# DEPRESSION AND ANXIETY:
# DIFFERING RELATIONSHIPS TO RESPIRATORY SINUS ARRHYTHMIA

by

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## Abstract

Many theoretical models addressing the role of the parasympathetic branch of the autonomic nervous system in psychopathology predict decreased respiratory sinus arrhythmia (RSA) in disorders such as depression and anxiety. However, decreased RSA in depression is not consistently observed across studies. Research on the relationship between anxiety and RSA has also been mixed, but the results may be more robust than that of depression. Before the theoretical models can be re-examined based on these findings, researchers must clarify the nature of these relationships. Specifically, three things should be determined: a) is there a relationship between RSA and depression; b) is there a relationship between anxiety and RSA; and c) could comorbid anxiety in depression be playing a role in the mixed findings to date.

This study was specifically designed to address those three questions. Based on the empirical literature, we hypothesized that: 1) depression would have a small but significant relationship to RSA; 2) anxiety would have a significant relationship to RSA that would be stronger than that of depression to RSA; 3) the anxiety-RSA relationship would persist when controlling for depression, whereas the depression-RSA relationship would not persist when controlling for anxiety. Additionally, the Cardiac Sympathetic Index (CSI) was used to explore the potential relationships that depression and anxiety may have with sympathetic-related heart rate variability and sympathovagal balance.

One-hundred and twenty-eight physically healthy undergraduate students completed a questionnaire measure assessing depression and anxiety symptoms.

Participants' ECG recordings were taken both at rest and during a stressful arithmetic task to obtain measures of RSA and CSI. Regression analysis revealed a significant inverse relationship between anxiety and RSA, and a marginally significant inverse relationship between depression and RSA, during the stressful arithmetic task. No significant relationships were observed at rest, or with CSI. Importantly, the relationship between anxiety and RSA persisted when controlling for depression, whereas the opposite was not true: the relationship between depression and RSA is almost eliminated when controlling for anxiety. These results suggest that some of the positive findings in the depression-RSA literature may be due to uncontrolled, co-occurring anxiety symptoms.

## Preface

This study was designed and implemented by the author, Anita Hibbert. Similarly, data analysis and the writing of the manuscript were the author's responsibility. Data collection was conducted by the author and Ms. Lalonde. Dr. Klonsky kindly provided suggestions and feedback throughout the project, and edited the manuscript during the write-up. All procedures and methods were approved by the UBC Behavioural Research Ethics Board (certificate # H11-01163).

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## Introduction

Heart rate variability (HRV), defined as the cyclical changes in the interval between consecutive heart beats, or the oscillations in consecutive instantaneous heart rates (Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology, 1996), has come a long way from its original status as artifactual noise (Porges, 2007). Since its first clinical application in fetal distress (Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology, 1996), HRV has moved from the realm of medicine and physiology to be widely used by researchers in psychology and psychopathology.

The role of the autonomic nervous system (ANS) in the genesis of heart rate variability has been extensively studied. HRV has in fact come to be used to assess the ANS, as it is partly responsible for regulating cardiac activity. More specifically, HRV is used as a tool to investigate sympathetic and parasympathetic influence on the heart (Acharya, Joseph, Kannathal, Lim, & Suri, 2006). The heart's pacemaker, the sinoatrial node of the heart, is enervated by both the sympathetic and the parasympathetic branches of the ANS. These branches have opposing, but independent, effects on heart rate: the sympathetic branch acts to increase heart rate, whereas the parasympathetic branch decreases heart rate. Resting heart rate is under tonic control of the parasympathetic branch of the ANS, which acts through the vagus nerve. This tonic level of vagal influence on the heart results in a resting heart rate which is slower than the intrinsic rate at which the cardiac pacemaker would otherwise contract (Porges, 2001).

Variability in heart rate has been characterized in many different ways (Allen, Chambers, & Towers, 2007), although metrics differ in their putative sources of this variability. Currently, many researchers are using HRV metrics which are supposed to index the influence of the parasympathetic nervous system (PNS) on the heart. Metrics assessing respiratory sinus arrhythmia (RSA) are most commonly used.

**Early Research in Heart Rate Variability and Depression**

Early research looking at the relationship between overall HRV and depression occurred largely in coronary artery disease (CAD) patients. Studies typically remarked that there was a higher-than-expected rate of depression in CAD populations (for a review, see Dalack & Roose, 1990) and that depression often predicted poorer outcomes in CAD samples (Ahern et al., 1990). For example, Carney, Rich, Freedland, et al., (1988) demonstrated that depression was the best predictor of cardiac events in the year following CAD diagnosis. HRV, along with increased sympathetic tone (e.g. Carney, Rich, teVelde, et al., 1988), was often suggested as a potential mediator between depression and increased morbidity and mortality in CAD. The potential for HRV to be mediating the depression-CAD link was strengthened by studies demonstrating a link between decreased HRV and increased mortality in CAD populations (e.g. Kleiger, Miller, Bigger, & Moss, 1987). Depression-related differences in HRV then began to be investigated, with several studies showing support for decreased HRV in depression (Carney et al., 1995; Krittayaphong et al., 1997).

Up to this point, researchers studying the depression-CAD link had been primarily focused on overall measures of HRV, which captured a mixture of both sympathetic and

parasympathetic influence on the heart. Gradually, researchers became interested in using metrics which were supposedly specific to the parasympathetic or sympathetic branches of the ANS in order to examine the decrease in HRV in depression more closely (e.g. Stein et al., 2000). Researchers noted that the decreased HRV seen in depressed CAD patients was primarily due to decreases in RSA-related metrics (e.g. Dalack & Roose, 1990).

**From Heart Rate Variability to Respiratory Sinus Arrhythmia**

The shift away from metrics of overall variability to more specific metrics of HRV as illustrated above was likely due in part to the increased understanding of the different contributors to overall HRV (Porges, 2007). Although metrics of overall variability in heart rate were useful as general outcome variables, they did not improve understanding of the underlying mechanisms. The emergence of HRV metrics specifically assessing parasympathetic or sympathetic influence on the heart deepened the understanding of heart rate variability and its link to clinical outcomes. Understandably, much research has been done to verify the origins of different metrics of HRV. RSA (which for ease of understanding will now refer to all metrics assessing RSA) has emerged as the most well-characterized of the HRV metrics, in that it is commonly understood to be a relatively 'pure' measure of parasympathetic influence on the heart.

From a purely mechanical view of the autonomic nervous system, the phenomenon of RSA occurs too quickly for the sympathetic branch of the ANS to contribute to the variance. The parasympathetic branch of the ANS exerts its influence at the order of hundreds of milliseconds, whereas the sympathetic branch of the ANS takes 10x longer, and decays 15x more slowly (Bernston, Cacioppo, & Quigley, 1993), meaning that only

the fluctuations in parasympathetic influence would occur quickly enough to match respiration speeds.

The neural mechanisms behind RSA have been extensively investigated in animal models. In dogs, parasympathetic blockade was shown to eliminate HF heart rate fluctuations, whereas sympathetic blockade had no effect on HF heart rate fluctuations (Akselrod et al., 1981, 1985). Katona & Jih, (1975) found that respiratory sinus arrhythmia in anesthetised dogs was proportional to the difference in pre- to post-vagal cooling (temporarily blocking the vagal influence). In rats, parasympathetic blockade (via atropine) eliminated the HF heart rate fluctuations (Japundzic, Grichois, Zitoun, Laude, & Elghozi, 1990).

Autonomic blockade studies in humans have also found substantial evidence that RSA arises primarily from parasympathetic influence on the heart. For example, researchers have documented that across several behavioural tasks, RSA was not attenuated by sympathetic blockade using both alpha and beta-adrenergic blockers (Grossman, Stemmler, & Meinhardt, 1990). Similarly, another study found that whereas atropine administration (a parasympathetic blocker) eliminated almost all HF power, propranolol (a sympathetic blocker) did not have a significant effect on HF power. This led the authors to conclude that RSA is mediated by the parasympathetic branch alone (Pomeranz et al., 1985).

One possible reason why RSA has come to dominate the psychophysiological non-invasive study of heart rate variability is that the mechanisms underlying the phenomenon are the most clearly understood. Other measures of heart rate variability, especially those

indexing overall variability (for example, SDNN), are influenced by numerous factors including both the sympathetic and parasympathetic branches of the autonomic nervous system (Allen et al., 2007), interacting in numerous feedback loops (Porges, 2007). The physiological correlates for high frequency power (HF power; a measure of RSA) are better characterized than those of very low frequency (VLF), and ultra-low frequency (ULF) power (Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology, 1996). In fact, despite being frequently cited as indexing sympathetic influence on the heart, low frequency (LF) power may in fact be influenced to a large extent by vagal input (Eckberg, 1997). Given the movement towards understanding the phenomenon of heart rate variability from a neurophysiological perspective, and away from using heart rate variability metrics as 'behaviours' (Porges, 2007), metrics which are well-characterized within a physiological framework have inherent appeal. RSA remains of significant interest to researchers, as the evidence supporting its validity as a relatively 'pure' index of parasympathetic efferent influence on the heart is substantial.

## RSA in Psychopathology

The previously discussed relationship between depression and RSA in CAD populations was discovered through empirical studies. However, several theoretical models also predict a relationship between depression and decreased RSA. Three of the most relevant theoretical models are discussed below.

**Polyvagal theory.** Polyvagal theory (Porges, 1995, 2001, 2003a, 2007, 2009) has been a highly influential theoretical framework in the investigation of the potential

relationship between psychopathology and parasympathetic functioning (Chambers & Allen, 2007a). In this theory, Porges posits that the human heart is innervated by two distinct vagal inputs: the 'smart vagus', consisting of myelinated fibres arising from the nucleus ambiguus (NA), and the 'vegetative vagus', consisting of unmyelinated fibres arising from the dorsal motor nucleus of the vagus (DMN). Whereas the smart vagus displays respiratory-linked oscillations in its activity and acts as a potent inhibitor of heart rate, the activity of the vegetative vagus is not linked with respiration, and under normal conditions it is not thought to greatly influence heart rate (Porges, 2001). These two branches of the vagus represent two different pathways that have evolved for responding to threat. According to polyvagal theory, the smart vagus represents a distinctly mammalian adaptation, allowing mammals to inhibit their sympathetic responses when they are in safe environments, thereby promoting engagement in social behaviours and interactions. Upon detection of threat in the environment, the influence of the smart vagus on the heart can be quickly withdrawn, allowing for a rapid increase in cardiac output without the metabolically costly activation of the sympathetic branch of the ANS. With the 'vagal brake' withdrawn, increasing threat or prolonged challenge can lead to the activation of the sympathetic nervous system, promoting a 'fight or flight' state that is uninhibited by opposing parasympathetic influence. Should engagement in fight or flight behaviours be impossible or ineffective, the vegetative vagus is thought to then induce bradycardia and more 'primitive' threat responses such as immobilization. These three phases are thought to reflex three stages of phylogenetic development, with first stage being an evolutionarily recent mammalian adaptation, in comparison with the third phase, which is thought to represent an evolutionarily older adaptation to threat.

According to polyvagal theory, physiological state limits the scope of possible social behaviours within an individual (Porges, 2003a). Deficits in parasympathetic influence increase the tendency of an individual to enter into states characterized by mobilization (aka. 'fight or flight') or immobilization (behavioural shutdown), and prevent the individual from adaptively engaging with those around them. The impairments in social engagement, and predominance of defensive reactions, are thought to mirror many of the symptoms observed in psychological disorders, such as anxiety and depression (Rottenberg, 2007).

**Polyvagal theory and Gray's motivational theory.** Beauchaine (2001; Beauchaine, Gatzke-Kopp, & Mead, 2007) has elaborated on polyvagal theory's application to psychopathology and development by integrating concepts from Gray's motivational theory, most notably the behavioural activation system (BAS) and the behavioural inhibition system (BIS). According to this theory (Beauchaine, 2001; Beauchaine et al., 2007), decreased tonic vagal control and excessive vagal withdrawal result in dysregulated emotional states and emotional lability, respectively. Whether this emotional dysregulation results in externalizing disorders (such as anger or aggression) versus internalizing disorders (such as anxiety or depression) depends on whether the BAS or the BIS motivational systems predominate within the individual. The BAS functions to motivate approach or active avoidance behaviours in order to maximize reward, whereas the BIS motivates passive avoidance, or inhibition of appetitive behaviours, in order to avoid aversive consequences (Beauchaine, 2001). In individuals whose SNS response is more highly influenced by the BAS motivational system, externalizing emotions and disorders predominate. In individuals whose SNS response is more highly influenced by

the BIS motivational system, internalizing emotions and disorders predominate.

**Autonomic flexibility – neurovisceral integration model.** A slightly different approach to HRV and psychopathology integrates research from both brain imaging studies and peripheral physiology (Friedman, 2007; Thayer & Lane, 2000, 2009; Thayer & Ruiz-Padial, 2006). In this model, the brain's central autonomic network (CAN) is tonically inhibited by areas in the prefrontal cortex. When presented with threatening stimuli, the inhibitory influence of the prefrontal cortex can be taken 'offline', which releases the inhibitory influence on the CAN. The resulting CAN disinhibition leads to increases in sympathetic activity and decreases in parasympathetic activity. In terms of HRV, these changes would be expected to lead to a decrease in RSA. In disorders such as anxiety or depression, this model posits that there is hypoactivation in key areas of the prefrontal cortex, related to an inability to inhibit threat-related neural pathways and resulting in a chronic lack of inhibition of the CAN. As such, disorders such as anxiety and depression should be related to increases in sympathetically mediated HRV, and decreases in RSA (Thayer & Lane, 2009).

## Current Research: Depression

The three theories outlined above predict, directly or indirectly, that depression should be associated with decreased levels of RSA. As discussed previously, this relationship has been demonstrated in CAD populations, but it has also been more recently investigated in medically healthy populations.

**Depression and RSA at rest.** Research into RSA in depression has frequently led

to mixed results. Many studies have found that depression or depressed mood is associated with low RSA at rest, both in clinically depressed patients (Agelink, Boz, Ullrich, & Andrich, 2002; Kemp, Quintana, Felmingham, Matthews, & Jelinek, 2012; Rechlin, Weis, Spitzer, & Kaschka, 1994; van der Kooy et al., 2006; Light, Kothandapani, & Allen, 1998), and in non-clinical samples (O'Connor, Allen, & Kaszniak, 2002). However, many other studies have failed to find a relationship between depression or depressed mood and low RSA at rest, both in clinical (Agelink et al., 2001; Dawood et al., 2007; Lehofer et al., 1997; Moser et al., 1998; O'Connor et al., 2002; Tulen et al., 1996; Udupa et al., 2007; Yeragani et al., 2002) and non-clinical samples (Hughes & Stoney, 2000). Several possibilities have been suggested to explain the variability in results, such as medication effects, or differences in physical health and physical fitness. However, investigations that have attempted to control for these variables have not had any more consistency in their results.

Two meta-analyses were recently conducted to try to clarify the inconsistent relationship between depression and RSA in medically healthy samples (Kemp et al., 2010; Rottenberg, 2007). Both papers concluded that there is a significant inverse relationship between depression and RSA ($r$ = -.364, $p$ < .001 in Kemp et al., 2010), and a small to medium effect size (e.g., $d$ = 0.3 in Rottenberg, 2007). These results suggest the existence of a real, but relatively small relationship between RSA and depression.

**Depression and RSA during physical and mental stressors.** In addition to baseline measures of RSA, many studies have also examined the relationship between depression and RSA during stressor tasks. However, the findings tend to be comparable to

the studies of baseline RSA, in that several studies have found a relationship between depression or depressed mood and low RSA (Hughes & Stoney, 2000; Light et al., 1998; Tulen et al., 1996) whereas others have not (Taylor et al., 2006; Yeragani et al., 1991, 2002). Furthermore, many of the studies which have found differences during the stressor tasks have not found baseline differences, indicating that trait-like differences in RSA may only become apparent under certain physical or emotional conditions.

The fluctuation or pattern of reactivity of RSA has also been examined in relation to depression. For example, major depression has been shown to relate to altered fluctuation during challenging speech and mirror-tracing tasks (Rottenberg, Clift, Bolden, & Salomon, 2007). This study found that depressed participants' RSA levels stayed the same or *increased* during the stressful tasks relative to their baseline measurements, and stayed elevated or continued to increase during the recovery period. Conversely, healthy controls exhibited decreased RSA during the stressful tasks relative to their baseline measurements, and their RSA levels increased back to baseline levels during the recovery period.

**Depression and RSA in ambulatory studies.** Several researchers have used 24-hour monitoring systems to collect RSA data in order to look for differences occurring in a more naturalistic setting. Their mixed findings are similar to the laboratory-based results. Neither Boettger et al., (2008) nor Sayar, Güleç, Gökçe, and Ak, (2002) found a difference between controls and patients with depression in measures of RSA. Khaykin et al., (1998) examined treatment responders and non-responders, but did not find a relationship between depression outcome and RSA. Similarly, Carney et al., (2000) also failed to find

a find a difference between depressed and non-depressed groups at baseline, but found that RSA significantly improved in those who were severely depressed but responded to CBT treatment.

**The course of depression and RSA.** Other longitudinal studies involving RSA and depression have been conducted to further explore the relationship between depression and RSA. RSA levels have been shown to be related to treatment outcomes: patients whose level of depression improves pre- to post- treatment tend to show increases in measures of RSA (acupuncture: Chambers & Allen, 2002; but see Rottenberg, Chambers, Allen, & Manber, 2007; cognitive behavioural therapy: Carney et al., 2000). Similarly, worsening of depression symptoms in patients who experienced a coronary event was shown to be associated with decreases in RSA (de Guevara et al., 2004). However, RSA did not change during pharmacological treatment of depression (e.g. Agelink et al., 2001; Dawood et al., 2007; for a meta-analytic review see: Kemp et al., 2010). Similarly, after electroconvulsive treatment, RSA has been shown to remain the same, or paradoxically decrease, despite alleviation of depressive symptoms (Nahshoni et al., 2004; Schultz, Anderson, & van de Borne, 1997). The lack of change in RSA-related measures after non-psychological treatments might reflect direct medication effects on RSA, or might indicate that differing methods of treatment may alleviate symptoms via differing pathways.

The utility of RSA as a predictor of the course of depression has also been investigated. However, the results are similarly mixed. One study found that larger decreases in RSA which occurred when watching a sad film significantly predicted

recovery from depression 6 months later (Rottenberg, Salomon, Gross, & Gotlib, 2005). However, the same research group also found that higher levels of a respiration-adjusted measure of RSA was associated with *poorer* outcome in a sample of depressed individuals (Rottenberg, Wilhelm, Gross, & Gotlib, 2002). This may have been due to their method of measuring RSA (involving paced breathing cued by rising and falling tones, as well as silent breaks), which may have increased mental effort enough to decrease RSA in some participants (see Bernston et al., 1997). Overall, there is only sparse evidence that RSA may have significant predictive value in treatment outcome.

**Summary.** Overall, the inconsistent relationship between depression and RSA is curious. Meta-analyses have demonstrated that depression is likely associated with decreased levels of RSA, either at rest or during stressors. However, the occurrence of both significant and non-significant results across study methods, durations, and approaches seems to indicate that researchers may be missing a piece of the puzzle. One possibility is that the small effect size is leading studies with smaller samples sizes to incorrectly conclude that there is no relationship. Clearly, studies with comparatively larger sample sizes are needed. It is also possible that the inconsistent inclusion of medicated populations is increasing the variability in the findings. Further research trying to clarify the relationship between depression and RSA should focus on medically healthy participants in order to avoid medication as a potential confound.

## Current Research: Anxiety

**Anxiety and RSA at rest.** The relationship between anxiety and RSA has also been examined in resting or supine conditions. Similar to depression, the findings have

been mixed both within and across anxiety disorders. For example, there are several studies showing that, versus controls, PTSD patients have lower RSA at rest (Blechert, Michael, Grossman, Lajtman, & Wilhelm, 2007; Cohen et al., 1997, 2000; Jovanovic, Norrholm, Sakoman, Esterajher, & Kozarić-Kovačić, 2009). Similarly, studies looking at autonomic functioning in GAD have also found differences between GAD patients and controls (Kemp et al., 2012; Kollai & Kollai, 1992; Thayer, Friedman, & Borkovec, 1996; although see Kollai & Kollai, 1992 for negative findings when using parasympathetic blockade). However, PD patients often do not differ from controls in terms of RSA (Blechert et al., 2007; Rechlin et al., 1994; Yeragani et al., 1990, 1993, 1995) although some instances of resting differences exist (Cohen et al., 2000; Klein, Cnaani, Harel, Braun, & Ben-Haim, 1995). The non-clinical literature on anxiety and RSA shows a similar mixed pattern of findings, with some studies finding a significant relationship (Lyonfields, Borkovec, & Thayer, 1995; Miu, Heilman, & Miclea, 2009; Piccirillo et al., 1997; Watkins, Grossman, Krishnan, & Sherwood, 1998), whereas others do not (Dishman et al., 2000; Friedman et al., 1993).

Since different anxiety disorders may display different relationships to RSA, it would be beneficial to approach 'anxiety' from a dimensional perspective, in order to seek out any underlying relationship using 'anxiety' as a construct. Findings from this type of study would complement the more in depth examination of the specific patterns of parasympathetic and sympathetic functioning in clinical disorders.

**Anxiety and RSA during a stressor.** Similar to the findings at rest, researchers have found significant relationships between clinical anxiety and measures of RSA during

various emotional and physical stressors (Lyonfields et al., 1995; Thayer et al., 1996; Yeragani et al., 1990, 1991). Dimensional measures of anxiety in non-clinical populations have yielded similar findings (Lyonfields et al., 1995; Miu et al., 2009). However, several other studies have found no significant relationships (Blechert et al., 2007; Friedman et al., 1993; Mauss, Wilhelm, & Gross, 2003; Piccirillo et al., 1997; Yeragani et al., 1993, 1995). As in the depression literature, many studies which have found differences only during stressor tasks, again indicating that it is important to assess RSA both at rest and during a stressor in order to gain a more comprehensive picture of parasympathetic-related HRV.

**Anxiety and RSA in ambulatory studies.** Few studies have used ambulatory measures to examine RSA and anxiety in physically healthy populations. One such study found a relationship between anxiety and a measure of RSA, but this relationship did not survive covariate analysis (Brosschot, Van Dijk, & Thayer, 2007). Another did not find a significant difference in 24-hour measures of RSA between PD and control participants (McCraty, Atkinson, Tomasino, & Stuppy, 2001). Overall, evidence collected using 24-hour ambulatory monitoring has not yielded insight into the relationship between anxiety and RSA. It is difficult to say whether the lack of significant findings indicates that there is no real difference between anxious and non-anxious individuals in their level of RSA, or whether the lack of findings is due to other, uncontrolled factors. For example, it might be possible that anxious individuals actively mitigate their anxious experiences during their daily lives by avoiding anxiety-provoking situations. If that were the case, both anxious and non-anxious individuals could potentially display similar 24-hour HRV metrics. Laboratory-based stressors, which can be standardized across participants, would be beneficial in avoiding this potential confound.

**The course of anxiety disorders and RSA.** Several studies have examined the longitudinal relationship between anxiety and RSA. One study found that, among PD treatment responders, CBT treatment was associated with increased RSA, whereas CBT with sertraline was not (Garakani et al., 2009). These results seem to echo the findings in the more extensive depression-RSA treatment literature, which also tend to find increases in RSA metrics only in non-pharmacological treatments. Again, this may be due to the effects of the drugs themselves, which seem to decrease RSA to varying extents.

**Summary.** Anxiety also seems to display an inconsistent relationship to RSA, although this relationship may be stronger and more consistent than the relationship between depression and RSA (Rottenberg, 2007). Importantly, anxiety and depression frequently co-occur, both clinically and on a symptom level. If there is a significant relationship between anxiety and RSA, it would be important to verify that co-occurring but statistically uncontrolled anxiety symptoms are not confounding the results of depression-RSA studies. In fact, several research groups have raised this issue as an important next step in research on the depression-RSA link (Rottenberg, 2007; Tulen et al., 1996).

Additionally, since past research has suggested that there may be differences in the relationships between RSA and anxiety across anxiety disorders, studies using dimensional measures of anxiety would complement the more extensive literature examining clinically anxious individuals. The use of dimensional measures would provide the opportunity to examine underlying relationships between 'general' anxiety

levels and RSA, which may not be as easily extrapolated from distinct clinical populations.

Finally, the assessment of RSA during standardized laboratory conditions is particularly important, especially when examining the basic, underlying relationship between anxiety and RSA. Ambulatory studies have had more difficulty in identifying differences between anxious and non-anxious individuals, possibly due to self-selection into differing environments. Although ambulatory monitoring would provide a more comprehensive view of HRV as it is experienced in a normal day, standardized laboratory measures offer an opportunity to avoid those kinds of confounds.

**An Aside on the Constructs of Anxiety and Depression**

Some may question if depression and anxiety are truly distinguishable, given the psychiatric comorbidity between anxious and depressive symptoms and disorders. Anxiety and depression co-occur to a surprising extent, with one study finding 64% of patients with major depressive disorder (MDD) having a comorbid anxiety disorder (Brown, Campbell, Lehman, Grisham, & Mancill, 2001). Furthermore, when looking at life-time co-occurrence, the comorbidity increased to 73%. In the same study, 8-69% of patients with a principal anxiety disorder had an additional diagnosis of MDD. This number increased to 27-77% when lifetime diagnoses were considered (Brown et al., 2001).

Several explanations exist for why anxiety and depression tend to co-occur. One possibility is that symptoms which are common to both anxiety and depressive disorders

may be artificially increasing their correlation. Another is that they share a common genetic diathesis (see Mineka, Watson, & Clark, 1998 for a discussion), or that they are in fact two manifestations of a unified disorder. Certain structural models looking at the phenotypes of depression and anxiety, such as the influential tripartite model (Clark & Watson, 1991), have suggested that the co-occurrence of anxiety and depression may be due to a shared 'general distress' factor, or negative affect (NA). In the tripartite model, both anxiety and depression are characterised by the presence of high NA, meaning that when an individual has a tendency to experience high NA, they are more likely to develop one or more anxiety and depressive disorders.

Given the comorbidity between anxiety and depressive disorders, and the potential shared role of NA, Watson (2005) has in fact suggested that the anxiety and mood disorders (including MDD) be merged under an overarching class of 'emotional disorders'. The proposed 'emotional disorders' class would then have 3 subclasses: the bipolar disorders, the distress disorders (including MDD and GAD), and the fear disorders (including most of the currently classified 'anxiety disorders'). However, this suggestion has not been adopted in the current DSM-5 drafted revisions (www.dsm5.org).

In fact, despite the frequent co-occurrence of anxiety disorders and depression, and their posited shared association with NA, they are still generally understood to be two distinct disorders. At the most basic level, the symptom profiles of anxiety disorders and depressive disorders in both the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the International Classification of Diseases (ICD-10) are distinct. Certain symptoms, such as agitation and concentration difficulties, may be common to certain

anxiety and depressive disorders. However, the symptoms of anxiety disorders primarily revolve around intense fear, worry, or anxiety, whereas depressive disorders are primarily characterized by the occurrence of depressed mood and anhedonia.

As might be expected of disorders with differing core symptoms, psychological treatments for anxiety and depressive disorders differ in their focus. Although a new unified treatment for anxiety and depression exists (Allen, McHugh, & Barlow, 2008), the majority of empirically supported treatments for anxiety and depression involve differing components. For example, treatment for various anxiety disorders tend to involve re-examination of threat appraisals, and exposure to the feared sensations or situations, whereas treatments for depression may instead focus on re-examining negative beliefs about the self, solving current interpersonal problems, or behavioural activation (Barlow, 2008).

In addition to differences in taxonomy and treatment, the theoretical constructs of anxiety and depression are also thought to be related but different. For example, although the tripartite model of anxiety and depression mentioned previously (Clark & Watson, 1991) characterizes high NA as a shared factor between depression and anxiety, it also describes two additional, specific factors which differentiate between depression and anxiety: depression is characterized by low positive affect (PA), whereas anxiety disorders are characterized by high levels of autonomic arousal or nervous tension.

Finally, laboratory-based studies have found differing physiological correlates to anxiety and depression. For example, self-report depression has been shown to be associated with decreased right hemisphere bias in a chimeric faces task, whereas self-

report anxiety in the same task was associated with increased right hemisphere bias (Keller et al., 2000).

**Summary.** The comorbidity between anxiety and depression has led some to question whether anxiety and depression can be adequately distinguished. However, theoretical models, disorder taxonomy, treatment methods and laboratory tasks suggest that anxiety and depression are distinct entities, and that investigation of anxiety and depression as distinct constructs is possible.

## Current Research: Concurrent Anxiety and Depression

Much research has been conducted on both the depression-RSA, and anxiety-RSA relationships. However, studies that simultaneously investigate these two relationships are also important. Given the high correlation between anxiety and depression, there is a possibility that only anxiety has a unique relationship to RSA. This possibility is strengthened by the seemingly stronger and more consistent relationship observed between anxiety and RSA. In other words, the relationship between depression and RSA which is occasionally observed in the literature may have been driven by comorbid anxiety symptoms, rather than by depression itself. In fact, researchers have occasionally raised the question of whether comorbid anxiety symptoms might explain some of the relationship that is observed between depression and RSA (e.g. Kemp et al., 2010; Rottenberg, 2007).

Several studies have attempted to examine this question in clinical populations. Although some studies failed to support the possibility that comorbid anxiety symptoms

may be impacting the relationship between depression and RSA (e.g. Sayar et al., 2002), others indicated that anxiety may in fact be influencing the relationship (e.g. Tulen et al., 1996).

Most recently, this question was examined in a study comparing three unmedicated clinical groups (MDD alone, MDD + PD/PTSD, MDD + GAD) versus controls during a resting state (Kemp et al., 2012). Compared to controls, patients with MDD displayed lower HF power and RMSSD (measures of RSA), and higher LF/HF ratios (a putative measure of sympathetic influence on the heart). However, when examining the differences by individual groups, only the MDD+GAD group differed significantly from controls. These results would seem to indicate that comorbid GAD is responsible for much of the difference in the 'overall MDD' versus control comparison. The lack of difference between the MDD+PD/PTSD group and controls is surprising, but may have been caused by the inclusion of two anxiety disorders which may have differing sympathetic/parasympathetic alterations. Although the researchers did administer a continuous measure of anxiety and depression, they did not report the dimensional correlations. Given the pattern of findings suggesting that comorbid GAD might be highly influencing the relationship between MDD and the HRV metrics, it would be interesting to take a look at the dimensional relationships to see if there is something specific to GAD, or whether this difference reflects differing levels of anxious symptoms across the disorder groupings.

**Current Research: The Importance of Sympathetic Measures**

The primary goal of this study is to examine the relationship between depression,

anxiety and RSA, and thereby test (and potentially refute) specific assumptions about depression and RSA that have been stated in the literature for at least the past 22 years (e.g. Dalack & Roose, 1990). However, it is important to note that this focus represents a highly restricted examination of the ANS influence on the heart. Although several researchers have conducted studies which were focused primarily on the parasympathetic-related components of HRV (e.g. Francis et al., 2009; Lyonfields et al., 1995; Rottenberg, 2007; Watkins et al., 1998), the majority of researchers also examine putative sympathetic-related HRV metrics. By including a measure of sympathetic influence on the heart, these researchers are able to gain a more complete view of the influence of the ANS on the heart and its potential relationship to disorders such as anxiety and depression.

For example, anxiety disorders have been shown to relate to increases in the sympathetic components of HRV (e.g. Blechert et al., 2007; Cohen et al., 2000), even without alterations in parasympathetic-related HRV (e.g. Rechlin et al., 1994 although see Thayer et al., 1996). Depression has also been shown to relate to sympathetic-related HRV (e.g. Kemp et al., 2012), although opposing findings are also prevalent (e.g. van der Kooy et al., 2006). The specific relationship between depression, anxiety and RSA could be tested without inclusion of a sympathetic measure. However, it seems important to include a measure of sympathetic influence on the heart, even in an exploratory fashion.

Another way in which sympathetic influence in HRV has long been characterized is through the use of a sympathetic-parasympathetic ratio (e.g. Pagani et al., 1986). This ratio is thought to index the 'sympathovagal balance', or the balance between the contributions that the sympathetic and parasympathetic branches of the ANS have on the

heart during the measurement period (Malliani, Lombardi, & Pagani, 1994). The ratio has typically been operationalized as the ratio between the LF power and HF power of an individual's HRV (aka. LF/HF; Malliani, 1999) although the use of heart rate (Bootsma et al., 1994) and the standard deviation of interbeat intervals (SDNN; Malliani et al., 1994) have also been suggested as potential indices of sympathovagal balance. Eckberg (1997) has criticized the use of the LF/HF ratio as a measure of sympathovagal balance, due in part to the non-specific nature of LF power. However, metrics that can potentially assess the extent to which either the sympathetic or parasympathetic influence predominates remain intuitively appealing. A shift towards sympathetic predominance may be expected in disorders such as anxiety and depression, where difficulties in social engagement may be reflected in decreased parasympathetic influence on the heart.

**The Current Study**

Many studies have examined the relationship between depression and RSA, or anxiety and RSA, whereas relatively fewer studies have concurrently examined both depression and anxiety within the same sample. This study seeks to improve upon previous study designs in a number of ways. First, this study sought to eliminate several potential confounds by design. For example, the sample was relatively homogeneous in age, effectively avoiding the confounding effect of age. Also, many of the studies examining the direct anxiety-RSA and depression-RSA relationships have been in very small samples (e.g. with 10-30 individuals per group). This study used a relatively larger sample, in order to try to obtain more reliable results. Additionally, to avoid differential medication use as a potential confound, this study was based on a medically healthy

sample. Second, whereas many of the studies examining depression and anxiety concurrently have compared clinical groups, this study will examine anxiety and depression dimensionally, in order to examine whether depression and anxiety have unique direct relationships with RSA and CSI. Finally, this study will aim to examine both the parasympathetic and sympathetic influence on the heart, in order to explore any differences in the pattern of parasympathetic and sympathetic-related HRV.

**Specific aims and hypotheses.** The specific focus of this study was to clarify the unique and shared relationships that anxiety and depression may have to RSA. Additionally, a measure of sympathetic influence on the heart (CSI) was included to explore potential differences in sympathetic-related HRV, and the balance between sympathetic and parasympathetic influence. The following was hypothesized:

***Hypothesis 1.*** Depression will have a small but significant relationship to RSA, at baseline and during the stressor task.

***Hypothesis 2.*** Anxiety will have a significant relationship to RSA, at baseline and during the stressor task, and it will be stronger than that of depression to RSA.

***Hypothesis 3.*** At both time points, anxiety will maintain its relationship with RSA when controlling for depression, but depression will no longer significantly relate to RSA when controlling for anxiety.

***Hypothesis 4 (exploratory).*** The relationships that depression and anxiety may have with sympathetic-related HRV will be examined using CSI.

## Method

### Participants

One hundred and fifty undergraduate students participated in the study in exchange for 2 class credits or $20. Participants were recruited through the University of British Columbia's human subject pool pre-screening system. Participants were eligible to participate in the study if they were categorized as high or low in anxious and depressive symptoms by the depression and anxiety scales of the 21-item Depression Anxiety Stress Scale (DASS) which they completed through the pre-screening system. Participants with scores that fell within the 'severe' or 'extremely severe' range (as outlined in Lovibond & Lovibond, 1995) in anxiety or depression were considered to be 'high', and those with scores that fell within the range of 'normal' were considered to be 'low'. This meant that for the anxiety scale, scores between 0-7 were classified as 'low' and scores of 15 and above were classified as 'high'. For the depression scale, scores between 0-9 were classified as 'low' and scores of 21 and above were classified as 'high'. In order to be eligible for the study, both the anxiety and depression scores of participants must have fallen into one of these ranges. Of the 150 students who participated in the study, 22 were excluded from data analysis (11 due to the use of medications with known impacts on the nervous system, eight due to medical conditions, two due to recreational drug use immediately prior to study participation, one due to being more than twice the age of the study population). Additionally, three participants were excluded from baseline analyses and four from stressor task analyses due to ECG recording issues. Overall, the final sample contained 125 participants in the baseline condition, and 124 participants in the

stressor task condition.

## Procedure

After providing informed consent, the participants completed a brief questionnaire which assessed for any relevant physical illnesses. The experimenter then measured the participants' waist and hip circumference before seating the participants in front of a computer and attaching the ECG sensors. The electrodes were placed in a bipolar lead II configuration on participants' torsos in order to minimize movement artifacts. Participants then completed the rest of the questionnaires on the computer while they habituated to the sensors. Upon completion of the computerized questionnaires, a baseline ECG measurement was taken while participants sat quietly for a 5-minute period. Emotional state was measured before and after the baseline recording. After this, participants engaged in several rounds of the Paced Auditory Serial Addition Task – Computerized (PASAT-C; Lejuez, Kahler, & Brown, 2003), which has shown to induce emotional distress in the form of irritability, frustration, anger and anxiety. Emotional state was once again measured before and after the stressor task. Finally, the sensors were removed and participants were debriefed.

## Measures

**Laboratory measures.** This study used a modified version of the PASAT-C (Lejuez et al., 2003), to induce general distress. The PASAT-C was originally shown to increase 'dysphoria' in the form of combined irritability, frustration, anger and anxiety (e.g. McHugh et al., 2011). Recently, the task was shown to primarily elicit shame,

irritability, and hostility (Gratz, Rosenthal, Tull, Lejuez, & Gunderson, 2010).

During the task, numbers are briefly presented on the screen. Participants must sum each number with the previously-presented number and indicate the correct answer by clicking on the appropriate number. If the response is correct, the participant receives a point. If the response is incorrect, or if the participant does not answer before another number is presented, the participant hears an explosion and does not receive a point.

This version of the PASAT-C had three distinct phases. The first phase (low difficulty) lasted two minutes, during which there was a 3-second latency between the number presentations. The second phase (medium-high difficulty) began with two minutes of number presentations with a 2-second latency, and ended with one minute of number presentations with a 1-second latency. This second phase was followed by a brief 60 second resting period, at which point the third phase (high difficulty) began. During the third phase, the numbers were presented with a 1-second latency, and participants were given the option to quit at any time. For the purpose of this study, only the data from the second phase will be analyzed.

**Physiological measures.**

***Acquisition.*** Physiological data were collected using an integrated system and software package (BIOPAC 150, 2005). Cardiovascular signals were recorded with the BIOPAC electrocardiogram amplifier module (ECG100C), using a sampling rate of 1000Hz. Signals were collected during five minutes of quiet sitting and three minutes of stressful arithmetic using two disposable Ag/AgCl electrodes designed for the BIOPAC

system: one placed just below the right collarbone, and the second placed on or near the lowest left rib. Respiration was measured with a strain gauge placed around participants' chests, and recorded with the BIOPAC respiration amplifier module (RSP100C). Participant data were stored digitally as an .acq file in *AcqKnowledge* (2005).

The BIOPAC MP150 system is the latest in the BIOPAC line, and has previously been used to collect HRV data for a variety of successful studies. In particular, data acquired using the BIOPAC system indicated that RSA recovery from anticipatory threat was differentially related to state positive versus negative affect (Waugh, Panage, Mendes, & Gotlib, 2010). Of relevance to the proposed study, RSA data obtained from collection with the BIOPAC MP150 system have been shown to differentiate between PTSD patients and controls (Jovanovic et al., 2009), as well as patients with panic and PTSD (Blechert et al., 2007). Additionally, RSA data collected using this system has been shown to differentiate between mental stress and autogenic training conditions, and to relate to trait anxiety (Miu et al., 2009).

***Signal processing.*** The raw digitized ECG signals in *AcqKnowledge* (2005) were analyzed off-line using a freely-available software suite: QRSTool and CMetX. These two programs were developed by Allen et al., (2007) to facilitate the processing of IBI series data into commonly-used HRV metrics. The raw (.acq) files were converted into text (.txt) files and imported into QRSTool, which is a beat-detection software program. Each individual IBI series was visually inspected for artifacts, and any identified artifacts were corrected by hand in QRSTool. After artifact removal, the cleaned IBI series were exported to CMetX. CMetX converts the IBI series into a time-series by employing a 10

Hz sampling rate with linear interpolation (Allen et al., 2007), and then automatically calculates several indices of HRV, including RSA and CSI.

***Respiratory sinus arrhythmia.*** CMetX calculates RSA using a 241-point finite impulse response digital filter designed using FWTGEN V3.8 from Cook and Miller (1992), with a .12-.40 Hz bandpass. This filter is applied to the time-series converted IBI series, and the natural log of the variance of the filtered waveform is then calculated and used as a measure of RSA (Allen et al., 2007).

This particular metric of RSA has several advantages. Firstly, the CMetX metric of RSA correlates almost perfectly with the Bohrer and Porges metric of RSA derived from Porges' MXEdit V2.21. At rest, this correlation was r = .992, and during an arithmetic stressor this correlation was r = .995 (Allen et al., 2007). Secondly, CMetX's RSA has been shown to correlate r = .986 with HF spectral power (0.12-0.40 Hz range) at rest, and r = .992 for HF spectral power during an arithmetic stressor. Thus, the RSA values produced by CMetX are highly comparable to HF spectral power as well. This is in line with the conclusions reached by Grossman, van Beek, and Wientjes (1990) who found that Porges' RSA, spectral HF power, and peak-to-trough methods were highly correlated. However, other researchers (Lewis, Furman, McCool, & Porges, 2012) have found that in fact Porges' method of calculating RSA has several benefits, including being most sensitive to vagal blockade, and generating stronger effect sizes. As CMetX's RSA correlates extremely highly with Porges' RSA, it is possible that these strengths may also be seen in the metric of RSA used in this study.

In fact, several other studies using CMetX's RSA have found results which are in

line with the RSA literature that has employed other metrics of RSA (e.g. HF power, RMSSD, etc.): individuals in the clinical range of borderline personality disorder demonstrated lower levels of RSA (Weinberg, Klonsky, & Hajcak, 2009); higher self-esteem was associated with higher levels of RSA (Martens et al., 2010); higher levels of RSA (moderated by power) predicted higher levels of empathic accuracy (Côté et al., 2011); and gender differences were observed in a sample of depressed individuals (Chambers & Allen, 2007b).

Finally, RSA as a construct has demonstrated high 1-week test-retest reliability of RSA measured at baseline ($r = .86$, $p < .001$) and during a stressor ($r = .87$, $p < .001$) (Schmidt et al., 2012). Given our use of more dispositional measures of depression and anxiety symptoms, the high reliability of RSA is important.

***Cardiac sympathetic index.*** Toichi's Cardiac Sympathetic Index (CSI; Toichi, Sugiura, Murai, & Sengoku, 1997), is calculated by CMetX as an index of sympathetic activity. CSI is calculated in CMetX by first rotating a Lorenz plot of each IBI plotted against the subsequent IBI by -45°. In this plot, the length of the transverse axis (T; aka. the axis orthogonal to the line $IBI_n = IBI_{n+1}$) reflects beat-to-beat variability that are associated with parasympathetic influences. The length of the longitudinal axis (L) reflects the range of IBIs, and reflects variability associated with both sympathetic and parasympathetic influences. CMetX then outputs CSI as the ratio of L/T (Allen et al., 2007).

CSI has been validated with pharmacological blockades (Toichi et al., 1997), where mild blockade of sympathetic function using propanolol was reliably detected in

sitting, standing, and supine mental arithmetic. Additionally, this measure was shown to be more sensitive to propanolol blockade than LF power (Toichi et al., 1997). Its application to various research paradigms, CSI has behaved as would be expected of a measure of sympathetic activation. For example, CSI is elevated during pain, as compared to baseline (Paine, Kishor, Worthen, Gregory, & Aziz, 2009). CSI is also positively related to psychotic states in schizophrenia (Toichi et al., 1999), and is decreased in undergraduate students high on BPD symptoms (Weinberg et al., 2009). Additionally, CSI was shown to significantly increase during an arithmetic stressor in undergraduate students (Weinberg et al., 2009).

***Respiration.*** Respiration rate was calculated directly in *AcqKnowledge* (2005) by averaging the rate of 'breaths per minute' across the entire 5-minute or 3-minute recording period.

**Emotional State.** Emotional state was assessed before and after each measurement period (baseline and stressor) using the Self-Assessment Manikin (SAM; Bradley & Lang, 1994). The SAM is a pictorial measure used extensively to assess three dimensions of emotional experience: valence (negative to positive), arousal (low to high), and control/dominance (low to high). Participants rate current levels of valence, arousal, and control/dominance by indicating whether their experience falls closest to any of the five SAM pictures, or in between two of the pictures (resulting in a 9-point scale).

**Depression and anxiety.** Depression and anxiety were assessed once during the laboratory visit using the Depression Anxiety Stress Scales (DASS) developed by Lovibond and Lovibond (1995). This 42-item self-report questionnaire consists of three

14-item scales measuring current symptoms of depression, anxiety and stress. Responses are made on a four point scale (0 = did not apply to me at all, 3 = applied to me very much), with higher scores indicating higher levels of emotional distress. The questionnaire was originally constructed to maximize discrimination between symptoms of anxiety and depression, and has shown excellent internal consistency (Lovibond, & Lovibond, 1995). A shortened 21-item DASS was used for pre-screening using the human subject pool. It consisted of seven items assessing each of the three scales, and has demonstrated reliability, convergent validity, and discriminant validity, comparable to the full 42-item DASS (Antony, Bieling, Cox, Enns, & Swinson, 1998).

**Demographic confounds.** A demographics questionnaire was administered to assess participants' age, gender and ethnicity. All three demographic variables have been shown to relate to RSA or HRV (age: De Meersman & Stein, 2007; gender: Greaves-Lord et al., 2007; Thayer, Smith, Rossy, Sollers, & Friedman, 1998; ethnicity: Wang, Thayer, Treiber, & Snieder, 2005). Additionally, participants' waist and hip circumference were measured to create a waist-to-hip ratio, to use as a proxy for abdominal adiposity and cardiovascular fitness.

## Results

### Sample Characteristics

Descriptive statistics and intercorrelations for major study variables are presented in Tables 1 and 2. The majority of the sample consisted of female undergraduate students (71.1%), with 78.9% of the sample being of East Asian (46.9%) or European (32.0%)

descent.

In this sample, anxiety and depression scores were highly correlated at $r = 0.59$, $p < .001$. Age did not significantly correlate with RSA at rest or during the stressor task, nor did it significantly correlate with depression or anxiety (see Table 2). Waist-to-hip ratio similarly failed to significantly correlate with measurements of RSA at either time-point, or with depression and anxiety scores (see Table 2).

Gender-related differences in HRV variables were not observed in this sample (see Table 3). Females did have a smaller waist-to-hip ratio ($r = -.20$, $p = .03$), and rated themselves as significantly higher on anxiety ($r = .24$, $p = .01$), with females reporting higher levels of anxiety (see Table 3 for means).

The majority of HRV variables were not significantly different among racial groups (grouped as: East Asian, Caucasian, and Other). The exception to this was baseline RSA, which was significantly lower in the East Asian participants ($M = 6.48$, $SD = .82$) than in Caucasian participants ($M = 7.09$, $SD = 1.10$), $p < .05$. East Asian participants also differed from Caucasian participants in their BMI ($M = 21.01$, $SD = 2.89$ vs. $M = 23.42$, $SD = 3.56$) and their waist-to-hip ratio ($M = 0.79$, $SD = .06$ vs. $M = .83$, $SD = 0.10$). No other race-related differences were observed (see Table 4).

Finally, the DASS-42 distribution from the current sample was compared to the non-clinical sample in Lovibond & Lovibond (1995), in order to examine the effects of the pre-screening. As compared to the normative sample, the standard deviation of the current sample's depression scores was slightly increased (8.35 vs. 6.85), as was the mean (8.59

vs. 6.34). The standard deviation of the current sample's anxiety scores was similar to that of the normative sample (5.07 vs. 4.91), whereas the mean was higher (6.46 vs. 4.70).

Table 1. *Sample Characteristics (N = 128)*

| Variable | Mean +/- *SD* or Number (%) |
|---|---|
| Gender | |
| Male | 37 (28.9) |
| Female | 91 (71.1) |
| Age | 19.61 +/- 2.32 |
| Ethnicity | |
| East Asian/East Asian Descent | 60 (46.9) |
| European/European Descent | 41 (32.0) |
| Latin American or Hispanic/Latin American or Hispanic | 3 (2.3) |
| Descent | 7 (5.5) |
| Indian or South Asian/Indian or South Asian Descent | 5 (3.9) |
| Middle Eastern/Middle Eastern Descent | 12 (9.4) |
| Other | |
| Waist to Hip Ratio | 0.81 +/- 0.07 |
| Heart Rate | |
| At rest | 69.15 +/- 10.78 |
| During stressor task | 72.79 +/- 10.81 |
| Respiratory Sinus Arrhythmia | |
| At rest | 6.78 +/- 0.99 |
| During stressor task | 6.22 +/- 1.02 |
| Cardiac Sympathetic Index | |
| At rest | 2.56 +/- 0.86 |
| During stressor task | 2.18 +/- 0.96 |
| Respiration Rate (breaths per minute) | |
| At rest | 13.66 +/- 3.31 |
| During stressor task | 18.63 +/- 3.55 |
| DASS-42 | |
| Depression Scale | 8.59 +/- 8.35 |
| Anxiety Scale | 6.46 +/- 5.07 |

Table 2. *Correlations Among Major Study Variables.*

| | Dep | Anx | Age | BMI | W:H | $RSA_{rest}$ | $RSA_{stress}$ | $CSI_{rest}$ |
|---|---|---|---|---|---|---|---|---|
| Anx | .59** | | | | | | | |
| Age | .04 | -.11 | | | | | | |
| BMI | .07 | -.06 | .0.3 | | | | | |
| W:H | .02 | -.15 | .13 | .34** | | | | |
| $RSA_{rest}$ | -.09 | -.13 | -.10 | .34** | .15 | | | |
| $RSA_{stress}$ | -.15 | -.22* | -.10 | .31** | .06 | .76** | | |
| $CSI_{rest}$ | .02 | .05 | .01 | -.11 | -.05 | -.59** | -.52** | |
| $CSI_{stress}$ | .07 | -.02 | .10 | -.02 | -.09 | -.47** | -.52** | .55* |

Note: * = $p < 0.05$, ** = $p < .001$ (Pearson correlations, 2-tailed).

Table 3. *Major Study Variables by Gender*

| | Male ($N = 37$) | Female ($N = 91$) |
|---|---|---|
| Depression | 9.27(8.17) | 8.32(8.45) |
| Anxiety | 4.54(3.36) | 7.24(5.45)* |
| BMI | 22.48(3.25) | 21.97(3.25) |
| Waist-to-Hip | 0.83(0.05) | 0.80(0.08)* |
| $RSA_{rest}$ | 6.81(0.95) | 6.77(1.01) |
| $RSA_{stress}$ | 6.25(0.91) | 6.21(1.06) |
| $CSI_{rest}$ | 2.79(0.63) | 2.47(0.93) |
| $CSI_{stress}$ | 2.24(0.77) | 2.15(1.03) |

*Note.* * = differed from males at $p < .05$, two-tailed.

Table 4. *Major Study Variables by Race*

| | East Asian ($N = 60$) | Caucasian ($N = 41$) | Other ($N = 27$) |
|---|---|---|---|
| Depression | 8.62(8.98) | 7.88(7.68) | 9.63(8.03) |
| Anxiety | 7.10(5.08) | 5.22(4.92) | 6.93(5.12) |
| BMI | 21.01(2.89)* | 23.42(3.56) | 22.65(2.70) |
| Waist-to-Hip | .79(.06)* | .83(.10) | .80(.01) |
| $RSA_{rest}$ | 6.48(.82)* | 7.09(1.10) | 6.98(1.01) |
| $RSA_{stress}$ | 5.98(0.88) | 6.42(1.15) | 6.47(1.00) |
| $CSI_{rest}$ | 2.68(1.00) | 2.43(0.67) | 2.50(0.78) |
| $CSI_{stress}$ | 2.19(1.06) | 2.16(0.68) | 2.18(1.12) |

*Note.* * = $p < .05$, as compared to the Caucasian racial group.

**Manipulation Check**

The effect of the baseline rest period and stressful arithmetic manipulation on emotional state was examined using the SAM. Results can be seen in Table 5. Participants' ratings of their emotional state changed significantly from pre- to post- 5-minute resting baseline. Specifically, participants endorsed feeling less happy, less physiologically aroused, and less dominant after the 5-minute baseline measurement (see Table 5). Participants' ratings also changed significantly from pre- to post-stressor task. After the stressor task, participants felt less happy, more physiologically aroused (see Table 5).

Scores on the anxiety and depression scales of the DASS-42 were correlated with the SAM ratings (see Table 6). The pattern of correlations was similar for both anxiety and depression scores, with the only major difference being that depression had a medium-to-large inverse correlation with baseline arousal ($r = -.45$, $p < .001$), whereas anxiety had a small-to-medium inverse correlation with baseline arousal ($r = -.20$, $p < .05$). This difference was negligible by the end of the baseline measurement period ($r = -.39$, $p < .001$ vs. $r = -.36$, $p < .001$).

Table 5. *SAM Ratings Pre- and Post-Baseline*

| | Baseline: *M(SD)* | | Stressor: *M(SD)* | |
|---|---|---|---|---|
| SAM scale | Pre | Post | Pre | Post |
| Valence | 6.17(1.19) | 5.55(1.20)** | 5.41(1.29) | 4.59(1.68)** |
| Arousal | 3.55(1.78) | 2.45(1.57)** | 2.79(1.71) | 5.61(1.95)** |
| Dominance | 5.46(1.85) | 5.14(2.09)* | 5.29(1.95) | 4.06(1.98)** |

*Note.* * = $p < .05$, ** = $p < .001$ ($N = 128$, paired-samples t-test, two-tailed).

Table 6. *Correlations Among SAM Ratings, Anxiety, and Depression Scores*

| | Baseline | | Stressor | |
|---|---|---|---|---|
| | Depression | Anxiety | Depression | Anxiety |
| Pre | | | | |
| Valence | -.45** | -.20* | -.33** | -.39** |
| Arousal | .07 | -.08 | -.00 | -.04 |
| Dominance | -.17 | -.10 | -.22* | -.18* |
| Post | | | | |
| Valence | -.39** | -.36** | -.27** | -.28** |
| Arousal | .06 | .07 | .00 | .11 |
| Dominance | -.16 | -.14 | -.15 | -.14 |

*Note.* * = $p < .05$, ** = $p < .001$ ($N = 128$, Pearson correlation, two-tailed).

**Statistical Approach**

Regression analyses were performed in order to examine the relationships between anxiety, depression, and RSA. To test their respective relationships to RSA, anxiety and depression were each used as predictors in three models. Model 1 was the direct prediction of the dependent variable (RSA) by the independent variable (anxiety or depression). Model 2 included respiration rate in addition to the independent variable (anxiety or depression), to predict the dependent variable (RSA). To verify that the relationship is not attributable to potential biological confounds, model 3 includes theoretically relevant covariates (age, gender, ethnicity, waist-to-hip ratio, BMI) in addition to the independent variable (anxiety or depression), in predicting the dependent variable (RSA). As ethnicity was a categorical variable, ethnicity was collapsed into three racial groups (Asian, European/Caucasian, and Other) and dummy coded. The results are presented in Tables 7 through 10.

To test the relative predictive power of both anxiety and depression, both were placed into models predicting resting and stressor task RSA. Biological covariates were not included, in order to test the direct effects. The results are presented in Table 11, along with the individual direct relationships for comparison.

Finally, the potential relationship between depression, anxiety and CSI were explored both directly (model 1) and when controlling for potentially relevant demographic variables (model 2) both at rest and during the stressor task. The results are presented in Tables 12 through 15.

**Depression and RSA At Rest**

At rest, depression did not significantly predict RSA either alone, $\beta$ = -0.09, $t$(123) = -.96, $p$ = .34, or when controlling for relevant demographic variables (age, gender, ethnicity, waist-to-hip ratio, and BMI), $\beta$ = -0.11, $t$(116) = -1.31, $p$ = .19 (see Table 7 for model details). When anxiety and depression were simultaneously entered into a regression equation predicting RSA, depression did not significantly predict RSA, $\beta$ = -.02, $t$(122) = -0.14, $p$ = .89 (see Table 11).

**Depression and RSA During a Stressor**

During the stressor task, depression alone did not significantly predict RSA, however there was a marginal trend towards higher levels of depression predicting lower levels of RSA, $\beta$ = -0.15, $t$(122) = -1.72, $p$ = 0.09. This relationship remained marginally significant when controlling for respiration, $\beta$ = -.16, $t$(121) = -1.82, p = .07, and became significant when controlling for relevant demographic variables (age, gender, ethnicity, waist-to-hip ratio, and BMI), $\beta$ = -0.18, $t$(115) = -2.10, $p$ = .03 (see Table 8 for model details). Importantly, when anxiety and depression were simultaneously entered into a regression equation predicting RSA, there was no significant relationship between depression and RSA, $\beta$ = -0.03, $t$(121) = -0.25, $p$ = .80 (see Table 11).

Table 7. *Depression Predicting RSA at Rest*

| | *β* | *t* | *p* |
|---|---|---|---|
| Model 1 | | | |
| Depression | -0.09 | $t(123) = -0.96$ | .34 |
| Model 2 | | | |
| Respiration | -0.36 | $t(122) = -4.31$ | <.001 |
| Depression | -0.09 | $t(122) = -1.07$ | .29 |
| Model 3 | | | |
| Age | -0.17 | $t(116) = -1.98$ | .05 |
| Gender (male=0) | 0.01 | $t(116) = -0.07$ | .94 |
| Ethnicity (D1) | -0.22 | $t(116) = -2.12$ | .04 |
| Ethnicity (D2) | -0.01 | $t(116) = -0.15$ | .88 |
| Waist-to-Hip Ratio | 0.05 | $t(116) = 0.55$ | .59 |
| BMI | 0.27 | $t(116) = 2.96$ | <.01 |
| Depression | -0.11 | $t(116) = -1.31$ | .19 |

Table 8. *Depression Predicting RSA During the Stressor Task*

| | *β* | *t* | *p* |
|---|---|---|---|
| Model 1 | | | |
| Depression | -0.15 | $t(122) = -1.72$ | .09 |
| Model 2 | | | |
| Respiration | -0.32 | $t(121) = -3.75$ | <.001 |
| Depression | -0.16 | $t(121) = -1.82$ | .07 |
| Model 3 | | | |
| Age | -0.17 | $t(115) = -1.94$ | .06 |
| Gender | -0.03 | $t(115) = -0.31$ | .76 |
| Ethnicity (D1) | -0.12 | $t(115) = -1.14$ | .26 |
| Ethnicity (D2) | 0.06 | $t(115) = 0.57$ | .57 |
| Waist-to-Hip Ratio | -0.04 | $t(115) = -0.40$ | .69 |
| BMI | 0.30 | $t(115) = 3.20$ | <.01 |
| Depression | -0.18 | $t(115) = -2.10$ | .03 |

**Anxiety and RSA At Rest**

At rest, anxiety did not significantly predict RSA alone, $\beta$ = -0.13, $t$(123) = -1.44, $p$ = .15, or when controlling for demographic variables (age, gender, ethnicity, waist-to-hip ratio, and BMI), $\beta$ = -0.12, $t$(116) = -1.31, $p$ = .20 (see Table 9 for model details). When anxiety and depression were simultaneously entered into a regression equation predicting RSA, anxiety continued to fail to predict RSA, $\beta$ = -0.12, $t$(122) = -1.07, $p$ = .29 (see Table 11 for model details).

**Anxiety and RSA During a Stressor**

During the stressor task, anxiety did significantly predict RSA, $\beta$ = -0.22, $t$(122) = -2.52, $p$ = 0.01. This relationship remained significant when controlling for respiration, $\beta$ = -0.22, $t$(121) = -2.58, p = 0.01, and relevant demographic variables (age, gender, ethnicity, waist-to-hip ratio, and BMI), $\beta$ = -0.24, $t$(116) = -2.69, $p$ = .01 (see Table 10 for model details). Importantly, when entered simultaneously with depression in a regression equation predicting RSA, anxiety maintained a marginally significant relationship to RSA, $\beta$ = -0.21, $t$(121) = -1.83, $p$ = .07 (see Table 11 for model details).

Table 9. *Anxiety Predicting RSA at Rest*

| | *β* | *t* | *p* |
|---|---|---|---|
| Model 1 | | | |
| Anxiety | -0.13 | $t(123) = -1.44$ | .15 |
| Model 2 | | | |
| Respiration | -0.36 | $t(122) = -4.25$ | <.001 |
| Anxiety | -0.11 | $t(122) = -1.36$ | .18 |
| Model 3 | | | |
| Age | -0.18 | $t(116) = -2.09$ | .04 |
| Gender | 0.04 | $t(116) = 0.43$ | .67 |
| Ethnicity (D1) | -0.21 | $t(116) = -2.05$ | .04 |
| Ethnicity (D2) | -0.01 | $t(116) = -0.14$ | .89 |
| Waist-to-Hip Ratio | 0.04 | $t(116) = 0.46$ | .65 |
| BMI | 0.27 | $t(116) = 2.88$ | .01 |
| Anxiety | -0.12 | $t(116) = -1.31$ | .20 |

Table 10. *Anxiety Predicting RSA During the Stressor Task*

| | *β* | *t* | *p* |
|---|---|---|---|
| Model 1 | | | |
| Anxiety | -0.22 | $t(122) = -2.52$ | .01 |
| Model 2 | | | |
| Respiration | -0.32 | $t(121) = -3.75$ | <.001 |
| Anxiety | -0.22 | $t(121) = -2.58$ | .01 |
| Model 3 | | | |
| Age | -0.19 | $t(116) = -2.26$ | .03 |
| Gender | 0.03 | $t(116) = 0.35$ | .73 |
| Ethnicity (D1) | -0.11 | $t(116) = -1.03$ | .31 |
| Ethnicity (D2) | 0.06 | $t(116) = 0.57$ | .57 |
| Waist-to-Hip Ratio | -0.05 | $t(116) = -0.58$ | .56 |
| BMI | 0.29 | $t(116) = 3.12$ | <.01 |
| Anxiety | -0.24 | $t(116) = -2.69$ | .01 |

Table 11. *Anxiety and Depression Predicting RSA at Rest and During the Stressor Task*

| | $\beta$ | $t$ | $p$ |
|---|---|---|---|
| At Rest | | | |
| Individually | | | |
| Depression | -0.09 | $t(123) = -0.96$ | .34 |
| Anxiety | -0.13 | $t(123) = -1.44$ | .15 |
| Combined | | | |
| Depression | -0.02 | $t(122) = -0.14$ | .89 |
| Anxiety | -0.12 | $t(122) = -1.07$ | .29 |
| During Stressor | | | |
| Individually | | | |
| Depression | -0.15 | $t(122) = -1.72$ | .09 |
| Anxiety | -0.22 | $t(122) = -2.52$ | .01 |
| Combined | | | |
| Depression | -0.03 | $t(121) = -0.25$ | .80 |
| Anxiety | -0.21 | $t(121) = -1.83$ | .07 |

**Depression and CSI**

There was no significant relationship between depression and CSI at rest, $\beta = 0.02$, $t(123) = 0.26$, $p = .79$, or during the stressor task, $\beta = 0.07$, $t(122) = 0.78$, $p = .44$. The addition of potentially relevant demographic variables to the regression equation did not change the small and non-significant relationship: $\beta = 0.02$, $t(116) = 0.20$, $p = .84$ at rest (see Table 12 for model details); $\beta = 0.08$, $t(115) = 0.88$, $p = .38$ during the stressor task (see Table 13 for model details).

**Anxiety and CSI**

Similarly, there was no significant relationship between anxiety and CSI at rest, $\beta = 0.05$, $t(123) = 0.51$, $p = 0.61$, or during the stressor task, $\beta = -0.02$, $t(122) = -0.19$, $p = .85$. The addition of the potentially relevant demographic variables to the regression equation did not change the small and non-significant relationship between anxiety and CSI: $\beta = 0.07$, $t(116) = 0.78$, $p = .44$ at rest (see Table 14); $\beta = 0.01$, $t(115) = 0.07$, $p = .94$ during the stressor task (see Table 15).

Table 12. *Depression Predicting CSI at Rest*

| | *β* | *t* | *p* |
|---|---|---|---|
| Model 1 | | | |
| Depression | 0.02 | $t(123) = 0.26$ | .79 |
| Model 2 | | | |
| Age | 0.03 | $t(116) = 0.34$ | .73 |
| Gender | -0.18 | $t(116) = -1.99$ | .05 |
| Ethnicity (D1) | 0.13 | $t(116) = 1.15$ | .25 |
| Ethnicity (D2) | 0.04 | $t(116) = 0.37$ | .72 |
| Waist-to-Hip Ratio | -0.04 | $t(116) = -0.40$ | .69 |
| BMI | -0.07 | $t(116) = -0.74$ | .46 |
| Depression | 0.02 | $t(116) = 0.20$ | .84 |

Table 13. *Depression Predicting CSI During the Stressor Task*

| | $\beta$ | $t$ | $p$ |
|---|---|---|---|
| Model 1 | | | |
| Depression | 0.07 | $t(122) = 0.78$ | .44 |
| Model 2 | | | |
| Age | 0.13 | $t(115) = 1.41$ | .16 |
| Gender | -0.04 | $t(115) = -0.44$ | .66 |
| Ethnicity (D1) | -0.02 | $t(115) = -0.14$ | .89 |
| Ethnicity (D2) | < -0.01 | $t(115) = -0.04$ | .97 |
| Waist-to-Hip Ratio | -0.01 | $t(115) = -0.11$ | .92 |
| BMI | -0.11 | $t(115) = -1.07$ | .29 |
| Depression | 0.08 | $t(115) = 0.88$ | .38 |

Table 14. *Anxiety Predicting CSI at Rest*

| | *β* | *t* | *p* |
|---|---|---|---|
| Model 1 | | | |
| Anxiety | 0.05 | $t(123) = 0.51$ | .61 |
| Model 2 | | | |
| Age | 0.04 | $t(116) = 0.43$ | .67 |
| Gender | -0.20 | $t(116) = -2.14$ | .04 |
| Ethnicity (D1) | 0.12 | $t(116) = 1.06$ | .29 |
| Ethnicity (D2) | 0.03 | $t(116) = 0.31$ | .76 |
| Waist-to-Hip Ratio | -0.03 | $t(116) = -0.35$ | .73 |
| BMI | -0.07 | $t(116) = -0.74$ | .46 |
| Anxiety | 0.07 | $t(116) = 0.78$ | .44 |

Table 15. *Anxiety Predicting CSI During the Stressor Task*

| Variable | *β* | *t* | *p* |
|---|---|---|---|
| Model 1 | | | |
| Anxiety | -0.02 | *t*(122) = -0.19 | .85 |
| Model 2 | | | |
| Age | 0.13 | *t*(115) = 1.40 | .16 |
| Gender | -0.05 | *t*(115) = -0.49 | .62 |
| Ethnicity (D1) | -0.01 | *t*(115) = -0.07 | .95 |
| Ethnicity (D2) | <0.01 | *t*(115) = 0.04 | .97 |
| Waist-to-Hip Ratio | -0.01 | *t*(115) = -0.11 | .91 |
| BMI | -0.10 | *t*(115) = -1.00 | .32 |
| Anxiety | 0.01 | *t*(115) = 0.07 | .94 |

## Discussion

The inconsistently observed relationship between depression and decreased levels of RSA has been puzzling for researchers. Although certain current psychological theories regarding parasympathetic influence would seem to suggest that RSA should be decreased in many psychological disorders, including depression and anxiety, the mixed findings in the literature render it unclear as to whether these theoretical predictions are supported. This thesis aimed to investigate whether depression and anxiety symptoms were in fact related to RSA, both at rest and during an arithmetic stressor task. I predicted that depression and anxiety would both have a significant relationship to RSA at rest and during the stressor task, but that the relationship between anxiety and RSA would be stronger. Additionally, I predicted that anxiety would maintain a unique relationship when controlling for concurrent depression, but that the reverse would not be true; I predicted that depression would no longer significantly relate to RSA when controlling for concurrent anxiety.

Although neither anxiety nor depression scores significantly predicted RSA at rest, anxiety was significantly related to RSA during the stressor task. Depression, however, was only marginally related to RSA during the stressor task. Additionally, during the stressor task, anxiety demonstrated a marginally significant relationship with RSA when controlling for depression scores. Conversely, when controlling for anxiety, the relationship between depression and RSA during the stressor task was non-significant. The results were consistent with anxiety as a potential 'third variable' which might be driving the previously observed associations between depression and RSA. These results

further our knowledge about RSA's relationship with anxiety and depression by suggesting that parasympathetic functioning, specifically the parasympathetic influence on the heart, may differ between them.

**Depression and RSA (Hypothesis 1)**

Previous research has found an inconsistent relationship between depression and RSA, with a small-to-medium effect size observed in clinical samples (Rottenberg, 2007). As such, we predicted that depression would have a small but significant relationship to RSA, at baseline and during the stressor task. The results partially support this hypothesis, in that a marginally significant relationship was observed during the stressor task, with higher levels of depression predicting lower levels of RSA as expected. However, at baseline, depression exhibited a negative but non-significant relationship to RSA. Although the lack of relationship between depression and RSA at baseline was counter to our predictions, it is not surprising given the many studies which have also failed to find a relationship between depression and RSA at rest (Lehofer et al., 1997; Moser et al., 1998; O'Connor et al., 2002; Watkins et al., 1998; Yeragani et al., 2002).

**Anxiety and RSA (Hypothesis 2)**

The previous literature on the relationship between anxiety and RSA has been mixed but more robust than that of depression and RSA. As such, we predicted that anxiety would have a significant relationship to RSA, at baseline and during the stressor task, and that this relationship would be stronger than that of depression to RSA. The prediction that anxiety would be significantly related to RSA was partially supported by

the data. During the stressor task, higher levels of anxiety were related to lower levels of RSA as predicted. However, at rest this relationship was not observed. Additionally, the direct relationship between anxiety and RSA during the stressor task was stronger than that of depression and RSA (although the latter represents non-significant relationship, and should be considered with caution). The lack of a relationship at rest was unexpected, but in line with previous studies which have failed to find a significant relationship between anxiety and RSA during baseline measurements (e.g. Watkins et al., 1998).

**Anxiety, Depression and RSA (Hypothesis 3)**

This study's third hypothesis was that, at both time points, anxiety would maintain its relationship with RSA when controlling for depression, whereas depression would no longer significantly relate to RSA when controlling for anxiety. To test this hypothesis, we employed a regression model containing anxiety and depression as predictors of RSA, to compare their relative predictive contributions. The hypothesis was supported during the stressor task, but not at rest. During the stressor task, upon the addition of anxiety to the regression model, the relationship between depression and RSA decreased to almost nothing. This finding suggests that depression may be related to RSA only in that higher levels of depression are related to higher levels of anxiety.

Our hypothesis was further supported when we examined the impact that the addition of depression scores to the regression model had on the relationship between anxiety and RSA. Importantly, the relationship between anxiety and RSA remained qualitatively similar and marginally significant when depression scores were included in the model predicting RSA from anxiety scores (from $\beta$ = -0.22, $p$ = .013 to $\beta$ = -0.21, $p$ =

.070).

These findings support the idea that anxiety has a robust relationship with RSA, and that depression may exhibit relationships to RSA only to the extent that it co-occurs with increased anxiety. This pattern is in line with previous studies which have found that anxiety but not depression are significantly related to decreased parasympathetic functioning (e.g. Watkins, Grossman, Krishnan, & Blumenthal, 1999). Additionally, the findings complement a recent study which examined the effect of comorbid anxiety disorders in MDD on RSA (Kemp et al., 2012) which found that patients with comorbid GAD showed the largest decreases in RSA. Although the researchers in that study concluded that unmedicated MDD patients had decreased RSA relative to controls, they did not account for differing levels of anxiety symptoms within the MDD groups. Had the authors examined the effect of comorbid anxiety symptoms dimensionally, they may have reached conclusions more similar to our own.

**Depression, Anxiety and CSI (Hypothesis 4)**

As RSA captures only one branch of the autonomic nervous system, we used CSI to explore potential patterns of SNS activity in relation to anxiety and depression. CSI's relationships with depression and anxiety were examined directly, with anxiety and depression individually predicting CSI. This represented an exploratory endeavor, and so we did not have any specific predictions. The results failed to support a relationship between sympathetic influence on the heart and either anxiety or depression. However, this HRV metric is relatively new (Toichi et al., 1997) and has not yet been extensively investigated in relation to either anxiety or depression. Given findings suggesting altered

sympathetic activity in both anxiety (Hoehn-Saric & McLeod, 2000) and depression (Musselman, Evans, & Nemeroff, 1998; Veith et al., 1994), it is possible that a different method of characterizing sympathetic activity might have produced different results.

**The Question of Rest vs. Stressor**

The discrepancy between the results at rest and during the stressor task is important to note. The difference is somewhat surprising given the theorized significance of RSA as a trait marker of emotion regulation abilities (Beauchaine, 2001; Beauchaine et al., 2007; Porges, Doussard-Roosevelt, & Maiti, 1994), especially when considering past studies which have found differences between clinically depressed or anxious individuals and controls at rest.

One possibility which may account for this lack of relationship between either depression or anxiety and RSA was the administration of questionnaires before the recording of the baseline measurement. All participants completed several questionnaires for approximately 30-45 minutes before the baseline measurements, perhaps giving them additional time to habituate to the research environment. Had we begun the study with a baseline measurement as has been done in several other studies (Agelink et al., 2002; Thayer et al., 1996), it is possible that participants' emotional states have been impacted by the stress of an unfamiliar environment (for example, making individuals who are prone to anxiety more anxious than the controls). This would have rendered the 'baseline' measurements in other studies, supposedly measuring resting RSA, more similar to a stressor condition. In our study, participants may have been more uniformly relaxed, as they had just completed 35-45 minutes of questionnaires.

Another possibility is that differences in parasympathetic activity related to psychopathology only emerge when individuals are subjected to stressors. For this reason, certain researchers have argued for the importance in looking at RSA reactivity (the change from rest to stressor condition) to assess differences in how individuals' parasympathetic system responds to stressors (e.g. Rottenberg et al., 2005). The results from this study could be seen to support the idea that it is only when participants are in the midst of stressful experiences that the relationship between anxiety symptoms and decreased RSA become apparent. This would mirror what some researchers have found in regards to sympathetic responding in anxious individuals (for a review, see Hoehn-Saric, & McLeod, 2000) where anxious individuals' sympathetic responses are only heightened as compared to controls during anxiety-relevant stressors. Conversely, at rest anxious participants tended to display normal SNS activity, or even blunted sympathetic responses to anxiety-irrelevant stressors.

A third possibility is that our study may have lacked the power to detect small relationships during the resting RSA measurement. Although the author acknowledges that non-significant relationships should not be interpreted in and of themselves, it is interesting to note that the pattern of findings at rest was similar to those during the stressor: both anxiety and depression had a negative relationship to RSA; the relationship between anxiety and RSA was stronger than that of depression and RSA; the small relationship between depression and RSA disappeared when controlling for concurrent anxiety symptoms; and the small relationship between anxiety and RSA did not disappear when controlling for concurrent depression symptoms. It is possible that these patterns represented relationships which were too small to be significant in this dataset.

## Implications and Future Directions

**RSA and psychopathology.** The results from this study indicate that comorbid anxiety symptoms may have played a role in the previously observed significant findings regarding the relationship between depression and RSA. These findings lend credence to the concern raised by researchers (e.g. Rottenberg, 2007) that anxiety symptoms in the depression-RSA relationship be investigated, so as to identify any potential confounding effects. The results presented here suggest that uncontrolled comorbid anxiety symptoms may explain the inconsistent findings in the literature on depression and RSA: where comorbid anxiety symptoms were significantly different between depressed participants versus non-depressed controls, researchers would have been more likely to find significant differences in RSA between the groups. In samples where the difference in anxiety symptoms was not as pronounced, researchers would have been less likely to find significant differences in RSA between the groups. Future studies are needed to verify this finding, both in clinical and non-clinical samples.

**Anxiety vs. depression.** The results from this study also have implications for the theoretical differentiation between anxiety and depression. These findings suggested that symptoms of anxiety, but not depression, may be related to decreases in RSA during a stressful task. If this difference continues to be replicated, it could indicate that there may be alterations in the autonomic functioning of anxious individuals when they are operating in stressful situations. Specifically, in individuals prone to anxiety, there may be a hyper-responsive withdrawal of the autonomic influence on the heart. Individuals with depression, on the other hand, may not demonstrate this altered autonomic functioning as

compared with 'healthy' individuals. This potential physiological difference between anxiety and depression may aid in the theoretical differentiation between the two disorders.

**Theoretical implications.** In addition to indicating a potential physiological and conceptual difference between anxiety and depression, future replication of the results from this study would indicate that the theories behind the role of RSA in psychopathology need to be revisited. For example, Porges' polyvagal theory (Porges, 1995, 2001, 2003a, 2007, 2009; Porges et al., 1994) implies that deficits in vagal activation would be associated with impaired social engagement behaviours. As both anxiety and depression often involve impairments in social engagement, both should be related to decreased vagal influence on the heart (Porges, 2003b). However, in this study only anxiety was significantly related to reduced vagal influence on the heart. It is possible that future elaborations on polyvagal theory may clarify why anxiety and depression differ in their vagal impairments, however the theory does not currently predict a difference between anxiety and depression.

Similarly, the results from this study are inconsistent with what would be expected from the theoretical integration of polyvagal theory with Gray's motivational theory (Beauchaine, 2001; Beauchaine et al., 2007). According to this theory, both anxiety and depression would be expected to relate to decreased RSA. As depression did not demonstrate a significant relationship to RSA, these predictions were not completely supported. Additionally, anxiety (and perhaps depression) would be expected to relate to increased CSI, since the theory implies that elevated sympathetic activity motivated

primarily by the BIS would result in internalizing disorders. Elevated CSI was not observed in this study.

Finally, the autonomic flexibility - neurovisceral integration model (Friedman, 2007; Thayer & Lane, 2000, 2009; Thayer & Ruiz-Padial, 2006) also suggests that hypoactivation of the prefrontal cortex in anxiety and depression should lead to decreases in RSA and increases in CSI. Other than a relationship between anxiety and decreased RSA during the stressor task, the results did not support this model's predictions. It should be noted, however, that these changes depend on concurrent inhibitory activity in the cortex, which was outside the scope of our study. It is possible that the levels of anxiety and depression in our sample were not severe enough to display the hypoactivation of the prefrontal cortex that is assumed by the neurovisceral integration model. However, as a significant relationship was observed between RSA and anxiety during the stressor task, this is unlikely to be the sole reason for discrepant findings. Additionally, in the context of this theory it is unclear how a relationship between anxiety and RSA could have been observed without a concurrent relationship between anxiety and CSI.

**A role for the sympathetic nervous system.** In this study, CSI was selected as a measure of sympathetic influence, as it could be derived from an EKG along with RSA. As CSI is a relatively new metric assessing sympathetic influence on the heart, future studies should compare CSI to more traditional measures of sympathetic activity (such as electrodermal activity). The parasympathetic branch represents only one half of the ANS, and it is likely that future research that is able to incorporate the relative contributions of

both the PNS and SNS will yield a more in depth understanding of the relationship between the ANS and psychopathology. Past research has attempted to measure this 'sympathovagal balance' by calculating the ratio of low-frequency power to high frequency power (Malliani et al., 1994). The theory behind this metric is that LF power indexes the sympathetic contributions to HRV, and the HF power is a reflection of vagal control of the heart. However, several issues exist with this particular measure (for a review see Eckberg, 1997), the most important of which is that LF power does not in fact seem to reflect sympathetic contributions to HRV. The use of electrodermal measure of SNS activity may circumvent this issue.

**Emotion-specific inductions.** The results from this study are limited in their emotional scope. Future studies may also benefit from looking at the parasympathetic and sympathetic influence on the heart during different kinds of tasks, as autonomic responses may vary based on the type of affective experience induced (Kriebig, Wilhelm, Roth, & Gross, 2007). The current study used a stressful arithmetic task to examine parasympathetic and sympathetic influence during a generalized stressor condition. However, specific emotional stressors or inductions may be useful in the future to take a more fine-grained approach to looking at differences in how anxious and depressed individuals respond in terms of their sympathetic and parasympathetic activity. For example, one might wonder if the sympathetic and parasympathetic systems in anxious and depressed individuals would respond differently across different emotional inductions (e.g. fear versus sadness versus happiness inductions). It is possible that autonomic functioning in anxious individuals may differ from healthy controls during fearful inductions but not during other emotional experiences. Conversely, alterations in ANS

functioning may only become apparent in individual with depression during sadness or happiness inductions. These differences remain relatively unexplored and interesting avenues for future research.

**Limitations**

Finally, this study has several limitations which should be considered. In terms of the study sample, all participants were young undergraduate students at the University of British Columbia who were registered in the psychology human subject pool. This very specific sample makes limits our ability to generalize the findings to other populations such as older adults, as age has been shown to relate to decreased RSA (De Meersman & Stein, 2007). Of particular relevance is the generalizing of the results to clinically anxious and depressed populations. Although there were a number of students who endorsed suffering from anxiety disorders or depression in our sample, the results are not necessarily representative of what would be found in clinical samples.

An additional limitation due to study design is the use of only one measure assessing depression and anxiety. The DASS was selected to assess depression and anxiety symptoms in this study as it was specifically designed to distinguish between the two, which was of utmost importance given the topic under study. However, the use of additional measure of anxiety and depression may have strengthened the persuasiveness of the results and also increased our ability to compare the current results with previous research.

Finally, the laboratory-based measurement of RSA allowed for standardization of

measurement conditions across participants. However, those conditions may differ from what is experienced by participants in their daily lives. The use of ambulatory measures would have enabled a greater understanding of how RSA and CSI behave in more natural settings.

## Conclusions

In summary, the results from this study indicate that anxiety, but not depression, has a real relationship to decreased RSA during stress. The relationship between anxiety and decreased RSA remained after controlling for respiration, and theoretically relevant demographic variables. However, the relationship between depression and decreased RSA was not supported in this study for two reasons. Firstly, the relationship between depression and decreased RSA was only marginally significant during stress. Secondly, the small relationship that did exist between depression and decreased RSA was rendered negligible when co-occurring anxiety was considered. This suggests that uncontrolled comorbid anxiety symptoms may have been responsible for some of the previously observed positive findings in the depression-RSA literature. These findings represent a potential explanation for some of the inconsistencies observed in the depression-RSA literature, and indicate that further investigation is warranted.

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