques to improve anxiety sensitivity (i.e., interoceptive exposures) could be a target of treatment. Future research may also want to examine anxiety related to physical changes during stressor tasks more directly. It may be beneficial for participants to rate their anxiety to physical changes happening throughout stressor paradigms and see how that type of self-report maps onto cardiovascular reactivity. This may be a better way of capturing anxiety sensitivity to cardiovascular changes as opposed to the ASI-3 subscale.

Summary

The purpose of this study was to examine cardiovascular reactivity during stress in PTSD, and specifically better understand how the sympathetic and parasympathetic nervous system influence this response. The study found that those with PTSD have higher heart rate reactivity compared to controls. This heightened heart rate reactivity in PTSD was more likely to be driven by sympathetic activation as opposed to parasympathetic withdrawal. The study also found those with PTSD have lower pre-ejection period at baseline compared to controls, suggesting pre-ejection period may be the best measure of resting cardiovascular psychophysiology in PTSD. Finally, this study sought to understand whether anxiety sensitivity contributes to cardiovascular reactivity. There was no evidence to suggest anxiety sensitivity can predict cardiovascular reactivity. However, anxiety sensitivity pertaining to physical changes was higher in those with PTSD compared to controls.

In sum, study findings support heightened heart rate reactivity in PTSD is more likely influenced by sympathetic activation. Treatment outcome research should further examine heart rate reactivity during stress and pre-ejection period at rest over the course of treatment. Future research should also continue to examine pre-ejection period reactivity, both individual and in conjunction with parasympathetic measures in PTSD, in hopes of further understanding sympathetic activation influences on cardiovascular reactivity.

REFERENCES

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. American Psychiatric Pub.

American Psychiatric Association. (1980). *DSM-III-R: Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association.

Arditi-Babchuk, H., Feldman, R., & Gilboa-Schechtman, E. (2009). Parasympathetic reactivity to recalled traumatic and pleasant events in trauma-exposed individuals. *Journal of Traumatic Stress: Official Publication of The International Society for Traumatic Stress Studies*, *22*(3), 254-257. doi: 10.1002/jts.20417.

Asmundson, G. J. G., Norton, G. R., Wilson, K. G., & Sandler, L. S. (1994). Subjective symptoms and cardiac reactivity to brief hyperventilation in individuals with high anxiety sensitivity. *Behaviour Research and Therapy*, *32*(2), 237. doi: 10.1016/0005-7967(94)90117-1.

Asmundson, G. J., & Stein, M. B. (1994). Vagal attenuation in panic disorder: an assessment of parasympathetic nervous system function and subjective reactivity to respiratory manipulations. *Psychosomatic Medicine, 53*(3), 187-193. doi: 10.1097/00006842-199405000-00002.

Asmundson, G. J., & Stapleton, J. A. (2008). Associations between dimensions of anxiety sensitivity and PTSD symptom clusters in active-duty police officers. *Cognitive Behaviour Therapy*, *37*(2), 66-75. doi: 10.1080/16506070801969005.

Barkay, G., Freedman, N., Lester, H., Louzoun, Y., Sapoznikov, D., Luckenbaugh, D., Shalev, A.Y., Chisin, R.G., & Bonne, O. (2012). Brain activation and heart rate during script-driven traumatic imagery in PTSD: Preliminary findings. Psychiatry Research: Neuroimaging, 204(2-3), 155-160. doi:10.1016/j.psychresns.2012.08.007.

Becker, C. B., & Zayfert, C. (2001). Integrating DBT-based techniques and concepts to facilitate exposure treatment for PTSD. *Cognitive and Behavioral Practice*, *8*(2), 107-122. doi: 10.1016/s1077-7229(01)80017-1.

Berenz, E. C., Vujanovic, A. A., Coffey, S. F., & Zvolensky, M. J. (2012). Anxiety sensitivity and breath-holding duration in relation to PTSD symptom severity among trauma exposed adults. *Journal of Anxiety Disorders, 26*(1), 134-139. doi: 10.1016/j.janxdis.2011.10.004.

Berntson, G. G., Bigger, J. T., Eckberg, D. L., Grossman, P., Kaufmann, P. G., Malik, M., ... & Van Der Molen, M. W. (1997). Heart rate variability: origins, methods, and interpretive caveats. *Psychophysiology*, *34*(6), 623-648. doi: 10.1111/j.1469-8986.1997.tb02140.x.

Berntson, G.G., Cacioppo, J.T., & Quigley, K.S. (1993). Cardiac psychophysiology and autonomic space in humans: empirical perspectives and conceptual implications. *Psychological Bulletin, 114*(2), 296-232. doi: 10.1037/0033-2909.114.2.296.

Berntson, G. G., Cacioppo, J. T., & Quigley, K. S. (1991). Autonomic determinism: the modes of autonomic control, the doctrine of autonomic space, and the laws of autonomic constraint. *Psychological Review*, *98*(4), 459-487. doi: 10.1037/0033-295X.98.4.459.

Berntson, G. G., Quigley, K. S., & Lozano, D. (2007). Cardiovascular psychophysiology. *Handbook of Psychophysiology,* 3, 182-210. doi: 10.1017/CBO9780511546396.008.

Bertram, F., Jamison, A. L., Slightam, C., Kim, S., Roth, H. L., & Roth, W. T. (2014). Auton arousal during actigraphically estimated waking and sleep in male veterans with PTSD. *Journal of Traumatic Stress*, *27*(5), 610–617. doi: 10.1002/jts.21947.

Bisson, J. I., Roberts, N. P., Andrew, M., Cooper, R., & Lewis, C. (2013). Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults. *Cochrane Database of Systematic Reviews*, (12). doi: 10.1002/14651858.cd003388.pub4.

Blanchard, E. B., Hickling, E. J., Buckley, T. C., Taylor, A. E., Vollmer, A., & Loos, W. R. (1996). Psychophysiology of posttraumatic stress disorder related to motor vehicle accidents: replication and extension. *Journal of Consulting and Clinical psychology*, *64*(4), 742. doi: 10.1037/0022-006X.64.4.742.

Blascovich, J. J., & Katkin, E. S. (1993). *Cardiovascular Reactivity to Psychological Stress & Disease*. American Psychological Association. doi: 10.1037/10125-000.

Blechert, J., Michael, T., Grossman, P., Lajtman, M., & Wilhelm, F. H. (2007). Autonomic and respiratory characteristics of posttraumatic stress disorder and panic disorder. *Psychosomatic Medicine*, *69*(9), 935–943. doi: 10.1097/PSY.0b013e31815a8f6b.

Blevins, C.A., Weathers, F.W., Davis, M.T., Witte, T.K., & Domino, J.L. (2015). The posttraumatic stress disorder checklist for DSM-5 (PCL-5): Development and initial psychometric evaluation. *Journal of Traumatic Stress, 28*(6), 489-498. doi:10.1002/jts.22059.

Bornas, X., Llabrés, J., Noguera, M., López, A. M., Barceló, F., Tortella-Feliu, M., & Fullana, M. A. (2005). Looking at the heart of low and high heart rate variability fearful flyers: self-reported anxiety when confronting feared stimuli. *Biological Psychology*, *70*(3), 182-187. doi: 10.1016/j.biopsycho.2005.01.002.

Boscarino, J. A., & Chang, J. (1999). Electrocardiogram abnormalities among men with stress-related psychiatric disorders: implications for coronary heart disease and clinical research. *Annals of Behavioral Medicine*, *21*(3), 227-234. doi: 10.1007/BF02884839.

Bovin, M.J., Marx, B.P., Weathers, F.W., Gallagher, M.W., Rodriguez, P…, & Keane, T.M. (2016). Psychometric properties of the PTSD checklist for diagnostic and statistical manual of mental disorders-fifth edition (PCL-5) in veterans. *Psychological Assessment, 28*(11), 1379-1391. doi: 10.1037/pas0000254.

Bradley, R., Greene, J., Russ, E., Dutra, L., & Westen, D. (2005). A multidimensional meta-analysis of psychotherapy for PTSD. *American Journal of Psychiatry*, *162*(2), 214-227. doi: 10.1176/appi.ajp.162.2.214.

Breuninger, C., Sláma, D. M., Krämer, M., Schmitz, J., & Tuschen-Caffier, B. (2017). Psychophysiological reactivity, interoception and emotion regulation in patients with agoraphobia during virtual reality anxiety induction. *Cognitive Therapy and Research*, *41*(2), 193-205. doi: 10.1007/s10608-016-9814-9.

Brown, T. A., Chorpita, B. F., & Barlow, D. H. (1998). Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *Journal of Abnormal Psychology*, *107*(2), 179. doi: 10.1037/0021-843X.107.2.179.

Burker, E. J., Fredrikson, M., Rifai, N., Siegel, W., & Blumenthal, J. A. (1994). Serum lipids, neuroendocrine, and cardiovascular responses to stress in men and women with mild hypertension. *Behavioral Medicine*, *19*(4), 155-161. doi: 10.1080/08964289.1994.9935186.

Burckhardt, D., Raeder, E., Müller, V., Imhof, P., & Neubauer, H. (1978). Cardiovascular effects of tricyclic and tetracyclic antidepressants. *JAMA*, *239*(3), 213-216. doi: 10.1001/jama.1978.03280300045019.

Busscher, B., Spinhoven, P., van Gerwen, L. J., & de Geus, E. J. (2013). Anxiety sensitivity moderates the relationship of changes in physiological arousal with flight anxiety during in vivo exposure therapy. *Behaviour Research and Therapy, 51*(2), 98-105. doi: 10.1016/j.brat.2012.10.009.

Cacioppo, J. T., Berntson, G. G., Binkley, P. F., Quigley, K. S., Uchino, B. N., & Fieldstone, A. (1994). Autonomic cardiac control. II. Noninvasive indices and basal response as revealed by autonomic blockades. *Psychophysiology*, *31*(6), 586-598. doi: 10.1111/j.1469-8986.1994.tb02352.x.

Campbell, A. A., Wisco, B. E., Silvia, P. J., & Gay, N. G. (2019). Resting respiratory sinus arrhythmia and posttraumatic stress disorder: A meta-analysis. *Biological Psychology*, *144*, 125–135. doi: 10.1016/j.biopsycho.2019.02.005.

Castro-Chapman, P. L., Orr, S. P., Berg, J., Pineles, S. L., Yanson, J., & Salomon, K. (2018). Heart rate reactivity to trauma-related imagery as a measure of PTSD symptom severity: examining a new cohort of veterans. *Psychiatry Research*, *261*, 574-580. doi: 10.1016/j.psychres.2018.01.024.

Cohen, J. R., Thomsen, K. N., Tu, K. M., Thakur, H., McNeil, S., & Menon, S. V. (2019). Cardiac autonomic functioning and post-traumatic stress: A preliminary study in youth at-risk for PTSD. *Psychiatry Research, 284*. doi: 10.1016/j.psychres.2019.112684.

Coughlin, S. S. (2011). Post-traumatic stress disorder and cardiovascular disease. *The Open Cardiovascular Medicine Journal*, *5*, 164. doi: 10.2174/1874192401105010164.

Craske, M. G., Rauch, S. L., Ursano, R., Prenoveau, J., Pine, D. S., & Zinbarg, R. E. (2011). What is an anxiety disorder? *Depression and Anxiety*, *26*, 1066-1085. doi: 10.1002/da.20633.

D'Andrea, W., & Pole, N. (2012). A naturalistic study of the relation of psychotherapy process to changes in symptoms, information processing, and physiological activity in complex trauma. *Psychological Trauma: Theory, Research, Practice, and Policy*, *4*(4), 438. doi: 10.1037/a0025067.

Diamond, A. E., & Fisher, A. J. (2017). Comparative autonomic responses to diagnostic interviewing between individuals with GAD, MDD, SAD and healthy controls. *Frontiers in Human Neuroscience*, *10*, 677. doi: 10.3389/fnhum.2016.00677.

Fetzner, M. G., Collimore, K. C., Carleton, R. N., & Asmundson, G. J. (2012). Clarifying the relationship between AS dimensions and PTSD symptom clusters: are negative and positive affectivity theoretically relevant constructs? *Cognitive Behaviour Therapy*, *41*(1), 15-25. doi: 10.1080/16506073.2011.621971.

Fisher, A. J., & Newman, M. G. (2013). Heart rate and autonomic response to stress after experimental induction of worry versus relaxation in healthy, high-worry, and generalized anxiety disorder individuals. *Biological Psychology*, *93*(1), 65-74. doi: 10.1016/j.biopsycho.2013.01.012.

Foa, E. B., & Rothbaum, B. O. (1998). *Treating the Trauma of Rape.* New York: Guilford Press.

Friedman, B. H., & Thayer, J. F. (1998). Anxiety and autonomic flexibility: a cardiovascular approach. *Biological Psychology*, *47*(3), 243-263. doi: 10.1016/S0301-0511(98)00051-9.

Gaebler, M., Daniels, J. K., Lamke, J. P., Fydrich, T., & Walter, H. (2013). Heart rate variability and its neural correlates during emotional face processing in social anxiety disorder. *Biological Psychology*, *94*(2), 319-330. doi: 10.1016/j.biopsycho.2013.06.009

Gotlib, I. H., & Cane, D. B. (1989). Self-report assessment of depression and anxiety. In P. C. Kendall & D. Watson (Eds.), *Personality, psychopathology, and psychotherapy. Anxiety and depression: Distinctive and overlapping features* (pp. 131-169). San Diego, CA, US: Academic Press.

Grossman, P., & Taylor, E.W. (2007). Toward understanding respiratory sinus arrhythmia: Relations to cardiac vagal tone, evolution, and biobehavioral functions. *Biological Psychology, 74,* 263-285. doi: 10.1016/j.biopsycho.2005.11.014.

Grossman, P., Wilhelm, F. H., Kawachi, I., & Sparrow, D. (2001). Gender differences in psychophysiological responses to speech stress among older social phobics: congruence and incongruence between self-evaluative and cardiovascular reactions. *Psychosomatic Medicine*, *63*(5), 765-777. doi: 10.1097/00006842-200109000-00010.

Hammel, J. C., Smitherman, T. A., McGlynn, F. D., Mulfinger, A. M., Lazarte, A. A., & Gothard, K.D. (2011). Vagal influence during worry and cognitive challenge. *Anxiety, Stress, & Coping*, *24*(2), 121-136. doi: 10.1080/10615806.2010.490912.

Harris, W. S., Schoenfeld, C. D., & Weissler, A. M. (1967). Effects of adrenergic receptor activation and blockade on the systolic preejection period, heart rate, and arterial pressure in man. *The Journal of Clinical Investigation*, *46*(11), 1704-1714. doi: 10.1172/JCI105661.

Hauschildt, M., Peters, M. J., Moritz, S., & Jelinek, L. (2011). Heart rate variability in response to affective scenes in posttraumatic stress disorder. *Biological Psychology*, *88*(2-3), 215-222. doi: 10.1016/j.biopsycho.2011.08.004.

Hirsch, J. A., & Bishop, B. (1981). *Respiratory sinus arrhythmia (RSA) in man: Altered inspired O2 and CO2.* Budapest: Pergamon Press.

Hopper, J. W., Spinazzola, J., Simpson, W. B., & van der Kolk, B. A. (2006). Preliminary evidence of parasympathetic influence on basal heart rate in posttraumatic stress disorder. *Journal of Psychosomatic Research*, *60*(1), 83–90. doi: 10.1016/j.jpsychores.2005.06.002.

Johnsen, G. E., Kanagaratnam, P., Nordling, T., Wilberg, C., & Asbjørnsen, A. E. (2017). Psychophysiological responses to an executive task in refugees with chronic PTSD and comorbid depression. *Nordic Psychology*, *69*(3), 177-194. doi: 10.1080/19012276.2016.1245157.

Jovanovic, T., Norrholm, S. D., Sakoman, A. J., Esterajher, S., & Kozarić-Kovačić, D. (2009). Altered resting psychophysiology and startle response in Croatian combat veterans with PTSD. *International Journal of Psychophysiology*, *71*(3), 264-268. doi: 10.1016/j.ijpsycho.2008.10.007.

Kamkwalala, A., Norrholm, S. D., Poole, J. M., Brown, A., Donley, S., Duncan, E., Bradley, B., Ressler, K. J., & Jovanovic, T. (2012). Dark-enhanced startle responses and heart rate variability in a traumatized civilian sample: Putative sex-specific correlates of posttraumatic stress disorder. *Psychosomatic Medicine*, *74*(2), 153–159. doi: 10.1097/PSY.0b013e318240803a.

Kibler, J. L. (2009). Posttraumatic stress and cardiovascular disease risk. *Journal of Trauma & Dissociation*, *10*(2), 135-150. doi: 10.1080/15299730802624577.

Kikuchi, M., Hanaoka, A., Kidani, T., Remijn, G. B., Minabe, Y., Munesue, T., & Koshino, Y. (2009). Heart rate variability in drug-naive patients with panic disorder and major depressive disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *33*(8), 1474-1478. doi: 10.1016/j.pnpbp.2009.08.002.

Kircanski, K., Waugh, C. E., Camacho, M. C., & Gotlib, I. H. (2016). Aberrant parasympathetic stress responsivity in pure and co-occurring major depressive disorder and generalized anxiety disorder. *Journal of Psychopathology and Behavioral Assessment*, *38*(1), 5-19. doi: 10.1007/s10862-015-9493-y.

Kotianova, A., Kotian, M., Slepecky, M., Chupacova, M., Prasko, J., & Tonhajzerova, I. (2018). The differences between patients with panic disorder and healthy controls in psychophysiological stress profile. *Neuropsychiatric Disease and Treatment*, *14*, 435-441. doi: 10.2147/NDT.S153005.

Krantz, D. S., & Manuck, S. B. (1984). Acute psychophysiologic reactivity and risk of cardiovascular disease: a review and methodologic critique. *Psychological Bulletin*, *96*(3), 435. doi: 10.1037/0033-2909.96.3.435.

La Rovere, M. T., Pinna, G. D., & Raczak, G. (2008). Baroreflex sensitivity: measurement and clinical implications. *Annals of Noninvasive Electrocardiology*, *13*(2), 191-207. doi: 10.1111/j.1542-474X.2008.00219.x.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1998). Emotion, motivation, and anxiety: Brain mechanisms and psychophysiology. *Biological Psychiatry, 44*, 1248–1263. doi: 10.1016/S0006-3223(98)00275-3.

Levine, J.C., Fleming, R., Piedmont, J.I., Cain, S.M., & Chen, W.J. (2016). Heart rate variability and generalized anxiety disorder during laboratory-induced worry and aversive imagery. *Journal of Affective Disorders*, *205*, 207-215. doi: 10.1016/j.jad.2016.07.019.

Levy, M. N., & Warner, M. R. (1994). Parasympathetic effects on cardiac function. *Neurocardiology,* 53-76.

Lewis, R. P., Leighton, R. F., Forester, W. F., & Weissler, A. M. Systolic time intervals, In A. M. Weissler(Ed.), *Noninvasive Cardiology*. New York: Grune and Stratton, 1974. Pp. 301-369.

Licht, C. M., de Geus, E. J., van Dyck, R., & Penninx, B. W. (2010). Longitudinal evidence for unfavorable effects of antidepressants on heart rate variability. *Biological Psychiatry*, *68*(9), 861-868. doi: 10.1016/j.biopsych.2010.06.032.

Llera, S. J., & Newman, M. G. (2010). Effects of worry on physiological and subjective reactivity to emotional stimuli in generalized anxiety disorder and nonanxious control participants. *Emotion*, *10*(5), 640. doi: 10.1037/a0019351.

Malik, M., Bigger, J. T., Camm, A. J., Kleiger, R. E., Malliani, A., Moss, A. J., & Schwartz, P. J. (1996). Heart rate variability: Standards of measurement, physiological interpretation, and clinical use. *European Heart Journal*, *17*(3), 354-381. doi: 10.1093/oxfordjournals.eurheartj.a014868.

Marshall, G. N., Miles, J. N., & Stewart, S. H. (2010). Anxiety sensitivity and PTSD symptom severity are reciprocally related: Evidence from a longitudinal study of physical trauma survivors. *Journal of Abnormal Psychology*, *119*(1), 143. doi: 10.1037/a0018009.

McCorry, L. K. (2007). Physiology of the autonomic nervous system. *American Journal of Pharmaceutical Education*, *71*(4), 78. doi: 10.5688/aj710478.

Meeten, F., Davey, G. C., Makovac, E., Watson, D. R., Garfinkel, S. N., Critchley, H. D., & Ottaviani, C. (2016). Goal directed worry rules are associated with distinct patterns of amygdala functional connectivity and vagal modulation during perseverative cognition. *Frontiers in Human Neuroscience*, *10*, 553. doi: 10.3389/fnhum.2016.00553.

Metzger, L. J., Orr, S. P., Berry, N. J., Ahern, C. E., Lasko, N. B., & Pitman, R. K. (1999). Physiologic reactivity to startling tones in women with posttraumatic stress disorder. *Journal of Abnormal Psychology, 108*, 347–352. doi: 10.1037/0021-843X.108.2.347.

Meyer, T., Albrecht, J., Bornschein, G., Sachsse, U., & Herrmann-Lingen, C. (2016). Posttraumatic stress disorder (PTSD) patients exhibit a blunted parasympathetic response to an emotional stressor. *Applied Psychophysiology and Biofeedback*, *41*(4), 395-404. doi: 10.1007/s10484-016-9341-1.

Morris, M. C., Hellman, N., Abelson, J. L., & Rao, U. (2016). Cortisol, heart rate, and blood pressure as early markers of PTSD risk: A systematic review and meta-analysis. *Clinical Psychology Review*, *49*, 79–91. doi: 10.1016/j.cpr.2016.09.00.

Newlin, D. B., & Levenson, R. W. (1979). Pre-ejection period: Measuring beta-adrenergic influences upon the heart. *Psychophysiology*, *16*(6), 546-552. doi: 10.1111/j.1469-8986.1979.tb01519.

Nishith, P., Griffin, M. G., & Weaver, T. L. (2002). Utility of the heart rate response as an index of emotional processing in a female rape victim with posttraumatic stress disorder. *Cognitive and Behavioral Practice*, *9*(4), 302-307. doi: 10.1016/S1077-7229(02)80024-4.

Norte, C. E., Souza, G. G. L., Vilete, L., Marques-Portella, C., Coutinho, E. S. F., Figueira, I., & Volchan, E. (2013). They know their trauma by heart: an assessment of psychophysiological failure to recover in PTSD. *Journal of Affective Disorders*, *150*(1), 136-141. doi: 10.1016/j.jad.2012.11.039.

Olatunji, B. O., Armstrong, T., Fan, Q., & Zhao, M. (2014). Risk and resiliency in posttraumatic stress disorder: Distinct roles of anxiety and disgust sensitivity. *Psychological Trauma: Theory, Research, Practice, and Policy*, *6*(1), 50. doi: 10.1037/a0029682.

Olatunji, B. O., & Wolitzky-Taylor, K. B. (2009). Anxiety sensitivity and the anxiety disorders: a meta-analytic review and synthesis. *Psychological Bulletin*, *135*(6), 974. doi: 10.1037/a0017428.

Orr, S. P., & Roth, W. T. (2000). Psychophysiological assessment: Clinical applications for PTSD. *Journal of Affective Disorders*, *61*(3), 225-240. doi: 10.1016/S0165-0327(00)00340-2.

Ottaviani, C., Watson, D. R., Meeten, F., Makovac, E., Garfinkel, S. N., & Critchley, H. D. (2016). Neurobiological substrates of cognitive rigidity and autonomic inflexibility in generalized anxiety disorder. *Biological Psychology*, *119*, 31-41. doi: 10.1016/j.biopsycho.2016.06.009.

Pelcovitz, D., Van der Kolk, B., Roth, S., Mandel, F., Kaplan, S., & Resick, P. (1997). Development of a criteria set and a structured interview for disorders of extreme stress (SIDES). *Journal of Traumatic Stress*, *10*(1), 3-16. doi: 10.1023/A:1024800212070.

Peterson, R. A., & Reiss, S. (1992). *Anxiety Sensitivity Index*. Lawrence Erlbaum Associates.

Petrowski, K., Wichmann, S., Siepmann, T., Wintermann, G. B., Bornstein, S. R., & Siepmann, M. (2017). Effects of mental stress induction on heart rate variability in patients with panic disorder. *Applied Psychophysiology and Biofeedback*, *42*(2), 85-94. doi: 10.1007/s10484-016-9346-9.

Pitman, R. K., Shalev, A. Y., & Orr, S. P. (2000). Posttraumatic stress disorder: Emotion, conditioning, and memory. *The New Cognitive Neurosciences*, *2*, 1133-1147.

Pole, N. (2007). The psychophysiology of posttraumatic stress disorder: a meta-analysis. *Psychological Bulletin*, *133*(5), 725. doi: 10.1037/0033-2909.133.5.725.

Porges, S. W. (1995). Orienting in a defensive world: Mammalian modifications of our evolutionary heritage. A polyvagal theory. *Psychophysiology*, *32*(4), 301-318. doi: 10.1111/j.1469-8986.1995.tb01213.x.

Rabellino, D., D'Andrea, W., Siegle, G., Frewen, P. A., Minshew, R., Densmore, M., ... & Lanius, R. A. (2017). Neural correlates of heart rate variability in PTSD during sub-and supraliminal processing of trauma-related cues. *Human Brain Mapping*, *38*(10), 4898-4907. doi: 10.1002/hbm.23702.

Reiss, S., & McNally, R.J. (1985). The expectancy model of fear. In S. Reiss & R. R. Bootzin (Eds.), *Theoretical Issues in Behavior Therapy* (pp. 107-121). NY: Academic Press.

Roberts, N. A., Burleson, M. H., Weber, D. J., Larson, A., Sergeant, K., Devine, M. J., ... & Wang, N. C. (2012). Emotion in psychogenic nonepileptic seizures: responses to affective pictures. *Epilepsy & Behavior*, *24*(1), 107-115. doi: 10.1016/j.yebeh.2012.03.018.

Rothbaum, B. O., Kozak, M. J., Foa, E. B., & Whitaker, D. J. (2001). Posttraumatic stress disorder in rape victims: Autonomic habituation to auditory stimuli. *Journal of Traumatic Stress*, *14*(2), 283–293. doi: 10.1023/A:1011160800958.

Rottenberg, J. (2007). Cardiac vagal control in depression: a critical analysis. *Biological Psychology, 74*(2), 200-211. doi: 10.1016/j.biopsycho.2005.08.010.

Sack, M., Lempa, W., & Lamprecht, F. (2007). Assessment of psychophysiological stress reactions during a traumatic reminder in patients treated with EMDR. *Journal of EMDR Practice and Research*, *1*(1), 15-23. doi: 10.1891/1933-3196.1.1.15.

Sack, M., Lempa, W., Steinmetz, A., Lamprecht, F., & Hofmann, A. (2008). Alterations in autonomic tone during trauma exposure using eye movement desensitization and reprocessing (EMDR)—results of a preliminary investigation. *Journal of Anxiety Disorders*, *22*(7), 1264-1271. doi: 10.1016/j.janxdis.2008.01.007.

Sahar, T., Shalev, A. Y., & Porges, S. W. (2001). Vagal modulation of responses to mental challenge in posttraumatic stress disorder. *Biological Psychiatry*, *49*(7), 637-643. doi: 10.1016/S0006-3223(00)01045-3.

Schmidt, N. B., Santiago, H. T., & Wernicke, R. (2001). Evaluating the etiology of anxiety sensitivity: Relation to cardiovascular perception and reactivity. *Journal of Psychopathology and Behavioral Assessment*, *23*(2), 85-92.

Schottenbauer, M. A., Glass, C. R., Arnkoff, D. B., Tendick, V., & Gray, S. H. (2008). Nonresponse and dropout rates in outcome studies on PTSD: Review and methodological considerations. *Psychiatry: Interpersonal and Biological Processes*, *71*(2), 134-168. doi: 10.1521/psyc.2008.71.2.134.

Shinba, T. (2017). Major depressive disorder and generalized anxiety disorder show different autonomic dysregulations revealed by heart-rate variability analysis in first-onset drug-naïve patients without comorbidity. *Psychiatry and Clinical Neurosciences*, *71*(2), 135-145. doi: 10.1111/pcn.12494.

Simon, E., Meuret, A. E., & Ritz, T. (2017). Sympathetic and parasympathetic cardiac responses to phobia-relevant and disgust-specific emotion provocation in blood-injection-injury phobia with and without fainting history. *Psychophysiology*, *54*(10), 1512-1527. doi: 10.1111/psyp.12900.

Stewart, S. H., Buffett-Jerrott, S. E., & Kokaram, R. (2001). Heartbeat awareness and heart rate reactivity in anxiety sensitivity: A further investigation. *Journal of Anxiety Disorders*, *15*(6), 535-553. doi: 10.1016/s0887-6185(01)00080-9.

Stewart, S. H., & Pihl, R. O. (1994). Effects of alcohol administration on psychophysiological and subjective-emotional responses to aversive stimulation in anxiety-sensitive women. *Psychology of Addictive Behaviors*, *8*(1), 29. doi: 10.1037/0893-164x.8.1.29.

Stone, R. A., & De Leo, J. (1976). Psychotherapeutic control of hypertension. *New England Journal of Medicine, 294*(2), 80-84. doi: 10.1056/NEJM197601082940204.

Sturges, L. V., & Goetsch, V. L. (1996). Psychophysiological reactivity and heartbeat awareness in anxiety sensitivity. *Journal of Anxiety Disorders*, *10*(4), 283-294. doi: 10. 1016/0887-6185(96)00012-6.

Tan, G., Dao, T. K., Farmer, L., Sutherland, R. J., & Gevirtz, R. (2011). Heart rate variability (HRV) and posttraumatic stress disorder (PTSD): A pilot study. *Applied Psychophysiology and Biofeedback*, *36*(1), 27-35. doi: 10.1007/s10484-010-9141-y.

Taylor, S. (2003). Anxiety sensitivity and its implications for understanding and treating PTSD. *Journal of Cognitive Psychotherapy, 17*(2), 179–186. doi:10.1891/088983903780906147.

Taylor, S., Zvolensky, M. J., Cox, B. J., Deacon, B., Heimberg, R. G., Ledley, D. R., ... & Coles, M. (2007). Robust dimensions of anxiety sensitivity: development and initial validation of the Anxiety Sensitivity Index-3. *Psychological Assessment*, *19*(2), 176. doi: 10.1037/1040-3590.19.2.176.

Thayer, J. F., & Lane, R. D. (2000). A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders*, *61*(3), 201-216. doi: 10.1016/S0165-0327(00)00338-4.

Tucker, P., Pfefferbaum, B., Jeon-Slaughter, H., Khan, Q., & Garton, T. (2012). Emotional stress and heart rate variability measures associated with cardiovascular risk in relocated Katrina survivors. *Psychosomatic Medicine*, *74*(2), 160-168. doi: 10.1097/PSY.0b013e318240a801.

Turpin, G. (1991). The psychophysiological assessment of anxiety disorders: Three-systems measurement and beyond. *Psychological Assessment: A Journal of Consulting and Clinical Psychology*, *3*(3), 366. doi: 10.1037/1040-3590.3.3.366/

Wald, J., & Taylor, S. (2008). Responses to interoceptive exposure in people with posttraumatic stress disorder (PTSD): a preliminary analysis of induced anxiety reactions and trauma memories and their relationship to anxiety sensitivity and PTSD symptom severity. *Cognitive Behaviour Therapy*, *37*(2), 90-100. Doi: 10.1080/16506070801969054.

Weathers, F.W., Blake, D.D., Schnurr, P.P.. Kaloupek, D.G., Marx, B.P., & Keane, T.M, (2013). *The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5).* Interview available from the National Center for PTSD at www.ptsd.va.gov.

Weathers, F.W., Keane, T.M., & Davidson, J.R. (2001). Clinician-Administered PTSD Scale: A review of the first ten years of research. *Depression and Anxiety, 13*, 132-156. Doi:10.1002/da.1029.

Zoellner, L. A., Rothbaum, B. O., & Feeny, N. C. (2011). PTSD not an anxiety disorder? DSM committee proposal turns back the hands of time. *Depression and Anxiety*, *28*(10), 853. Doi: 10.1002/da.20899.

APPENDIX A

TABLES

Table A1

Demographic, Trauma Type, and Health Behavior Information

	PTSD (n = 53)	Controls (n = 68)	Total (n = 121)
	n (%)	n (%)	n (%)
Gender (percent Female)	45 (84.9%)	54 (79.4%)	99 (81.8%)
Race/Ethnicity			
American Indian/ Alaskan Native	1 (1.9%)	1 (1.5%)	2 (1.7%)
Asian/Pacific Islander	1 (1.9%)	1 (1.5%)	2 (1.7%)
Black/African American	20 (37.7%)	29 (42.6%)	49 (40.5%)
Hispanic Latino	3 (5.7%)	5 (7.4%)	8 (6.6%)
White (not Hispanic)	24 (45.3%)	23 (33.8%)	47 (38.8%)
Biracial	3 (5.7%)	7 (10.3%)	10 (8.3%)
Other	0	1 (1.5%)	1 (0.8%)
Trauma Type			
Sexual Assault	27 (50.9%)	29 (42.6%)	56 (46.3%)

Physical Assault	8 (15.1%)	12 (17.6%)	20 (16.5%)
Illness or Death	10 (18.9%)	8 (11.8%)	18 (14.9%)
Natural Disaster or Accident	7 (13.2%)	15 (22.1%)	22 (18.2%)
Other	1 (1.9%)	1 (1.5%)	2 (1.7%)
Any Cigarette/Nicotine Use Last 24 Hours	9 (17.0%)	7 (10.3%)	7 (13.22%)
Daily Cigarette Users	2 (3.77%)	4 (5.9%)	6 (5%)
Exercise Last 24 Hours			
Less than 1 Hour	33 (62.3%)	40 (58.8%)	73 (60.3%)
1-3 Hours	18 (34.0%)	22 (32.4%)	40 (33.1%)
4 or More Hours	2 (3.77%)	6 (8.8%)	8 (6.6%)
Exercise Average per Week			
Less than 1 Hour	11 (20.8%)	13 (19.1%)	24 (19.8%)
1-3 Hours	20 (37.7%)	22 (32.4%)	42 (34.7%)
4-5 Hours	12 (22.6%)	19 (27.9%)	31 (35.6%)
6-10 Hours	10 (18.9%)	9 (13.2%)	19 (15.7%)
More than 10 Hours	0	5 (7.4%)	5 (4.1%)
	M (SD)	M (SD)	M (SD)

Age	24.3 (8.2)	25.6 (9.9)	25 (9.2)
Total CAPS Symptom Score	32.2 (7.2)*	12.0 (7.6)*	20.9 (12.5)
ASI Physical Subscale Score	7.7 (5.4)*	4.5 (4.4)*	5.9 (5.1)
Cups of Coffee Last 24 Hours	1.0 (2.36)	.51 (.86)	.74 (1.72)
Cups of Coffee Average Day	.87 (1.40)	.75 (.81)	.80 (1.1)
Cups of Soda/Tea Last 24 Hours	.53 (.72)	.54 (.77)	.54 (.75)
Cups of Soda/Tea Average Day	.62 (.92)	.53 (.75)	.57 (.83)

*Values varied as a function of PTSD status.

Table A2

Medication and Substance Use 24 hours Prior to Day 2 Session

	PTSD (n = 53)	Controls (n = 68)	Total (n = 121)
	n (%)	n (%)	n (%)
Medication Class			
Birth Control	9 (17.0%)	9 (13.2%)	18 (14.9%)
Anti-Histamine	0	0	0
Analgesic	0	1 (1.5%)	1 (<1%)
Steroid	0	0	0
Expectorant	0	0	0
Non-steroidal anti-inflammatory drug (NSAID)	0	1 (1.5%)	1 (<1%)
Anti-convulsant	1 (1.9%)	0	1 (<1%)
Antacid	0	0	0
Benzodiazepine	1 (1.9%)	0	1 (<1%)
Antiemetic	1 (1.9%)	0	1 (<1%)
Antibiotic	0	0	0
Antifungal	0	0	0
Stimulant	0	0	0
Antitussives	0	0	0
Alcohol	3 (5.7%)	6 (8.8%)	9 (7.4%)
Marijuana	4 (7.5%)	4 (5.9%)	8 (6.6%)

Table A3

Medication and Substance Use One Week Prior to Day 2 Session

	PTSD (n = 53)	Controls (n = 68)	Total (n = 121)
	n (%)	n (%)	n (%)
Medication Class			
Birth Control	9 (17.0%)	13 (19.1%)	22 (18.2%)
Anti-Histamine	6 (11.3%)	9 (13.2%)	15 (12.4%)
Analgesic	5 (9.4%)	5 (7.4%)	10 (8.3%)
Steroid	0	1 (1.5%)	1 (<1%)
Expectorant	1 (2.0%)	0	1 (<1%)
Non-steroidal anti-inflammatory drug (NSAID)	8 (15.1%)	5 (7.4%)	13 (10.7%)
Anti-convulsant	1 (2.0%)	1 (1.5%)	2 (1.7%)
Antacid	0	1 (1.5%)	1 (<1%)
Benzodiazepine	1 (2.0%)	0	1 (<1%)
Antiemetic	2 (3.8%)	0	2 (1.7%)
Antibiotic	1 (2.0%)	0	1 (<1%)
Antifungal	0	1 (1.5%)	1 (<1%)
Stimulant	1 (2.0%)	2 (2.9%)	3 (2.5%)
Antitussives	1 (2.0%)	0	1 (<1%)
Alcohol	10 (18.9%)	14 (20.6%)	24 (19.8%)
Marijuana	7 (13.2%)	5 (7.4%)	12 (9.9%)

Table A4

Repeated Measures ANOVA Results for Cardiovascular Measures

	df	Mean Square	F	p
Heart Rate				
Within-Subjects				
Time*	1	802.35	34.27	<0.001
Time x PTSD*	1	141.20	6.03	0.015
Error	119	23.41		
Between-Subjects				
Intercept	1	1386505.71	5623.15	<0.001
PTSD	1	467.0	1.90	0.170
Error	119	246.57		
Respiratory Sinus Arrhythmia				
Within-Subjects				
Time*	1	9.52	24.07	<0.001
Time x PTSD	1	0.34	0.86	0.355
Error	119	0.40		
Between-Subjects				
Intercept	1	9769.12	3519.13	<0.001
PTSD	1	0.71	0.26	0.613
Error	119	2.78		
Pre-Ejection Period				
Within-Subjects				
Time	1	41.32	1.01	0.318
Time x PTSD	1	124.73	3.04	0.084
Error	110	40.99		
Between-Subjects				

Intercept	1	2674449.86	7233.66	<0.001
PTSD*	1	2648.08	7.16	0.009
Error	110	369.72		

*Significant main or interaction effects.

Table A5

Repeated Measures ANOVA Results for Anxiety Sensitivity

	df	Mean Square	F	p
Heart Rate				
Within-Subjects				
Time*	1	239.02	10.15	0.002
Time x ASI	1	7.58	0.32	0.571
Time x PTSD*	1	108.87	4.62	0.034
Error	118	23.54		
Between-Subjects				
Intercept	1	552062.77	2234.33	<0.001
ASI	1	186.26	0.75	0.387
PTSD	1	616.51	2.50	0.117
Error	118	247.08		
Respiratory Sinus Arrhythmia				
Within-Subjects				
Time	1	1.09	2.81	0.096
Time x ASI	1	1.25	3.21	0.076
Time x PTSD	1	0.04	0.11	0.740
Error	118	0.39		
Between-Subjects				
Intercept	1	3846.36	1375.98	<0.001
ASI	1	0.49	0.18	0.676
PTSD	1	0.34	0.12	0.727
Error	118	2.80		
Pre-Ejection Period				
Within-Subjects				

Time	1	58.50	1.42	0.236
Time x ASI	1	21.62	0.53	0.470
Time x PTSD	1	145.66	3.54	0.063
Error	109	41.16		
Between-Subjects				
Intercept	1	1058578.97	2841.23	<0.001
ASI	1	58.48	0.16	0.693
PTSD*	1	2143.38	5.75	0.018
Error	109	372.58		

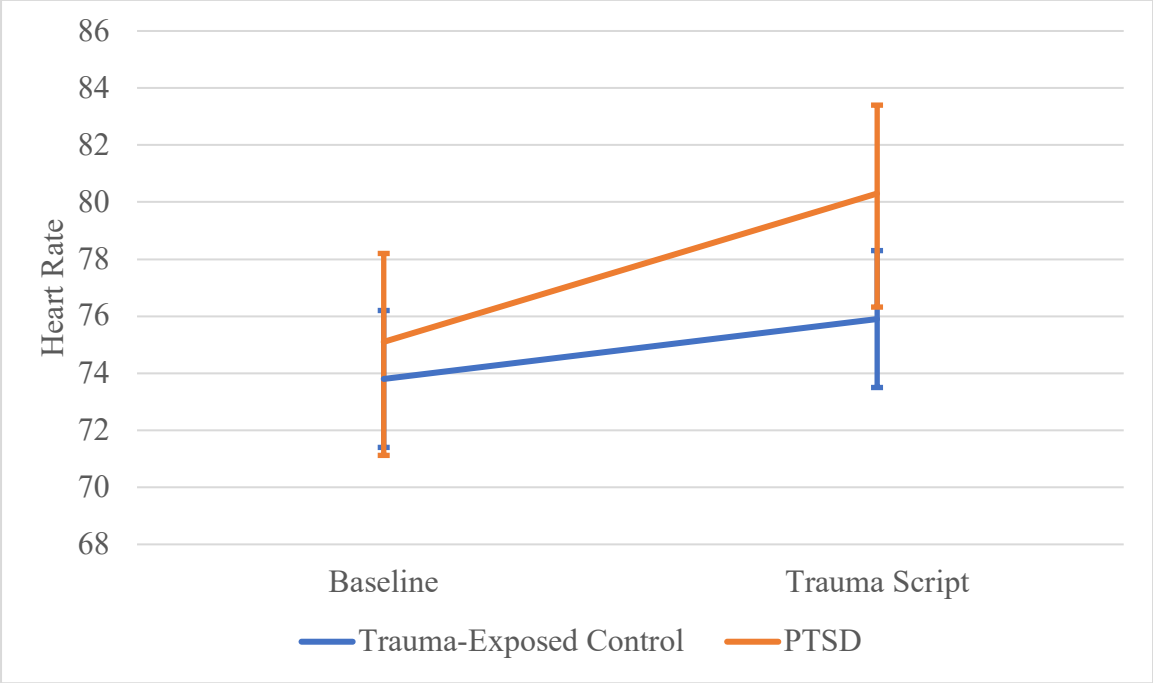
*Significant main or interaction effects.

APPENDIX B

FIGURES

Figure B1

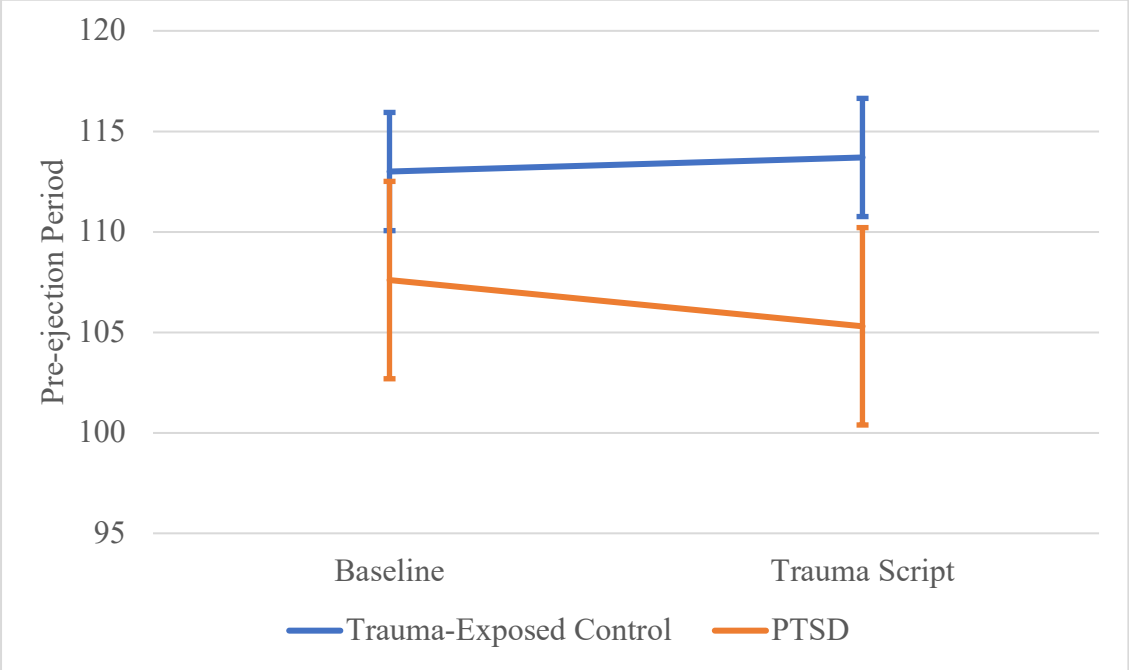
Heart Rate Results



*Error bars display 95% confidence interval.

Figure B2

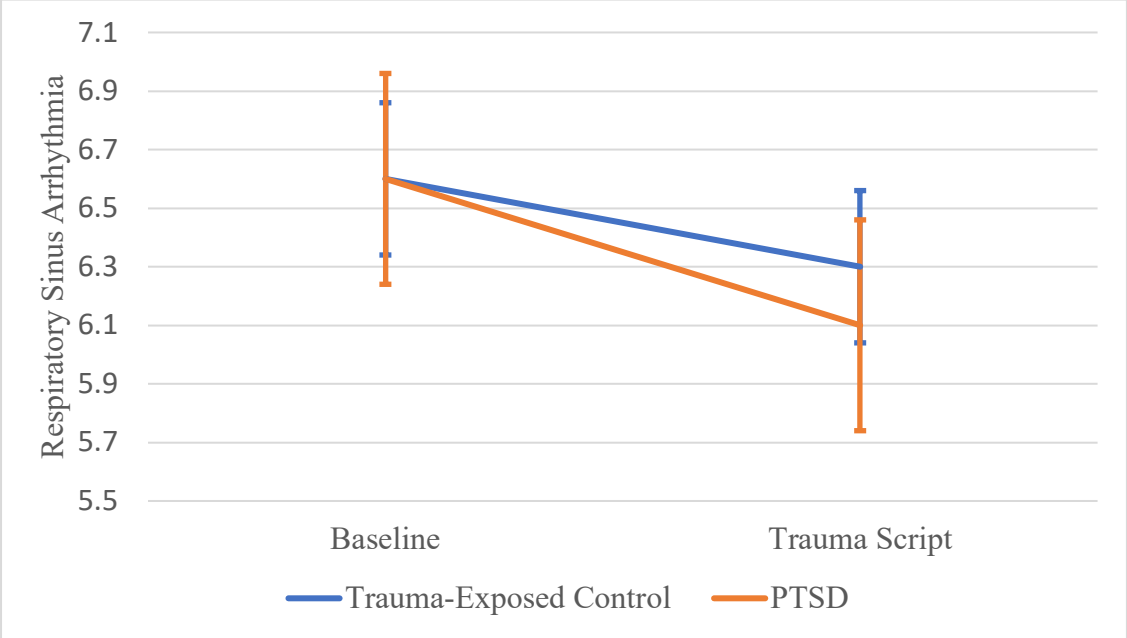
Pre-ejection Period Results



*Error bars display 95% confidence interval.

Figure B3

Respiratory Sinus Arrhythmia Results



*Error bars display 95% confidence interval.