THREAT BIAS AND HEART RATE VARIABILITY IN TRAIT ANXIETY

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An attentional bias favoring threat-related information and reduced cardiac vagal control are both prominent features of anxiety. However, relationships of threat bias to indicators of vagal tone, such as high frequency heart rate variability (HF-HRV), have primarily been examined among non-anxious individuals. The present study examined associations of threat bias, HF-HRV, and trait anxiety among 86 participants preselected for having high or low trait anxiety (M age= 26, 58% Female, 69% White), and tested whether experimentally manipulating threat bias via attention bias modification (ABM) would influence HF-HRV among high trait anxious individuals. Extent of threat bias, mood, and resting HF-HRV were assessed at baseline among all study participants. High trait anxious participants were then randomized to complete either a bias enhancing or bias attenuating ABM protocol after which extent of bias was re-assessed, and HF-HRV and mood were collected at rest, in response to stress, and during stress recovery. Results indicated that extent of vigilance toward threat (but not HF-HRV) predicted level of trait anxiety (OR = .995, p = .04), but that threat bias and HF-HRV were unrelated. In addition, ABM did not influence extent of bias or mood; however, HF-HRV increased from pre- to post-ABM among participants in the bias enhancement group, and decreased from post-ABM to stress among participants in the bias attenuation group [F (2.61, 130.61) =3.81, p=.02]. These results highlight vigilance toward threat as a salient component of threat bias and are the first to demonstrate an effect of ABM on HF-HRV among trait anxious individuals.

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PREFACE

I would like to extend my sincerest gratitude to the many people who made the completion of this dissertation possible. First and foremost, I thank my advisor Dr. Stephen Manuck for the time, resources, professional opportunities, and expert guidance which comprised the unmatched quality of training he provided. Many thanks also to Dr. Rebecca Price for her expertise, assistance, and encouragement during my foray into attention bias research, and Drs. Peter Gianaros, Richard Jennings and Anna Marsland for their invaluable contributions to not only this work, but to my professional development as a whole. I would also like to recognize Victoria Walker, Olivia Miller, Sarah Zale, and Mary Donahue for their assistance with data collection, Janet Lower, whose willingness to help, camaraderie, and overall support has been instrumental to the success of this and numerous other endeavors, and the countless other faculty, staff, students, and colleagues who contributed to my intellectual and personal growth at the University of Pittsburgh.

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1.0 INTRODUCTION

1.1 ANXIETY

1.1.1 Definition

Anxiety is a commonly occurring affective state characterized by feelings of fear, tension, apprehension, and worry, as well as accompanying autonomic changes such as increases in heart rate and blood pressure. States of anxiety fluctuate across circumstances and typically arise in response to perceived threat (Barlow, 2004; Spielberger, 2010). A cognitive vulnerability toward perceiving threat in many situations may predispose susceptible individuals to experience states of anxiety more frequently than others (Eysenck, 2013; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). These individual differences in proneness to anxiety comprise a stable personality trait -referred to as trait anxiety- that emerges early in life, is stable over time, and reflects both genetic and environmental influences (Spielberger, Gorsuch & Lushene, 1970; Kessler, Berglund, Demler, Jin, Merikangas, & Walters, 2005; Usala & Hertzog, 1991; Legrand, McGue & Iacono, 1999; Kendler, Neale, Kessler, Heath & Evans, 1992). High trait anxiety is also a prominent risk factor for developing anxiety disorders (Mundy, Weber, Rauch, Killgore, Simon, Pollack, Rosso, 2015), the most commonly experienced class of pathologies in Western countries (Michael, Zetsche & Margraf, 2007). Some of the most prevalent of these disorders include:

generalized anxiety disorder (GAD), characterized by persistent and uncontrollable anxiety, usually without a specific precipitant; social anxiety disorder (SAD) and specific phobias (SP), in which either social (e.g. social interactions, evaluation) or some other specific stimuli (e.g. spiders, heights) elicit strong and impairing states of anxiety; and panic disorder (PD), characterized by episodic experiences of intense anxiety strongly tied to sensitivity to bodily changes (Kessler et al., 2005; Wells, 2013). While a disposition toward general threat appraisal has been considered especially relevant to the development of GAD (Eysenck, 2013), individual differences in particular threat referents (e.g. social circumstances, a specific stimulus, bodily changes) may explain how trait anxiety predisposes to other anxiety disorders (Barlow, 2004; Mundy et al., 2015; Hishinuma, Miyamoto, Nishimura, Goebert, Yuen, Makini…& Carlton, 2001; Brandes & Bienvenu, 2006).

1.1.2 Consequences

When experienced acutely, anxious states are thought to adaptively motivate responses to threat, including facilitation of attention to potential danger, and harm avoiding behaviors (e.g. "fight or flight") supported by nervous and endocrine system changes (Barlow, 2004; Eysenck, 2013). On the other hand, anxiety can be maladaptive in so far as high trait anxiety associates with a number of disruptive emotional, cognitive, and behavioral sequelae, such as diminished subjective well-being, impairments in cognitive performance and stress coping, and behavioral avoidance that can negatively influence social, work, and other aspects of life (Barlow, 2004). In clinical populations, where anxiety occurs with greater frequency, intensity, and duration, psychological and physical functioning is even more severely affected (Barlow, 2004; Rosen & Schulkin, 1998), with the annual economic burden imposed by anxiety disorders in the United

States estimated to be at least $42 billion (Greenberg, Sisitsky, Kessler, Finkelstein, Berndt, Davidson & Fyer, 1999), though this figure is likely much higher (Kessler & Greenberg, 2002).

1.1.3 Autonomic Correlates

States of anxiety are regularly accompanied by changes in peripheral physiology mediated by the autonomic nervous system (ANS), including elevations in heart rate, blood pressure, vasoconstriction, and skin conductance (Hoehn-Saric, McLeod, & Zimmerli, 1989; Thyer, Papsdorf, Davis & Vallecorsa, 1984). The bulk of early literature establishing associations of anxiety with these various markers of ANS activity primarily examined activation of the sympathetic nervous system (SNS) and largely ignored parasympathetic nervous system (PNS) influences. However, observations of autonomic "inflexibility" in anxious relative to non-anxious individuals (e.g. reduced variability in skin conductance, larger physiological responses to stress but slower recovery and habituation) led to subsequent research examining the dynamic interplay between both branches of the ANS among anxious individuals (see Friedman & Thayer, 1998; Friedman, 2007 for review). From the 1990s on, anxiety studies began investigating both parasympathetic (vagal) withdrawal and relative balance of SNS and PNS activity, emphasizing the importance of physiological variability (and lack thereof among anxious individuals) for adaptive responding to changing environments (see Thayer, Friedman & Borkovec, 1996; Friedman, 2007). In this view, frequent experiences of elevated anxiety are both accompanied and perpetuated by heightened sympathetic responsivity, and reduced parasympathetic activity (Friedman, 2007). A large body of contemporary research on the ANS correlates of anxiety has focused on PNS influences on the cardiovascular system, which have

been established as an important component of healthy cardiac functioning (Levy & Schwartz, 1994).

1.1.4 Heart Rate Variability

One index of PNS activity particularly relevant to anxiety is heart rate variability (HRV), the variation in time interval between successive heart beats. Each heartbeat originates from a specialized group of cells in the sino-atrial (SA) node, which generates 100-120 electrical impulses per minute at rest, well above the normative resting heart rate (HR) of 50-70 beats per minute in healthy individuals. Both the SNS and PNS innervate the heart, exerting opposing influences on HR, with PNS dominance reflected in a lower resting HR relative to SA node activity. Spectral analyses of electrocardiogram (ECG) recordings are often used to distinguish factors that influence HR fluctuations occurring at different frequencies. For instance, low frequency (~0.10 Hz) fluctuations in HR are primarily due to blood pressure regulation, achieved by both SNS and PNS pathways, while high-frequency (~0.25 Hz) oscillations in HR are predominately mediated by PNS activity. The balance of sympathetic and parasympathetic activity continually changes in response to internal and external stimuli, and greater variability in HR reflects an adaptive predominance of parasympathetic cardiac control (see Thayer, Yamamoto & Brosschot, 2010).

One circumstance that temporarily influences the relative balance of sympathetic and parasympathetic cardiac control is psychological stress, in which increased sympathetic and decreased parasympathetic activity characterizes the “fight-or-flight” response to threat (Cannon, 1929). In healthy individuals, psychological stress has been associated with both a reduction in high frequency HRV (HF-HRV), a marker of vagal withdrawal, and increased low frequency

HRV (LF-HRV), which, in these circumstances is thought to primarily reflect increased SNS activity (Berntson & Cacioppo, 2004). These stress-related changes in HRV have been shown to occur in studies using both laboratory and naturalistic stressors. Examples of the former include speech preparation, mental arithmetic, shock avoidance, and Stroop interference tasks (Berntson, Cacioppo, Binkley, Uchino, Quigley & Fieldstone, 1994; Friedman, Thayer & Tyrell, 1996; Delaney & Brodie, 2000), and of the latter, college exams, earthquakes, and daily hassles (Lucini, Norbiato, Clerici & Pagani, 2002; Lin & Hughson, 2001; Sloan, Shapiro, Bagiella, Boni, Paik, Bigger… & Gorman, 1994). Additionally, low cardiac vagal tone has been construed as a physiological marker of stress sensitivity (e.g. Porges, Doussard-Roosevelt & Maiti, 1994; Thayer, Yamamoto & Brosschot, 2010), with a number of studies showing lower HRV to predict more adverse reactions to variously-defined stressors among infants (Porges et al., 1994), children (Whitson & El-Sheikh, 2003), adolescents (Mclaughlin, Rith-Najarian, Dirks, & Sheridan, 2015), and adults (Fabes & Eisenberg, 1997; Gouin, Deschenes & Dugas, 2014). Because anxious individuals are thought to have compromised flexibility in physiological responding to environmental challenges, characterized by hyperactive SNS activity and reduced PNS inhibition, much research has examined HRV among anxious individuals (see Berntson & Cacioppo, 2004).

Most research examining associations of anxiety with HRV have focused on HRV at rest in case-control studies of clinically anxious participants, though resting HRV in high trait anxious individuals has also been examined. Among studies involving anxiety disorders, PD predominates, likely because of the heightened sensitivity to bodily sensations in panic, though associations with HRV have been examined in a number of other anxiety disorders as well. A recent meta-analytic review reported lower HRV among individuals with anxiety disorders,

regardless of diagnosis, when compared to controls, with medium effects among individuals with GAD and SAD, and small effects among patients with PD (Chalmers, Quintana, Abbott, & Kemp, 2014). These effects were specific to HF-HRV, with no differences in low frequency HRV (LF-HRV) between patients and controls (Chalmers et al., 2010), supporting the hypothesized impairments in cardiac vagal control among anxious individuals. A similar pattern of results has emerged in studies of HF-HRV in sub-clinical anxiety. Specifically, high (relative to low) trait anxiety has been associated with lower HF-HRV in healthy adolescent, young adult, and mid-life samples (Fuller, 1992; Danilova, Korshunova, Sokolov & Chernyshenko, 1994; Watkins, Grossman, Krishnan & Sherwood, 1998; Bleil, Gianaros, Jennings, Flory & Manuck, 2008; Miu, Heilman & Miclea, 2009; Mujica-Parodi, Korgaonkar, Ravindranath, Greenberg, Tomasi, Wagshul…& Chon, 2009; but see also Dishman, Nakamura, Garcia, Thompson, Dunn, & Blair, 2000; Mezzacappa, Tremblay, Kindlon, Saul, Arseneault, Seguin… & Earls, 1997), as well as in individuals with hypertension and implanted cardiac defibrillators (Bajkó, Szekeres, Kovács, Csapó, Molnár, Soltész, ... & Csiba, 2012; Francis, Weinstein, Krantz, Haigney, Stein, Stone…& Kop, 2009). Similarly, number of self-reported symptoms of anxiety show strong inverse associations with HF-HRV in both healthy (Piccirillo, Elvira, Bucca, Viola, Cacciafesta & Marigliano, 1997) and hypertensive (Piccirillo, Elvira, Viola, Bucca, Durante, Raganato & Marigliano, 1998) individuals. Commonly-used pharmacological (paroxetine, benzodiazepines) and psychological (cognitive behavioral therapy, exposure therapy) treatments have been shown to increase vagal tone among individuals with anxiety disorders (Phebe, Adamson, Scarborough, Williams, Groff & McClean, 1997; Baker, Khaykin, Devins, Dorian, Shapiro & Newman, 2003; Mathewson, Schmidt, Miskovic, Santesso, Duku, McCabe, ... & Moscovitch, 2013; Bornas, Del Amo, Tortella-Feliu & Llabrés, 2012; Prasko, Latalova, Diveky, Grambal, Kamaradova,

Velartova, ... & Silhan, 2010; Garakani, Martinez, Aaronson, Voustianiouk, Kaufmann & Gorman, 2009), and it has been suggested that a number of other interventions that improve symptoms of anxiety (e.g. zen meditation, diaphragmatic breathing) may work through effects on HRV (Friedman, 2007; Henriques, Keffer, Abrahamson & Horst, 2011). Indeed, there is evidence that biofeedback interventions used to increase HF-HRV have shown corresponding reductions in anxiety symptoms among individuals with clinical and sub-clinical levels of anxiety (e.g. Reiner, 2008; Nada, 2008; Henriques et al., 2011), and a recent meta-analytic review found a large effect (g = .83) of these interventions relative to control training on self-reports of anxiety (Goessl, Curtiss & Hofmann, 2017).

While associations of anxiety with HF-HRV assessed at rest are largely consistent, findings from a smaller literature investigating stressor-evoked HF-HRV among anxious individuals are more mixed. Although anxious individuals are expected to show enhanced vagal withdrawal under stress –reflecting elevated stress sensitivity (Eysenck, 2013) - available evidence is equivocal. In clinically anxious participants compared to controls, greater vagal withdrawal in response to a laboratory stressor has been reported in women (but not men) with SAD (Grossman, Wilhelm, Kawachi & Sparrow, 2001). Individuals with PD have also been reported to show greater vagal withdrawal in response to a stressor, though here, differences in magnitude of change in patients versus controls were not tested (Petrowski, Herold, Joraschky, Muck-Weymann, & Siepmann, 2010). On the other hand, both patients with GAD and controls showed similar reductions in HF-HRV after a worry induction task (Thayer et al., 1996). Similarly inconsistent results are reported in studies comparing stressor-evoked HRV in high and low trait anxious participants. Specifically, high (relative to low) trait anxious participants have shown lower HF-HRV during laboratory stressors in some investigations (Miu et al., 2009;

Sanchez-Gonzalez, 2015), but not in one other similar study (Mauss, Wilhelm, & Gross, 2003) or in response to a naturalistic (exam) stressor (Fuller, 1992). Some authors have suggested that HRV differences between anxious and non-anxious individuals may not emerge during, but only after, stress exposure, such that anxious individuals may show sustained post-stress lowering of HRV (e.g. Mauss et al., 2003; Davidson, 1998). However, two studies reported opposite results during stress recovery (Mauss et al., 2003; Sanchez-Gonzales, Guzik, May, Koutnik, Hughes, Muniz… & Fincham, 2015). It is important to note that even among studies finding no differences between anxious and non-anxious individuals in stressor-evoked HRV, mean levels of HRV tended to be lower in anxious individuals across all experimental conditions (e.g. Fuller 1992; Mauss et al., 2003; Thayer, et al., 1996), further supporting an inverse association of anxiety with tonic cardiac vagal activity.

1.2 THREAT BIAS

In addition to examining anxiety's physiological correlates, a large body of contemporary anxiety research has focused on the cognitive aspects of anxiety (Eysenck, 2013). Specifically, because threat appraisal is a fundamental component of anxiety, cognitive approaches to anxiety research focus on processes involved in the evaluation of sensory stimuli as threatening or non-threatening. One area of interest involves cognitive biases, which broadly refer to systematic selectivity in information processing, usually occurring outside of conscious awareness and resulting in one type of information being favored over another (MacLeod & Mathews, 2012). Most of this research has focused on attentional bias, a type of cognitive bias characterized by preferential allocation of early attentional resources to a particular stimulus type (MacLeod &

Mathews, 2012). These studies have informed numerous cognitive models of anxiety, all of which center on attentional bias toward threat-related information (or threat bias) in the etiology and maintenance of anxiety (Williams, Watts, Macleod & Mathews, 1988; Beck & Clark, 1997; Wells & Matthews, 1996; Eysenck, 2013; Öhman, 1996; Mathews & Mackintosh, 1998; Mogg & Bradley, 1998; Bar-Haim, Lamy, Paergamin, Bakermans-Kranenburgh & van Ijzendoorn, 2007; Beck & Clark, 1997). Although these models share a focus on threat biases, conceptual ambiguities may arise owing to the many facets of what is broadly referred to as "attention" having been variously examined.

1.2.1 Attention

Generally speaking, attention refers to the ways in which an individual selects among all sensory information available at a given moment and can be parsed into four broad categories: orienting, filtering, searching, and preparing (Coren, 2003). Briefly, orienting refers to a change in the focus of attention and includes the orienting response (automatic physical adjustments to optimally receive information from a source of sudden sensory change) and shifting (disengagement of attention from one stimulus in order to attend to another). Filtering is an ongoing process whereby some information is preferentially processed while other sensory information is ignored. Searching refers to scanning of the sensory world for particular features or combinations of features, and preparing occurs when relatively "empty" information is attended to while anticipating something to transpire. Importantly, these categories are not independent, often occurring simultaneously, as a result of one another, or in various combinations. Research establishing the existence of attentional biases typically does so using tasks that conflate the aforementioned components of attention. Though muddying of attentional

processes can generate variability in interpretation of results among the various cognitive models of anxiety, that these processes are subsumed by attention explains the convergence of such models on biases in attention to threat.

1.2.2 Selective Attention

The first studies involving attentional biases (also referred to as selective attention), explored the nature of attention, and helped to develop two influential attention theories, referred to as structural (early versus late selection) and resource theories (Coren, 2003). Structural theories, which primarily focused on filtering, suggested that a bottleneck in information processing exists through which few stimuli can pass at once; in early selection models, this bottleneck occurs very early in perceptual processing, whereby most information about other stimuli is largely filtered out (e.g. Broadbent, 1977). In contrast, in late selection models, all sensory information receives some level of preliminary encoding, after which the bottleneck occurs at an initial stage of conscious processing (e.g. Deutsch & Deutsch, 1963). Attentional resource theories, on the other hand, focus more on performance in the search and preparation components of attention, and presume there exists a limited amount of cognitive resources that are "used up" by these attentional processes (e.g. Treisman & Gelade, 1980). Modern conceptualizations of attention tend to draw from both models in that some degree of filtering and capacity limits are thought to occur both in early (bottom up) and late (top down) perceptual processing (Goldstein, 2008). An important concept shared by these models of attention, which factors prominently in attention research today, is that the perceptual system is unable to process all available sensory information, and as such, must select what will be attended to from competing stimuli.

1.2.3 Assessments

Interest in how certain information is preferentially processed gave rise to more direct studies of selective attention. However, because early researchers were interested in largely different phenomena (i.e. filtering versus search and preparation), a variety of different paradigms were developed. For instance, studies conducted by structural theorists examined factors influencing selection in filtering through various dichotic listening tasks, where participants are asked to repeat aloud only one of two auditory messages presented simultaneously to either ear (e.g. Cherry 1953) or similar visual tasks, where participants are instructed to attend to only one of two simultaneously-presented visual stimuli (e.g. Neisser & Becklen, 1975; Long, 1979). Conversely, popular methods used by resource theorists to study selection in the context of preparing and searching are visual probe and visual search tasks, respectively. In probe tasks, participants identify the location of a particular visual probe as quickly as possible, with a popular variation having the probe preceded by a valid cue (e.g. arrow pointing to location of the next probe), an invalid cue (arrow pointing to incorrect location), or no cue (neutral). These probe studies explored cue-related benefits and costs to preparation, with faster probe identification occurring when visual attention is directed toward the location of the probe, and slower identification when attention is directed away from the probe. Importantly, these studies were the first to establish that spatial attention can be measured using reaction time (RT) to visual probes (Posner, Snyder, & Davidson, 1980; Navon & Margalit, 1983). Search tasks require participants to select (preferentially process) a target from among distractors, and have been used to examine search strategies and influences on resources used for searching. Despite their differences, each of these paradigms quantify bias via its hindrance or enhancement of task

performance, and this operationalization continues on in current research, as most studies of selective attention to threat make use of modified versions of these original tasks.

Like early selective attention studies, most assessments of threat bias quantify degree of bias as latency to respond to cues, but with modifications such that these cues appear either as, or in the presence of, threatening stimuli. The emotional Stroop presents threatening and neutral words in various colors that participants are asked to quickly name (disregarding word meaning), and longer latency to respond to threat-related words is interpreted as a bias in which attention to threat meaning interferes with performance (McKenna & Sharma, 1995). In the dot probe detection task two stimuli, one neutral and one threatening, are simultaneously flashed on either side of a computer screen, followed immediately by a target probe (e.g. a dot) appearing in place of one of the former stimuli. Participants are asked to indicate on which side the probe appeared as quickly as possible, with threat bias reflected in shorter latencies to detect probes in the location preceded by threatening stimuli and longer latencies to detect probes preceded by neutral stimuli (Macleod, Mathews & Tata, 1986). Similar to the dot probe, emotional spatial cueing requires participants to identify the location of a probe, but here the probe is cued by either a threatening or neutral stimulus, and the probe is either in same location as the cue (referred to as "valid") or opposite the cue ("invalid"). Threat bias in emotional spatial cueing is indicated by a shorter latency to respond to valid threat versus valid neutral cues (similar to the dot probe) and as slower latency after presentation of invalid threat versus invalid neutral cues (Posner, 1980; Fox, Russo, Bowles & Dutton, 2001). Finally, search tasks present a threat target among neutral distractors, or a neutral target among threat distractors, and threat bias presents as faster detection of threat targets or slower detection of neutral targets. Although varied application of these and other paradigms (e.g. eye tracking) and variations within each paradigm

(e.g. by stimulus type or exposure time) has given rise to much methodological diversity among threat bias studies, it is important to note that each task has been able to demonstrate the presence of a threat bias among anxious individuals.

1.2.4 Threat Bias in Anxiety

Interest in biased attentional processing of threat-related information among anxious individuals spurred hundreds of studies examining threat biases in anxiety. Until recently, the emotional Stroop task was largely favored in such studies, but concerns that latencies to name a color might reflect behavioral and cognitive processes other than attention (e.g. freezing in response to threat, memories and prior experiences with a word; MacLeod et al., 1986; Algom, Chajut & Lev, 2004) led to a shift toward the dot probe task, which remains the most commonly-used task in the literature. In terms of stimulus type, many of the earlier studies used word stimuli, but newer studies tend to rely on faces expressing neutral, positive and negative emotions. The two types of stimuli are relatively evenly distributed across the literature, though pictures and phobia-specific stimuli (e.g. spiders) are also used. Duration of stimulus presentation also varies, with most studies relying on exposure times that allow for conscious recognition of the stimulus, while a smaller proportion have used subliminally-presented stimuli. Population differences across threat bias studies also exist. For instance, while more of these studies have been conducted in adults, a large number examine threat biases in children. In addition, a subset of studies have examined threat biases during episodes of state anxiety or in anxious individuals with depression or substance abuse comorbidities, but most have examined threat biases in either trait or clinically anxious individuals. Regarding the latter, threat biases have been examined in all major anxiety disorders, most commonly GAD and SAD, though PD and SP are also often studied.

A meta-analytic review of 173 studies based on use of the dot probe, emotional Stroop, and emotional spatial cueing tasks found evidence of threat bias among anxious individuals that was not present among non-anxious controls (Bar-Haim et al., 2007). Similarly, a bias toward threat among clinically anxious and high trait anxious relative to non-anxious individuals has been established using other laboratory tasks, including visual search, eye tracking, and more recently-developed paradigms (see Van Damme, Crombez, Hermans, Koster & Eccleston, 2006; Lipp & Waters, 2007; Armstrong & Olantunji, 2012; Grafton & MacLeod, 2014; Rudaizky, Basanovic & MacLeod, 2014). Not only has threat bias been established among anxious relative to non-anxious individuals independently of experimental task, but this effect is also independent of stimulus type (words, faces, pictures) and duration of stimulus presentation (including subliminal presentations; Bar-Haim et al., 2007). Such results provide task-independent support for the aforementioned cognitive theories, which emphasize biases in attention toward threat-related information among anxious individuals.

Consistencies across study population were also established in the meta-analytic review by Bar-Haim and colleagues (2007). Specifically, there was no evidence of bias among non-anxious individuals, and effects did not differ between anxious children and anxious adults, nor were these effects altered when studies that included relevant comorbidities (substance abuse, depression) were excluded. It is also important to note that there is evidence for more robust attentional biases toward disorder-congruent versus -incongruent stimuli (e.g. threatening faces in SAD, physical harm in PD, and specific stimuli, i.e. spiders, in SP), suggesting some specificity of threat biases across different anxiety disorders (Pergamin-Hight, Naim, Bakermans-Kranenburgh, van Ijzendoorn, Bar-Haim, 2015). One of the most important consistencies in the Bar-Haim meta-analysis is that the moderate effects of threat bias were

significant in studies of persons with high trait anxiety (*d*= .43) as well as individuals with various anxiety disorders (*d*= .45), compared to non-anxious indivdiuals. Taken together, this evidence suggests that selective attention to threat is a prominent feature of anxiety.

1.2.5 Threat Bias and Anxiety Sequelae

While the existence of threat bias among anxious individuals has been studied extensively, a smaller area of research has examined associations of threat bias with correlates of anxiety, such as stress sensitivity and HRV. Exaggerated responding to stress is often implicated in the etiology and maintenance of anxiety (see Eysenck, 2013). In addition, because sensitivity to stress among anxious individuals is often attributed to heightened threat appraisals of stressful circumstances (Eysenck, 2013), we might expect a bias toward processing threat to similarly associate with stress sensitivity. Indeed, in non-anxious individuals, degree of threat bias has been associated with extent of distress, symptoms of anxiety, and cortisol levels in response to laboratory stressors and stressful life events (Nay, Thorpe, Roberson-Nay, Heckor, Sigman, 2004; Fox, Cahill & Zoughou, 2009; MacLeod & Hagan, 1992; van den Hout, Tenney, Huygens, Merkelbach & Kindt, 1995). Because low vagal tone has been construed as a physiological indicator of sensitivity to stress (e.g. Porges et al., 1994; Thayer, Yamamoto & Brosschot, 2010; Whitson & El-Sheikh, 2003; Mclaughlin, Rith-Najarian, Dirks, & Sheridan, 2015; Fabes & Eisenberg, 1997; Gouin, Deschenes & Dugas, 2014), we might also expect greater extent of threat bias to relate to lower HRV.

With respect to HRV, threat bias research in non-anxious individuals has extended a much older line of research on the relationships of HR and HRV to attentional processes (e.g. Porges, Arnold & Forbes, 1973; Lacey & Lacey 1974). More recent evidence has shown that

individuals with greater HRV are better able to shift (disengage) attention from threatening stimuli, inhibit the return of their attention to threatening distractors, and show less vigilance (less rapid orienting of attention) to threatening stimuli (Park, Van Bavel, Vasey, & Thayer, 2012; Park, Van Bavel, Vasey, & Thayer, 2013; Hansen, Johnsen & Thayer, 2003). Because threat biases have been characterized by both delayed disengagement from and vigilance toward threatening stimuli, reported associations of greater threat bias with lower HRV (Park & Thayer, 2014; Park, Vasey, Van Bavel, Thayer, 2013; Miskovic & Schmidt, 2010; Booij, Swenne, Brosschot, Haffmans, Thayer & Van der Does, 2006) are consistent with the corresponding literature on anxiety. Though threat biases have been associated with lower HRV among non-anxious individuals, the relationship between threat biases and HRV among anxious individuals is less clear. A single study found that high trait anxiety and low HRV were associated with both vigilance for threat and delayed disengagement from threat, but HRV moderated associations of trait anxiety with delayed disengagement (but not vigilance; Cocia, Uscatescu & Rusu, 2012). However, the effects of respiration, which are known to influence HF-HRV (Berntson et al., 1997), were not controlled for in this study and it is important to note that extent of this bias was associated with lower HRV only among high trait anxious individuals (Cocia et al., 2012). Because HR changes accompany attentional processes, it has been suggested that a rigid pattern of attention to threat might contribute to elevated sympathetic, and reduced parasympathetic cardiac control giving rise anxiety susceptibility (Lee, Park & Kalinin, 2011; Friedman, 2007). However, no studies to date have examined whether HRV might underlie associations of threat bias with trait anxiety. Additional studies are needed to further explore the nature of these relationships, and experimental manipulations of threat bias may help to resolve some ambiguities in the direction of associations between these variables.

1.3 BIAS MODIFICATION

1.3.1 Tasks

To the extent that threat bias underlies vulnerability to anxiety, attenuating biases toward threat might be used to reduce anxiety and its behavioral and physiological correlates and sequelae. Procedures aiming to manipulate bias – broadly referred to as attention bias modification (ABM) –have been developed and used for two main purposes, 1) to examine potential causal associations of threat bias with anxiety, and 2) to evaluate the potential therapeutic benefits of reducing threat biases. Most ABM interventions use modified versions of standard tasks (dot probe, emotional spatial cueing, visual search) in order to either enhance or attenuate attentional biases toward threat. Generally, enhancing threat bias is accomplished by fixing probes or cues to appear either as, or in place of, threatening (instead of neutral) stimuli in all trials. Here, quick and accurate detection of probes is favored by attention to threat. Conversely, fixing probes and cues to appear as or in place of neutral stimuli in all trials is used to attenuate threat bias because task performance is aided by attention to the neutral (not threatening) information. In the dot probe task, probes commonly appear behind neutral and threatening stimuli an equal number of times to assess extent of bias. When adapted for ABM, probes appear in place of either the neutral (to reduce threat bias) or threatening (to enhance threat bias) stimuli in the majority (often 100%) of trials (MacLeod et al., 1986). The emotional spatial cueing and visual search tasks have been similarly altered for ABM. Emotional spatial cueing modifications used to reduce bias most often have valid neutral cues and invalid threatening cues in most trials, such that attending to neutral cues helps with probe identification and attending to threatening cues hinders probe identification. To enhance bias in emotional spatial cueing, the opposite is used –

neutral cues are invalid and threatening cues are valid (Fox et al., 2001). In visual search tasks, bias toward threat is reduced by placing a neutral target stimulus in an array of threatening stimuli on all trails, and threat bias is enhanced by the use of threatening targets among neutral distractors on all trials (e.g Dandeneau & Baldwin, 2004). In most of these tasks, bias modification is thought to occur outside of participant awareness, -resulting from implicit learning of where to direct attention in order to more quickly detect probes/targets, but some ABM procedures more directly involve participants by disclosing the purpose of the training and providing continuous feedback about extent of bias (e.g. Price, Greven, Siegle, Koster, De Raedt, 2016; Bernstein & Zvielli, 2014). Despite differences in methodology, each of the various ABM tasks has been used to successfully alter extent of bias toward threat.

Studies employing ABM to reduce a bias toward threat most often use the modified dot probe task, followed by emotional spatial cueing, and then visual search, though a number of newly developed tasks are also being utilized. As with threat bias assessment, stimuli used in ABM include words, pictures, disorder-specific stimuli (e.g. spiders), and most often, faces. Bias modification is typically conducted in a laboratory setting, though some studies have examined internet-based home delivery of ABM, and number of sessions range from 1 to 28, with single sessions being the most common. Studies of threat bias reduction most often compare the effects of ABM to sham training, which is typically roughly identical to the corresponding bias assessment (i.e., a modified dot probe training toward neutral stimuli is compared to a dot probe in which the probe appears behind threatening and neutral stimuli equally often), but bias attenuation has also been compared to bias enhancement. Investigations comparing bias attenuation to bias enhancement have been conducted almost exclusively in non-anxious individuals, while the effects of bias attenuation relative to sham training have also been studied

among clinical populations (typically GAD and SAD) and in high trait anxious individuals. In terms of outcome, studies have most often examined the effects of ABM on extent of bias, post-ABM mood, state anxiety, stress reactivity, and in anxious individuals, number of symptoms of anxiety and percentage of individuals meeting criteria for an anxiety disorder have also been assessed (on occasion again during a follow-up session).

1.3.2 Effects of Bias Modification

Studies using ABM to enhance threat biases in non-anxious individuals have primarily aimed to examine the causal role of threat biases in generating anxiety, and as mentioned previously, typically compare effects of bias enhancement to bias attenuation. These studies have not only shown that threat biases can be altered in a single session of ABM, but also reliably demonstrate that bias enhancement and attenuation associate with the same outcomes in opposing directions. Specifically, individuals randomized to receive ABM training toward threat show small to moderate elevations in post-ABM levels of anxiety, negative mood, and worry relative to both baseline levels of these factors within subjects (Cret, 2013) and to post-ABM levels among individuals in the "train away" from threat condition (Mathews & MacLeod, 2002; Hayes, Hirsch & Matthews, 2010). The effects of bias enhancement and attenuation are even larger when participants are exposed to a laboratory stressor, with studies reporting moderate to large effects of training toward (relative to away from) threat on levels of anxiety following an anagram stress task (MacLeod, Rutherford, Campbell, Ebsworthy & Holker, 2002; Eldar, Ricon & Bar-Haim, 2008), and distressing video (Hoppitt, Mathews, Yiend & Mackintosh, 2010), as well as higher frustration and less persistence during an unsolvable anagram (Johnson, 2009). Moreover, the effects of a single administration of ABM on mood tend to be most reliable when

participants are exposed to a stressor. These results have typically been interpreted as evidence that a bias toward threat may play a causal role in the development of anxiety via increases in stress sensitivity (e.g. Mathews & MacLeod, 2002).

In comparison to research examining potential causal associations of threat bias enhancement with anxiety, a larger number of studies have addressed the therapeutic benefits of bias reduction. Adding to results showing that threat bias attenuation associates with lower post-ABM anxiety, negative mood, worry, and stress sensitivity when compared to threat bias enhancement, a number of studies in non-anxious individuals report similar effects when comparing threat bias attenuation to sham training. Specifically, relative to sham training controls, individuals receiving ABM designed to reduce threat bias report lower levels of stress and anxiety both post-ABM (Wadlinger & Isaacowitz, 2008) and in response to laboratory (speech task) and naturalistic stressors (e.g. final exams, work stress, and moving to another country; Amir, Weber, Beard, Bomyea & Taylor, 2008; Dandeneua, Baldwin, Baccus, Sakellaropoulo, Pruessner, 2007; See, MacLeod & Bridle, 2009). Bias attenuation in non-anxious individuals has also been associated with better performance during a speech stressor (Amir et al., 2008) and reduced thought intrusion following a distressing video (Verwoerd, Wessel & de Jong, 2012). The beneficial effects of bias attenuation have been extended also to anxious individuals. For instance, relative to sham ABM, bias attenuation in high trait anxious participants has been associated with lower levels of post-ABM anxiety (Li, Tan, Qian & Liu, 2008; Reese, McNally, Najmi & Amir, 2010) and worry (Hazen, Vasey & Schmidt, 2009), as well as lower levels of anxiety and negative mood in response to both anagram and speech task stressors (Bar-Haim, Morag, Glickman, 2011; Taylor, Bomyea & Amir, 2011; Amir et al., 2008). In clinically anxious participants, bias attenuation (relative to sham ABM) has reduced self- and

clinician-reported number and severity of anxiety symptoms post-ABM (Eldar, Apter, Lotan, Edgar, Naim, Fox, Pine & Bar-Haim, 2012; Amir, Beard, Burns & Bomyea, 2009) and lower self-reported ratings of anxiety during a speech task (Heeren, Reese, McNally & Phillippot, 2012; Heeren, Lievens & Philippot, 2011). Even more promising are results showing that 72% of participants with SAD who were randomized to receive ABM no longer met criteria for this disorder following bias reduction (relative to 11% of controls) and that these differences were maintained at a 4-month follow-up (Schmidt, Richey, Buckner & Timpano, 2009). These results were replicated in another study of adults with SAD (Amir, Beard, Taylor, Klumpp, Elias, Burns & Chen, 2009), and a more recent investigation similarly reported that 50% of children randomized to receive ABM (relative to 8% of controls) no longer met criteria for an anxiety disorder diagnosis following training (Waters, Pittaway, Mogg, Bradley & Pine, 2013).

The clinically meaningful effects of threat bias attenuation sparked much interest in the use of ABM for anxiety treatment. However, results are not consistent across all studies, with some reporting no effect of ABM on bias, anxiety or stress sensitivity. Numerous meta-analytic reviews of ABM have been conducted that take into account differences in experimental paradigms and population across the literature (e.g. Hakamata, Lissek, Bar-Haim, Britton, Fox, Leibenluft, et al., 2010; Hallion & Russo, 2011; Beard, Sawyer & Hofmann, 2012; Mogoaşe, David, Koster, 2014; Cristea, Kok & Cuijpers, 2015). Across experimental tasks, these reviews report medium to large effects of ABM on bias attenuation when compared to sham training (g's= .45-.80), and even stronger effects when bias attenuation is compared to bias enhancement (g=1.06). There is evidence of greater bias modification in studies conducted in laboratory (versus home) settings, in those using the modified dot probe task, and in studies of younger participants. Also, there is some evidence that extent of change in threat bias is greater with

training of longer duration (Hallion & Russo, 2011; Beard Sawyer, & Hofmann, 2012), though a dose-response relationship has not emerged in all meta-analyses (Hakamata et al., 2010; Mogoaşe et al., 2014; Cristea et al., 2015).

Although these meta-analytic reviews of ABM differ with respect to inclusion criteria, results generally indicate similar effects of ABM on both extent of bias and post-ABM anxiety and stress sensitivity among individuals with high trait anxiety and those diagnosed with an anxiety disorder. In terms of outcome, these reviews show small to medium effects of even single administrations of ABM on pre- to post-training anxiety symptom reduction in both high trait anxious and clinically anxious individuals, but not among non-anxious individuals. Additionally, these reviews report moderate to large effects of threat bias reduction on various measures of reactivity to laboratory stressors, again with even single administrations of ABM yielding fewer post-stressor anxiety symptoms, and less reported distress and negative mood in both anxious and non-anxious individuals. Importantly, most studies reporting null effects of ABM on symptom-related outcomes also failed to reduce threat bias (see Clarke, Notebaert & MacLeod, 2014; MacLeod & Clarke, 2015). Conversely, symptom-related improvements are typically reported among studies in which threat bias is attenuated (Clarke et al., 2014), showing that therapeutic benefits accompany successful bias attenuation.

Although there is compelling evidence that attenuating a bias toward threat can produce therapeutic changes in anxiety and stress sensitivity, few studies have examined whether the salubrious effects of ABM extend also to anxiety-related peripheral physiology. One study of individuals with SAD found a single session of ABM to lower stressor-evoked changes in skin conductance, an indicator of SNS activation (Heeren, Reese, McNally & Phillippot, 2012). Another investigation found that adolescent girls at a high familial risk for depression who were

randomized to receive online threat bias attenuation had significantly lower HR during anticipation of a speech stressor relative to those who received sham ABM (Joomann, Kircanski & Gotlib, 2016). A single previous investigation has examined the effect of threat bias attenuation on HF-HRV among participants not selected for anxiety (Baert, Casier, De Raedt, 2012. In this study, participants randomized to receive six sessions of online ABM had significantly higher HF-HRV during recovery from a speech stressor, though there were no group differences in HF-HRV assessed at rest or during speech anticipation. It is important to note that this particular investigation had a relatively small sample (14 in each group), and considering that the effects of home-delivered ABM tend to be smaller and less reliable than laboratory administrations, may have been underpowered. Because meta-analytic reviews report consistent effects of ABM on correlates of anxiety among anxious, but not non-anxious, individuals we might expect stronger effects of ABM on HF-HRV in anxious individuals. Additionally, while ABM did not affect HF-HRV assessed at rest, two considerations suggest that ABM might increase resting HF-HRV among anxious individuals and persons high in trait anxiety. First, high trait anxiety associates with lower vagal control of heart rate, so that baseline values may be depressed; and second, ABM tends to improve mood and bias more strongly among anxious than non-anxious individuals. However, no studies to our knowledge have examined the effects of ABM on tonic or stressor-evoked HF-HRV specifically among anxious participants.

1.4 SUMMARY

Anxiety is a commonly-occurring affective state that when experienced acutely is thought to motivate adaptive threat responding, but can be maladaptive among individuals with a predisposition to experience anxiety more frequently, as well as in individuals with anxiety disorders (Barlow, 2004). Frequent experiences of anxiety are both accompanied and sustained by heightened sympathetic responsivity and sensitivity, and reduced parasympathetic activity (Friedman & Thayer, 1998). Because anxious individuals show compromised flexibility in physiological responding to environmental challenges, often characterized by increased SNS activity and reduced PNS inhibition, a large body of work has examined HRV as a measure of autonomic SNS-to-PNS "balance" among anxious individuals (Friedman, 2007). These studies find that individuals with anxiety have lower resting HF-HRV, reflecting reduced cardiac vagal control (Chalmers et al., 2010; Fuller, 1992; Danilova, Korshunova, Sokolov & Chernyshenko, 1994; Mezzacappa, Tremblay, Kindlon, Saul, Arseneault, Seguin… & Earls, 1997; Watkins, Grossman, Krishnan & Sherwood, 1998; Miu, Heilman, Miclea, 2009; Mujica et al., 2009). Because lower HF-HRV predicts increased sensitivity to stress (Porges et al., 1994; Whitson & El-Sheikh, 2003; Mclaughlin, Rith-Najarian, Dirks & Sheridan, 2015; Fabes & Eisenberg, 1997; Gouin, Deschenes & Dugas, 2014), reduced cardiac vagal control may, in part, contribute to anxiety through elevated stress sensitivity (Eysenck, 2013). Commonly-used pharmacological and psychological treatments have been shown to increase vagal tone among individuals with anxiety disorders (Phebe, Adamson, Scarborough, Williams, Groff & McClean, 1997; Baker, Khaykin, Devins, Dorian, Shapiro & Newman, 2003; Mathewson, Schmidt, Miskovic, Santesso, Duku, McCabe, ... & Moscovitch, 2013; Bornas, Del Amo, Tortella-Feliu & Llabrés, 2012; Prasko, Latalova, Diveky, Grambal, Kamaradova, Velartova, ... & Silhan, 2010; Garakani,

Martinez, Aaronson, Voustianiouk, Kaufmann & Gorman, 2009) and it has been suggested that a number of other effective anxiety interventions may work through effects on HRV (Friedman, 2007; Henriques et al., 2011). Indeed, there is evidence that biofeedback used to increase HF-HRV elicits corresponding reductions in anxiety (Reiner, 2008; Nada, 2008; Henriques, Keffer, Abrahamson & Horst, 2011; Goessl et al., 2017).

States of anxiety and their physiologic correlates typically arise in response to threat, and cognitive approaches to anxiety research focus on processes involved in the evaluation of sensory stimuli as threatening or non-threatening (Eysenck, 2013). One area of particular interest involves attentional biases toward threat, in which early attentional resources are preferentially allocated to threatening information (MacLeod & Mathews, 2012). An attentional bias toward threatening stimuli is considered a prominent feature of anxiety and is consistently demonstrated among anxious, but not non-anxious, individuals (Bar-Haim et al., 2007). Numerous cognitive models of anxiety implicate threat biases in the etiology and maintenance of anxiety (Williams, et al., 1988; Beck & Clark, 1997; Wells & Matthews, 1996; Eysenck, 2013; Öhman, 1996; Mathews & Mackintosh, 1998; Mogg & Bradley, 1998; Bar-Haim, Lamy, Paergamin, Bakermans-Kranenburgh & van Ijzendoorn, 2007; Beck & Clark, 1997), evidence for which often derives from studies using ABM to enhance or attenuate selective attention to threat. Such studies have shown that enhancing threat biases can increase anxiety-related sequelae, while threat bias attenuation has been used to improve indicators of anxiety such as negative mood, worry, sensitivity to stress, and in clinically anxious participants, number of self- and clinician reported symptoms and number of participants meeting criteria for an anxiety disorder (e.g. Cret, 2013; Mathews & MacLeod, 2002; Hayes, Hirsch & Matthews, 2010; Amir, Weber, Beard, Bomyea & Taylor, 2008; Eldar, Apter, Lotan, Edgar, Naim, Fox, Pine & Bar-Haim, 2012;

Schmidt, Richey, Buckner & Timpano, 2009). Because the effects of bias modification tend to be strongest and most reliable when participants are exposed to a stressor, ABM influences on anxiety are thought to occur via changes in sensitivity to stress (Mathews & MacLeod, 2002). Indeed, extent of threat bias has been associated with increased sensitivity to both laboratory and naturalistic stressors (Nay, Thorpe, Roberson-Nay, Heckor, Sigman, 2004; Fox, Cahill & Zoughou, 2009; MacLeod & Hagan, 1992; van den Hout, Tenney, Huygens, Merkelbach & Kindt, 1995) and has been shown to predict lower resting HF-HRV, a physiological correlate of stress sensitivity, among non-anxious individuals (Park & Thayer, 2014; Park, et al., 2013a; Miskovic & Schmidt, 2010; Booij, Swenne, Brosschot, Haffmans, Thayer & Van der Does, 2006). There is some evidence that bias modification may influence HF-HRV among individuals not selected for anxiety (Baert, Casier & De Raedt, 2012), but no studies have yet examined effects of bias modification on HF-HRV among high trait anxious individuals.

1.4.1 Current Study

An attentional bias toward threat and reduced cardiac vagal control are both prominent features of anxiety. However, relationships between threat bias and HF-HRV have been examined primarily among non-anxious individuals, and the ways in which anxiety, threat bias, and HF-HRV are associated in a causal chain is unclear. Experimental manipulations might be used to resolve ambiguity in the direction of association between these variables, and evidence of a directional relationship between threat bias and HF-HRV was found in a study of non-anxious participants that showed that experimentally attenuating threat bias increased HF-HRV. Given that both attenuating threat bias and increasing HF-HRV have separately been shown to decrease anxiety, and preliminary evidence that threat bias attenuation influences HF-HRV, low HRV

may be one pathway through which threat bias contributes to anxiety. However, no studies have examined whether HF-HRV might underlie associations of threat bias with anxiety. As such, the first aim of the current investigation is to examine associations among trait anxiety, threat bias and HF-HRV. We hypothesize that extent of threat bias and HF-HRV will predict level of trait anxiety, and that extent of threat bias and HF-HRV will be inversely related. If each of the above relationships are obtained, we will test for cross-sectional mediation of threat bias associations with anxiety by HF-HRV.

If low cardiac vagal control underlies associations of threat bias with anxiety, it may be that the clinically meaningful reductions in symptoms of anxiety elicited by ABM occur via changes in HF-HRV. Given that anxious individuals consistently show lower resting HF-HRV, and that threat bias modification can be used to both enhance and attenuate a number of prominent correlates of anxiety, we might expect ABM to similarly elicit changes in HF-HRV among anxious individuals. Moreover, that the effects of ABM are most pronounced when participants are exposed to a stressor suggests that bias modification improves anxiety-related outcomes via effects on sensitivity to stress, and low vagal tone has been construed as a physiological marker of stress sensitivity. To the extent that ABM effects on anxiety occur via alterations in stress sensitivity, and low vagal tone predicts sensitivity to stress, changes in HF-HRV tone may represent one pathway through which ABM-related changes in anxiety occur. However, no studies have examined the effects of ABM on HF-HRV among individuals predisposed to experience anxiety, nor have any examined whether ABM-elicited reductions in negative mood might be explained by changes in resting or stressor-evoked HF-HRV. Accordingly, the second aim of the current investigation is to examine whether bias modification influences HF-HRV at rest, during a stressor, and during stress recovery among individuals high

in trait anxiety. We will also attempt to replicate the effects of ABM on extent of bias and mood among high trait anxious participants. We hypothesize that individuals randomized to receive bias attenuation will have higher HF-HRV and better mood at rest, during stress, and during stress recovery relative to those randomized to receive bias enhancement. If we find that ABM affects both mood and HF-HRV, aim 2 will also examine whether effects of ABM on HF-HRV mediate effects of ABM on mood.

2.0 METHOD

2.1 OVERVIEW

With respect to our first aim, threat bias and resting HF-HRV were assessed in study participants preselected for having high or low trait anxiety. To test our second aim, high trait anxious participants were randomized to receive ABM to either enhance or attenuate threat bias. Upon completion of ABM, extent of bias was re-assessed and HF-HRV and ratings of mood were collected at rest, in response to stress, and during stress recovery.

2.2 PARTICIPANTS

A total of 86 participants were recruited from the introductory psychology participant pool and Clinical and Translational Science Institute volunteer registry at the University of Pittsburgh. Participants in the top (N=52) and bottom (N=34) tertiles of trait anxiety, as defined by distribution of scores in an independent sample, were selected to participate based on a priori power analyses (see Appendix A). Stratified sampling was used in order to ensure an equal proportion of males and females in the high and low trait anxiety groups, as women tend to score higher on trati anxiety than men (Spielberger et al., 1970). Participants were included if they were 18 years of age or older, with no history of cardiovascular disease and having normal or

corrected-to-normal vision. In line with previous investigations, participants were instructed to refrain from caffeine 4 hours prior to their appointment, alcohol and exercise 12 hours prior to their scheduled session, and over the counter medications 24 hours before their appointment to minimize the effects of these on heart rate (e.g. Jennings, Allen, Gianaros, Thayer & Manuck, 2015). Adherence to these restrictions was verified on the day of testing. Participants from the introductory psychology pool received course credit for participation, and participants not receiving course credit were entered into a raffle to receive one of two $50 payments upon study completion. All participants signed an informed consent agreement and the protocol was approved by the University of Pittsburgh Human Research Protection Office.

2.3 MEASURES

2.3.1 Anxiety

Trait levels of anxiety (assessed online and verified upon arrival to the study) were assessed using the State-Trait Anxiety Inventory-Trait form Y (STAI; Spielberger, 1985). The STAI-Trait form consists of twenty items, and responses to each item are chosen from a four-point Likert scale. The trait scale of the STAI is used to assess an enduring disposition to feel stress, worry, and discomfort, and consists of statements such as “I worry too much over something that really doesn’t matter,” and “I am a steady person,” (reverse coded) with responses ranging from 1- “almost never” to 4- “almost always.” An online version of the STAI was used for screening, and only those scoring in the upper and lower ranges of STAI scores were invited to participate. Cutoff scores defining upper and lower tertiles of trait anxiety were derived from the STAI

administered to community volunteers in the Adult Health and Behavior study phase 2 (AHAB-2). Analyses in the full sample (N=490) indicated that a score of 28 or below for males and females would place participants in the lowest tertile of trait anxiety, while a score of 36 or above for males and 34 or above for females would place participants in the highest tertile. Restricting these analyses to younger participants (under the age of 35; N=113) yielded the same score cut-offs for the bottom tertile in both males and females, but showed a score of 38 or above for males and 39 or above for females would place participants in the highest tertile. Thus, males and females scoring 28 or below (low trait anxiety), and 38 or 39 (respectively) or above (high trait anxiety) on the online-administered STAI were invited to participate in the current study. Eligible participants completed the STAI a second time upon arrival to the study in order to confirm their trait anxiety level.

2.3.2 Threat Bias

Extent of threat bias was determined using two different tasks presented in succession: First the dot probe, which is the most widely used assessment of threat bias, followed by a newly-developed task - the attentional response to distal versus proximal emotional information (ARDPEI; Grafton & MacLeod, 2014). In the dot probe task, shorter latencies to detect probes preceded by threatening relative to neutral stimuli can arise from relatively faster orienting of attention to threat (often referred to as vigilance) as well as difficulties in disengaging attention from threat. Specifically, threat vigilance provides 1) a time benefit for detecting a probe appearing in place of the threatening stimulus and 2) a time cost for detecting a probe appearing in place of a neutral stimulus because attention must be shifted from the location to which it was initially oriented. Because difficulties disengaging attention away from threat also provide a time

cost for detecting a probe appearing in place of a neutral stimulus, the dot probe task has been criticized for being unable to differentiate vigilance from disengagement in threat bias. To control for the effects of vigilance in assessments of disengagement, the stimulus from which individuals are disengaging must be able to capture attention equally regardless of its emotional valence (or anxiety level of the participant) so that individual differences in disengaging from that stimulus can be assessed independently of influences from vigilance for that stimulus (Clarke, MacLeod & Guastella, 2013). In addition, assessments of vigilance should ensure attention is secured to a neutral fixation so that differences in orienting to simultaneously-presented threatening and neutral stimuli can be determined (Clark et al., 2013). These criteria are met in the ARDPEI, where attention to a neutral anchor (horizontal or vertical line) that is briefly flashed on either side of the screen is verified by requiring that participants identify the orientation of the anchor, and by using an abstract image to accompany both threatening and neutral images so that attention might be equally captured by either side of the screen.

Participants were seated behind a PC computer at a distance of approximately 60 cm from the screen to perform the probe detection and ARDPEI tasks, which were separated by a 3 minute rest period to reduce fatigue. E-prime software (version 2.0) was used to program, present, and collect response time latencies for both tasks. In the dot probe task, extent of bias was assessed using face stimuli from twenty four actors, each expressing fearful and neutral expressions (Karolinska Directed Emotional Faces; Lundqvist, Flykt, & Ohman, 1998). An equal number of male and female models displaying the two expressions was used. Participants first completed a practice trial consisting of 18 picture pairs that differ from models used in the primary dot probe task. Each dot probe trial began with a central fixation point presented for 100ms, after which two faces (one fearful and one neutral) appeared in vertical orientation on the

screen for 500ms. Face pairs were followed immediately by either the letter ‘E’ or ‘F’ appearing in place of one of the two faces, and participants were instructed to indicate which letter appeared as quickly and as accurately as possible using a keyboard. Threatening and neutral pictures and letter probes were presented equally often on the top and bottom of the screen. For the main task, 4 blocks of 24 picture pairs (24 fearful, paired with the neutral expression of the same actor) were presented and the order of trials was randomized for each participant.

In the ARDPEI, bias was assessed using 128 images (64 negative and 64 neutral) from the International Affective Picture System (IAPS; Lang, Bradley, Cuthbert, 2008), along with 128 abstract images. Participants first completed a practice trial consisting of 32 picture pairs that differ from images used in the primary ARDPEI task. Each trial of the ARDPEI began with the presentation of two white square outlines, with a smaller red square outline appearing inside of either of the two white outlines. Participants were asked to direct their attention to the red outline, within which an anchor probe (horizontally- or vertically-presented red line) was presented for 150ms. Immediately after offset of the anchor probe, a threatening or neutral “representational image” was presented either proximally (in the same white box as the anchor probe) or distally (in the white box on the opposite side of the screen) with equal frequency randomized within participants. These images were accompanied by an abstract image in the box not housing the representational image. Image pairs were displayed for 500ms, after which a target probe (horizontal or vertical red line) appeared in either of the two screen locations and participants were asked to indicate whether the target probe matched the anchor probe as quickly and accurately as possible. In the ARDPEI, faster latencies to identify probes replacing distally-presented threatening versus neutral images indicate faster orienting of attention to threat

(vigilance), and slower latencies to identify probes replacing proximally-presented threatening versus neutral images indicates difficulties disengaging attention from threat.

2.3.3 Bias Modification

Bias modification was also implemented using two different tasks administered in succession and separated by a 3 minute rest period: first, the modified dot probe (the most commonly used ABM procedure), followed by a newer ABM task, the person-identity-matching (PIM) task (Notebaert, Clarke, Grafton & MacLeod, 2015). Though anxiety-related therapeutic benefits accompany successful bias modification, ABM does not always succeed in reducing a threat bias. The need for more reliably effective ABM procedures (Bar-Haim, 2010) has spurred the development of a number of new ABM tasks, including the PIM. In this task, two "cards," both of which display a threatening and happy face pair, are presented on the screen, and participants in the train-away from threat condition are asked to indicate whether the happy faces from each card match (are the same person), while participants in the train-toward threat condition are asked to indicate whether the threatening faces match. Notebaert and colleagues (2015) compared the PIM and modified dot-probe task in terms of their effects on bias modification and stress sensitivity among individuals with mid-range trait anxiety. In this study, the modified dot-probe task did not successfully alter bias or stress vulnerability, while the PIM training toward happy faces significantly reduced threat bias and post-stress negative mood (Notebaert et al., 2015). Though further studies are needed to replicate the effects of the PIM for threat-bias and subsequent stress sensitivity, the large effects of the PIM on bias reduction (d=.63) and stress sensitivity (d=.62) relative to previously-reported effects of the modified dot-probe on either of

these (e.g. Hakamata et al., 2010; Hallion & Ruscio, 2011; Beard, Sawyer & Hofmann, 2012; Mogoaşe, David, Koster, 2014) are promising.

Participants in the upper tertile of trait anxiety were randomized to either threat bias enhancement or attenuation ABM via modified dot probe and PIM tasks administered on the same PC computer using E-Prime 2.0 software for programming and presentation. The modified dot probe task was similar to the dot probe assessment, but with the location of the probe manipulated to appear behind either a fearful or happy face (to enhance or attenuate bias, respectively) in 100% of trials. For bias modification, 4 blocks of 32 picture pairs were used (32 fearful, paired with the happy expression of the same actor). Crossing person identity, picture location and number of blocks resulted in a total of 256 trials, the order of which was randomized for each participant.

In the PIM (Notebaert et al., 2015) task, participants were presented with two virtual cards, each with two different KDEF actors – one depicting a happy expression and the other an angry expression. Participants randomized to receive bias enhancement were asked to indicate whether the actor depicting the angry expression on the top card matched the identity of the actor depicting the angry expression on the bottom card, while those in the bias attenuation condition were asked to match the actors depicting happy expressions. After each response, the bottom pair of faces moved up to replace the top pair, a new pair appeared at the bottom of the screen, and the border of the top pair of faces changed color to provide feedback about whether the previously-presented faces matched (green to signal a match or red to indicate a mismatch). The 32 actors used in this task were grouped into eight sets of eight identities with each identity appearing in two sets, and each set contained four different identities (two male, two female). Pairing each identity carrying one expression with each of three identities carrying an opposite

expression created 24 “cards,” or trials in each set. Each set was completed once, and two were repeated, resulting in a total of 240 trials.

2.3.4 Heart Rate Variability

High frequency HRV (HF-HRV) was assessed from inter-beat interval (IBI) data obtained at four collection epochs (baseline, post-ABM, during stress, and post-stress) via continuous electrocardiogram (ECG) recording from a modified lead II configuration. Participants were instructed to remain as still as possible during each collection epoch. For adequate resolution to conduct HRV analysis, signals were obtained at 1000 Hz (Berntson, 1997). MindWare technologies software version 3.1.4 (MindWare Technologies LTD., Gahanna, OH) was used to edit raw data and derive high frequency (0.12-0.40) spectral power values for each 1-minute segment of IBI data. In addition, respiration was assessed using a respiratory belt in order to statistically control for the effects of respiration on HF-HRV (Egizio, Eddy, Robinson, & Jennings, 2011)

2.3.5 Stress Task

A speech preparation task modeled after a task shown previously to evoke decreases in HRV (Gianaros, Salomon, Zhou, Owens, Edmundowicz, Kuller & Matthews, 2005) was used to assess changes in HF-HRV and mood in response to a stressor. In this task, participants were asked to imagine that they were being detained by authorities on an accusation of shoplifting and were given 3 minutes to mentally prepare a 2 minute speech defending themselves against the accusation. To assist with the preparation, participants were provided with instructions to discuss

1) the events that led to the accusation, 2) whether the accusation was issued wrongfully, and 3) the responsibility of authorities for preventing such incidents. Participants were told that their speeches would be recorded and rated by a panel of judges on persuasiveness, clarity, and style, though speeches were not actually rated or recorded. HF-HRV was derived from the 3 minute speech preparation period, and a mood assessment was taken at the end of the 3 minute period before speech delivery. Following the speech delivery, participants were told that their speech was not recorded and would not be rated.

2.3.6 Mood

Stress-related mood changes were assessed via two 11 point (range 0-10) mood scales used in previous assessments of ABM effects on stress sensitivity (e.g. MacLeod et al., 2002; Notebaert et al., 2015) and administered on the computer. One scale was anchored with the labels happy (0) and sad (10), and the other with relaxed (0) and anxious (10). In order to disguise the purpose of the study, three other 11-point scales were included, anchored with interested (0) and bored (10), full (0) and hungry (10), and alert (0) and tired (10).

2.4 PROCEDURE

The sequence of study procedures is displayed in Figure 1. Participants interested in the study completed an online version of the STAI-trait form, and individuals with scores in the upper and lower tertiles were contacted and invited to participate. Upon arrival, informed consent was obtained. Next, standard demographic information (age, sex, and race), as well as study

eligibility and compliance with instructions regarding pre-study restrictions (caffeine, alcohol, over the counter medications and exercise) were assessed via questionnaire, followed by the STAI-trait form to verify trait levels of anxiety. Next, the ECG electrodes and respiration belt were fitted, participants were seated in front of the computer monitor, and continuous ECG recording began. After five minutes of resting ECG recording, participants completed a mood rating, immediately followed by the dot probe and ARDPEI bias assessments. Low trait anxious participants were debriefed at this time, while high trait anxious participants who were randomly assigned to either threat bias enhancement or attenuation continued on to complete the ABM after a 3 minute rest. Bias modification was followed by another 3 minute rest, after which the second block of bias assessment (via dot probe and ARDPEI) was completed. Next, post-ABM HF-HRV was collected during a five minute rest period, after which post-ABM mood was assessed. Participants were then given instructions about the speech task and three minutes to prepare their speech during which stressor-evoked HF-HRV was derived followed by another mood assessment. After the speech delivery, participants were informed that their speech was not recorded and asked to rest prior to a final mood assessment. HF-HRV during stress recovery was assessed during this five minute rest period. Following the final mood rating, ECG electrodes and the respiration belt were removed, and participants were debriefed.

3.0 ANALYSES

3.1 DATA REDUCTION

Statistical analyses were performed using SPSS, version 25 (SPSS Inc., Chicago, IL), and prior to hypothesis testing, all study variables were examined to verify assumptions of normality.

3.1.1 Threat Bias

Threat bias scores (Table 1) were derived using response time (RT) data collected from the dot probe and ARDPEI tasks. Prior to calculating bias, all RT data were cleaned following procedures outlined previously (Price, Kuckertz, Siegle, Ladouceur, Silk, Ryan, Dahl & Amir, 2015). First, RT data from the initial three trials of each assessment were excluded to account for acclimation to the task, as were any trials on which participants provided an inaccurate response (mean accuracy was 96.32% for the dot probe and 94.36% for the ARDPEI). Next, RT values outside of 1.5 interquartile ranges below the 25^{th} percentile and above the 75^{th} percentile were Winzorized to the last value within that range for each distribution, and bias scores were derived from these rescaled distributions. For both dot probe assessments, threat bias was calculated by subtracting mean RT on fearful trials from mean RT on neutral trials, with higher scores indicating greater extent of bias toward threat. For both ARDPEI assessments, engagement with, and disengagement from threat were calculated using the following equations provided by

Grafton and Macleod (2014), where higher engagement scores reflect greater vigilance for threat-related information and higher disengagement scores reflect greater difficulty disengaging from threat-related information:

Engagement: [(RT for probes in same location as neutral image – RT for probes in location opposite to neutral image) – (RT for proves in same location as negative image – RT for probes in opposite location to negative image)]

Disengagement: [(RT for probes in location opposite to negative image – RT for probes in same location as negative image) – (RT for probes in location opposite to neutral image – RT for probes in same location as neutral image)]

In addition, an overall bias score for both ARDPEI assessments was derived by averaging vigilance and disengagement scores. Outliers on any of the dot probe or ARDPEI threat bias scores were similarly rescaled to 1.5 interquartile ranges below the 25th percentile and above the 75th percentile for that distribution. Because threat bias scores derived from the dot probe were unrelated to engagement, disengagement, and overall scores derived from the ARDPEI (Table 2), these indices were examined separately in all analyses.

3.1.2 Heart Rate Variability

MindWare Heart Rate Variability scoring software version 3.1.4 was used to derive HF-HRV from ECG data. Following automatic artifact detection, IBI data were corrected manually for extra and missing R spikes, and 1-minute segments containing more than 5 seconds of noise were omitted. Less than 1% of all R's were corrected manually (.0081), and only a single segment contained more than 5 seconds of noise and was omitted. High frequency (0.12-0.40) spectral power values were derived by a fast Fourier Transformation algorithm for each 1-minute

segment of IBI data and used as an indicator of HF-HRV for each segment. Because a repeated measures ANOVA showed that mean respiration rate varied across the four collection epochs [F (3, 49) = 13.04, p <.001], HF-HRV values were adjusted for the effects of respiration. To adjust for respiration, HF-HRV was regressed onto respiration rate within each 1-minute segment of data collection, with the standardized residuals representing respiration-adjusted HF-HRV (mean HF-HRV for each segment was added to these residual values for ease of interpretation). Respiration-adjusted values for each 1-minute segment were then averaged across each collection epoch (pre-ABM, post-ABM, stress, and recovery) and used as outcomes in subsequent analyses. These outcomes were normally distributed, and are displayed with mean respiration and heart rate (HR) for each collection epoch in Table 3.

3.2 PRIMARY ANALYSES

3.2.1 Question 1. Associations of threat bias, HF-HRV and trait anxiety

Prior to regression analyses, univariate associations between continuous measures (age, bias indicators, HF-HRV) were examined via zero-order correlation analyses, and independent samples t tests were used to examine mean differences between categorical measures (sex, race, level of trait anxiety) on each of these continuous variables. Separate logistic regression analyses controlling for standard demographic covariates (age, sex, and race) were used to test whether level of trait anxiety (high versus low) was predicted by 1) extent of threat bias, and 2) resting HF-HRV. In addition, linear regression analyses controlling for standard demographic covariates were used to determine whether extent of threat bias predicted HF-HRV.

3.2.2 Question 2. Effects of Attention Bias Modification

Randomization and Manipulation Checks. Prior to testing effects of ABM, independent samples t-tests were used to examine baseline group differences between participants randomized to receive bias attenuation versus bias enhancement. In addition, the efficacy of our stress induction was examined using paired samples t-test comparisons of mean anxiety, heart rate, and HF-HRV assessed during, and prior to stress.

Pre- to post-ABM changes in bias, resting HF-HRV, and mood. Separate 2 X 2 repeated measures analyses of variance (ANOVA) were used to test group (bias enhancement v. bias attenuation) by time (pre- to post- ABM) interactions on extent of bias, resting HF-HRV, and mood. We hypothesized there to be an interaction of group by time such that differences in post-ABM threat bias, resting HF-HRV, and mood would depend on whether participants were randomized to the bias enhancement or bias attenuation. Specifically, we anticipated individuals randomized to bias enhancement to show more threat bias, lower resting HF-HRV, and greater negative mood post-ABM relative to individuals randomized to bias attenuation.

Effects of ABM on HF-HRV and mood during stress and recovery. To examine whether the effects of ABM can be extended also to HF-HRV during stress and stress recovery, and determine whether we can replicate previously reported effects of ABM on stressor-evoked mood, a series of 2 X 4 repeated measures ANOVAs were used to examine whether there were group (bias enhancement v. bias attenuation) by time (post-ABM, stress, recovery) interactions on HF-HRV and mood. We hypothesized there would be a main effect of time, reflecting stressor-evoked decreases in HF-HRV and increases in negative mood among both groups. In addition, we hypothesized an interaction between group and time such that stressor-evoked

decreases in HF-HRV and increases in negative mood would be greater among participants randomized to the bias enhancement than among participants randomized to bias attenuation.

4.0 RESULTS

4.1 PARTICIPANT CHARACTERISTICS

A total of 52 high trait anxious (HTA), and 34 low trait anxious (LTA) individuals participated in the current study. Summary statistics for participant characteristics are provided in Table 4. Participants were 26 years of age on average, and LTA participants were significantly older (M=33.26, SD=19.06) than HTA participants (M=22.04, SD=5.76); t (36.97)= 3.34, p= .002; df adjusted for unequal variances). The majority of the sample was female (58%), and sampling procedures ensured that we had a similar gender distribution in both trait anxiety groups. Participants were predominantly White (69%), and in the LTA group, there were more African American participants (18%) and fewer Asian participants (6%), relative to the HTA group (2% and 21%, respectively); χ^2 (4, N=86)= 10.76, p= .03). Because none of these race groups predicted trait anxiety, HF-HRV, or any of our bias indicators when explored independently, race was recoded as white/nonwhite and used as a covariate along with age and sex in subsequent analyses.

4.2 QUESTION 1. ASSOCIATIONS OF THREAT BIAS, HF-HRV AND TRAIT ANXIETY

Prior to regression analyses examining associations of threat bias, HF-HRV and trait anxiety, univariate associations between continuous measures in these models (age, bias indicators and HF-HRV) were examined, as were mean differences between categorical measures (sex, race, and level of trait anxiety) on each of these continuous variables. Univariate associations (Table 5) indicated that older age was associated with lower HF-HRV, but was unrelated to any of the threat bias indices, and none of the threat bias indices were associated with HF-HRV. Independent samples t tests (Table 6) indicated there were no gender or race differences in age, threat bias, or HF-HRV, and only age differed by trait anxiety level.

A series of logistic regression analyses was conducted to examine whether level of trait anxiety was predicted by extent of threat bias or HF-HRV. In each model, age, sex, and race were entered in step 1, followed by a threat bias indicator (dot probe, engagement, disengagement, and ARDPEI overall) or HF-HRV entered at step 2 (Table 7). When tested against a constant only model, each of the full models was significant, indicating that together, the predictors were able to distinguish between high and low trait anxiety (overall classification success = 70.9 - 74.4%). However, these effects were largely driven by age (OR = .93, 95% CI = .88 - .97, p = .003). Neither HF-HRV, nor dot probe-derived bias, disengagement, or overall bias scores from the ARDPEI contributed to the prediction of trait anxiety, though a 1-unit increase in engagement (vigilance) was associated with a slight decrease in the likelihood of being classified as high trait anxiety (OR = .995, 95% CI = .99 – 1.00, p = .04). In order to examine whether threat bias predicted HF-HRV, a series of linear regression analyses were conducted, where age, sex, and race were entered in step 1, followed by each of the threat bias indicators (entered

separately) in step 2. In these analyses, older age and female sex were associated with lower HF-HRV (β = -.50, p < .001, and β = -.20, p = .04, respectively), though none of the threat bias indicators predicted HF-HRV (Table 8). Though we expected both extent of threat bias and HF-HRV to predict level of trait anxiety, and that greater extent of threat bias would be associated with lower HF-HRV, these hypotheses were largely unsupported. Because the above associations were not found, we did not test for mediation of threat bias associations with anxiety by HF-HRV.

4.3 QUESTION 2. EFFECTS OF ATTENTION BIAS MODIFICATION

4.3.1 Randomization check

Prior to analyses examining effects of ABM, baseline group differences between participants randomized to receive bias attenuation versus bias enhancement were examined using independent samples t-tests. Results of these analyses showed that the randomization was successful. Specifically, participants in the bias attenuation and bias enhancement groups did not differ in terms of mean trait anxiety, age, or baseline extent of threat bias, HF-HRV or mood (Table 9). Similarly, a chi square analysis indicated that the proportion of white versus non-white participants did not differ significantly between the two bias modification groups; χ^2 (1, N=52)= .09, p= .77).

4.3.2 Manipulation check

Prior to testing ABM effects during stress and recovery, the efficacy of our stress induction was examined by comparing mean anxiety, heart rate, and HF-HRV between stress and pre-stress (post-ABM) measurements. These analyses showed that 1) Anxiety increased from post-ABM (M= 3.90, SD= 1.82) to stress [M= 6.08 SD= 2.17; t (51)= -5.85, p<.001], 2) Heart rate increased from post-ABM (M= 76.48, SD= 10.33) to stress [M= 81.70, SD= 13.17; t (51)= -4.25, p<.001], and 3) HF-HRV decreased from post-ABM (M= 6.50, SD= 0.81) to stress [M= 6.22 SD= 0.89; t (51)= 3.49, p=.001].

4.3.3 Pre- to post-ABM changes in bias, resting HF-HRV, and mood

Separate 2 X 2 repeated measures ANOVAs were used to examine group (bias enhancement versus bias attenuation) by time (pre- to post-ABM) interactions on extent of bias, resting HF-HRV, and mood (Table 10). Because there were no significant effects of age, sex, or race in any of the models, statistics from models without demographic characteristics are reported here. Overall, these analyses showed no effect of ABM type on extent of bias, HF-HRV, or mood. Specifically, each of the analyses examining the effects of ABM on extent of bias showed that there was no main effect of time, nor were there any group by time interactions, indicating that extent of bias was not successfully altered by our bias modification paradigm. While there was a main effect of time on resting HF-HRV [F (1, 50) = 10.67, p=.002] indicating an overall increase from pre-ABM (M=6.30, SD=.77) to post-ABM (M=6.50, SD=.81), these effects did not differ by bias modification group. In addition, there was no main effect of time on ratings of anxiety, but there was a main effect on ratings of sadness, [F (1, 50) = 22.19, p<.001] with results

showing an overall increase in ratings from pre-ABM (M=3.54, SD=1.35) to post-ABM (M=5.02, SD=2.18). However, there were no group by time interactions on either mood rating. Our hypotheses that ABM groups would differ in terms of extent of bias, mood, and HF-HRV from pre- to post-ABM were not supported, and as such, we did not test for mediation of ABM effects on mood by HF-HRV.

4.3.4 Effects of ABM on HF-HRV and mood during stress and recovery

A series of 2 X 4 repeated measures ANOVAs was used to test for group (bias attenuation versus bias enhancement) by time (pre-ABM, post-ABM, stress, and recovery) interactions on mood and HF-HRV. For these analyses, a Greenhouse-Geisser correction was applied to correct for violations of sphericity. Because these analyses similarly showed no significant age, sex, or race interactions, statistics from models without these demographic variables are reported here.

Mood. Analyses examining group by time differences in mean ratings of anxiety showed a main effect of time [F (2.36, 117.79)= 23.02, p<.001], with post-hoc analyses indicating that ratings of anxiety were significantly higher during the stress task relative to all other time points, which did not differ from one another (Table 11). However, ratings of anxiety over time did not vary by ABM group, as there was no group by time interaction on ratings of anxiety (Table 12). A similar pattern of results emerged in analyses examining mean ratings of sadness, where there was a significant main effect of time [F (2.36, 117.79)= 23.02, p<.001], but no group by time interaction (Table 12). Post-hoc analyses of sadness indicated that ratings were significantly lower at pre-ABM relative to all subsequent ratings taken at post-ABM, during stress, and stress recovery, which did not differ from one another (Table 11). Though we expected negative mood

to be higher among participants who received bias enhancement, these results indicate that our hypothesis was not supported.

Heart Rate Variability. In terms of HF-HRV, there was a main effect of time [F (2.61, 130.61)=9.75, p<.001], with post-hoc comparisons showing an overall pattern in which HF-HRV increased from pre- to post-ABM, decreased during stress (from post-ABM), and then returned to post-ABM levels during stress recovery (Table 13). In addition, there was a group by time interaction (Table 12), indicating that HF-HRV differed over time between ABM groups [F (2.61, 130.61)=3.81, p=.02]. While results from independent samples post-hoc comparisons showed that mean differences in HF-HRV did not differ between ABM groups at any of the collection epochs (Table 14), paired sample within group comparisons showed a slightly different pattern of mean differences in HF-HRV over time for each group (Table 15; Figure 2). Specifically, among individuals who received bias enhancement, there was a significant increase in HF-HRV from pre- to post-ABM, and from stress to recovery, but HF-HRV during stress did not differ from resting HF-HRV assessed previously (at pre- or post-ABM). On the other hand, pre-to post-ABM HF-HRV did not differ among individuals who received bias attenuation, but in this group, HF-HRV was significantly lower during stress than at all other assessments. In both groups, HF-HRV returned to post-ABM levels during stress recovery. These results show our hypothesis that HF-HRV would be lower following ABM among participants who received bias enhancement was not supported.

4.4 SUPPLEMENTAL RELIABILTY ANALYSES

Because previous studies have found the dot probe to have poor internal consistency, and the psychometric properties of newer bias assessment tasks, such as the ARDPEI have not yet been established, we examined the internal reliability of each of these, along with our trait anxiety and HF-HRV measures. Internal consistency of each of our threat bias measures was examined using the split-half method wherein bias scores derived from RTs on odd numbered trials were correlated with scores derived from even numbered trials (e.g. Schmukle, 2005). To assess internal reliability of our HF-HRV measures, Cronbach's α for each epoch of data acquisition (pre-ABM, post-ABM, stress, recovery) was computed using HF-HRV indicators derived from each 1 minute period within each epoch (e.g. Francisco, Porges, Lamb & Rosenberg, 1994). Cronbach's α was also used to determine internal consistency of the STAI. Results of these analyses showed poor internal consistency in the dot probe as well as ARDPEI-derived disengagement and overall threat bias. Conversely, ARDPEI-derived vigilance was internally stable, and we also found high internal consistency in the STAI, and HF-HRV (Table 16).

5.0 DISCUSSION

The present study aimed to examine relationships among trait anxiety, threat bias, and HF-HRV and test whether threat bias modification influences HF-HRV among high trait anxious individuals. Rationale for this investigation was derived from evidence that biased attention toward threat and reduced HF-HRV are both prominent features of anxiety, and that attention bias modification can be used to influence anxiety-related sequelae. Given evidence suggesting that ABM improves anxiety by reducing sensitivity to stress, and that greater stress sensitivity may be reflected in lower HF-HRV, we intended to examine HF-HRV as a potential pathway through which threat biases influence anxiety in two research questions. In question 1, cross sectional relationships of threat bias and HF-HRV among high and low trait anxious individuals were examined. We hypothesized that extent of bias and HF-HRV would both predict level of trait anxiety, that extent of bias and HF-HRV would be inversely associated, and that HF-HRV might cross-sectionally mediate threat bias associations with trait anxiety. For question 2, high trait anxious participants were randomized to either a bias-enhancing or bias-attenuating ABM protocol, after which HF-HRV and mood were assessed at rest and in response to a stressor. Here we hypothesized that HF-HRV and mood would be lower among individuals who received bias enhancement, higher among individuals who received bias attenuation, and that HF-HRV might mediate the effects of ABM on mood. Results of our analyses indicated these hypotheses were

largely unsupported, and are discussed in terms of each research question in the following sections.

5.1 RELATIONSHIPS OF ANXIETY, THREAT BIAS, AND HF-HRV

Our first research question examined cross sectional relationships of threat bias and HF-HRV among individuals selected for high and low trait anxiety. Results indicated that HF-HRV did not predict level of trait anxiety, extent of bias and HF-HRV were unrelated, and only one indicator of bias successfully predicted level of trait anxiety.

5.1.1 HF-HRV and trait anxiety

That we did not find HF-HRV to predict level of trait anxiety was unexpected, as previous studies have generally found individuals higher in trait anxiety to have lower HF-HRV relative to low trait anxious participants (Fuller, 1992, Watkins et al., 1998; Danilova et al., 1994; Mujica et al., 2009; Bleil et al., 2008; Miu et al., 2009). However, these findings are not entirely consistent, and our results are in line with other investigations that have reported null effects (Dishman et al., 2000; Mezzacappa et al., 1997). Inconsistencies in the literature may in part derive from methodological differences among studies (e.g. psychometric instruments, ECG recording procedures, conditions). In particular, many of the studies reporting a relationship between variously-assessed vagal tone and trait anxiety did not control for effects of respiration (Fuller, 1992, Watkins et al., 1998; Danilova et al., 1994; Mujica et al., 2009). Moreover, among the better controlled studies that find an association between continuous measures of trait anxiety

and HF-HRV, effects are modest (*r's* < .3; Brosschot et al., 2007; Bleil et al., 2008). Because meta-analytic results show lower HRV at a moderate effect size among clinically anxious individuals, lower HF-HRV may be more apparent at higher levels of anxiety. Indeed, when we examined the relationship of HF-HRV and trait anxiety scores assessed on a continuous scale (separately within each trait anxiety group), we found the expected inverse association (r= -.29, p= .037) among high trait anxious participants only. This suggest that there may exist a non-linear association between trait anxiety and HF-HRV such that lower HF-HRV is only observed at higher levels of trait anxiety.

5.1.2 Extent of bias and trait anxiety

With the exception of ARDPEI-derived vigilance, no other measure of bias successfully predicted level of trait anxiety in the current study. Given that the presence of a bias toward threat-related information has been well established among anxious individuals using a number of bias assessment tasks, and unlike HRV, the strength of this relationship does not differ between clinically anxious and high trait anxious participants, our results were unexpected and contradict a large literature including numerous investigations with methodologies and participant characteristics similar to the current study (Bar-Haim et al., 2007). Still, not all published reports find a relationship between extent of threat bias and trait anxiety, and these inconsistencies have been attributed to psychometric properties of the dot probe task (see Schmukle, 2005). Specifically, previous studies have found the dot probe to have poor internal consistency and test-retest reliability in non-anxious (Schmukle, 2005; Staugaard, 2009), trait-anxious (Kappenman, Farrens, Luck, & Proudfit, 2014), and clinically-anxious participants (Price et al., 2015; Waechter, Nelson, Wright, Hyatt, & Oakman, 2013). As such, we examined

the internal consistency of each of our threat bias measures and found that the dot probe showed poor internal consistency, as did ARDPEI-derived disengagement and overall threat bias. Conversely, ARDPEI-derived vigilance was internally stable, and we also found high internal consistency in the STAI. As vigilance was the only threat bias measure to successfully predict level of trait anxiety in the current study, null associations of trait anxiety with our other bias indicators could have been the result of poor reliability in the measures.

Moreover, that greater extent of vigilance toward threat was associated with a slight decrease in the likelihood of being classified as high trait anxiety was also contrary to our expectations that high trait anxious individuals would show more threat vigilance. Though previous studies using various methodologies have found hypervigilance toward threat among individuals with anxiety (see Cisler & Koster, 2010), dysfunction in attentional processes in anxiety may also manifest as excessive avoidance of threat-related material. According to the vigilance-avoidance hypothesis (Mogg, Bradley, Miles & Dixon, 2004), individuals with anxiety show altered attentional patterns that give rise to both threat vigilance and subsequent avoidance of threat-related information, and a number of investigations have found evidence of threat avoidance among individuals with anxiety (e.g. Mogg, Bradley, Miles & Dixon, 2010; Koster, Verschuere, Crombez & Van Damme; Koster, Crombez, Verschuere, Van Damme & Wiersema, 2006). As such, reduced vigilance for threat among high, relative to low trait anxious participants in the current study may reflect attentional avoidance of threat-related material among these individuals.

5.1.3 Extent of bias and HF-HRV

None of the threat bias indicators used in the current study were associated with HF-HRV. Because previous studies have established a relationship between HRV and various attentional processes, and the few that have directly examined threat bias tend to find it inversely associated with HRV (Park et al., 2013a; Park et al., 2013b; Miskovic & Schmidt, 2010; Coscia et al., 2012; Johnson et al., 2003, but see also Schwerdtfeger & Derakhshan, 2010), we expected to find the same inverse association. While null effects could be the result of poor internal consistency in our bias measures, ARDPEI-derived threat vigilance did not suffer from the same unreliability but was similarly unrelated to HF-HRV, which was also internally stable ($\alpha = .91$) in the current study. Vigilance derived via the ARDPEI has not previously been examined in relation to HF-HRV, and previous research has relied almost exclusively on the emotional spatial cueing task. Among emotional spatial cueing studies that separately examined vigilance in relation to HRV, lower HRV was found among individuals showing greater threat vigilance in some (Coscia et al., 2012, Park et al., 2013a; Park et al., 2013b) but not all investigations (Schwerdtfeger & Derakhshan, 2010), and the time course of stimulus presentation may moderate these associations. Specifically, two investigations found that individuals with lower (relative to higher) HRV had greater threat vigilance during rapid (e.g. $\leq$ 300ms) presentations of stimuli only, and difficulties disengaging only during longer (e.g. $\geq$ 500ms) presentations (Park et al., 2013a; Park et al., 2013b). As such, we may not have found a relationship between vigilance and HF-HRV in the current study because stimuli in the ARDPEI were presented for a longer duration (500ms). Because the ARDPEI is an improved measure of vigilance and disengagement as it was specifically developed to remediate the methodological limitations of the emotional spatial cueing and modified dot probe tasks (Grafton & Macleod, 2014), additional studies

utilizing varying stimulus presentation durations may provide better insight into the relationship of these components of bias to HF-HRV.

5.2 EFFECTS OF ATTENTION BIAS MODIFICATION

The second aim of the current study was to test the effects of threat bias modification on HF-HRV among high trait anxious individuals, and to determine whether such effects might mediate ABM-related changes in mood. Though we expected to find lower HF-HRV and better mood among individuals randomized to receive bias attenuation, and the converse among those who received bias enhancement, results indicated that ABM groups did not differ in terms of either of these outcomes. Evidence of ABM-related changes in HRV is limited to a single investigation that reported an effect of ABM on HF-HRV during stress recovery (Baert et al., 2012). Because this study was conducted among individuals not selected for anxiety and utilized home-delivery of ABM, which may be less effective (e.g. Heeren et al., 2015; Price, Wallace, Kuckertz, Amir, Graur, Cummings… & Bar-Haim, 2016), we expected to find stronger evidence of an effect of ABM on HF-HRV, though results indicated that was not the case. On the other hand, our predictions regarding the effects of ABM on mood were derived from a much larger literature, with numerous meta-analytic reviews reporting small to moderate decreases in anxiety and negative mood following bias attenuation, and even stronger effects when participants are exposed to a stressor (Hakamata et al., 2010; Mogoaşe et al., 2014; Heeren et al., 2015).

That we did not find ABM-related changes in either mood or HF-HRV is likely due to a failure of our protocol to effectively modify threat bias. Though medium to large effects of ABM on extent of threat bias have been reported, not all studies find biases to be successfully modified

by ABM (see MacLeod & Clarke, 2015). Given that ABM interventions specifically target attention biases, and change in bias is considered the mechanism through which ABM influences anxiety, it follows that we may not see an effect of ABM on anxiety-related sequelae without successful modification of threat bias. Indeed, a review of the literature by MacLeod & Clarke (2015) suggests that improvements in anxiety-relevant outcomes reliably accompany successful bias attenuation by ABM, whereas null effects of ABM tend to be reported in studies where bias modification was similarly unsuccessful. Further illustrating change in bias as the mechanism by which ABM acts is evidence from an investigation that pooled participant-level data from numerous randomized controlled trials and found degree of change in threat bias mediated effects of ABM on anxiety (Price et al., 2016). Importantly, this mediation was significant only among subgroups wherein ABM was found to be most effective (younger participants, laboratory-administrations, clinician-assessed anxiety), suggesting that refinement of ABM methodology is needed in order to maximize its benefit.

Bias modification in the current study was conducted in a laboratory setting among a group of relatively young participants, and although there is evidence that both of these contextual factors may improve the efficacy of ABM (e.g. Price et al., 2016), other methodological considerations may have contributed to the failure of our protocol to modify bias. For instance, ABM was conducted in a single session, and two meta-analytic reviews of the ABM literature have found stronger effects of ABM to accompany repeated administrations (Beard et al., 2012; Hallion & Ruscio, 2011). While there is evidence that single sessions of ABM can influence extent of bias (Hakamata et al., 2010; Mogoaşe et al., 2014; Cristea et al., 2015), a number of single session studies have reported no effect of ABM (Clarke et al., 2014). Considering the increased interest in effects of ABM, and that single sessions are relatively quick

and easy to administer, there may exist an even larger single session literature that is obscured by a publication bias against null results. It is also important to note recent evidence that, within multi-session ABM protocols, the efficacy of ABM on anxiety reduction *decreased* unexpectedly as the total number of training trials across all sessions increased, suggesting that the best ABM "dosage" is an important and complex factor that is not yet understood (Price, Kuckertz, Amir, Bar-Haim, Carlbring, Wallace, 2017).

In addition, effects of ABM in the current study may have been obscured by the poor psychometric properties of our threat bias indicators. Not only were baseline threat bias measures largely unreliable in the current study, but the same pattern of unreliability in these indicators was found for post-ABM assessments of threat bias. Though ARDPEI-derived vigilance did not show the same poor reliability, the effects of ABM on this newer measure of threat bias have not been examined previously. While it may be that we did not see a change in the ARDPEI because modified dot probe ABM effects do not always generalize to non-dot probe bias assessments (Van Bockstaele, Salemink, Bogels & Wiers, 2017), ABM here also included the PIM task, and additional studies examining these newer tasks (e.g. ARDPEI and PIM) together are needed. Finally, bias modification in the current study was comprised of two different tasks that were administered in succession, and though the use of two tasks was intended to increase the effects of bias modification, no studies to our knowledge have examined the cumulative effects of multiple ABM tasks on extent of threat bias. It is possible that if only one of the ABM tasks effectively reduced threat bias in the current study, the addition of an ineffective task may have masked these results.

5.2.1 Changes in HF-HRV over time

Though we did not see an effect of ABM on extent of bias, we did find a slight difference within ABM groups in the pattern of changes in HF-HRV across the course of the study. Specifically, a main effect of time showed that overall, HF-HRV increased from pre- to post-ABM, decreased during stress, and then returned to post-ABM levels during stress recovery. However, this pattern was qualified by a group by time interaction that showed the increase from pre- to post-ABM was only significant among participants who received bias enhancement, while the decrease in response to stress was only significant among those in the bias attenuation group. It is also important to note that while we expected to find group differences in HF-HRV following ABM, post-hoc analyses indicated that HF-HRV did not differ between groups at any time point. Because there was no effect of ABM on extent of bias, it is unclear why we observed a different pattern of change in HF-HRV among participants in each group. Since both ABM tasks were identical in all respects other than to which stimulus participants were directed to attend, it may be that there was a slight effect of ABM on the attentional patterns of participants in each group that was not apparent in our post-ABM assessment due to the psychometric properties of our bias indices. Indeed, while most studies reporting no effect of ABM on extent of bias similarly find no effect on other outcomes, there are a handful that have found ABM to influence anxiety-relevant outcomes in the absence of a measurable change in bias (see MacLeod & Clarke, 2015 for review).

Assuming there was a slight effect of ABM on attentional patterns, that HF-HRV increased from pre- to post-ABM among participants in the bias enhancement group alone was unexpected. Given that attentional training toward threat-related information has been shown to increase anxiety-related sequalae, and that lower HF-HRV has been found among anxious

individuals, we hypothesized that attentional training toward threat-related information would decrease HF-HRV among participants in this group. It is unclear why HF-HRV increased among participants in the bias enhancement group as no prior studies have examined pre- to post-ABM changes in HF-HRV. Earlier work has shown HR decreases to a larger degree when participants are exposed to threatening, relative to positive or neutral images, and these HR decelerations are thought to reflect an increase in parasympathetic activity that facilitates sensory intake for salient information (e.g. Bradley, Codispoti, Cuthbert & Lang, 2001; Lang, Greenwald, Bradley & Hamm, 1993; Cuthbert, Bradley & Lang, 1996; Lacey & Lacey, 1974). As such, directing attention to threat-related stimuli may have elicited an increase in parasympathetic activity that was reflected in an increase in HF-HRV among participants in the bias enhancement group. Alternatively, an increase in parasympathetic activity may have accompanied habituation to threat stimuli among participants in the bias enhancement group. According to the vigilance-avoidance hypothesis (Mogg, Bradley, Miles & Dixon, 2004), excessive threat avoidance may also contribute to experiences of anxiety in that it impedes engagement with threat-related information that would allow for adaptive coping and habituation to threatening material (Mogg et al., 2004). Because high trait anxious individuals in the current study showed threat avoidance (as evidenced by greater avoidance on the ARDPEI engagement index relative to low trait anxious individuals), directing attention to threat-related information that might typically be avoided may have allowed for habituation to the threat which in turn, improved HF-HRV among participants in the bias enhancement group. As the single previous investigation that examined HF-HRV in relation to ABM did not assess pre-ABM HF-HRV, our results are the first to our knowledge that demonstrate an effect of ABM on pre- to post-ABM changes in HRV.

In terms of HF-HRV in response to stress, that only participants in the bias attenuation group showed a significant decrease in HF-HRV was similarly unexpected. Because stress-related decreases in HF-HRV reflect a normative autonomic response in which parasympathetic withdrawal facilitates increases in cardiac output that support defensive stress coping, we anticipated a decrease in HF-HRV among both groups during stress. In addition, because ABM has been shown to influence stress sensitivity among individuals with anxiety, we expected to see increased sensitivity to stress reflected in lower HF-HRV among individuals in the bias enhancement group. While we expected a decrease in HF-HRV in response to stress among both groups, potential habituation to threat in the bias enhancement group may have buffered the effects of the stressor. The increase in HF-HRV from pre- to post-ABM among participants in the bias enhancement group may have also carried through to the stress task, requiring a more potent stressor to elicit a decrease in HF-HRV among both groups of participants. Specifically, our speech anticipation stress task resulted in only a moderate increase in heart rate (5.22 beats per minute) and anxiety ratings (2.17), and participants, who were largely derived from undergraduate Psychology courses, may have gained knowledge from classmates that speeches were not actually recorded. Our results also contradict the single previous investigation testing effects of bias attenuation versus sham ABM on HF-HRV among non-anxious participants that found HF-HRV decreased among both groups of participants during stress, but remained lower during stress recovery among participants in the sham training only. In the current study, HF-HRV returned to pre-stress levels among both groups of participants, further suggesting that our stress task was not potent enough to elicit sustained decreases in HF-HRV among individuals who did not receive bias attenuation.

5.3 LIMITATIONS AND FUTURE DIRECTIONS

The current study was conducted in order to elucidate directional associations among anxiety, threat biases, and HF-HRV. That we were unable to replicate both previously-observed cross sectional relationships and effects of threat bias modification likely resulted from a number of methodological limitations. First, our assessment of trait anxiety was obtained through self-report, which is subject to biases in self-presentation. Measurement error was also introduced in our assessments of threat bias, which generally showed poor internal consistency. Indeed, an expected association between threat bias and trait anxiety was found for the only threat bias assessment that showed better internal reliability in the current study (ARDPEI-derived vigilance). In addition, a failure of our ABM protocol to successfully modify bias precluded further testing of the effects of bias modification on anxiety-relevant outcomes of interest, and our stress-induction task may not have been potent enough to detect meaningful differences in responses to stress. In spite of these limitations, this study was the first to include newly-developed bias assessment and modification tasks in the examination of bias associations with peripheral physiology, as well as the first to test effects of ABM on HF-HRV among anxious individuals. Future studies could improve upon the methodological considerations here to better examine directional relationships among trait anxiety, threat bias, and HF-HRV. Specifically, the psychometric properties of newer bias assessment and modification tasks need to be tested in order to refine these measures and improve the efficacy of ABM interventions before inferences about the role of vagal tone in ABM-related improvements in anxiety can be determined.

6.0 TABLES & FIGURES

Table 1. Threat bias descriptive statistics

	Pre-ABM (n=86)		Post-ABM (n=52)	
	Mean (SD)	*Min. – Max*	*Mean (SD)*	*Min. - Max*
Dot Probe	-.63 (20.75)	-55.24 – 47.30	-1.34 (16.41)	-49.44 – 28.21
Engagement	-11.48 (105.87)	-260.28 – 259.34	6.74 (78.20)	-151.16 – 198.96
Disengage	7.82 (97.50)	-246.70 – 182.33	8.90 (79.94)	-211.17 – 164.83
ARDPEI Total	-1.83 (75.34)	-162.51 – 159.35	7.82 (54.40)	-150.16 – 160.50

Table 2. Associations between threat bias scores

r (p)	Pre-ABM (n=86)			Post-ABM (n=52)		
	2.	3.	4.	2.	3.	4.
1. Dot Probe	-.07 (.50)	-.05 (.64)	-.09 (.44)	.04 (.79)	.14 (.32)	.15 (.29)
2. Engagement	--	.10 (.38)	.76 (.00)	--	.72 (.00)	.76 (.00)
3. Disengage		--	.72 (.00)		--	.56 (.00)
4. ARDPEI Total			--			--

Table 3. Heart rate variability, respiration, and heart rate descriptive statistics

Pre-ABM (n=86)	*Mean (SD)*	*Min. – Max.*
Respiration-adjusted HF-HRV	6.22 (.89)	3.79 – 8.24
Respiration (breaths/minute)	13.17 (3.14)	6.52 – 20.09
HR	76.51 (11.44)	49.76 – 108.91
Post-ABM (n=52)		
Respiration-adjusted HF-HRV	6.50 (.81)	3.74 – 8.37
Respiration (breaths/minute)	14.50 (3.12)	7.83 – 21.30
HR	76.48 (10.33)	56.52 – 106.85
Stress (n=52)		
Respiration-adjusted HF-HRV	6.22 (.89)	-3.43 – 8.29
Respiration (breaths/minute)	16.16 (3.41)	7.57 – 24.55
HR	75.04 (11.52)	39.88 – 103.47
Recovery (n=52)		
Respiration-adjusted HF-HRV	6.52 (.84)	4.00 – 8.13
Respiration (breaths/minute)	14.50 (3.06)	7.64 – 20.21
HR	81.70 (13.17)	57.92 – 110.23

Table 4. Participant Characteristics

		Total, n= 86 *Mean (SD)* *or % (n)*	HTA, n= 52 *Mean (SD)* *or % (n)*	LTA, n= 34 *Mean (SD)* *or % (n)*
Age, years		26.48 (13.84)	22.04 (5.76)	33.26 (19.06)
Sex	Female	58.1 (50)	57.7 (30)	58.8 (20)
	Male	41.9 (36)	42.3 (22)	41.2 (14)
Race	Caucasian	68.6 (59)	67.3 (35)	70.6 (24)
	Asian	15.1 (13)	21.2 (11)	5.9 (2)
	African American	8.1 (7)	1.9 (1)	17.6 (6)
	Other/Multiracial	5.8 (5)	5.8 (3)	5.9 (2)
	Latinx	2.3 (2)	3.8 (2)	0 (0)
Trait Anxiety		39.07 (11.05)	46.98 (6.13)	26.97 (2.61)

Table 5. Univariate associations between continuous measures

N= 86 *r (p)*	2.	3.	4.	5.	6.
1. Age	.08 (.48)	-.16 (.13)	-.13 (.23)	-.19 (.08)	-.50 (.00)***
2. Dot Probe	--	-.07 (.50)	-.05 (.64)	-.09 (.44)	.04 (.73)
3. Engagement		--	.10 (.38)	.76 (.00)***	.16 (.14)
4. Disengagement			--	.72 (.00)***	.09 (.41)
5. ARDPEI Overall				--	.16 (.15)
6. HF-HRV					--

***$p < .00$

Table 6. Mean comparisons between categorical measures

	Sex		Race		Trait Anxiety	
	Male	*Female*	*White*	*Non-white*	*Low*	*High*
Age						
Mean	26.94	26.14	27.20	24.89	33.26	22.04
± SD	± 15.03	± 13.06	± 15.40	± 9.65	± 19.06	± 5.75
t	*t* (68.84)= .26, *p*=.79		*t* (75.76)= .85, *p*=.40		*t* (36.97)= 3.34, *p*=.002	
Dot Probe						
Mean	-2.35	.60	-.18	-1.63	1.57	-2.07
± SD	± 21.24	± 20.51	± 20.97	± 20.61	± 21.40	± 20.39
t	*t* (73.96)= -.65, *p*=.52		*t* (51.30)= .30, *p*=.76		*t* (68.24)= .79, *p*=.43	
Engage						
Mean	-.58	-19.33	-7.70	-19.75	7.57	-23.94
± SD	± 94.60	± 113.57	± 104.15	± 111.08	± 94.95	±111.56
t	*t* (82.14)= .41, *p*=.41		*t* (47.67)= .48, *p*=.64		*t* (78.22)= 1.40, *p*=.17	
Disengage						
Mean	16.17	1.81	5.32	13.29	-8.08	18.21
± SD	± 99.72	± 96.44	± 101.07	± 90.81	± 120.10	± 78.94
t	*t* (74.03)= .67, *p*=.51		*t* (55.79)= -.36, *p*=.79		*t* (51.61)= -1.13, *p*=.27	
ARDPEI Total						
Mean	-6.75	-8.98	-2.01	-3.23	-1.68	-2.86
± SD	± 74.65	± 78.02	± 80.47	± 68.75	± 88.57	± 68.54
t	*t* (77.47)= .95, *p*=.35		*t* (58.51)= .07, *p*=.94		*t* (58.14)= .07, *p*=.95	
HF-HRV						
Mean	6.40	6.08	6.29	6.06	6.09	6.29
± SD	± .97	± .81	± .80	± 1.07	± 1.05	± .77
t	*t* (67.55)= 1.60, *p*=.11		*t* (39.90)= .98, *p*=.33		*t* (55.64)= -.96, *p*=. 34	

***p* < .001 All estimates were adjusted for unequal variances

Table 7. Summary results of logistic regression analyses predicting level of trait anxiety from HF-HRV and extent of threat bias

	OR (*p*)	95% CI	Step χ^2	R^2 *(Nagelkerke)*
Step 1: Covariates			14.97**	.22
Age	.93 (.003)**	.88 – .97		
Sex	.92 (.86)	.35 – 2.42		
Race	1.07 (.90)	.39 – 2.96		
Step 2: HF-HRV	.69 (.30)	.34 – 1.38	1.13	.23
Step 2: Bias†				
Dot Probe	.99 (.59)	.97 – 1.02	.30	.22
Engagement	.995 (.04)*	.99 – 1.00	4.81*	.28
Disengagement	1.00 (.41)	.98 – 1.01	.68	.23
ARDPEI Overall	.997 (.38)	.99 – 1.00	.80	.22

**p<.01, *p<.05. †Entered separately in analyses.
Note. Full analytic models are reported in Tables 17-21 (Appendix B)

Table 8. Summary results of linear regression analyses predicting HF-HRV from extent of threat bias.

	B (SE)	95% CI	β	Step F (*p*)	R^2
Step 1: Covariates				10.97 (.000)**	.29
Age	-.03 (.006)	-.04 – -.02	-.50**		
Sex	-.35 (.17)	-.69 – -.02	-.20*		
Race	.05 (.08)	-.11 – .22	.06		
Step 2: Bias†					
Dot Probe	.004 (.004)	-.004 – .013	.10	1.19 (.28)	.30
Engagement	.001 (.001)	-.001 – .002	.07	.49 (.48)	.29
Disengagement	.000 (.001)	-.002 – .002	.08	.01 (.94)	.29
ARDPEI Overall	.001 (.001)	-.002 – .003	.04	.20 (.67)	.29

**p<.01, *p<.05. †Entered separately in analyses
Note. Full analytic models are reported in Tables 22-25 (Appendix B)

Table 9. Results of independent samples t-tests examining group differences between participants randomized to receive bias attenuation versus bias enhancement

	Mean (SD)			
	Bias Attenuation (N=26)	Bias Enhancement (N=26)	*t*	*p*
Trait Anxiety	47.19 (6.08)	46.77 (6.30)	.25	.74
Age	21.77 (3.57)	22.30 (7.40)	-.33	.81
Extent of Bias				
Dot Probe	-2.64 (21.14)	-1.51 (20.02)	-.20	.84
Engagement	-12.97 (103.85)	-34.91 (119.81)	.71	.48
Disengagement	22.90 (86.57)	13.54 (71.92)	.42	.67
ARDPEI Overall	4.97 (63.58)	-10.69 (73.58)	.82	.42
HF-HRV	6.37 (.70)	6.23 (.84)	.68	.50
Mood Ratings				
Anxious	3.54 (1.61)	3.38 (1.88)	.32	.75
Sad	3.65 (1.16)	3.42 (1.53)	.61	.54

Table 10. Summary results of Repeated Measures ANOVA examining pre- to post-ABM changes in extent of bias, HF-HRV and mood.

		Mean (SD)			
Assessment	*Condition*	*Pre-ABM*	*Post-ABM*	*F*	*p*
Dot Probe	Bias Attenuation	-2.64 (21.14)	-3.74 (15.86)	.25	.62
	Bias Enhancement	-1.51 (20.02)	1.07 (16.91)		
Engagement	Bias Attenuation	-12.97 (103.85)	6.94 (86.63)	.36	.55
	Bias Enhancement	-34.91 (119.81)	6.54 (70.50)		
Disengagement	Bias Attenuation	22.90 (86.57)	7.43 (73.54)	.14	.71
	Bias Enhancement	13.54 (71.92)	10.38 (87.32)		
ARDPEI Overall	Bias Attenuation	4.97 (63.58)	7.18 (60.07)	.97	.33
	Bias Enhancement	-10.69 (73.58)	13.08 (53.31)		
HF-HRV	Bias Attenuation	6.37 (.70)	6.46 (.81)	3.10	.09
	Bias Enhancement	6.23 (.84)	6.53 (.83)		
Mood- Anxious	Bias Attenuation	3.54 (1.61)	4.03 (1.80)	.04	.84
	Bias Enhancement	3.38 (1.88)	3.77 (1.86)		
Mood- Sad	Bias Attenuation	3.65 (1.16)	5.15 (2.22)	.004	.95
	Bias Enhancement	3.42 (1.53)	4.88 (2.18)		

Note. Full analytic models are reported in Table 26 (Appendix B)

Table 11. Results of post-hoc comparisons examining the main effect of time on ratings of mood

			Post-ABM		Stress		Recovery	
	Mean	*SD*	*t (51)*	*p*	*t (51)*	*p*	*t (51)*	*p*
Mood - Anxious								
Pre-ABM	3.46	1.73	-1.53	.132	-1.89	.000	-1.12	.27
Post-ABM	3.90	1.82	--		-5.85	.000	-.06	.96
Stress	6.07	2.17			--		7.91	.000
Recovery	3.92	2.23					--	
Mood - Sad								
Pre-ABM	3.54	1.35	-4.76	.000	-4.36	.000	-4.29	.000
Post-ABM	5.02	2.18	--		.70	.49	.73	.47
Stress	4.94	2.21			--		.00	.99
Recovery	4.93	2.22					--	

Table 12. Summary results of Repeated Measures ANOVA examining group by time interactions on mood and HF-HRV

	Mean (SD)						
	Pre-ABM	*Post-ABM*	*Stress*	*Recovery*	*F*	*df*	*p*
Mood - Anxious							
Bias Attenuation	3.54 (1.61)	4.04 (1.80)	6.50 (1.79)	4.27 (2.22)	.46	2.36, 117.79	.67
Bias Enhancement	3.38 (1.88)	3.77 (1.86)	5.65 (2.45)	3.58 (2.23)			
Mood - Sad							
Bias Attenuation	3.65 (1.16)	5.15 (2.22)	5.15 (2.27)	5.08 (2.21)	.06	1.33, 66.69	.86
Bias Enhancement	3.42 (1.53)	4.88 (2.18)	4.73 (2.16)	4.81 (2.26)			
HF-HRV							
Bias Attenuation	6.37 (.70)	6.46 (.81)	6.07 (.88)	6.51 (.80)	3.81	2.61, 130.61	.02
Bias Enhancement	6.22 (.84)	6.54 (.83)	6.38 (.90)	6.54 (.90)			

Note. Full analytic models are reported in Table 27 (Appendix B)

Table 13. Results of post-hoc comparisons examining the main effect of time on HF-HRV

			Post-ABM		Stress		Recovery	
	Mean	*SD*	*t (51)*	*p*	*t (51)*	*p*	*t (51)*	*p*
Pre-ABM	6.30	.77	-3.20	.002	.89	.38	-3.97	.000
Post-ABM	6.50	.81	--		3.49	.001	-.34	.74
Stress	6.22	.89			--		-4.36	.000
Recovery	6.52	.84					--	

Table 14. Independent samples post-hoc comparisons of HF-HRV between ABM groups at each time point

		Mean	*SD*	*t* (50)	*p*
Pre-ABM	Bias Attenuation	6.37	.70	.68	.50
	Bias Enhancement	6.22	.84		
Post-ABM	Bias Attenuation	6.46	.81	-.33	.75
	Bias Enhancement	6.54	.83		
Stress	Bias Attenuation	6.07	.88	-1.23	.22
	Bias Enhancement	6.38	.90		
Recovery	Bias Attenuation	6.51	.80	-.13	.90
	Bias Enhancement	6.54	.90		

Table 15. Paired samples post-hoc comparisons of HF-HRV at each time point by ABM group

			Post-ABM		Stress		Recovery	
	Mean	*SD*	*t (51)*	*p*	*t (51)*	*p*	*t (51)*	*p*
Bias Attenuation								
Pre-ABM	6.37	.70	-1.42	.17	2.72	.01	-2.09	.05
Post-ABM	6.46	.81	--		3.86	.001	-.64	.53
Stress	6.07	.88			--		-3.98	.001
Recovery	6.51	.80					--	
Bias Enhancement								
Pre-ABM	6.23	.84	-2.97	.01	-1.39	.18	-3.46	.002
Post-ABM	6.54	.83	--		1.35	.19	.02	.98
Stress	6.38	.90			--		-2.15	.04
Recovery	6.54	.90					--	

Table 16. Internal consistency of study measures

	Split-Half *r* (*p)*				Cronbach's α	
	Dot Probe	ARDPEI Engage	ARDPEI Disengage	ARDPEI Overall	HF-HRV	STAI
Pre-ABM	.12 (.18)	.34 (.001)	-.10 (.37)	.02 (.88)	.99	.86
Post-ABM	-.18 (.20)	.30 (.03)	.22 (.11)	.02 (.87)	.94	--
Stress	--	--	--	--	.95	--
Recovery	--	--	--	--	.95	--

Figure 1. Study Design

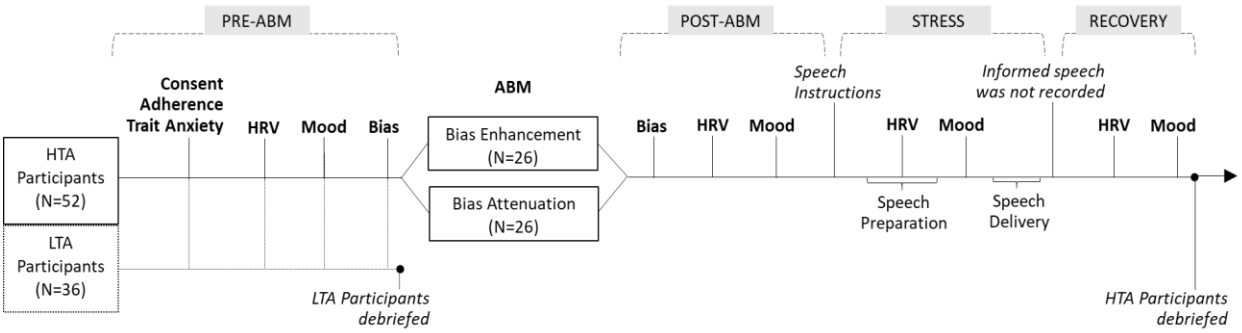
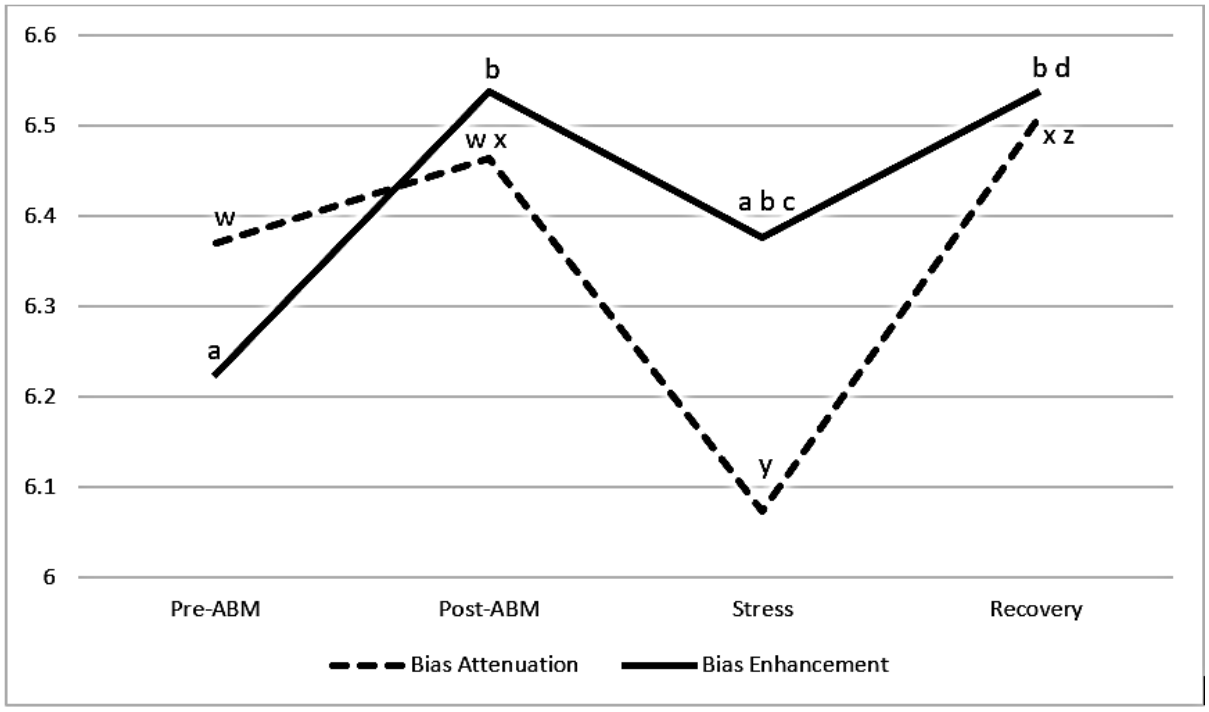


Figure 2. Differences in HF-HRV at each collection epoch by ABM group



Note. Shared letters indicate within group means are not statistically different

APPENDIX A

POWER ANALYSES

A priori power analyses were conducted using G*Power (Faul, Erdfelder, Lang, & Buchner, 2007). For question 1, three separate analyses using the bivariate correlation normal model were performed to determine sample sizes needed to detect (with at least 80% power) associations of 1) anxiety with threat bias, 2) anxiety with HF-HRV, and 3) threat bias with HRV. In terms trait anxiety and threat bias, parameters estimated from the effects (d=.63) reported by Grafton & MacLeod (2014) indicated that 67 participants would be sufficient to detect this association (power =.800). Similar analyses for trait anxiety associations with HF-HRV using effects (r= -.3) estimated from Watkins et al. (1998) also showed that a sample of 67 participants would allow us to detect this relationship (power = .803), and effects estimated from associations of threat bias and HF-HRV (r=.5) reported by Miskovic & Schmidt (2005) indicated that 21 participants would be needed to detect this association (power= .817).

For question 2, sample sizes needed to detect significant group (between subjects) by time (within subjects) interactions with at least 80% power were calculated separately for the effects of ABM on bias, mood, and HF-HRV. Estimates for the effects of ABM on bias and stressor-evoked mood were derived from previously-reported effects of the PIM task on both of

these (Notebaert et al., 2015). In terms of the effects of ABM on extent of bias, Notebaert and colleagues (2015) found a significant interaction (eta^2_p = .18) between assessment point (pre- to post-ABM) and training condition (threatening or happy faces) where threat bias increased from pre- to post-training in the train toward threat condition (*d*=.70), and decreased in the train toward happy condition (*d*=.66). Repeated-measures, within-between interaction ANOVA models in G*Power using each of the above-reported effect sizes resulted in effect size f estimates of .47, .35, and .33, respectively. An effect size f estimate of .3 and conservative repeated measures correlation estimate of .10 indicated that a total of 34 participants (16 per group) would be needed to detect an effect of ABM on bias (power= .804). The effects of ABM on stressor-evoked mood were estimated from the significant interaction (eta^2_p = .05) reported by Notebaert et al., (2015), where participants in the attend-threat condition had significantly greater negative mood following the stressor than participants in the attend-happy condition (*d*=.62). Effect size f estimates derived from these parameters were .23 and .31, respectively, and using the more conservative of the two (.23) with a conservative repeated measures correlation estimate of .1 indicated that 52 participants (26 per group) would allow us to detect an effect of ABM on stressor-evoked mood (power=.811). The sample size needed to detect an effect of ABM on post-stressor HRV was determined using previously-reported effects of ABM on HF-HRV (Baert et al., 2012) where participants receiving modified dot probe ABM to reduce threat bias (versus sham) had significantly higher HF-HRV (*d*=.69). This effect yielded an estimated effect size f of .34, and with a repeated measures correlation estimate of .1, we would need 28 total participants (14 per group) to detect a similar effect (power= .823). Though no previous studies have examined the effects of ABM on resting HRV, effects estimated from a previous report that found individuals in a bio feedback intervention to have higher resting HRV relative

to controls (*d*=.64; Bradley, McCraty, Atkinson, Tomasino, Daugherty & Arguelles, 2010) indicated that with an estimated f of .32, and repeated measures correlation of .1, a total of 30 participants (15 per group) would be needed to detect a similar effect in our sample (power =.802).

Finally, in the case that we were to find significant associations in either question 1 or question 2, we determined the sample size needed to detect (with at least 80% power) partial mediation of A) trait anxiety associations with threat bias by HRV (question 1), and B) ABM associations with mood by HF-HRV (question 2) using the linear multiple regression fixed R^2 increase model. Parameters derived from variance explained in the Cocia et al. (2012) report (ΔR^2=.22) resulted in an estimated effect size f of .28, which indicated that a sample of 38 participants would allow us to detect partial mediation with these variables and three additional predictors (e.g. standard demographic covariates, age sex and race) added to the model (power = .805). Taken together, the most conservative estimated number of participants needed to test question 1 (which includes both high and low trait anxious participants) was 67, while the most conservative estimate for question 2 (conducted in high trait anxious participants only) was 52 participants (26 in each ABM group). Thus, the current study recruited 86 participants total (52 high trait anxious participants and 34 low trait anxious participants).

APPENDIX B

FULL ANALYTIC MODELS

B.1 LOGISTIC REGRESSION ANALYSES

Table 17. Results of logistic regression analysis predicting level of trait anxiety from HF-HRV

	B	*SE*	*p*	Model χ^2	Model R^2 *(Nagelkerke)*
Age	-.09	.03	.002	16.09	.23
Sex	-.24	.52	.644		
Race	-.05	.54	.926		
HF-HRV	-.37	.35	.299		
Constant	5.18	2.76	.061		

Table 18. Results of logistic regression analysis predicting level of trait anxiety from dot probe

	B	*SE*	*p*	Model χ^2	Model R^2 *(Nagelkerke)*
Age	-.08	.03	.004	15.26	.22
Sex	-.08	.50	.879		
Race	-.06	.52	.911		
Dot Probe	-.006	.01	.588		
Constant	2.44	.77	.001		

Table 19. Results of logistic regression analysis predicting level of trait anxiety from ARDPEI engagement

	B	*SE*	*p*	Model χ^2	Model R^2 *(Nagelkerke)*
Age	-.09	.03	.001	19.78	.29
Sex	-.20	.51	.702		
Race	-.01	.54	.987		
Engagement	-.01	.003	.037		
Constant	2.78	.80	.001		

Table 20. Results of logistic regression analysis predicting level of trait anxiety from ARDPEI disengagement

	B	*SE*	*p*	Model χ^2	Model R^2 *(Nagelkerke)*
Age	-.08	.03	.004	15.64	.23
Sex	-.09	.50	.929		
Race	.06	.52	.908		
Disengagement	.002	.003	.412		
Constant	2.38	.77	.002		

Table 21. Results of logistic regression analysis predicting level of trait anxiety from ARDPEI Overall

	B	*SE*	*p*	Model χ^2	Model R^2 *(Nagelkerke)*
Age	-.08	.03	.002	15.76	.23
Sex	-.15	.50	.768		
Race	.04	.52	.935		
ARDPEI	-.003	.003	.376		
Constant	2.60	.79	.001		

B.2 LINEAR REGRESSION ANALYSES

Table 22. Results of linear regression analyses predicting HF-HRV from dot probe

	B	*SE*	β	*t*	*p*	Model R^2
Age	-.03	.01	-.51	-5.46	.000	.30
Sex	-.37	.17	-.21	-2.19	.032	
Race	.07	.08	.08	0.80	.427	
Dot Probe	.004	.004	.10	1.09	.279	
Constant	7.48	.39		19.29	.000	

Table 23. Results of linear regression analyses predicting HF-HRV from ARDPEI engagement

	B	*SE*	β	*t*	*p*	Model R^2
Age	-.03	.01	-.49	-5.17	.000	.54
Sex	-.34	.17	-.19	-2.02	.047	
Race	.06	.08	.06	0.67	.506	
Engagement	.001	.001	.07	0.70	.484	
Constant	7.44	.39		18.92	.000	

Table 24. Results of linear regression analyses predicting HF-HRV from ARDPEI disengagement

	B	*SE*	β	*t*	*p*	Model R^2
Age	-.03	.01	-.50	-5.29	.000	.54
Sex	-.35	.17	-.20	-2.07	.042	
Race	.05	.08	.06	0.62	.53	
Disengagement	.001	.001	.01	0.08	.94	
Constant	7.48	.39		19.02	.000	

Table 25. Results of linear regression analyses predicting HF-HRV from ARDPEI overall

	B	*SE*	β	*t*	*p*	Model R^2
Age	-.03	.01	-.49	-5.16	.000	.54
Sex	-.35	.17	-.19	-2.03	.046	
Race	.05	.08	.06	0.64	.525	
ARDPEI	.001	.001	.04	0.45	.656	
Constant	7.46	.40		18.84	.000	

B.3 REPEATED MEASURES ANOVAS

Table 26. Results of 2X2 repeated measures ANOVAs of pre- to post-ABM extent of bias by ABM group

Assessment	Effect	*MS*	*df*	F	*p*
Dot Probe	Time	14.27	1	0.04	.842
	Group	228.65	1	0.68	.413
	Time X Group	87.61	1	0.25	.623
	Error	357.19	50		
Engagement	Time	24465.57	1	2.95	.092
	Group	3243.49	1	0.31	.581
	Time X Group	3016.33	1	0.36	.549
	Error	8299.21	50		
Disengagement	Time	2256.82	1	0.33	.569
	Group	267.16	1	0.05	.834
	Time X Group	985.71	1	0.14	.706
	Error	6855.63	50		
ARDPEI Overall	Time	4387.81	1	1.42	.240
	Group	618.13	1	0.13	.723
	Time X Group	3018.93	1	0.97	.328
	Error	3098.54	50		

Table 27. Results of 2 X 4 repeated measures ANOVAs of HF-HRV and mood ratings by ABM group over time

Assessment	Effect	*MS*	*df*	F	*p*
HF-HRV	Time	1.30	2.61	9.75	.000
	Group	0.23	1	0.92	.762
	Time X Group	0.51	2.61	3.81	.016
	Error	0.13	130.61		
Mood: Anxiety	Time	91.66	2.36	23.02	.000
	Group	12.51	1	1.90	.174
	Time X Group	1.82	2.36	0.46	.666
	Error	3.98	117.79		
Mood: Sadness	Time	59.90	1.33	17.52	.000
	Group	4.62	1	0.38	.539
	Time X Group	0.21	1.33	0.06	.980
	Error	3.42	66.69		

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