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THE ROLE OF AFFECT AND THE AUTONOMIC NERVOUS SYSTEM (ANS) IN VISUOSPATIAL LEARNING AND SET-SHIFTING: MODULATING CARDIAC VAGAL TONE THROUGH HEART RATE VARIABILITY (HRV) BIOFEEDBACK TO IMPROVE COGNITIVE PERFORMANCE

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ABSTRACT

The fields of psychology and neuroscience have found an interconnection between the autonomic nervous system (ANS), affect, and cognitive performance. Heart rate variability (HRV) may be a useful index of this relationship, representing the regulatory processes that facilitate adapting to emotions and environments to modulate mood and executive function. The current project consists of a series of experiments to investigate the relationship between trait affect, HRV, learning, and set-shifting performance. In the first experiment associations are found between negative affectivity, HRV, and set-shifting performance during an attentional set-shifting variant of the Virtual Morris Water Task (VMWT). Participants that exhibited both higher trait negative affectivity and lower baseline HRV displayed lower behavioral flexibility performance in the task. In Experiment 2, VMWT effects on HRV are examined. HRV is compared for individuals who completed the

task and those that failed learning or failed shifting phases of the task. In the Complete group, HRV decreased during the task and remained low during a 5-minute recovery period. This pattern was not observed in the groups that failed to complete the task, suggesting ANS sregulation deficits potentially playing a role in failure to perform the task. When investigating changes by phase, it was found that the extradimensional shift condition elicited the significant decrease in HRV. In the final experiment, a single 10-minute HRV biofeedback training was given to participants to investigate if increases in vagal tone immediately elicit changes in flexibility and mood. The biofeedback group (BFB) showed increases in mood and HRV while exhibiting decreases in Wisconsin card sort task (WCST) preservative errors. These findings taken together aid in the understanding of underlying vagal mechanisms that effect the emotion-cognition relationship, and may provide evidence for novel, noninvasive, and quick interventions that target vagal modulation to enhance cognitive performance and executive function.

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CHAPTER 1

Introduction and Specific Aims

1.1 Introduction

Cognition and affect are interconnected processes. Previous research has identified overlap in underlying neurobiological indices of these two domains from the neurotransmitter level to functional neuroanatomy and autonomic control systems (Cornwell et al., 2010; Drevets et al., 1997; Herrero et al., 2006; Monsell, 2003a; A. C. Roberts, 2000; Rogers, 1998). Both transient and chronic affective differences have been associated with spatial navigation and behavioral flexibility performance, with a general pattern of negative affect decreasing and positive affect increasing performance (Brunyé et al., 2009; Gardony & Taylor, 2011; Kanske & Kotz, 2011; Nusbaum et al., 2018; Palmiero et al., 2016; Xue et al., 2013)**.** Cardiac vagal tone could be an index of this relationship, reflecting differences in central and autonomic nervous system (ANS) ability to adapt to changes in external and internal stimuli.

The connection between the brain and heart through the vagal nerve has been a fascination of scientists since the seminal work of physiologist Claude Bernard (Thayer and Lane, 2009). From a neuroanatomical perspective, the brain structures involved in self-regulation and those involved in cardiac control largely overlap (Beissner et al., 2013; Hovland et al., 2012; Thayer et al., 2009). This link between cardiac vagal tone, indexed using heart rate variability (HRV), and self-regulation abilities can be explained by a functional network linking the heart to the prefrontal cortex (Thayer et al., 2009, 2012), and through the physiology underlying the functioning of the vagus nerve (Thayer et al.,

2009, 2012). Three more modern theories explain this link and its impact on different variations of self-regulation properties in humans. The polyvagal theory (Porges, 2007) purports that vagal control facilitates prosocial behavior through appropriate physiological and behavioral states. The neurovisceral integration model (Thayer et al., 2009) builds on this previous theory and hypothesizes that higher cardiac vagal control is associated positive increases in executive functions, emotion, and health, displaying overall a enhancements in self-regulation (Thayer et al., 2009, 2012). Most recently, Laborde's (2018) vagal tank theory expands on the neurovisceral integration model, given its precise description of self-regulation at the cognitive level and describes how the ANS reacts and recovers from environment needs for the system to self-regulate.

Further investigation is necessary to parse apart how affect, cognitive performance, and the ANS interact and influence one another. The current set of studies attempts to expand on previous findings to delve further into this relationship. This project examines the affect-cognition-ANS connection, specifically in the domains of behavioral flexibility (cognitive control) and visuo-spatial learning (hippocampal dependent learning), while attempting to modulate HRV to modify cognitive performance. While studies investigating relationships between cognitive control, affect, and vagal tone have been conducted (Brunyé et al., 2009; Gardony & Taylor, 2011; Kanske & Kotz, 2011; Nusbaum et al., 2018; Palmiero et al., 2016; Xue et al., 2013), visuo-spatial learning has not. Spatial learning deficits have been found to be related to anxiety and depression in animal models but have not been fully transferred to human experimental paradigms (for review see Bannerman et.al., 2014, Conrad , 2010). Over the course of four experiments, this project will attempt to rectify this knowledge gap. Findings will not only aid in the understanding of underlying cardiac vagal mechanisms that

affect the emotion-cognition relationship, but may also provide evidence for novel, noninvasive, and quick interventions that target vagal modulation to enhance cognitive performance and executive function.

1.2 Specific Aims of Current Dissertation:

The current dissertation aims to build on previous research to elucidate the relationship between affect, cognitive performance, and the parasympathetic nervous system (PNS). Previous research has found relationships between affect, HRV, and cognitive performance (Caselli et al., 2004; Chalmers et al., 2014; Downes et al., 1989; Edwards et al., 2015; Kemp et al., 2010), however, no studies have investigated these variables simultaneously. Studies have also shown effects of mood induction on performance and the benefits of biofeedback on stress, clinical symptoms, and cognitive performance (Kanske & Kotz, 2011; Prinsloo et al., 2011; Sutarto et al., 2013; Xue et al., 2013), however, these studies have not investigated the effect of HRV biofeedback training on the affect-cognition-ANS connection. To gain insight into the relationship, this project investigates these associations, then attempts to modulate state affect and HRV to modify cognitive performance in place learning and attentional set-shifting.

Aim 1: **To investigate the relationship between trait affectivity, baseline HRV, and performance during a set-shifting variant of the VMWT.**

This aim sets a foundation for understanding the complex interplay between cognition, affect, and the ANS. It employs the set-shifting variant of the VMWT, which is a novel design that has not previously been examined. This task was chosen for its complexity,

inclusion of both visuospatial learning and set-shifting components, and translational capabilities from human to animal research domains.

Aim 2: **To study task effects on vagal tone by investigating differences in HRV before, during, and after the set-shifting VMWT.**

This aim explores the impact that performing in the VMWT has on a number of HRV metrics. By measuring differences in baseline, task, and recovery HRV, dynamic changes in vagal response to cognitive challenge can be investigated. If performing the VMWT decreases HRV, then that would be evidence of an increase in cognitive control resources being allocated to the task at hand.

Aim 3: **To examine the relationship between affect, HRV, and performance on set-shifting through HRV biofeedback training.**

a) Will biofeedback training increase HRV and positive affect? This would elucidate the direction of the relationship between HRV and affectivity.
b) Will biofeedback change performance during the WCST? This would be evidence of a causal relationship between vagal tone on task-switching performance.
c) Will HRV biofeedback influence performance during the VMWT? This would suggest that modulating the ANS leads to changes in cognitive performance.

The findings of this research could have many impacts and implications in the fields of affective science, cognitive psychology, and psychophysiology. Aim 1 provides a fill for knowledge gaps in the relationship between cognition, affect, and baseline PNS measures. This aim extends on previous findings in affect and behavioral flexibility, as well as the role of the ANS on the emotion-cognition connection. In Aim 2, cognitive task effects on vagal tone are investigated. These findings will elucidate the impact of active learning and

performance of task switching on the ANS. While there is some research investigating time on task and stress on HRV, no research investigates the effects of performing a behavioral flexibility task on HRV. Aim 3 attempts to enhance cognitive performance through HRV biofeedback training to get a deeper understanding of the mechanistic underpinnings associated with this connection. Furthermore, results may provide evidence of a quick, non-evasive technique to increase positive mood and cognitive abilities. If cognitive performance can be improved after a single 10-minute training session, this technique could be employed by specialists in many domains to quickly enhance mental performance. This research could provide evidence that expands the utilization of this tool outside of clinical and emotion applications.

CHAPTER 2

Review of Literature

This project pulls from previous research in a multitude of fields including affective psychology, cognition, and neuroscience. This chapter will discuss trait affectivity, spatial learning, behavioral flexibility, heart rate variability, and past research investigating the interplay of emotions, cognitive, and vagal response. Finally, the HRV biofeedback body of research will be covered to fully introduce the pertinent theories and background literature.

2.1 Affect:

Affect is a collective term for feeling states that include constructs such as emotion and mood. Affective processes can be distinguished from one another by several factors. They are predominately defined in terms of duration and whether they are objective or subjective (Alpert & Rosen, 1990). Emotions are brief, intense feelings that are related to a specific event while both mood and affect are more enduring and diffuse and lack specificity to a certain event (for review see Beedie et al., 2005). Emotion and mood states, however, are both highly variable and dependent on environmental factors (for review see Beedie et al., 2005). Also, at the foundation of the affective research path, many of the scales measuring emotion and mood lacked methodological consistency, had poor sampling of affect terms, and had response biases that falsely decreased the normally high negative correlations between opposite mood terms. This, in turn, prevented the bipolar nature of these factors from being apparent. Another limitation can be found in the analysis of these earlier studies. The majority relied on factor analysis for mood component creation, which has the tendency

to create a large number of factors when a large number of variables are input. This leads to variability in the number and nature of primary factors creating low reproducibility (Watson et al., 1988).

These disadvantages in scalability, along with the transient nature of mood and emotion, make these metrics difficult to investigate. Trait affectivity, or tendency to respond to specific classes of stimuli in a predetermined, affect-based manner, is a stable measure of affective differences. This measure relates to dispositional differences in affect and remains consistent over time. Watson and Tellegen (1985) applied a different scaling approach than previous studies by focusing on the dominant dimensions of affect. By conducting a meta-analysis of previous work in the field, they determined much of affectivity could be described by classification of negative and positive valence. The researchers combined levels of arousal with pleasantness-unpleasantness to create the bi-polar dimensions of positive and negative affect. High levels of positive affect (PA) are associated with high pleasantness and high arousal. High negative affectivity (NA) is related with high levels of unpleasantness and high arousal. Zevon and Telligen (1982) first created a self-report assessment of with a representative number of mood descriptors (60) to determine clear PA and NA affect factors.

Categories of affect were then created using principal-components factor analysis categories of affect were created. From the initial list of 60 words, words with a loading factor above .40 on both the R and P-analyses were included leaving 30 NA and 20 PA meeting this criterion. These factors were narrowed down to the unidimensional factors that would not correlate or load to the opposing factor, creating pure markers of PA and NA by excluding any affect words with an unacceptable loading factor. This reduced the quantity to 25 NA and 12 PA affect terms. To simplify and condense the test, the experimenters than cut

the PA terms to 10 words removing the 2 with the highest secondary loadings from the factor analysis. The final PA scale includes the following terms: attentive, interested, alert, inspired, enthusiastic, proud, determined, strong, active, and alive. They truncated the NA to a matching 10-item scale by including 2 terms from each of the 7 categories found during factor analysis barring contempt and revulsion terms. The final NA scale includes the following terms from the five remaining categories: distressed, angry, fearful, guilty, and jittery. The scale was named the Positive and Negative Affectivity Scale (PANAS).

2.2 Spatial learning, anxiety, and depression:

Spatial navigation and place learning have been studied by behavioral scientists since the mid-1900s (Restle, 1957). Animal researchers have measured performance on these abilities using the Morris Water Task (MWT) (D'Hooge & De Deyn, 2001; R. Morris, 1984). In this task, an animal is placed in a circular pool of water with a hidden platform below the surface of the water. The animal must navigate to the hidden platform, relying on cues that are present in the environment. The animal completes many trials to master the task and learn the location of the platform. The MWT enables researchers to study the underlying biological mechanisms of hippocampal dependent place learning in normal and abnormal genetic strains by changing a number of variables, such as cues available in the environment. This task has been used to test many psychological theories and evaluate effects of brain lesions (e.g. Fantie & Kolb, 1990), prenatal environment (e.g. Callan et al., 2017; Savage et al., 2002), pharmacology (e.g. Gacar et al., 2011), stress (e.g. Engelmann et al., 2006) and genetic strains (e.g. Upchurch & Wehner, 1988; Vandam et al., 2006). More recently, researchers have developed a virtual version of the MWT to expand the research to human

subjects (Astur et al., 1998; Hamilton & Sutherland, 1999; Korthauer et al., 2021). In this computerized environment, the participant gets a first-person perspective, similar to that of animals. They are placed in a virtual pool of water, provided certain cues depending on the experimental manipulation and instructed to find the platform. Previous findings show that human performance in this task is similar to rats, and that they rely on cues in the environment to navigate to the platform location. .

One pertinent area that has been extensively studied is individual differences in trait anxiety and spatial learning in laboratory rats. Herrero, Sandi, and Venero (2006) found that rats classified as high anxiety (HA) had slower learning and decreased memory than low anxiety (LA) rats while performing the Morris water task and an open arm elevated maze. They found higher levels of mineralocorticoid receptors in the homogenated hippocampus of LA rats than HA rats. Mineralocorticoid levels were found to be correlated with performance as well. The higher the mineralocorticoid expression the more time the animal spend in the open arms of the maze. Behavioral differences were found during the water maze performance with LA rats showing quicker learning acquisition and memory than HA rats. HA rats also exhibited more thigmotaxic activity. This indicates that there might be interaction between trait anxiety, hippocampal mineralocorticoid expression, and the performance of individuals in spatial orientation tasks under stress. In a similar vein, Hawley, Grissoma, and Dohanich (2011) conducted an experiment on place learning and investigating memory, bias, and place strategy in male rats. They found a positive correlation between lower levels of trait anxiety and better place recognition memory. Lower trait anxiety was also correlated with the preferred use of place learning strategy. These findings combined

suggest that higher levels of trait anxiety seem to inhibit performance of spatial learning tasks in animal models.

Human behavioral studies also report individuals with anxiety and mood disorders are impaired in visual memory (Vasa et al., 2007) and spatial navigation (Mueller et al., 2009, Gould et al, 2007) during a virtual MWT (VMWT) relative to controls. Relationships between lower mental rotation abilities, avoidance motivation, and higher trait anxiety predict impairments in VMWT learning and performance (Murty et al., 2011; Thoresen et al., 2016). Neuroimaging studies have found decreased performance and activation of the anterior hippocampus and parahippocampal cortices during spatial navigation in depressed and anxious patients compared to controls (Cornwell et al, 2010, Milne, 2012).

2.3 Set-shifting, anxiety, and depression:

Cognitive flexibility is broadly defined as the ability to adapt and respond to changes in an environment (Scott, 1962). This construct has been studied extensively in animals and humans in both healthy and pathological populations by investigating set shifting, or the ability to switch rule sets (Uddin, 2021 for review). The original attentional set shifting task (AST) was created as a measurement of set-shifting in animals (Birrell & Brown, 2000; Garner et al., 2006; Heisler et al., 2015). This task was modeled after the intradimensional/extradimensional component of the Cambridge Neuropsychology Test Automated Battery (CANTAB), a test battery utilized to determine cognitive dysfunction (e.g. McKirdy et al., 2009; Roberts et al., 2007).

In the AST an animal is taught a specific attentional set by differentiating between relevant and irrelevant cues. For example, animals may learn to respond to a visual cue that

elicits a reward, while ignoring an odor cue that does not elicit a reward. This association is reinforced through trials pairing this association. The AST protocol goes through reversal phases and extra-dimensional shift phases to measure aspects of cognitive flexibility. In the example provided above, the previously rewarded visual stimulus will not be rewarded and the visual stimulus that did not elect a reward now will (reversal stage). In the extradimensional shifting phase, the irrelevant dimension becomes relevant and animals are rewarded based on odor cues and are no longer rewarded based on visual cues (in this example). This phase challenges the attentional set creation and perseverating on previously learned dimension indicates cognitive inflexibility (Uddin, 2021 for review). In humans, a similar task has been developed to investigate deficits in extradimensional shifting called the Wisconsin Card Sorting Task (WCST) (Grant & Berg, 1948). In this card game-like task participants must match cards based on learned dimensions on color, number, or suit. Shifts in attentional sets are performed by changing the relevant dimension of card (Heaton et al, 1993).

Individuals with higher levels of trait and clinical anxiety, as well as patients with clinical depression, display decreased performance in set-shifting tasks. These findings have been interpreted as evidence of inflexible processing styles in clinically depressed and anxious populations (Murphy et al., 2012). In contrast, high trait anxiety does not appear to negatively affect performance in trail-making tasks or other, more simple task switching paradigms (Bunce et al., 2008; Purcell et al., 1997; Waldstein et al., 1997). Gustavson and colleagues (2017) have postulated that imbalances in task demands may account for these conflicting findings with higher anxiety eliciting deficits only for more cognitively demanding tasks.

Relationships between affectivity and behavioral flexibility could be associated with individual differences in the prefrontal cortex (PFC) and other neuroanatomy underlying attentional shifting and executive function. Medial prefrontal (mPFC) lesions in rats interfere with shifting, specifically extradimensional (ED) shifting (Birrell & Brown, 2000). Elevating 5-HT_6 and noradrenergic activity at α_1-receptors the mPFC also facilitates cognitive performance of rats in attentional set-shifting tasks, which may contribute to the role of norepinephrine in behavioral state changes such as arousal, or to the beneficial cognitive effects of psychotherapeutic drugs that target serotonin and norepinephrine neurotransmission (Burnham et al., 2010; Lapiz & Morilak, 2006). In humans, impaired cognitive control, inability to inhibit responses, and set-shifting problems can be attributed to damage and dysfunction of the PFC. Underactivation in these regions and overactivation in the amygdala is common in clinical depression, both at rest (Drevets et al., 1997) and during reversal learning tasks (Taylor Tavares et al., 2008).

Eysenck and colleagues developed the Attentional Control Theory (Eysenck et al., 2007) and the Processing Efficiency Theory (Eysenck & Calvo, 1992) to describe the mechanisms underlying these working memory deficits in individuals with high trait anxiety. Under these models, it is thought that anxiety impairs functioning of the goal-directed system of attention and increases the extent to which processing is influenced by the stimulus-driven attentional system. In addition to decreasing attentional control, anxiety also seems to increase focus on threat-related stimuli. Adverse effects of anxiety on processing efficiency depend on two central executive functions involving attentional control: inhibition and shifting. This model argues that anxiety may not impair quality of performance but might

employ compensatory strategies, such as enhanced effort or increased use of processing resources.

Trait anxiety has been found to have a negative impact on flexibility in set shifting, mainly using the Wisconsin Card Sorting Task (WCST). The WCST is used in numerous neuropsychological studies and assessments as a measure of set shifting abilities. Studies have shown that individuals with higher levels of trait anxiety perform worse on measures of performance effectiveness, including total errors (Caselli et al., 2004), perseverative errors (Caselli et al., 2004), processing efficacy (Edwards et al., 2015), and the failure to maintain sets (Gershuny & Sher, 1995). These deficits in task switching performance have not been found for Trail Making Tasks (switching between numbers and letters) or other, simpler task switching paradigms (Bunce et al., 2008; Waldstein et al., 1997). Gustavson and colleagues (2017) postulated that imbalances in task demands may account for the conflicting findings. They manipulated task difficulty by having participants respond when side of screen arrows were presented (easy) and when the directionality of the arrows were presented (difficult). The researchers found that higher levels of trait anxiety were associated with worse performance (slower RTs) when participants had to switch from the more demanding task to the less demanding task. This RT cost was not seen when the directionality was reversed.

2.4 Spatial learning, flexibility, and mood induction

The relationship between cognition and affect does not seem to be limited to chronic affective conditions. Mood induction studies have found that changing a participant's transient emotional state can affect attentional breadth, as well as flexibility in cognitive processing. Emotional states have also been found to effect attentional breadth and

flexibility. The ability to process global features (forest) takes precedence over local features (trees) (Kimchi, 1992; Navon, 1977) and attending to these local features requires flexibility in strategy to overcome the dominant and more accessible strategy of attending to global features.

Positive affective states have been found to increase the ability to attenuate to local, non-dominant features suggesting increased flexibility in cognitive processing (Dreisbach & Goschke, 2004; Gasper & Clore, 2002). Baumann and Kuhl (2005) found participants responded significantly faster to local targets after positive compared to neutral and negative prime words. These findings support the assumption that positive affect increases cognitive flexibility by allowing for access to different strategies. Furthermore, findings suggest that mood-related preferences in global versus local processing cannot be generalized to processing ability. Van Wouwe, Band, and Ridderinkhof (2011) found the neural correlates to this effect using a cuing paradigm called the continuous performance task (CPT). The authors found that inducing positive affect elicited larger N2 component (an event related potential signifying cognitive control function) and error-related negativity after incorrect responses which indicates increased flexibility, evaluation, and reactivity after an error is made. According to this flexibility hypothesis, positive affect does not necessarily promote accessibility to global processing but facilitates open and efficient processing (flexibility). Others have found increased flexibility during flanker and Simon tasks in positive trials when compared to neutral trials (Kanske & Kotz, 2011; Xue et al., 2013). Wang, Chen, and Yu (2017) investigated switch costs during a Stroop-like set-shifting task after mood induction using emotional pictures. The researchers found lower switch costs in the positive condition compared to negative and neutral conditions.

It is possible that positive affect does not always have an enhancing effect on behavior flexibility, specifically when motivational factors are taken into consideration. Dreisbach and Goschke (2004) argued that while positive affect could increase attentional and behavioral flexibility it also increases distractibility. The researchers modulated affect during performance of the CPT and found that positive affect reduced maintenance capacity in relation to negative and neutral affect conditions. This effect was magnified when the researchers' introduced distractors into the experimental paradigm. Marien et. al. (2012) investigated how goal-directed behavior of goals versus means could explain this effect using a switch paradigm. They found that attaching positive affect (via positive image) to the representation of the goal decreased switch cost (RT) and enhanced flexibility. When positive affect was attached to the means they found increased switch cost signifying more rigid behavior. Nusbaum and colleagues (2018) induced positive and negative affect in participants prior to a task switching and reversal learning task. While affect states were effectively altered, there was no difference in mood groups performance on the task, casting doubt in the positive affectivity's faciliatory effects on cognitive flexibility.

There has been less research into the effect of mood induction on spatial navigation. Studies have found that higher arousal, both in positive and negative valence, lead to less utilization of global environment cues in spatial tasks (Brunyé et al., 2009; Gardony & Taylor, 2011). Palmerio and colleagues (2016) investigated mood induction and sex differences in spatial navigation working memory performance. The positive affect group scored higher on spatial working memory tasks than negative and neutral valence groups. Males outperformed females on the tasks only in the negative valence group, while no differences were found for positive or neutral groups.

2.5 Neuroanatomy underlying the heart-brain connection

The vagus is one of ten cranial nerves and is purported to be the most important nerve in the parasympathetic nervous system (Porges, 2007). This nerve branches to most organs in the body with a majority innervating gastrointestinal and cardiovascular systems, allowing for widespread communications between the brain and body (Chang et. al., 2003, Laborde, 2018). The vagus nerve plays an important role in the integration of interoceptive information and organizes appropriate responses and adaptive feedback (Yuan & Silberstein, 2016). It contains both afferent and efferent fibers that both send and receive signals from body to brain and vice a versa releasing acetylcholine (Howland, 2014, Brodal, 2010). A subset of vagal efferent fibers control the heart and modulate its activity through the sinus node, which determine heart rate (Jose & Collison, 1970). The central nervous system (CNS) integrates these sensory outputs from the vagal activity and organizes them, creating the phasic output of cardiac vagal control (Fallen et al., 2001). This central autonomic network (CAN) supports goal-directed behavior and self-regulation (Benarroch, 1993). The CAN is a network of multiple brain structures that are all under the organization of the prefrontal cortex, which regulates bidirectional information between lower and higher levels to the CNS (Benarroch, 1993,Thayer et al., 2009). The structural network includes the cingulate cortex, amygdala, insula, and hypothalamus. Through the stellate ganglia and vagus nerve, the CAN outputs sympathetic and parasympathetic activity to the heart (Benarroch, 1993,Thayer et al., 2009, Laborde et. al, 2018). This functional network is theorized to facilitate regulation of vagal afferent and efferent activity (Berthoud & Neuhuber, 2000).

2.6 HRV, affect, and flexibility:

Heart rate variability (HRV), an index of cardiac vagal conrol, has become a popular method to track overall wellbeing. HRV is a measurement of variability in beat-to-beat intervals that are mediated by vagal nerves, to slow heart rate, and sympathetic nerves to increase heart rate (for review see Rajendra Acharya et al., 2006). There is complex coupling between the brain and body that underlies the HRV signal. The sinoatrial (SA) node of the heart initiates heartbeats, dictating the rhythm of R-R intervals. Control of the SA node is influenced by interactions between multiple regulatory systems as well as more mechanistic activities (e.g. breathing). Slow-time changes in HR are metrics of body fluctuations (e.g. hormones, circadian rhythms, metabolism) while short-time changes in R-R intervals reflect ANS cardiac influences along with the ANS's interaction with respiration and cardiovascular activity (Malik, 1996; Pham et al., 2021; Shaffer & Ginsberg, 2017). Measures of HRV in the time domain (example: RMSSD) as well as high frequency power (HF) reflect parasympathetic activity (Berntson et al., 2005, Acharya et al, 2006).

Reductions in these cardiac vagal HRV measures have been found in clinical populations. Patients with MDD and anxiety disorders exhibit lower HRV than controls (Koch et al., 2019; Udupa et al., 2007). Meta-analyses find effect sizes for both anxiety and depression to be moderate (Chalmers et al., 2014; Kemp et al., 2010). This association could be explained with the Neurovisceral Integration Model of HRV (Thayer & Lane, 2000a). In this model, the prefrontal cortex moderates parasympathetic activity, which in turn mediates inflammatory processes that potentially contribute to pathologies such as affective disorders (Friedman, 2007).

Previous research has found higher baseline HRV is associated with increased resilience and emotion regulation capabilities, as well as cognitive capabilities of attention, memory, and behavioral flexibility (Balzarotti et al., 2017; Chen et al., 2015; Colzato et al., 2018; Friedman, 2007; Hildebrandt et al., 2016; Hovland et al., 2012; Mathewson et al., 2010). The Neurovisceral Integration Model postulates that baseline HRV could be an index of the affect-cognitive relationship, reflecting central and autonomic nervous system adaption capabilities to external and internal stimuli (Thayer et al., 2009; Thayer & Lane, 2000b). Thayer's model of neurovisceral integration hypothesizes that differences in parasympathetic cardiac vagal tone are indictive of emotional and cognitive regulatory processes (Thayer & Lane, 2000a). HRV, the metric used to estimate vagal responses, can be examined in tandem with affect and behavioral flexibility performance. Decreased HRV has been observed in clinical populations with mood and anxiety disorders (Paniccia et al., 2017), leading to this metric being a possible mechanism of affective effects on cognitive performance.

2.7 HRV biofeedback, emotions, and cognitive performance:

HRV biofeedback has become a popular technique to improve emotion regulation, reduce clinical mood symptoms, and modulate behavior (Gevirtz, 2013; Goessl et al., 2017). This tool trains individuals to regulate their physiological responses. Training regimens anywhere from one 5-min training to multiple trainings spanning over a month have been shown to modulate affect and behavior (Goessl et al., 2017; Prinsloo, Derman, Lambert, & Laurie Rauch, 2013; Prinsloo, Derman, Lambert, & Rauch, 2013; Prinsloo et al., 2011; Sutarto et al., 2013).

HRV biofeedback, or resonance frequency feedback, was initially examined as cardiorespiratory intervention in the 1990's (Lehrer et al. 2000). There are many difference forms of HRV biofeedback training which all either train the subject to create parallel sinusoidal line graphs for respiration and heart rate or train them to increase the amplitude in the sinusoidal line graph. which can effectively be used to increase cardiac tone (Moss, 2004, Gevirtz, 2003, Lehrer et al., 2000). All HRV biofeedback procedures consist of providing the individual with their beat-by-beat heart rate data during resonance breathing techniques to maximize HRV during training through a physiological sensor. The participant is then lead through diaphragmatic breathing techniques, relaxation and/or mediations, and/or instructed to cultivate positive emotion. They attempt to create sine-wave like curves that match their cardiac response to peaks and valleys of their breath while viewing the increases in heart rate during inhalation and decreases during exhalation to a pace delivered to them through a feedback device (Lehrer et al., 2006, 2013). Modern computer interfaced biofeedback systems and apps can be programmed to guide the subject in each of the training strategies (eg. HeartMath emWave systems: Whithed et al., 2014, Jester et al., 2018).

HRV biofeedback training appears to be an effective treatment for mood disorders, such as generalized anxiety disorder and post-traumatic stress disorder (Goessl et al., 2017; Lande et al., 2010). In nonclinical populations, biofeedback can also reduce stress and trait/state anxiety in individuals. This reduction can be seen in as little as one training session (Prinsloo et al., 2011; Sherlin et al., 2009). In a meta-analysis, Goessl, Curtiss, and Hoffman (2017) report a large within-group pre-post effect size for HRV biofeedback reducing anxiety and stress in multiple populations.

There is also evidence that HRV biofeedback interventions improve cognitive performance in a handful of small studies (Suvorov, 2006, Sutarto et al., 2013, Prinsloo et al., 2011). Sutarto et al. (2013) conducted a 5-week biofeedback training in a sample of operator workers. Pre-treatment and post-treatment cognitive performance were tested in multiple domains and found cognitive enhancement post biofeedback. Research has also shown that even short-term biofeedback training can lead to immediate benefits to cognitive performance. Prinsloo and colleagues (2011) compared performance on a modified Stroop task as well as stress levels before and after receiving one 10-minute biofeedback training. Participants that received training exhibited quicker reaction times and made fewer mistakes after the intervention. They also reported feeling more relaxed. Research in this area is limited, and further investigation is needed to parse apart this relationship.

CHAPTER 3

General Methodology

3.1 Attentional Set-shifting in the VMWT:

The main task in this research project combines the VMWT and classic attention set-shifting paradigms to create the set-shifting variant of the VMWT. The Morris Water Task (MWT) was originally developed to study spatial navigation in animals (R. G. M. Morris, 1981). In this behavioral task, an animal is placed in a circular pool of water and must learn to navigate to a submerged platform based on visual cues in their environment (R. G. M. Morris, 1981; Sutherland & Dyck, 1984). This task is commonly used to study hippocampal dependent learning and memory performance (R. G. M. Morris et al., 1982; Sutherland et al., 2001). The MWT has been adapted over the past 40 years to study effects of strains, stress, age, sex, drug/alcohol exposure, and rodent models for neurocognitive disorders (for review see D'Hoode & De Deyn, 2001). Virtual versions of this task have also been created to study human navigation (VMWT). Classical attentional set-shifting tasks were designed to measure cognitive flexibility by changing rule sets within a given task (Heisler et al., 2015). The paradigm consists of a series of rule shifts either within a given learning dimension (intradimensional shifts) or outside of the previous learning dimension (extradimensional shift). The attention shifting variant of the VMWT combines these two tasks into one task that measures place learning and set-shifting in a virtual environment.

The attentional set-shifting variant of the VMWT has an environment that consists of a circular pool divided into four equal quadrants. Two diametrically opposed, easily distinguishable, and visible platforms extend approximately half the pool wall height out

from the pool surface. The platforms are 1.75% of the pool surface. A pool wall encircles the pool and extends approximately 10% of the pool diameter. Four walls are located twice the pool diameter from the center of the room. On each wall a picture (distal cue) is displayed. These distal cues are an indication of location in the VMWT and can provide the participant with spatial location information. Cues are placed off-center vertically by a fixed amount determined prior to experimentation. At the beginning of each trial, participants are placed in one of four pseudo-randomly selected locations. To navigate in the virtual environment, participants use keyboard arrow keys (up, right, left). It takes 4 seconds to completely move a distance equal to the diameter of the pool and 2.5 seconds to complete a full 360-degree rotation (Figure 1, Figure 2).

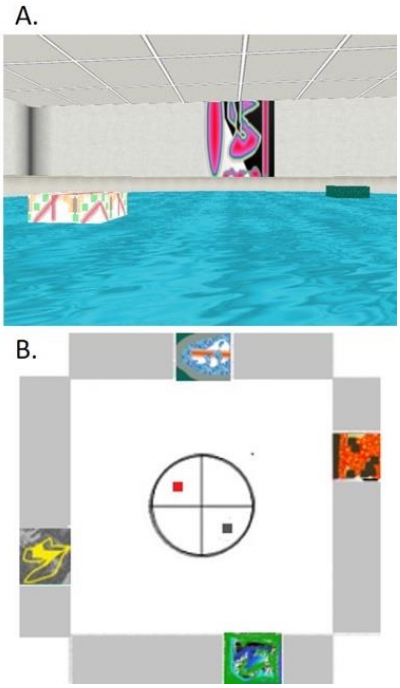

Figure 1: The VMWT schematic of the (A) aerial view and (B) from the participants vantage point.

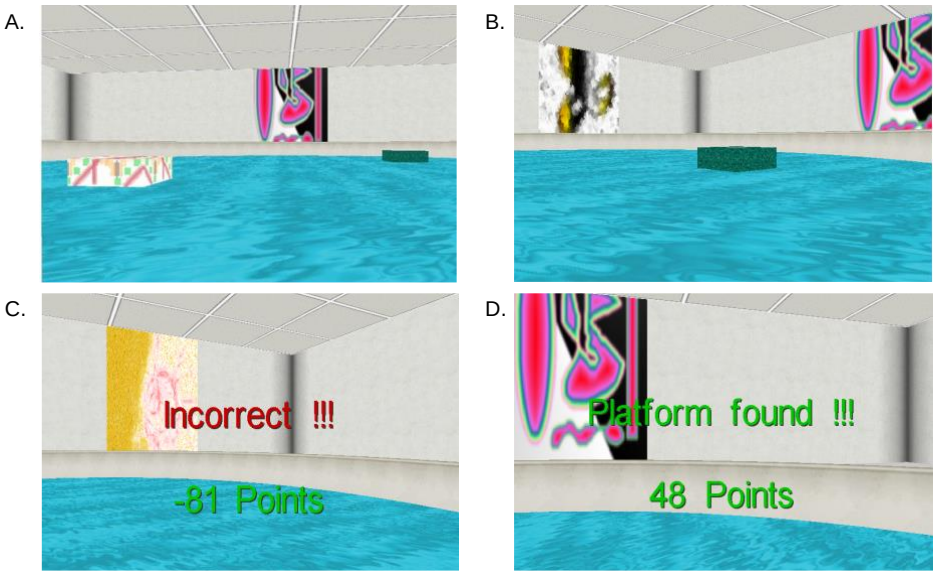

Figure 2: Participant's view during the set-shifting variant of the VMWT highlighting (A) object discrimination (platforms), (B) distal cues (wall pictures), and (C & D) performance feedback.

Participants complete six phases of the VMWT to assess initial learning and ID/ED set-shifting in the virtual environment (Table 1, Figure 3). To continue to the next phase, participants were required to reach trials-to-criteria of 9/10 correct. The experiment is discontinued if the participant fails to reach criteria after 150 trials. Phase 1 consists of an initial compound discrimination. Participants are randomly assigned to receive object discrimination or place discrimination for the initial learning rule. Once participants reach trials-to-criteria, they move to Phase 2 where the criterion changes, and the rule are reversed. Phase 3 consists of an intradimensional shift, where the cues change, but the rule remains the same. Phase 4 is the second reversal with the same cues and dimension rule set as Phase 3. In Phase 5, an extradimensional shift occurs, where the participant must learn a new rule set. The participants with initial learning phases of cue discrimination now must perform place learning and vice versa. Phase 6 is the final reversal in the same dimension and with the same

cues as Phase 5. After the task is completed, participants are given a brief questionnaire asking about strategies they employed, perceived task difficulty, and video game experience.

	Initial Compound Discrimination: Cue	Initial Compound Discrimination: Spatial
1: Initial Learning	Cue	Spatial
2: Reversal Learning	Cue	Spatial
3: ID Shift	Cue	Spatial
4: ID reversal	Cue	Spatial
5: ED Shift	Spatial	Cue
6: ED Reversal	Spatial	Cue

Table 1: Set-shifting Experimental Design shows the experimental design, highlighting the counterbalanced phases by relevant discrimination criteria for each phase. Columns represent the rules of the task by phases. Once the participant reaches trials-to-criteria of 9 out of 10 they move on to the subsequent phase.

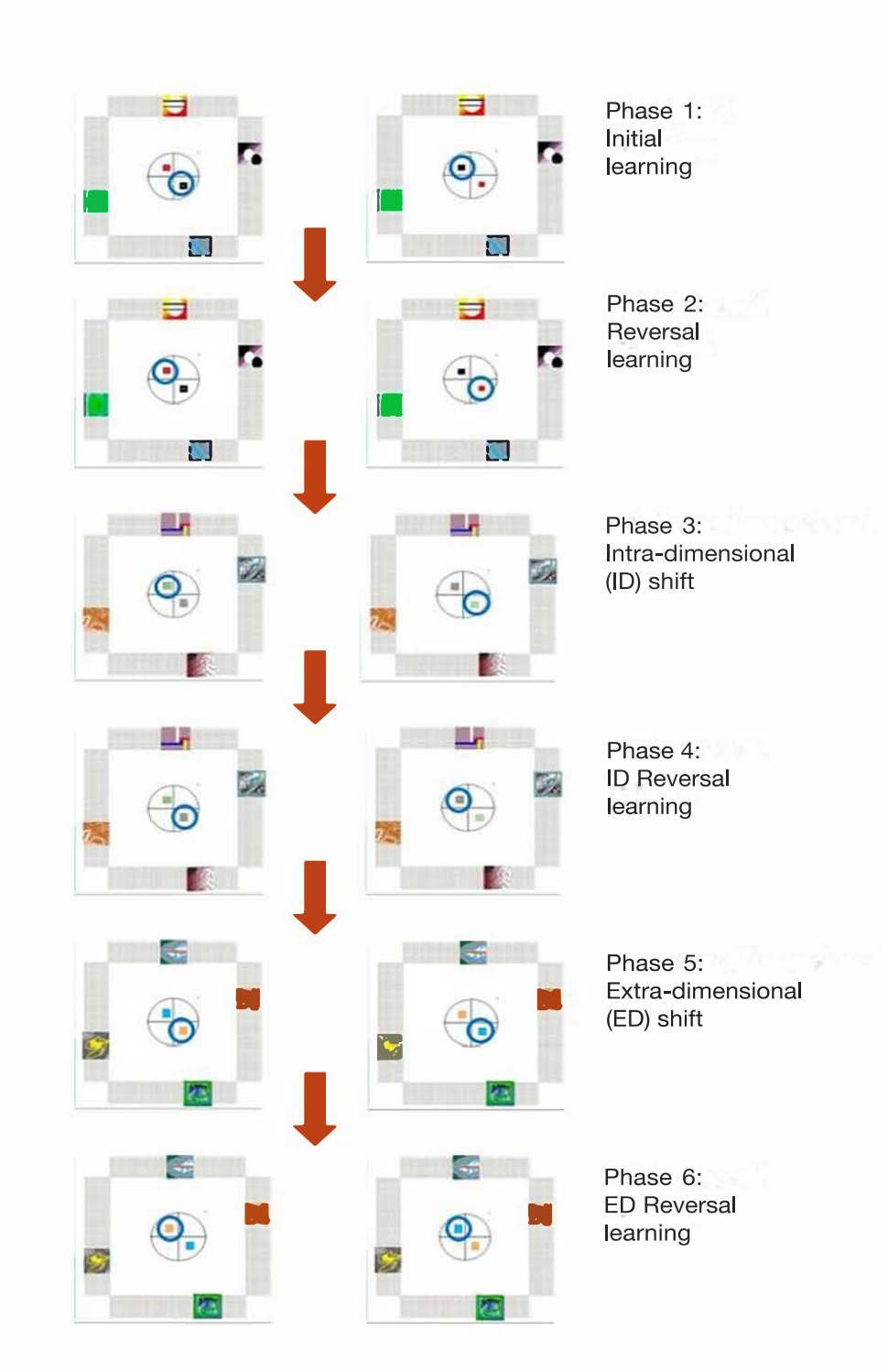

Figure 3: Phases of the attentional set-shifting variant of the VMWT. Initial learning in this example is cue discrimination. Once the participant reaches trials-to-criteria of 9 out of 10 they move on to the subsequent phase.

3.2 HRV Metric Methodology – Why RMSSD?

A large methodological consideration for this project was the selection of the HRV metric. There are over 70 variables that can calculate HRV in time, frequency, and non-linear domains (Bravi et al., 2011; Smith et al., 2013). The following section will present the most common HRV measurements that can be calculated using ECG signal only, focusing on variables indicating vagal tone, and justify the implementation of RMSSD as the main HRV metric of this project.

Time domain HRV measurements calculate HRV based on the variability of inter beat intervals (IBI) between successive heartbeats. Popular time domain measurements include the standard deviation of N-N intervals (SDNN), percentage of normal sinus differences above 50 ms (pNN50), and root mean square of successive differences (RMSSD). All of the most used measurements of HRV in the time domain measure variability in N-N intervals of HR. SDNN became popular for its cardiac risk prediction capabilities (Klieger et.a l, 1997). Both the sympathetic and parasympathetic nervous system play a role in SDNN (Umitani et al., 1998). SDNN does specify cardiac vagal tone but reflects all cyclic components of variability in the period of a recording (Malik, 1996). Therefore, this measurement would not be ideal for investigation into cardiac vagal tone. PNN50 represents the percentage of adjacent NN intervals that differ from each other by over 50 ms. RMSSD is the root mean square of successive differences between normal heartbeats. Each successive time difference is calculated then the values are squared (Shaffer & Ginberg, 2017). PNN50 and RMSSD both reflect differences in cardiac vagal tone (Kleiger et al., 2005; Laborde et al., 2017a; Shaffer & Ginsberg, 2017; Thayer & Lane, 2000a). While the measurements tend to be highly related to one another, RMSSD has been found to provide a better metric of

cardiac vagal tone and is preferred over pNN50 in parasympathetic research (Laborde et al., 2017a; Otzenberger et al., 1998, Shaffer & Ginsberg). RMSSD is the most robust measure against differences in respiration (Hill and Siebenbrock, 2009) and has been shown to be a pure index of vagal tone (Laborde et al., 2017b; Malik, 1996),

Frequency indices of HRV measures are separated into powerbands reflecting different underlying mechanisms. The bands are separated into ultra-low (ULF: below .0033 HZ), very-low (VLF: .0033 - .04), low (LF: .04 - .15), and high frequency (HF: .15 - .40) HRV. ULF HRV is reflecting bodily processes of core body temperature, circadian cycles, and metabolism, and requires 24 hr recordings to assess differences. VLF HRV reflects thermoregulation and hormonal and other long-term regulation mechanisms (Berntson & Stowell, 1998; Malik, 1996). LF-HRV band is influenced by both sympathetic and parasympathetic branches of the ANS, as well as blood pressure regulation via baroreceptors, and reflects a mixture of both vagal and sympathetic tone, as well as baroreflex activity during rest conditions (Malik, 1996; Berntson et al., 1997). HF-HRV reflects cardiac vagal tone and is highly correlated with RMSSD (Kleiger et al., 2005). This frequency band is also referred to as the respiration band and reflects phasic heart rate variations of the respiration cycle (Eckberg and Eckberg, 1982), meaning HF-HRV is highly affected by differences in breathing. These HR variations (known as RSA) may not be the pure index of vagal control it was once thought to be (Grossman & Taylor, 2007). Population characteristics also play a major role in differences in this metric with age, health, sex, and many other factors changing HF-HRV (Shaffer & Ginsberg, 2017). Laborde et. al (2017) advises that reports of HF-HRV should be paired with other time-domain measures of vagal tone to assure these population differences in respiration do not contaminate the results.

For the current project, a stable measure of cardiac vagal tone that is not influenced by respiration is the ideal metric. Out of all the measurements listed above, RMSSD fulfills all these requirements. RMSSD is more influenced by the PNS than SDNN and more reliable than PNN50 (Shaffer & Ginsberg, 2017). It is also less affected by respiration differences than HF-HRV and RSA (Shafer & Ginsberg, 2017), thought to be a pure metric of vagal tone (Laborde et al, 2017), and the preferred measurement of cardiac vagal tone by many HRV researchers (Laborde et al, 2018, Thayer & Lane, 2009, Shaffer & Ginsberg, 2017). For these reasons, RMSSD was chosen as the main biometric of vagal HRV for the current project. In Aim 2, we expand our measures to include frequency measurements of HF- and LF- HRV to fully investigate task effects on vagal tone.

CHAPTER 4.

Aim 1. To Investigate the Relationship Between Affectivity, HRV, And Performance During a Set-Shifting Variant of the VMWT.

4.1 Aim 1 Introduction

Previous research has studied affective differences in executive function and attention processes (Baumann & Kuhl, 2005; Dreisbach & Goschke, 2004; Gasper & Clore, 2002; Nusbaum et al., 2018), however, the relationship between spatial behavior, flexibility, and trait affectivity have not been adequately studied. The majority of spatial navigation and behavioral flexibility research has been conducted on clinical populations or by modulating emotional states, while measurements of trait affect have not been fully investigated. Further, whether positivity is associated with elevated cognitive abilities such as behavioral flexibility and spatial learning while negativity relates to diminished performance has not been examined. Previous ANS research has investigated the effects of mood induction modulating cognition and autonomic responses, HRV dysregulation and executive functioning deficits in mood disorders, and the relationship between HRV and affective flexibility (Grol & De Raedt, 2020), but none have investigated the relationship with HRV, trait NA, and set-switching concurrently in a purely cognitive task.

To address these knowledge gaps and develop a foundation of findings in the relationship between affective measures, vagal tone, and our novel VMWT, two experiments were conducted. Two samples were collected; the first consisted of 80 participants, with affective measures and VMWT, and the second (n = 73) with affective measures, VMWT, and ECG/pulse measures.

The preliminary behavioral study investigated the relationship between affectivity and the cognitive processes of behavioral flexibility and place learning in a variant of the VMWT. The connection between affective measures, spatial learning, and set-shifting in this task were assessed. In the second experiment, baseline ECG measures were collected along with affectivity measures to investigate the relationship between vagal tone, affect, and performance in the set-shifting variant of the VMWT.

It was hypothesized that positive affectivity would be associated with enhanced performance in initial learning and set-shifting while negative affective measures would be related to decreased performance. Following the same line of thought, it was hypothesized that lower baseline HRV would be associated with lower performance in the task. It is possible that these effects may bridge to performance in discrimination learning as well, however no previous research has examined the association between HRV and spatial or discrimination learning have been reported. Further, because of previous research finding differing NA effects on cognitive performance and ANS regulatory indices in clinical and normal populations (Holzman & Bridgett, 2017), it was postulated that theaccociation between HRV and performance would be modulated by individual differences in NA, with higher trait NA eliciting negative outcomes in performance and cardiac vagal regulation. Experiment 1.1 and 1.2 have recently been published in peer reviewed journals (Howell & Hamilton, 2021, 2022).

4.2 Experiment 1.1: The relationship between affect and performance on the VMWT.

4.2.1 Methods and Materials

4.2.1.1 Participants

Eighty-two undergraduate students ages 18 – 36 (M = 21.1, SD = 4.72, 55 female) were recruited from psychology classes at the University of New Mexico using an online recruitment system. This study was approved by the university's institutional review board. Participants were randomly assigned to the four conditions by sex in each condition. Inclusion criteria was normal or corrected vision and age limits of 18 - 36. All participants gave informed consent and were fully debriefed upon completion of the experimental session. were randomly assigned to the four conditions by sex in each condition. Two participants were excluded for clinical levels of depression or suicidal ideation making the final sample 80.

4.2.1.2 Survey Measures

Three electronic surveys were given to participants to measure affectivity. The Positive and Negative Affective Scale (PANAS) consists of a list of 60 adjectives that describe feelings and emotions (ex: cheerful, guilty, or distressed) in order to assess self-reported affect. Participants rate the extent to which they experienced these emotions over the past six weeks on a 5-point Likert scale with answers between 1 = very slightly/not at all to 5 = extremely. The subscales used in this experiment were the Positive Affectivity subscale (PA) and the Negative Affectivity subscale (NA). Higher scores indicate higher reports of positivity and negativity respectively. Beck Depression Inventory-II (BDI) and Beck Anxiety Inventory (BAI) were collected to assess levels of depression and anxiety in the population. Both questionnaires consisted of 21 questions with higher scores indicating higher levels of

depression/anxiety. were asked to answer BAI and BDI questions based on their affectivity over the past 6 weeks.

Measure		Complete		Failed Learning		Failed Shift	
		N = 56 (37 F)		N = 8 (8 F)		N = 16 (12 F)	
		M	SD	M	SD	M	SD
BDI	Total	9.96	7.67	14.37	11.86	13.56	10.08
	Male	8.47	8.33	–	–	21.50	11.90
	Female	10.31	7.36	14.37	11.86	10.91	8.33
BAI	Total	15.33	11.56	24.50	13.63	19.00	11.23
	Male	11.00	9.72	–	–	27.75	12.09
	Female	17.56	12.60	24.50	13.63	16.08	9.75
NA	Total	19.59	5.99	20.00	4.72	25.63	8.94
	Male	20.16	7.36	–	–	35.25	7.14
	Female	19.54	5.29	20.00	4.72	22.44	7.07
PA	Total	31.95	6.86	29.63	6.71	30.69	7.13
	Male	33.26	7.75	–	–	34.00	7.45
	Female	32.08	6.29	29.63	6.71	29.58	6.70

Table 2. Mean and standard deviation of the sum affective measures: BDI: Beck Depression Inventory-II, BAI: Beck Anxiety Inventory, NA: Negative Affectivity Subscale, PA: Positive Affectivity Subscale (PANAS)

4.2.1.3 Experimental Design and Procedure:

Intradimensional/extradimensional set-shifting (ID/ED) in the VMWT was assessed for two dimensions, platform cue identity and spatial location. Participants were randomly assigned to receive platform cue discrimination or spatial discrimination as the initial

learning condition. Within each phase, each of the four start locations was sampled once without replacement until all four locations were selected, after which the selection process was repeated for all four locations. For each phase, a criterion of 9 out of 10 trials correct was required to proceed to the subsequent phase. If the participant completed all phases of the trial they were grouped as Complete. If participants did not complete all phases they were placed into Failed Learning or Failed Shifting depending on the phase that they did not reach trials to criteria.

4.2.1.4 Statistical Analyses:

4.2.1.4.1 MANOVA analysis comparing Failed Learning and Failed Switch to Complete:

Twenty-four participants failed to meet criteria in one phase of the experiment, and therefore, failed to complete the task. Participants either failed to meet criteria during Phase 1 when the relevant dimension was spatial location (Failed Learning) or an ID/ED shift condition in Phases 4, 5, or 6 (Failed Shift). Participants who completed all phases were compared with those in the Failed Learning and Failed Shift group on affective measures. No males were in the Failed Learning group, so the two separate models were run on Complete vs. Failed Learning and Complete vs. Failed Shift with the Complete x Failed Learning model not including sex as a factor. A MANOVA with group as a between-subject factor and BDI scores, BAI scores, and negative and positive scales on the PANAS as dependent measures.

To investigate differences between Complete and Failed Shift participants, a 2 (Group) x 2 (Sex) MANOVA for the four affective dependent measures was performed. Pillai's Trace

was utilized because of the uneven and smaller sample sizes in some groups. All statistical analyses were performed using SPSS version 26. Effect sizes were reported using Pillai's V and partial eta squared. Family-wise alpha of the two models were controlled using FDR corrections. Model assumptions of normality and homogeneity of variance were checked. Measures for the affective dependent variables were within an acceptable range (skewness: .10 - .84, kurtosis: -.07 – 1.03). Levene's test of equality of variance did not reach significance for any affective measures for either model (p's = .18 - .86).

4.2.1.4.1 Regression analyses of phase trials to criteria:

Separate hierarchical regression models were run for each of the 6 phases with trials-to-criteria as the criterion variable. Predictor variables were the affectivity measures (BDI, BAI, PA, NA) and sex. If a participant reached maximum number of trials-to-criteria (150) in any phase the task was discontinued. The participant was then removed from further regression models of later phases in which they did not participate.

4.3 Results:

4.3.1 Affect and Learning:

There was no significant multivariate effect of group (Complete vs. Failed Learning) for affectivity measures ($V = .10$, $F_{(4, 59)} = 1.65$, $p = .17$). There were also no significant main effects of group for separate analyses of each variable, however, a trend for higher BAI total sum in the Failed Learning group was observed ($F_{(1,59)} = 3.93$, $p = .05$) (Figure 4).

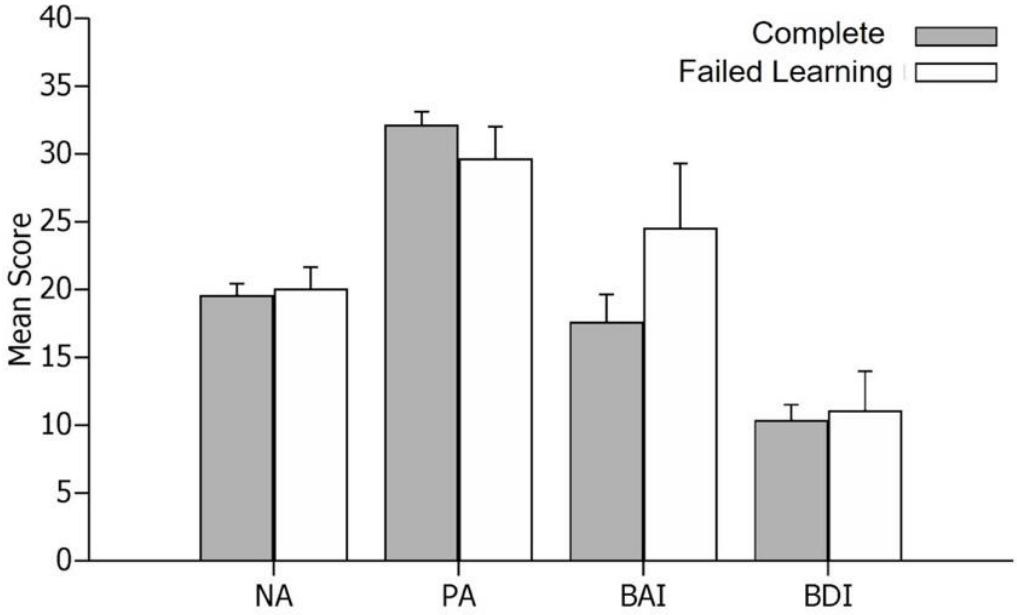

Figure 4: Main effect of group Complete vs Failed Learning. Mean and standard deviation bars are shown for: BDI, BAI, NA, PA. all ns.

4.*3.2 Affect and Set shifting:*

There was a significant effect of group for affectivity measures (V = .26, $F_{(4, 68)}$ = 6.65, p < .001). Between-subjects tests revealed that the Failed Shift group was significantly higher in BDI ($F_{(1,68)}$ = 6.95, p = .01, n_p^2 = .05), BAI ($F_{(1,68)}$ = 4.31 p = .04, n_p^2 = .06), and NA ($F_{(1, 68)}$ = 22.78, p < .001, n_p^2 = .13) compared to the Complete group. There was no significant relationship with PA (Figure 5).

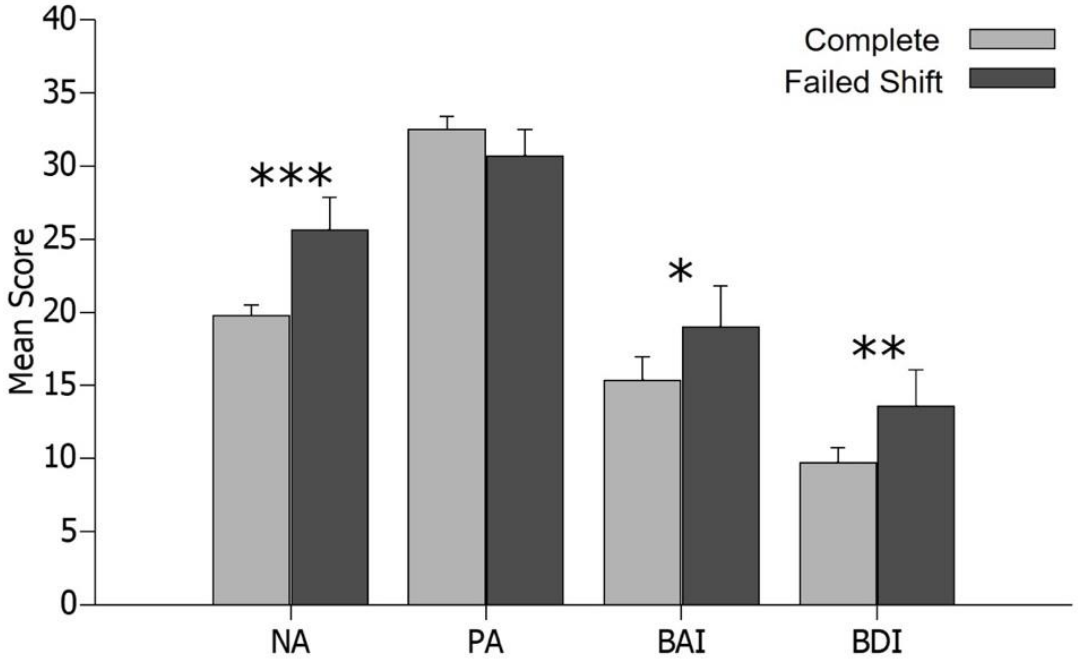

Figure 5: Main effect of Complete x Failed Switching. Mean and standard deviation bars are shown for: Beck Depression Index (BDI), Beck Anxiety Index (BAI), Positive and Negative Affectivity Scale (NA, PA). *p < .05, **p < .01, ***p < .001.

There was also a significant main effect of sex on affectivity measures ($F_{(4, 68)}$ = 6.35, p = .001, V = .28). Between-subjects tests revealed that females were significantly higher in NA ($F_{(1, 68)}$ = 12.77, p = .001, n_p^2 = .23). There were no significant mean differences between sex and BAI, BDI, or PA (p's > .05). Females scored higher in NA than males.

2.3.3 Interaction of Group and Sex:

There was a significant interaction between Complete and Failed Shift groups and sex, with affectivity measures ($F_{(4, 65)}$ = 3.83, p = .007, V = .19). Males who did not complete the switch during ID/ED VMWT had higher scores on the BDI ($F_{(1, 68)}$ = 8.68, p = .01, n_p^2 =

.11), BAI ($F_{(1, 68)}$ = 7.08, p = .01, n_p^2 = .09), and NA ($F_{(1, 68)}$ = 21.93, p < .001, n_p^2 = .24) than Complete males as well as their Failed Switch female counterparts. There were no significant mean differences for the group and sex interaction for PA (Figure 6).

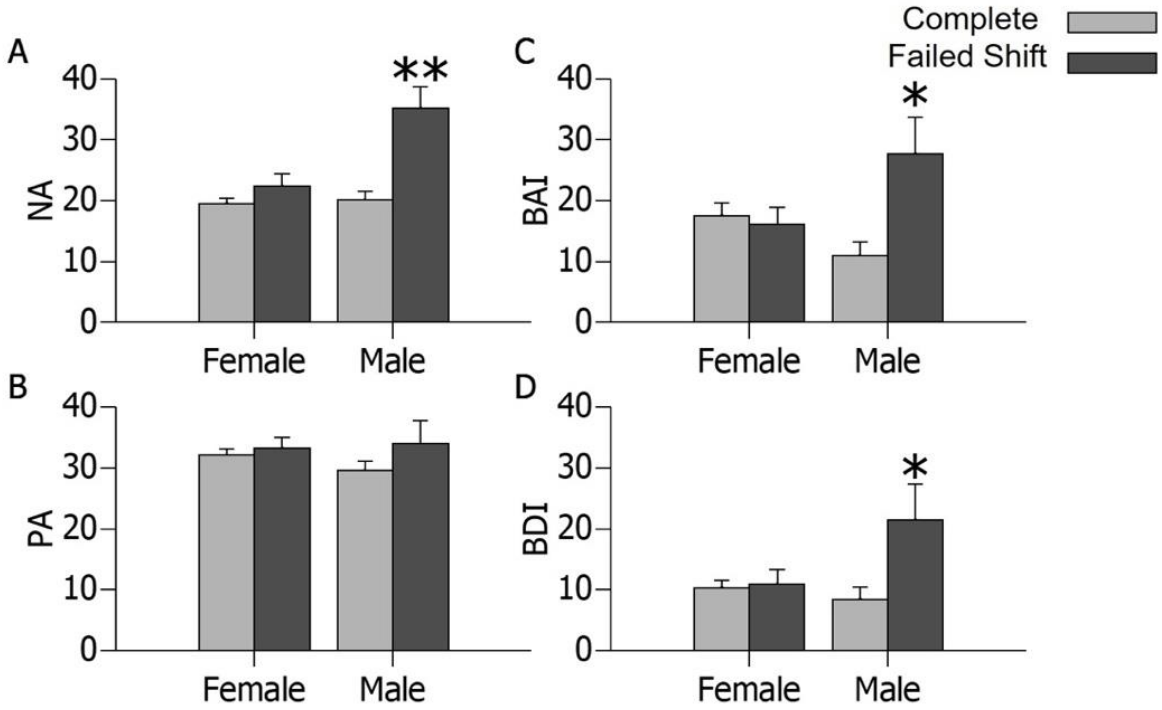

Figure 6: Interaction of VMWT and sex with affectivity. Means and standard deviation bars are shown for: (A) Negative Affect (NA), (B) Positive Affect (PA), (C) Beck Anxiety Index (BAI), (D) Beck Depression Index (BDI). *p < .05, **p < .01.

4.3.4 Regression models:

Models for Phases 1 – 3 failed to reach significance (R^2 range = .08 - .09, p's > .05). Phase 4, Phase 5, and Phase 6 regression models reached significance. Performance on the 2nd reversal (Phase 4; R^2 = .16, $F_{(5,71)}$ = 2.56, p = .04) ,extradimensional shift (Phase 5; R^2 = .21, $F_{(5,68)}$ = 2.89, p = .02), and following reversal phase (Phase 6; R^2 = .21, $F_{(5,58)}$ = 2.74, p = .03) were predicted by affectivity measures controlling for sex. Pairwise comparisons show

significant predictors to be NA (Phase 5: = .63 p < .001, Phase 6: β = .35 p = .04), BAI (Phase 4: β = -.37 p = .04, Phase 5: β = -.38 p = .04), and BDI (Phase 4: β = .50 p = .01, Phase 6: β = -.48 p = .01) (Table S#).

4.4 Experiment 1.2: HRV and Performance on the VMWT

4.4.1 Methodology:

Experiment 1.2 employed the same methodology as Experiment 1.1 with the addition of HRV measures. HRV study design, data collection, and data analysis plans were developed using guidance and recommendations from HRV Taskforce (Electrophysiology, 1996) and Laborde, Mosley and Thayer (2017a). Electrocardiographic inter beat interval (IBI) measures were collected with the BIOPAC acquisition system (MP150 system; BIOPAC systems Inc., Goleta, CA). During survey collection, ECG electrodes are be placed in a 3-lead configuration, a triangular arrangement with one electrode on the right collar bone and one on the lower left rib bone. A ground electrode is placed on the left collar bone. The ECG signals are amplified using the BIOPAC ECG100C amplifier and digitized with a sampling rate of 1000 Hz. The signal is bandpass filtered from .5 to 35 Hz. Baseline ECG data was collected for 5-minutes immediately prior to the VMWT.

ECG and were processed and analyzed using QRS Tool, MATLAB 19, and the HRVTool 1.04 application. R-R artifacts will be removed using automated settings in line with the HRV Taskforce recommendations (50:50 window and 20 Hz filter). Root mean square of successive differences (RMSSD) of the R-R intervals (RMSSD) was chosen as an index of HRV due to previous research indicating the measure's applicability to short term ECG recordings and robust tolerance to differences in respiration (Laborde, Mosley,

&Thayer, 2017). QRS Tool will be employed to calculate RSA, a metric commonly used in HRV biofeedback research.

4.4.2 *Participants:*

Seventy-three students (M = 21.32 years, SD = 5.89, 50 female) enrolled in undergraduate psychology courses at the University of New Mexico were recruited using an online system. They received course credit for the experiment. All participants had normal or corrected vision and were between 18 – 36 years old. The experiment was approved by the university's review board. Following informed consent, participants completed online surveys and the experimental task while ECG indices were being collected. Participants were debriefed following completion of the task. Three participants were removed for high clinical levels on the BDI scale, one participant for missing survey data, one participant was removed for unusable ECG data, and one participant was removed for having an RMSSD score of over three standard deviations above the mean, making the final sample size sixty-seven.

4.4.3 *Affective surveys:*

Affective surveys remained consistent with Experiment 1.1 (PANAS, BDI-II, BAI). Participants were asked to answer the questions based on their affectivity over the past 6 weeks. Beck Depression Inventory-II (BDI-II) and Beck Anxiety Inventory (BAI) were collected to assess levels of depression and anxiety in the population. Both questionnaires consisted of 21 questions with higher scores indicating higher levels of depression/anxiety.

4.4.4 *Heart rate measures and analysis*

Electrocardiographic inter beat interval (IBI) measures were collected with the BIOPAC acquisition system (MP150 system; BIOPAC systems Inc., Goleta, CA). During survey collection, ECG electrodes were placed in a 3-lead configuration, a triangular arrangement with one electrode on the right collar bone and one on the lower left rib bone. A ground electrode was placed on the left collar bone. The ECG signals were amplified using the BIOPAC ECG100C amplifier and digitized with a sampling rate of 1000 Hz. The signal was bandpass filtered from .5 to 35 Hz. Once participants had completed the surveys (15 - 20 minutes post-electrode application), baseline recordings were collected for 5-minutes at rest before the experimental task. ECG data were processed and analyzed using MATLAB 19 (MathWorks) and the HRVTool 1.04 application (Vollmer, 2019). R-R artifacts were filtered using automated settings in line with the HRV Taskforce (1996) recommendations (50:50 window and 20 Hz filter). Heart rate (HR) beats-per-minute and root mean square of successive differences in ms (RMSSD) of the R-R intervals were calculated. RMSSD was chosen as an index of HRV due to previous research indicating the measure's applicability to short term ECG recordings and robust tolerance to differences in respiration. While many studies have found RMSSD to be positively skewed, our data did not exhibit this effect (skewness = .37). Therefore, mean RMSSD (ms) was employed without manipulation to correct for skewness.

	Complete *N = 45* *(35 F)*		*Failed Learning* *N = 7* *(6 F)*		*Failed Shift* *N = 15* *(10 F)*	
Measure	*M*	*SD*	*M*	*SD*	*M*	*SD*
BDI	8.60	7.59	4.71	4.99	7.87	6.55
BAI	14.29	8.69	12.29	10.6	12.33	9.47
NA	17.62	5.23	17.14	6.30	15.00	6.35
PA	30.38	5.83	29.71	2.13	30.47	7.17
HR	74.16	7.80	79.9	8.02	81.00	9.78
RMSSD	51.79	15.85	36.45	9.51	34.99	10.93

Table 3: Mean and standard deviation of the sum affective measures and ECG measures. Notes: BDI: Beck Depression Inventory-II, BAI: Beck Anxiety Inventory, NA: Negative Affectivity Subscale, PA: Positive Affectivity Subscale (PANAS), HR: Heart Rate (beats per minute), RMSSD (root mean square of successive differences (ms)).

4.4.5 *Statistical analysis:*

4.4.5.1 MANOVA analysis on Group Differences:

Subjects who did not meet criteria failed either in Phase 1 during place learning (Failed Learning, N = 7, 1 M) or failed to ID/ED set-shift (Failed Shift, N = 15, 5 M) (Table 2). The remaining participants completed all phases of the task (Complete, N = 45, 10 M). Only one male failed learning, making the sample too small to perform significance tests including sex for this group. Because of this, two separate models were analyzed: Complete vs. Failed Learning (sex not included) and Complete vs. Failed Shift. For Complete x Failed Learning, a MANOVA with group as a between-subject factor and BDI scores, BAI scores, NA scale, PA scale, HR, and RMSSD as dependent measures was run.

To investigate differences between Complete and Failed Shift groups, a 2 (Group) x 2 (Sex) x 6 MANOVA for the four affective and two electrocardiography dependent measures

was performed. To control for uneven and small sample sizes of some groups, Pillai's Trace was utilized, and model assumptions were checked. All statistical analyses were performed using SPSS version 26 (IBM SPSS Statistics for Macintosh, Version 25.0). Covariance matrices of the dependent variables were equal across groups were not significantly different. (Complete and Failed Learning: Box's M = 42.903 $F_{(21, 402.70)} = 1.2$, p = .24; Complete and Failed Switch: Box's M = 36.34 $F_{(21, 2581.01)} = 1.4$, p = .10). Effect sizes were reported using Pillai's V and partial eta squared. Family-wise alpha of the two models were controlled using FDR corrections.

4.4.5.2 Regression models by phase:

To investigate the moderating effects of NA on HRV and trials-to-criteria, separate hierarchal regression models were run for each phase. Centered predictor variables of sex, BDI, BAI, NA, PA, HR, RMSSD, and NA x RMSSD were regressed on log-transformed trials-to-criteria. If a participant reached maximum number of trials-to-criteria (150) in any phase the experiment terminated, and the participant was removed from further regression models of phases in which they did not participate. For models that reached significance, follow-up regressions were run on split mean NA (high NA: H-NA and low NA: L-NA) groups separately. Centered predictor variables of sex, BDI, BAI, PA, HR, and RMSSD were regressed on log-transformed trials-to-criteria.

4.*5.1 Learning, HRV, and affect:*

There was no significant multivariate effect of group (Complete vs. Failed Learning) for affectivity and electrocardiography measures (V = .20, $F_{(6, 45)} = 1.85$, p = .11). There was

a significant main effect of group for separate analyses of RMSSD, with the Failed Learning group exhibiting significantly lower RMSSD ($F_{(1,50)} = 6.14$, $p = .02$, $n_p^2 = .11$) (Figure 7A). There were no significant differences in affectivity measures (p's > .05) (Figure 7B).

4.5.2 Behavioral flexibility, HRV, and affect:

There was a significant multivariate effect of Group (Complete vs. Failed Shift) for affectivity and electrocardiography measures ($V = .23$, $F_{(6, 51)} = 2.5$, $p = .03$). No significant differences were found for Sex ($V = .08$, $F_{(6, 51)} = .78$, $p = .59$) or the interaction of Group x Sex ($V = .08$, $F_{(6, 51)} = .68$, $p = .58$). There was a significant main effect of group for RMSSD (Failed Shift < Complete; $F_{(1,56)} = 12.61$, $p = .001$, $n_p^2 = .18$) (Figure 7A). There were no significant differences in affectivity measures (p's > .05) (Figure 7B.

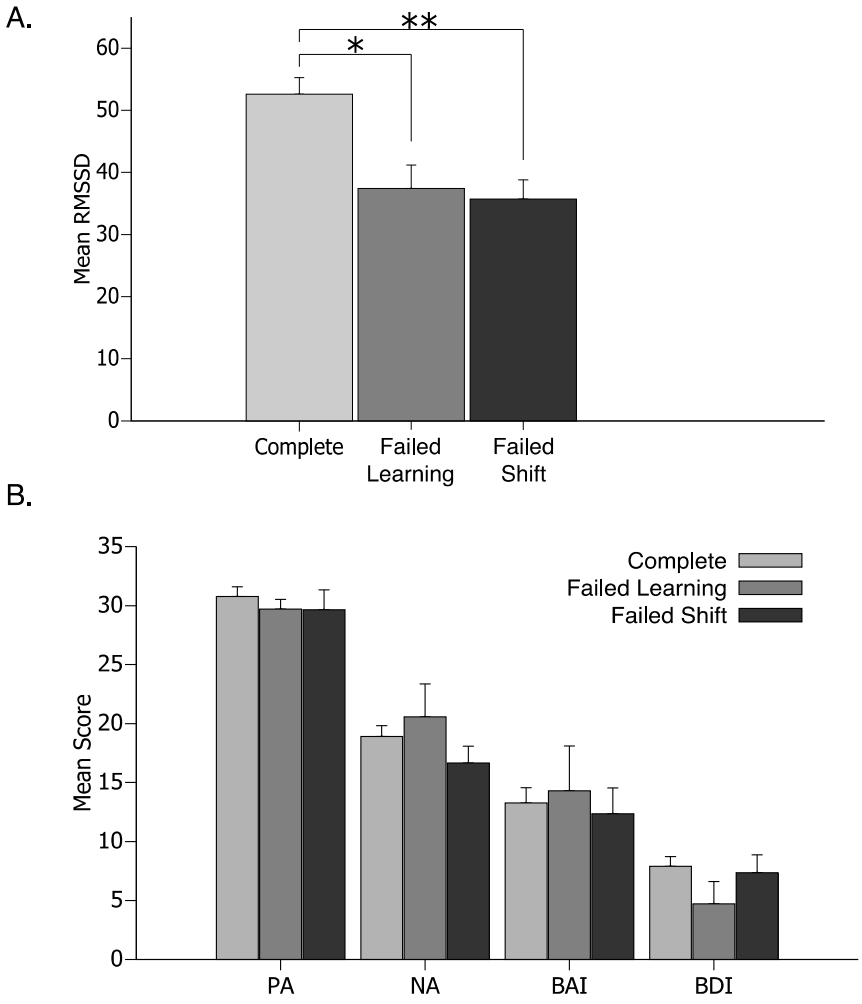

Figure 7: Group Differences in mean/standard deviation A) RMSSD (ms) and B) affectivity measures. RMSSD (ms) and B) Affectivity measures. Notes: BDI: Beck Depression Inventory-II, BAI: Beck Anxiety Inventory, NA: Negative Affectivity Subscale, PA: Positive Affectivity Subscale (PANAS).** $p < 0.01$

4.*5.3 Regression models:*

Regression models for Phases 1 – 4 and 6 failed to reach significance (R2 range = .13 - .22, p's > .05). The model for Phase 5 (ED Shift) significantly predicted trials-to-criteria (R2 = .36, $F_{(8,58)} = 3.36$ p = .004). Pairwise comparisons show significant predictors RMSSD

(β = -.45 p = .004) and the RMSSD x NA interaction (β = .30 p = .02) . All other predictors were non-significant (p's > .05) (Table 3).

Independent Variables	*Phase 1 (N = 67)* *β (p-value)*	*Phase 2 (N = 62)* *β (p-value)*	*Phase 3 (N = 60)* *β (p-value)*	*Phase 4 (N = 59)* *β (p-value)*	*Phase 5 (N = 59)* *β (p-value)*	*Phase 6 (N = 49)* *β (p-value)*
sex	*-.10(.43)*	*-.03(.85)*	*-.20(.15)*	*-.14(.34)*	*.19(.14)*	*.04(.78)*
PA	*-.23(.10)*	*-.04(.76)*	*.04(.78)*	*-.03(.86)*	*.04(.78)*	*.17(.29)*
NA	*.09(.3)*	*-.22(.25)*	*-.16(.39)*	*-16(.41)*	*-.15(.37)*	*.17(.43)*
BDI	*.31(.05)**	*.12(.49)*	*.12(.45)*	*.08(.64)*	*.11(.45)*	*.18(.34)*
BAI	*.02(.89)*	*.20(.28)*	*.07(69)*	*.11(.55)*	*-.21(.21)*	*.09(.69)*
HR	*.02(.90)*	*-.09(.55)*	*.08(.63)*	*.07(.66)*	*-.01(.96)*	*.27(.13)*
RMSSD	*-.22(.18)*	*-.28(.11)*	*-.31(.07)*	*-.20(.24)*	*.45(.004)***	*.17(.38)*
NA x RMSSD	*-.04(.75)*	*.21(.13)*	*.01(.93)*	*.04(.79)*	*.30(.02)**	*.3(.45)*

Table 4: Regressions by VMWT phase. All IVs were centered for analysis. Phase 5 is the only model that reached significance. Notes: BDI: Beck Depression Inventory-II, BAI: Beck Anxiety Inventory, NA: Negative Affectivity Subscale, PA: Positive Affectivity Subscale (PANAS). * p < .05, ** p < .01.

Follow-up regression models were run separately on L-NA and H-NA for Phase 5 trials-to-criteria. No significant relationship was found for the H-NA group (p > .05). The regression model was significant for the L-NA group (R^2 = .64, $F_{(6,30)}$ = 4.72, p > .001). Pairwise comparisons found significant negative relationships between trials-to-criteria and RMSSD (β = -.79, p =.001) and PA (β = -.32, p = 02) (Figure 8A and B) (Table 4). No other predictors reached significance (p's > .05). Analysis of Covariance with Allowances for Heterogeneity of Regression Slopes (ANCOHET) was then run to determine if the slopes were significantly different between H-NA and L-NA groups for the linear relationship between Phase 5 and RMSSD, and Phase 5 and PA. Tests of model effects were significant

for NA Group x RMSSD (Wald $\chi 2_{(2,58)} = 9.86$, $p = .007$) and trending towards significance for NA Group x PA (Wald $\chi 2_{(2,58)} = 5.39$, $p = .068$).

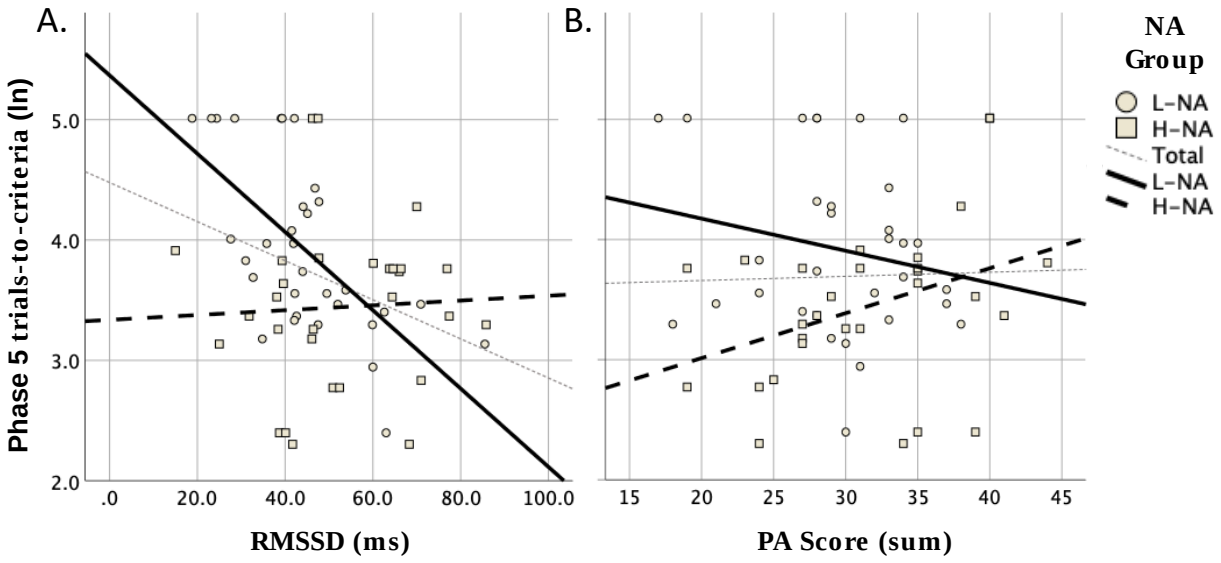

Figure 8: Plots by NA group for significant predictors of A) Mean RMSSD and ln Phase 5 trials-to-criteria for l-NA (Low Negative Affectivity), H-NA (High Negative Affectivity), and the overall sample, and B) Sum Positive Affectivity (PA) score and ln Phase 5 trials-to-criteria for l-NA, H-NA, and the overall sample.

Independent Variables	*L-NA (N = 31) β (p-value)*	*H-NA (N = 28) β (p-value)*
sex	*.14(.32)*	*.99(.34)*
PA	*-.32(.02)**	*.43(.06)*
BDI	*.27(.09)*	*.34(.13)*
BAI	*-.24(.12)*	*-.41(.07)*
HR	*.01(.94)*	*.22(.38)*
RMSSD	*-.79(.001)***	*.10(.72)*

Table 5: Phase 5 regression model for L-NA and H-HA. * p < .05, ** p < .01.

4.6 Aim 1. Discussion

In Experiment 1.1 and Experiment 1.2 robust relationships were found with negative affectivity and ANS measures. In Experiment 1.1, a significant relationship between negative affectivity and behavioral flexibility in the virtual spatial learning environment was found. Regression models identified that higher levels of trait negative affectivity were significantly related to higher trials-to-criteria during the set shifting conditions. Higher levels of trait negative affectivity, anxiety, and depression were observed in participants who failed to meet criteria for set-shifting and this effect was more pronounced in males**.** In Experiment 1.2, individuals who successfully completed the VMWT had significantly higher HRV than those that failed learning and failed shifting conditions. During the extradimensional shift condition, there was a significant negative relationship between HRV and performance on the task. Higher RMSSD was related to lower trials-to-criteria during this set-shifting phase. The effect was moderated by NA, with H-NA negating the relationship between HRV and extradimensional set-shifting performance.

While consistencies were found in the two experiments, Experiment 1.2 did not completely replicate findings from Experiment 1.1. There were no sex differences found in Experiment 1.2. While there was a moderating effect of negative affectivity on the relationship between HRV and behavioral flexibility, there was not a direct effect of affectivity measures on VMWT performance. The results of both experiments support the connection between affectivity, HRV, and performance on the set-shifting VMWT, however. Negative affectivity is significantly related to worse performance during set-shifting and lower HRV is significantly related to decreased performance in both spatial learning and flexibility in the VMWT.

CHAPTER 5.

Aim 2. To Study Task Effects on Vagal Tone by Investigating Differences in HRV Before, During, and After the Set-shifting VMWT.

5.2 Aim 2 Introduction:

Heart rate variability (HRV) has been associated with differences in executive function and regulation capabilities in both normal and clinical populations (Forte et al, 2016). HRV also appears to be negatively affected by the environmental factors, with effects being reported in response to both physical and mental demands (Melo et al., 2020; Segerstrom & Nes, 2007). These task effects on HRV have been examined in a very limited capacity, however. A handful of studies investigating vagal response to task demands, as well as time on task have found progressively decreasing cardiac vagal HRV throughout blocks of cognitive task trials (Luque-Casado et al., 2013, 2016; Melo et al., 2020). Experimental designs with stress conditions have been shown to actively decrease HRV as well (for review see Castaldo et al., 2015). To date, no studies have examined the effect of complex cognitive set-shifting and learning tasks on HRV by comparing vagal response before, during, and after task completion.

Findings from Aim 1 supported previous research and provided evidence that baseline HRV and negative affectivity have a relationship with performance during the set-shifting variant of the VMWT, with the most consistent findings showing a negative effect of both factors on behavioral flexibility. To fully understand the relationship between cardiac vagal tone and cognitive performance, the current experiment investigates this relationship from the inverse side of Aim 1 to study effects of VMWT on HRV. In addition to RMSSD,

the main HRV metric in this project, HF-HRV, LF-HRV, and HR are calculated to examine other ECG indices relationship with VMWT. HF-HRV (0.15 - .40 Hz) is highly correlated with RMSSD, and evidence indicates that both index the same measurement, cardiac vagal tone (Kleiger et al., 2005; Laborde et al., 2017a). LF-HRV (0.04 - 0.15 Hz) was once thought to measure sympathetic activation, however, it has been found that LF-HRV signal reflects both sympathetic and parasympathetic activation and may not be as significant a metric as once thought (Berntson & Stowell, 1998; Laborde et al., 2017a; Malik, 1996).

In Experiment 2, changes in HRV from baseline, during the VMWT, and a post-task recovery period were investigated. Like Experiment 1.2, individuals were grouped by completion of task. It was postulated that changes in HRV from baseline to task and task to recovery would be significantly different for those in the complete group and those that failed learning and failed to switch. For those that completed the task, HRV indices were compared over time from 5-minute baseline, through the 6 phases of the VMWT, as well as during the 5-minute recovery period. It was hypothesized that vagal HRV would decrease as task demands increase over the phases of the VMWT. These findings elucidate the impact that performance of the VMWT elicits on HRV.

5.3 Aim 2 Methodology:

5.*3.1 Participants:*

ECG data was collected for three time periods baseline (Baseline, 5-minutes), during task (Task), and during recovery (Recover, 5-minutes) from a subset of 60 participants in Experiment 1.2. HRV, task, and survey measure methodologies were consistent with

Experiments 1.1 and 1.2. Of these 60 participants, 7 had unusable, messy task ECG data making the final sample 53 (38 F, M(SD) = 20.62(5.21) years old).

3.3.2 HRV Methodology:

HRV collection and processing remained consistent with Experiment 1.2. Data were collected using a BIOPAC acquisition system (MP150 system; BIOPAC systems Inc., Goleta, CA). Electrodes were placed prior to survey collection in the 3-lead configuration described in Experiment 1.2. 5-minute recordings were collected for Baseline (reported in Experiment 1.2) and Recover. For Task measures, data collected during the VMWT was binned into 5-minute blocks and heart rate, RMSSD, HF-HRV, LF-HRV were calculated using Kubios HRV (Tarvainen et al., 2013). Data processing and analysis settings were consistent with Experiment 1.2. For group comparisons, the average of the binned 5-minute blocks was computed to create a grand average task measure. For phase comparisons, the time of the binned 5-minute HRV blocks were manually compared to time stamps from the behavioral task output and averaged for each phase.

5.*3.3 Statistical analysis:*

Subjects who did not meet criteria failed either in Phase 1 during place learning (Failed Learning, N = 6, 1 M) or failed to ID/ED set-shift (Failed Shift, N = 12, 5 M) . The remaining participants completed all phases of the task (Complete, N = 35, 9 M). Mixed repeated measures 3 (Group) x 3 (Task) ANOVAs for vagal HRV (RMSSD and HF-HRV), LF-HRV, and heart rate (HR), were run to investigate within group and between task differences in ECG measures at rest, during the VMWT, and during recovery (Table 6).

Changes in HRV response to the different phases (Base, P1, P2, P3, P4, P5, P6, Recover) were investigated for those that completed the task (Complete). A 1 x 8 Repeated Measures ANOVA was run for the four ECG measures. All statistical analyses were performed using SPSS version 26 (IBM SPSS Statistics for Macintosh, Version 25.0) and jamovi (Sahin and Aybek, 2019). Model assumptions were checked. Effect sizes were reported using partial eta squared. Family-wise alpha of the models were controlled using Tukey corrections.

To investigate the relationship between changes in HRV during the VMWT, reactivity and variability between phases were calculated for RMSSD. HRV Reactivity to task was calculated by subtracting the Task HRV from Base HRV. This measure has been used in previous research in the field and is a main component of the Vagal Tank Theory (Laborde et al., 2017c, 2018). A regression model was run predicting Reactivity by Group with NA, PA, BAI, and BDI as covariates. Further investigation into differences in HRV response to task was investigated by calculating successive sum standard deviations (SSSD) by phase for participants that completed up to Phase 5 of the experiment (Complete and Failed Switch groups). A regression model was run predicting SSSD by Group (Complete and Failed Switch) with NA, PA, BAI, and BDI as covariates.

ECG Measure	Task	Complete N = 36 (24 F) M(SD)	Failed Learning N = 6 (5 F) M(SD)	Failed Shifting N = 12 (7 F) M(SD)
HR	Base	74.36(8.18)	80.12(9.11)	80.08(10.04)
	Task	75.36(8.26)	77.42(12.27)	80.24(9.41)
	Recover	74.32(8.86)	77.52(10.39)	75.05(8.33)
RMSSD	Base	50.80(17.99)	36.26(9.92)	32.99(10.79)
	Task	45.31(12.46)	39.61(15.49)	36.81(10.62)
	Recover	47.25(15.92)	38.27(11.84)	43.46(14.72)
HF-HRV	Base	7.09(1.12)	6.25(1.05)	5.94(.89)
	Task	6.60(0.73)	6.67(1.19)	6.30(1.19)
	Recover	6.73(0.80)	6.29(0.91)	6.46(0.81)
LF-HRV	Base	6.99(0.94)	6.87(0.81)	6.62(0.89)
	Task	7.06(0.54)	6.81(0.20)	7.04(0.95)
	Recover	7.14(0.68)	7.21(0.44)	6.77(0.68)

Table 6: Means and SD of HRV measures by Task (Base, Task, Recover) and Group (Complete, Failed Learning, Failed Shifting) for task effects.

Phase	HR M(SD)	RMSSD M(SD)	HF-HRV M(SD)	LF-HRV M(SD)
P1	74.42(9.57)	47.63(15.61)	6.58(0.85)	6.86(0.65)
P2	75.31(9.90)	45.16(14.12)	6.58(0.84)	6.91(0.61)
P3	75.34(8.30)	45.98(13.08)	6.65(0.75)	7.13(0.66)
P4	75.25(8.11)	45.26(11.83)	6.61(0.72)	7.14(0.64)
P5	75.97(8.94)	43.15(12.23)	6.45(0.91)	7.13(0.63)
P6	75.27(9.10)	45.20(12.53)	6.67(0.69)	7.13(0.59)

Table 7: Means and SD of HRV measures for Complete by Phase for Task Effects.

5.4 Aim 2 Results:

5.*4.1 Group differences:*

5.4.1.1 Heart Rate:

There was a significant within subjects main effect for HR and Task (Baseline, Task, Recover) ($F_{(2,98)}$ = 3.18 p = .05, n^2_p = .06). Baseline HR was significantly higher than Recover HR ($t_{(1,49)}$ = 2.17, p = .035). No significant between subject effect was found for group (Complete, Failed Switch, Failed Learning) ($F_{(2,49)}$ = 1.19, p > .05, n^2_p = .05). A significant interaction was also found for Group (Complete, Failed Learning, Failed Shifting) and Task ($F_{(4,98)}$ = 2.58, p = .04, n^2_p = .09). Pairwise comparisons did not reach significance (p's > .05).

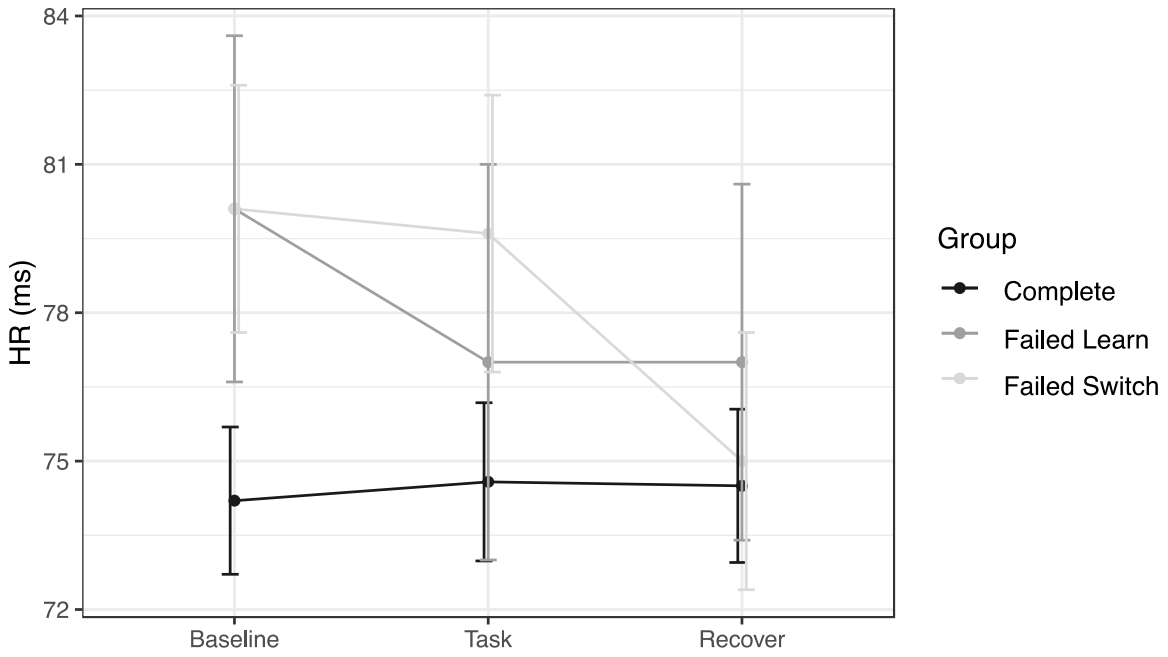

Figure 9: Heart rate (HR) mean and standard deviation by Group (Complete, Failed Learning, Failed Switching) for Base, Task, and Recover.

5.4.1.2 RMSSD:

There was no significant main effect for RMSSD and Task (Baseline, Task, Recover) ($F_{(2,98)} = 1.49$, $p > .05$, $n^2_p = .03$). A significant interaction was found for Group (Complete, Failed Learning, Failed Shifting) and Task ($F_{(4,98)} = 5.12$, $p < .001$, $n^2_p = .17$). Tukey corrected post-hoc comparisons for Group * RMSSD task found significantly higher Baseline RMSSD in Complete compared to Failed Switch ($t_{(1,49)} = 3.49$, $p = .001$) and Failed Learn ($t_{(1,49)} = 2.18$, $p = .034$). RMSSD Base significantly decreased in the Complete group during task (REACT: $t_{(1,49)} = 3.49$, $p = .001$) and stayed lower during Recover ($t_{(1,49)} = 2.03$, $p = .043$). Failed Switch exhibited a different pattern with RMSSD increasing from Baseline to Recover ($t_{(1,49)} = -3.36$, $p = .002$) and Task to Recover ($t_{(1,49)} = -2.52$, $p = .015$). No other pairwise comparisons were significant (p's > .05).

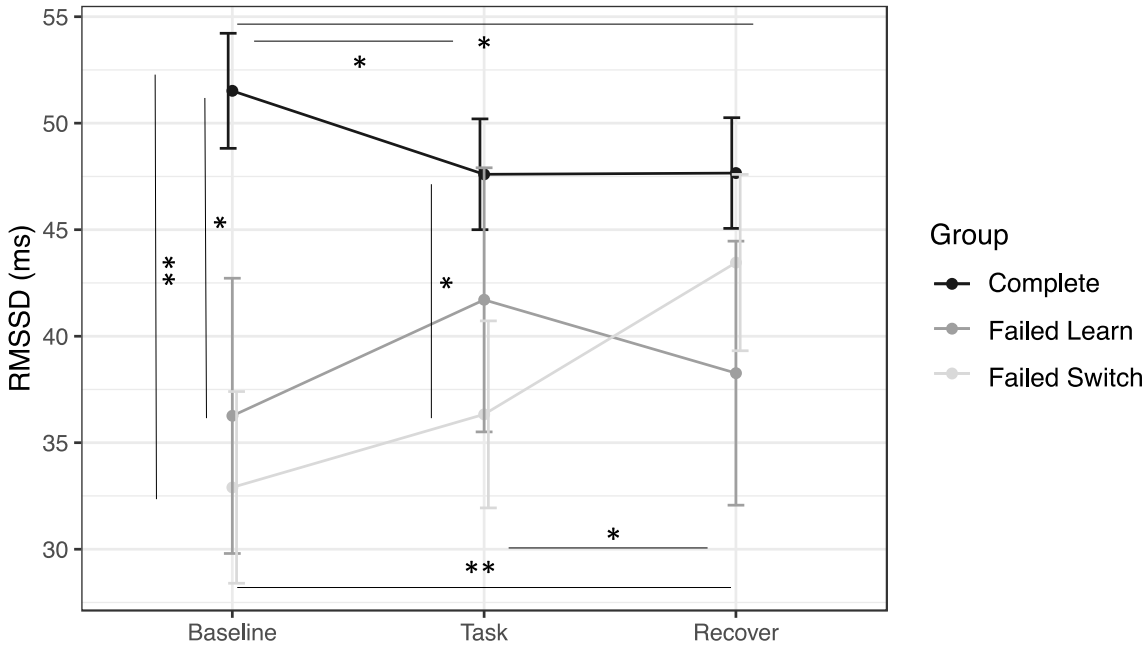

Figure 10: RMSSD mean and standard deviation by *Group (Complete, Failed Learning, Failed Switching)* for Baseline, Task, and Recover. *p < .05, ** p < 0.01.

5.4.2.3 HF-HRV:

There was no significant main effect for HF-HRV and Task (Baseline, Task, Recover) ($F_{(2,98)}$ = .11, p > .05, n^2_p = .002). A significant effect was found for group (Complete, Failed Switch, Failed Learning) ($F_{(2,49)}$ = 3.69, p = .03, n^2_p = .13). A significant interaction was also found for Group (Complete, Failed Learning, Failed Shifting) and Task ($F_{(4,98)}$ = 3.98, p = .005, n^2_p = .14). Tukey corrected post-hoc comparisons for Group * HF-HRV task found significantly higher Baseline HF-HRV in Complete compared to Failed Switch ($t_{(1,49)}$ = 3.43, p = .001). Baseline HF-HRV was significantly higher than Task ($t_{(1,49)}$ = 3.14, p = .003) and Recover($t_{(1,49)}$ = 2.51, p = .029) for the Complete group as well. No

other pairwise comparisons were significant when corrected for multiple comparisons (p's > .05).

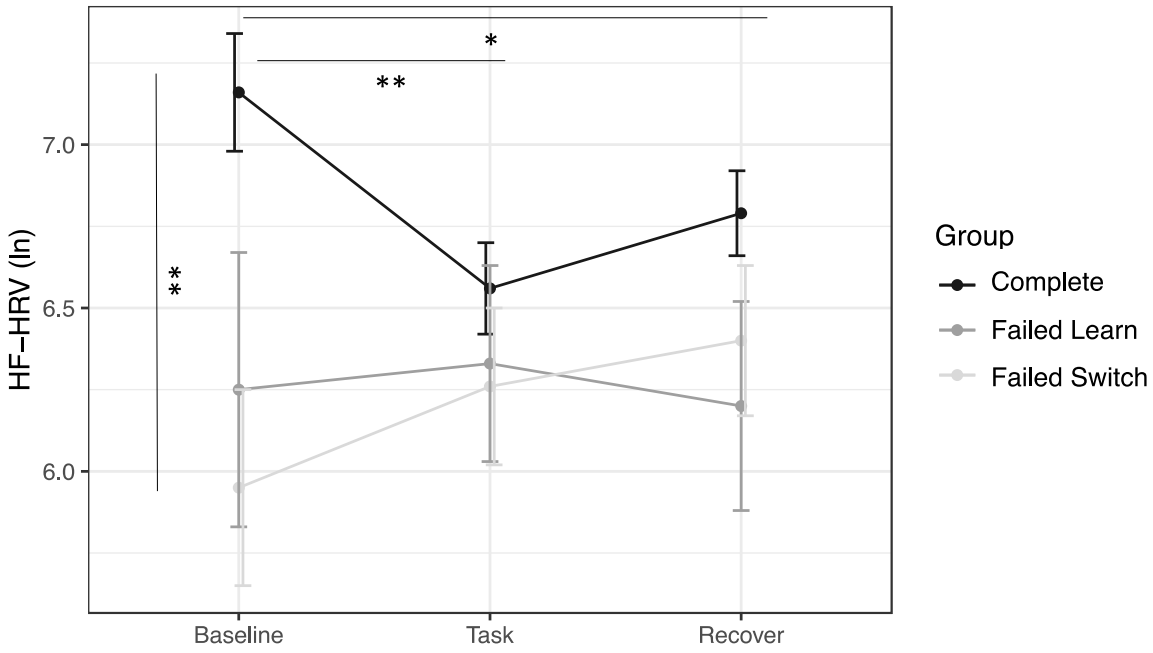

Figure 11: HF-HRV mean and standard deviation by *Group (Complete, Failed Learning, Failed Switching)* for Base, Task, and Recover. *p < .05, ** p < 0.01.

5.4.2.4 LF-HRV:

There was no significant main effect for LF-HRV and Task (Baseline, Task, Recover) ($F_{(2,98)}$= 1.10, p > .05, n^2_p = .02). No significant effect was found for group (Complete, Failed Switch, Failed Learning) ($F_{(2,49)}$ = .92, p > .05, n^2_p = .04). No significant interaction was also found for Group (Complete, Failed Learning, Failed Shifting) and Task ($F_{(4,98)}$ = .89, p > .05, n^2_p = .04) No further analyses were conducted.

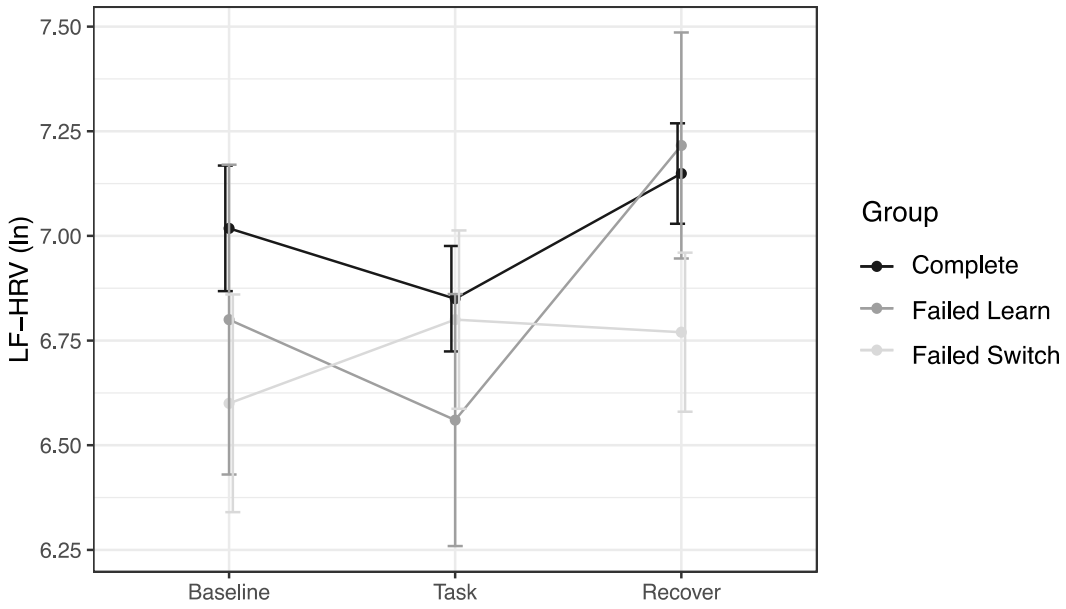

Figure 12: LF-HRV mean and standard deviation by Group (Complete, Failed Learning, Failed Switching) for Base, Task, and Recover

5.*4.3 Phase difference for Complete:*

5.4.3.1 Heart Rate:

There was no significant main effect for HR and Phase (Base, P1, P2, P3, P4, P5, P6, Recover) ($F_{(7,217)} = 1.21$, $p > .05$, $n^2_p = .04$). No further analyses were performed.

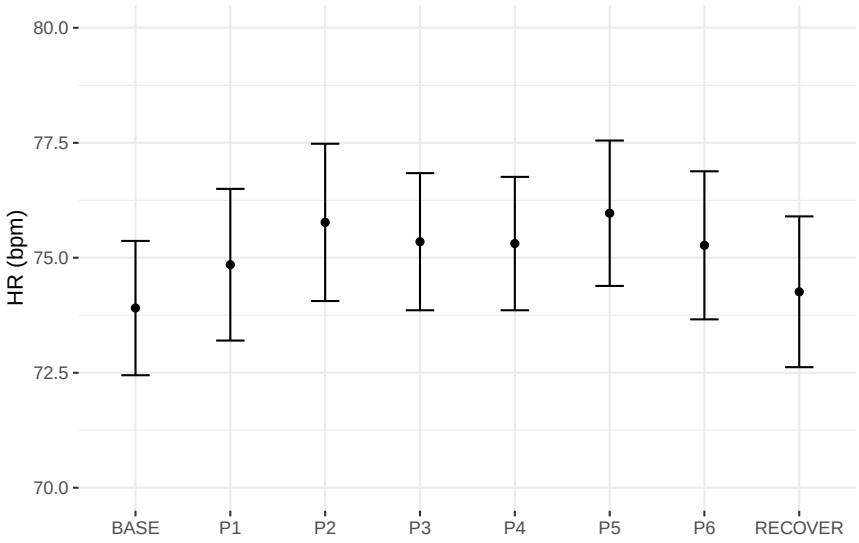

Figure 13: Mean and standard deviation of HR BPM by phase for Complete Group

3.4.3.2 RMSSD

There was a significant main effect for RMSSD and Phase (Base P1, P2, P3, P4, P5, P6, Recover) ($F_{(7.224)=}$ 5.456, p <.001, n^2_p = .145). Tukey corrected post-hoc comparisons exhibited significantly higher Rest RMSSD than P5 ($t_{(1,224)}$= 3.62, p = .02). A significant increase in RMSSD was found from P5 to Recover ($t_{(1,224)}$= -3.73, p = .02) No other pairwise comparisons were significant when corrected for multiple comparisons (p's > .05).

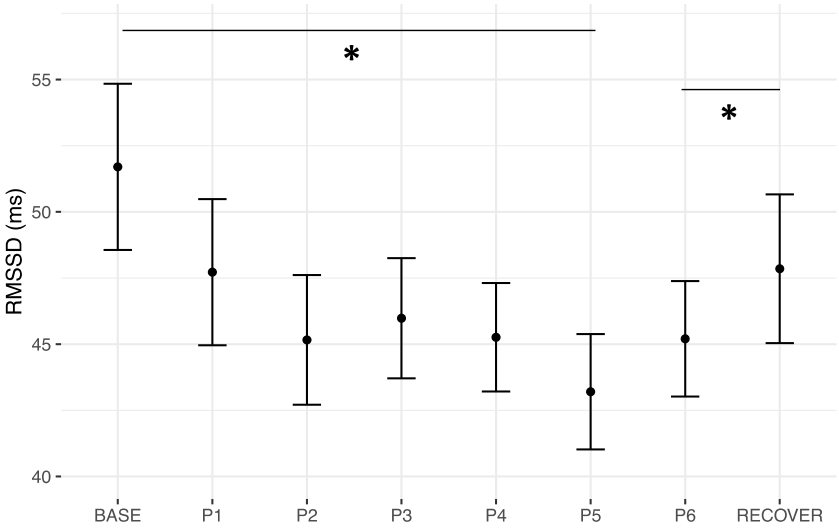

Figure 14: Mean and standard deviation of RMSSD by phase for Complete Group. * $p < .05$.

5.4.3.3 HF-HRV:

There was a significant main effect for HF-HRV and Phase (Base, P1, P2, P3, P4, P5, P6, Recover) ($F_{(7,217)} = 5.52$, $p < .001$, $n^2_p = .151$). Tukey corrected post-hoc comparisons exhibited significantly higher Base HF-HRV than P5 ($t_{(1,217)} = 3.28$, $p = .04$). No other pairwise comparisons were significant when corrected for multiple comparisons (p's > .05).

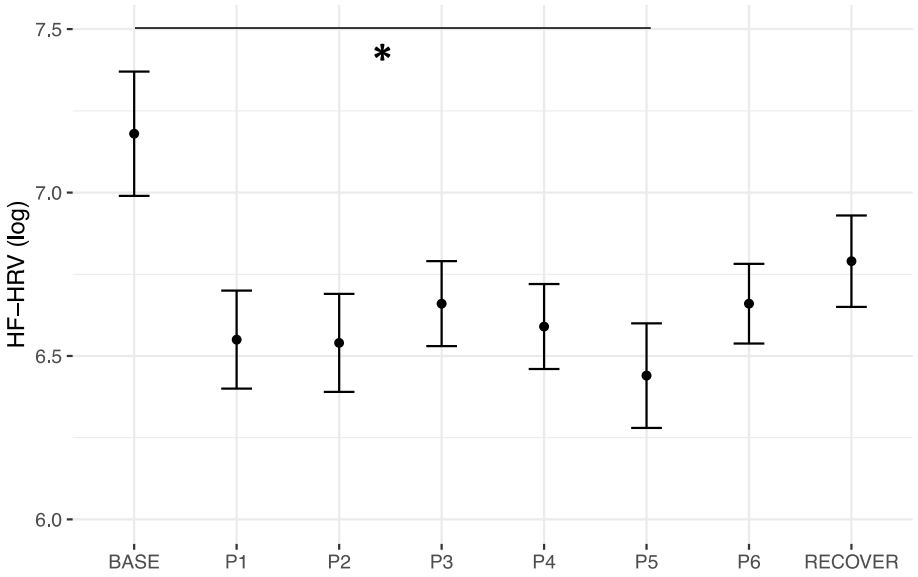

Figure 15:Mean and standard deviation of HF-HRV by phase for Complete Group. * $p < .05$.

5.4.3.4 LF-HRV

There was a significant main effect for LF-HRV and Phase (Base, P1, P2, P3, P4, P5, P6, Recover) ($F_{(7,217)} = 2.40$, $p = .02$, $n^2_p = .072$). Tukey corrected post-hoc comparisons exhibited significantly lower P2 than P5 ($t_{(1,217)} = -3.37$, $p = .04$). No other pairwise comparisons were significant when corrected for multiple comparisons (p's > .05).

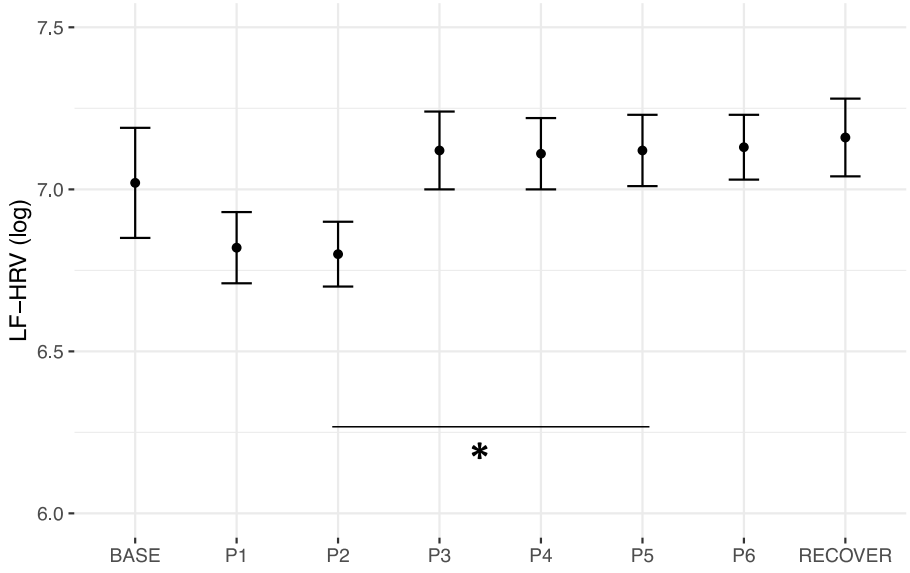

Figure 16: Mean and standard deviation of LF-HRV by phase for Complete Group

* p < .05.

5.*4.4 HRV task effects and affectivity*

5.4.4.1 Reactivity

While the full OLS model was not significant ($R^2_{(5,52)}$ = .28, p > .05), a significant effect was found for NA (β = -.442, p = .014) and Group (Complete – Failed Learn: β = -.95, p = .029, Complete – Failed Shift: β = -.683, p = .039). No other relationships were significant (p's > .05).

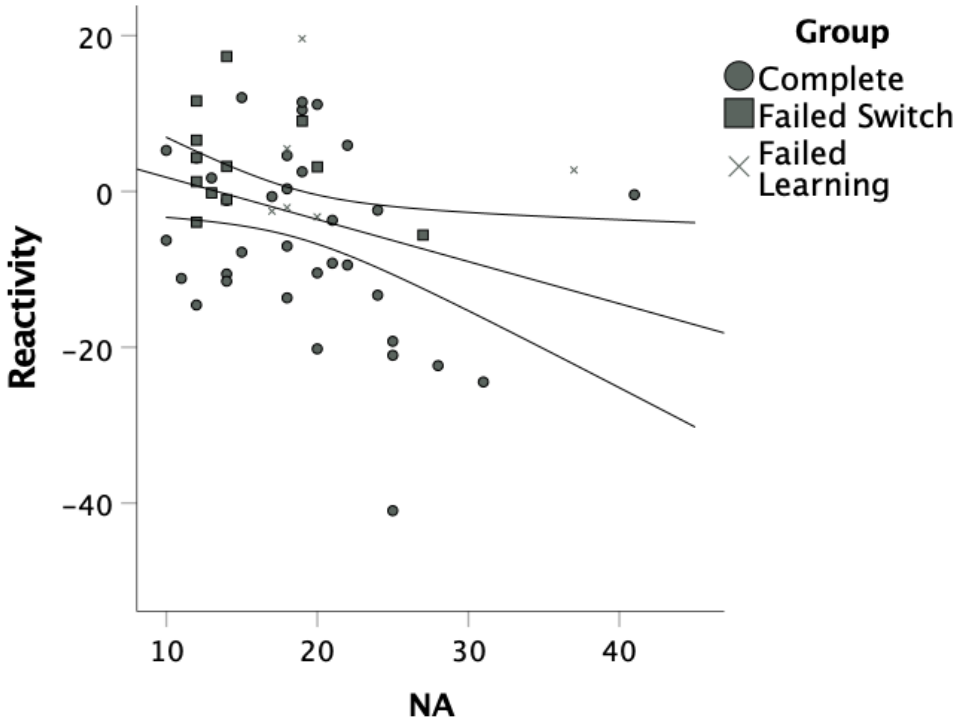

Figure 17. HRV Reactivity and NA scores with SD error lines for Complete, Failed Switch, and Failed Learning.

5.4.4.2 SSSD

While the full OLS model was not significant ($R^2_{(5,46)} = .15$, $p > .05$), a significant effect was found for BAI ($\beta = -.475$, $p = .036$). No other effects were significant.

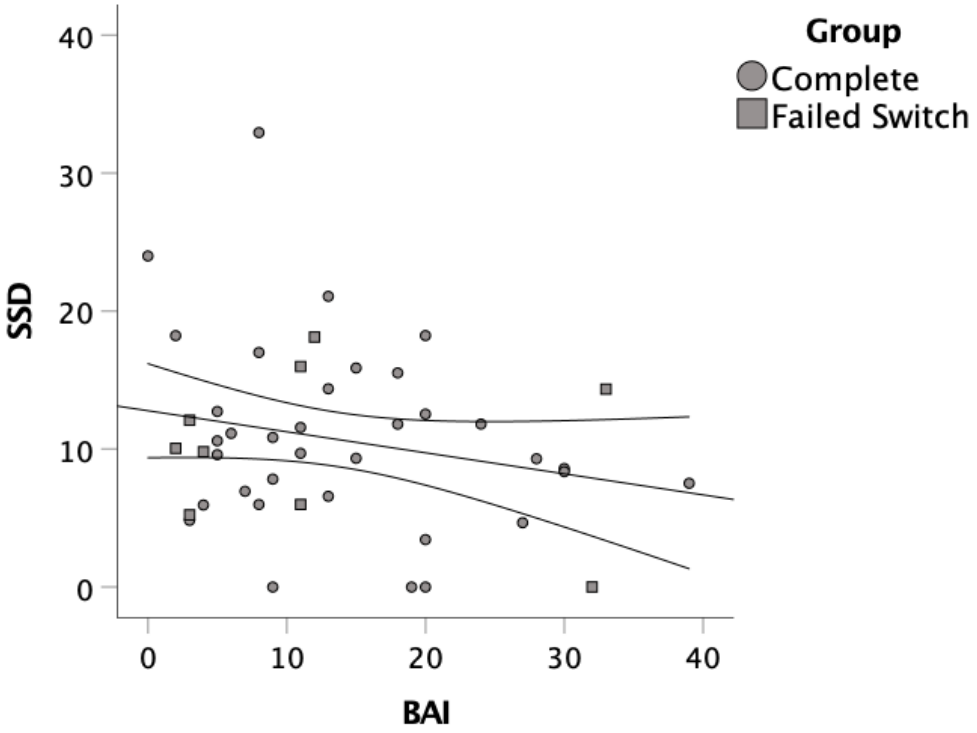

Figure 18. Relationship between SSD and BAI with SD error lines for Complete and Failed Switch groups.

Measure	Complete M(SD)	Failed Learning M(SD)	Failed Shifting M(SD)
PA	30.44(5.58)	30.00(2.19)	28.58(6.63)
NA	19.44(6.55)	21.50(7.66)	15.08(4.64)
BAI	13.94(9.17)	16.00(9.88)	11.83(10.40)
BDI	8.06(5.92)	4.50(5.43)	6.00(5.46)
Reactivity	-6.22(10.26)	3.34(8.68)	3.81(6.57)
SSSD	11.48(6.46)	-	10.18(5.74)

Table 8. Affectivity and HRV reactive measures for Complete, Failed Learning, and Failed Shifting groups.

5.5 Aim 2 Discussion:

In participants that completed the task, RMSSD and HF-HRV were significantly reduced during the VMWT and remained decreased during recovery when compared to HRV

at baseline. This relationship was not found in individuals that failed to complete the task. These findings suggest that the VMWT significantly negatively affects HRV during successful place learning and task-switching. Further, HRV remained lowered post-task during a 5-minute recovery period. Individuals that failed to perform initial learning and set shifting did not exhibit this effect, suggesting potential under regulation of cardiac vagal tone may be associated with decreased cognitive performance. When investigating phase differences in individuals that completed the task, significant task effects were also found, with both vagal HRV measurements showing the largest decrease in the extradimensional shift condition. RMSSD HRV then significantly increased from P5 to Recover. This is evidence that set-shifting in this virtual environment leads to lower HRV in response to cognitive stressors.

Associations between affect measures and vagal reactivity to the VMWT were also investigated. Changes in HRV were calculated in two ways, reactivity to VMWT (Task RMSSD – Baseline RMSSD) to investigate the overall effect of task performance on HRV, as well as by calculating the sum of successive standard deviations (SSSD) through each phase of the VMWT to investigate HRV fluctuations during VMWT performance. Reactivity was significantly associated with NA, with those scoring higher in NA showing larger decreases in HRV elicited by VMWT performance. When investigating the relationship between baseline affectivity measures and SSSD, higher BAI scores predicted lower SSSD, suggesting less flexibility and change in HRV during the task. Results will be discussed further in the general discussion.

CHAPTER 6.

Aim 3: Examine the Relationship Between Affect, HRV, and Set-Shifting Performance Through HRV Biofeedback Training.

6.1 Experiment 3: HRV biofeedback training effect on affect, HRV, and set-shifting performance

In Experiment 1 and Experiment 2, evidence supporting a connection between cardiac vagal activity, affectivity, and cognitive performance was found. To further examine this relationship, an intervention of HRV biofeedback training was performed to investigate the impact of a single short-term (10-minute) biofeedback training on mood, HRV, and set-shifting performance.

6.2 Aim 3 Introduction:

Previous research has found many benefits of HRV biofeedback training. HRV biofeedback training appears to be an effective treatment for mood disorders, such as generalized anxiety and post-traumatic stress disorder (Goessl et al., 2017; Lande et al., 2010). In nonclinical populations, biofeedback training can also reduce stress and trait/state anxiety in individuals. This reduction can be seen in as little as one training session (Prinsloo et al., 2011; Sherlin et al., 2009). In a meta-analysis, Goessl, Curtiss, and Hoffman (2017) report a large within-group pre-post effect size for HRV biofeedback reducing anxiety and stress in multiple populations.

There is also evidence that HRV biofeedback interventions improve cognitive performance in multiple domains (Suvorov, 2006, Sutarto et al., 2013, Prinsloo et al., 2011).

Sutarto et al. (2013) conducted a 5-week biofeedback training to operator workers. Pre-treatment and post-treatment cognitive performance were tested in multiple tasks, showing cognitive enhancement post-biofeedback. Research has also found that even short-term biofeedback training can lead to immediate benefits to cognitive performance. Prinsloo and colleagues (2011) compared performance on a modified Stroop task, as well as stress levels before and after receiving one 10-minute biofeedback training. Participants that received training exhibited quicker reaction times and made fewer mistakes after the intervention. They also reported feeling more relaxed.

Experiment 3 expands on these findings to investigate the mood, vagal tone, and set-shifting modulatory abilities of a one-time 10-minute HRV biofeedback training session. It was hypothesized that this training would immediately increase cardiac vagal tone which, in turn, would lead to better set-shifting performance and increased positive mood. If HRV biofeedback training improves performance on set-shifting, this would be evidence of a directional, causal relationship of HRV on cognition and provide a quick and simple avenue to improve cognitive performance in normal populations.

6.3 Aim 3 Methodology:

Affective measures, HRV collection and analysis, and VMWT protocols remained the same as Experiments 1.1, 1.2, 2, and 3. WCST, HRV biofeedback training (BFB) , and Progressive Muscle Relaxation (PMR) were added to the procedures. Additional surveys were collected to investigate alcohol use, stress from the COVID-19 pandemic, and mood before and after intervention.

6.3.1 *Participants*

Sixty (39 F, M(SD) = 22.28(5.57) years old) participants were recruited for the intervention experiment. Participants were recruited in three different methods. Some of the participants were recruited through Craigslist and the university registrar email listserv system. They were given a 35$ gift card as compensation for their time. Participants were also recruited through Sona, an online university recruitment system, and received 3.5 extra credits on coursework. Participants were pseudo-randomly grouped into the control relaxation group (Progressive Muscle Relaxation training: PMR) or biofeedback group (HRV biofeedback training: BFB) controlling for sex, age, history of mood disorder, and recruitment method. Demographics pertaining to age, sex, trait affect, COVID-19 stress, and alcohol use was collected (Table 9). 8 participants in each group (16 total) reported a history of a mood disorder. 8 participants total (4 in each intervention group) reported taking medications in the SSRI class. Two participants reported taking medications for attention deficits (1 BFB, 1 PMR). One participant was undergoing estrogen hormone therapy (BFB). Two participants (1 BFB, 1 PMR) were removed for having abnormal pre-intervention WCST preservative error scores (3+-std mean). 1 participant in the PMR group was removed for declining to have ECG measures collected leaving the final sample at 29 (19 F, M = 22.03 SD = 4.54) BFB and 28 (18 F, M = 22.56 SD = 5.83) PMR.

6.3.2 *Berg's Card Sorting Task (WCST)*

The WCST was be given to participants immediately before and after interventions to assess effects on set-shifting performance. This task was originally designed to assess deficits associated with brain damage in the prefrontal cortex, particularly in executive function, and has since been employed to study other patient and nonclinical populations (Berg, 1948,

Kopp et al., 2019; Merriam et al., 1999) . Executive function, along with learning and executive control are employed during the WCST and this task is particularly sensitive to set-shifting and set maintenance differences (Nyhus & Barceló, 2009). During the task the participant must learn, based on trial and error, the sorting rules for a set of cards differentiated by color, number, or shape. After 10 correct sorts, the rule changes and the participant must adjust to the novel rule set. Preservative errors occur when the participant continues responding to the previously learned rule and does not switch to the relevant rule set. These errors are regarded as a failure to maintain the current the set and reflect cognitive inflexibility (for review see Miles et al., 2021).

6.3.3 Vanilla Task:

ECG data collection differed slightly from the previous two experiments. In Experiment 3, participants performed a 5-minute vanilla task (Jennings et al., 1992) while ECG was recorded for pre-intervention, post-intervention, and recovery. This task requires minimal cognitive demands and focuses the participant's attention on a set of colored boxes. The participant is instructed to detect the number of a given color of boxes (e.g. "Count the number of blue boxes you see on the screen") presented on the screen. This task, in place of no task during baseline recordings, has been shown to elicit more accurate cardiovascular reactions in measures of between-within stability, amplitude and significance of responsivity, and generalizability between sessions on separate days (Jennings et. al., 1992).

6.3.4 *Interventions:*

6.3.4.1 HRV biofeedback:

HRV biofeedback training was conducted using HeartMath's emWavePro Plus and Coherence Trainer. The emWavePro Plus consists of PC based software and a USB sensory unit that is attached to the computer and a wired optode ear clip. The optode clips on the participant's earlobe and uses a small amount of infrared light to measure blood flow in the ear. HeartMath provides documentation on biofeedback training, and participants were shown 'the quick coherence technique' and three stages of 'effective coherence training'. The three stages first raise the participants' awareness of the physiology of their body then trains participants to alter their physiology by learning to control their HRV through slower breathing and positive emotions. Finally, participants are taught to reach an optimal HRV state (Parra et al., 2018). They then begin a 10 minute session using the 'Coherence Coach' which visualizes breathing and provides values of low, medium and high HRV coherence feedback on the screen to participants. Levels of HRV coherence are shown as the percentage of coherence and the traffic light indicator; red = low coherence; orange = medium coherence and green = high coherence. Participants employ this feedback to modulate their HRV.

6.3.4.2 Progressive Muscle Relaxation:

To control for respiration changes and stress relief effects of biofeedback training on performance and mood modulation, the control group in this experiment received a 10-minute Progressive Muscle Relaxation (PMR) session in place of biofeedback training. Progressive muscle relaxation is a guided meditation technique in which the participant is directed to progressively tense and release specific muscles to elicit a calming effect and stress relief (for review McCallie, Blum, and Hood, 2006). This technique has been used to improve quality of life, relieve pain, and decrease depression and anxiety symptoms in many

clinical populations (e.g. Paula, Carvaoho, and Santos, 2002, Ghafari et al, 2008, Essa, Ismail, and Hassan, 2017). Participants in this study listened to a 10-minute recording of a PMR session while in a seated position.

6.3.5 *Additional Surveys and Questionnaires:*

6.3.5.1 AUDIT:

To investigate alcohol use in the sample, the Alcohol Use Disorders Identification Test (AUDIT) was administered. The AUDIT is a commonly used tool to assess and screen for early stage alcohol problems (for review see Reinert & Allen, 2006). The AUDIT consists of 10 questions including "*How often do you drink alcohol?*", "*How often during the last year have you found you were unable to stop drinking once you had started?"* and "*Have you or someone else ever been injured by your drinking*?". Answers are scaled for 0 – 4 points with higher points being allocated to answers that are associated with higher amounts of drinking and more negative outcomes from drinking (Table 9).

6.3.5.2 *COVID Stress Identification:*

No validated measures of the effects of the COVID-19 pandemic on stress had been developed at the time of data collection. Stress effects from COVID-19 factors were measured using the 3 questions below. For each participant a COVID stress score was created by summing the questions together with higher scores relating to higher stress being associated with the COVID-19 pandemic (Table 9).

1. *"How stressful has the threat of the coronavirus been for you? (0 = not at all to 10 = a great deal)"*

2. *" How anxious have you been about the threat of the coronavirus? (0 = not at all to 10 = a great deal)"*
3. *" How depressed have you been about the threat of the coronavirus? (0 = not at all to 10 = a great deal)"*

6.3.5.3 *BMIS:*

Mood modulation was measured using the Brief Mood Introspective Scale (BMIS, Meyer & Gasche, 1988). The BMIS consists of 15 mood related words. Participants are asked on a scale of 1 (definitely do not feel) to 4 (definitely feel) how intensely they feel each adjective. Words include "*happy*", "*sad*", "*content*", and "*fed-up*". This scale is commonly used to investigate mood inductions and has been validated in normal populations (Mayer & Gaschke, 1988). BMIS scores were collected immediately prior to intervention and immediately following intervention to investigate the interventions mood modulation effects.

6.3.6 *Data Collection:*

Participants were consented and then completed all baseline surveys. While survey data was collected, ECG registration was set up using the same methodology as Experiment 1.2 and 2. Pre-intervention BMIS was administered, followed by a 5-minute baseline ECG recording. Participants then completed the WCST. A ten-minute intervention (HRV biofeedback training or Progressive Muscle Relaxation) was then conducted. The BMIS was readministered followed by a 5-minute post-intervention ECG session. Post-intervention computerized tasks were administered. The WSCT was then run followed by the VMWT. Recovery HRV was collected immediately following the VMWT (Figure 17).

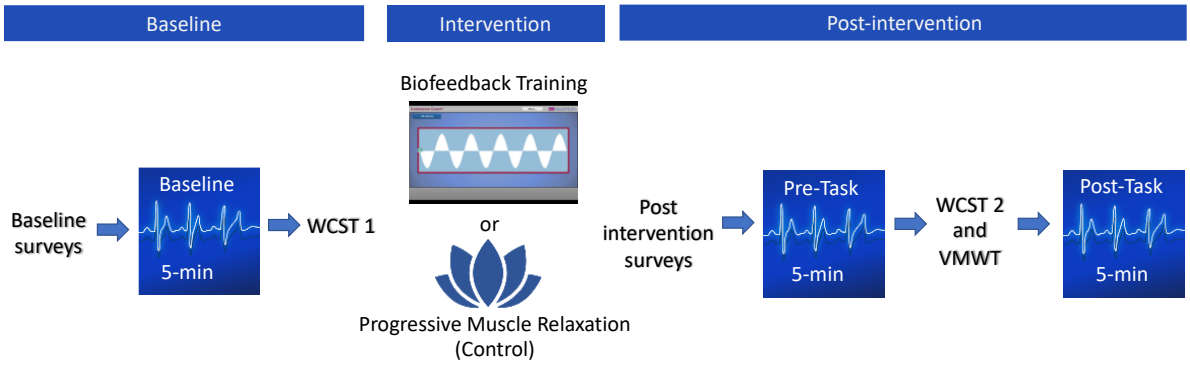

Figure 17: Experimental design of Experiment 3 (Aim 3).

6.3.7 *Statistical Analysis*

6.3.7.1 Repeated Measures ANOVAs on Pre- and Post-Intervention:

To investigate the impact of the interventions on HRV, mood, and set-switching performance, repeated measures ANOVAs were run by Group pre- and post-intervention for BMIS and WCST Preservative Errors. All statistical analyses were performed using SPSS version 26 (IBM SPSS Statistics for Macintosh, Version 25.0). Effect sizes were reported using partial eta squared. Family-wise alpha of the two models were controlled using Bonferroni corrections. For RMSSD, a repeated measures ANOVA was run for all three HRV 5-minute sessions collected in the study (pre-intervention baseline, post-intervention, and recovery).

Table 8: Mean and standard deviation of measures pre- and post-intervention

	BFB *N = 29* *(19 F)*		*PMR* *N = 28* *(18 F)*	
Measure	*Pre*	*Post*	*Pre*	*Post*
BMIS	1.76(7.56)	5.21(5.08)	4.54(6.23)	7.18(5.20)
RMSSD	45.93(30.43)	53.83(35.19)	37.20(23.66)	38.30(20.28)
P-ERR	17.66(5.14)	13.52(2.50)	15.32(4.24)	14.00(2.90)

Table 9: *Mean and standard deviation of measures pre- and post-intervention. Notes:* BMIS: Brief Mood Introspective Scale, RMSSD: Root Mean Square of Successive Differences, P-ERR: Wisconsin Card Sorting Task Preservative Error.

6.3.7.2 VMWT and intervention:

Nineteen participants were unable to complete the VMWT (8 BIO (7 F), 11 PMR (7F)). An independent non-parametric Chi Square test of independence was run to investigate count differences between groups in complete and incomplete VMWT performance. Associations between performance on the task by phase (trials-to-criteria) and BMIS, HRV, WSCT preservative errors were investigated using Pearson correlations. Correlations between individual differences in baseline affect, COVID-19 stress, and AUDIT scores were also investigated.

6.4 Aim 3 Results:

6.4.1 Demographics:

Independent samples t-tests were run to investigate baseline differences in BFB and PMR groups. T-tests were run for age, BAI, BDI, NA, PA, COVID, AUDIT, pre-

intervention BMIS, pre-intervention RMSSD, and pre-intervention WCST preservative errors. Differences between groups were not significant (p's > .05) (Table 9).

	BFB *N = 29* *(19 F)*		*PMR* *N = 28* *(18 F)*	
Measure	*M*	*SD*	*M*	*SD*
BDI	7.32	7.59	6.82	4.99
BAI	17.41	12.32	16.11	13.36
NA	21.41	9.16	19.60	7.04
PA	25.14	7.82	27.36	5.03
AUDIT	3.27	3.29	1.92	2.42
COVID	15.86	8.05	14.50	7.92

Table 10: *Mean and standard deviation of the sum affective measures. Notes:* BDI: Beck Depression Inventory-II, BAI: Beck Anxiety Inventory, NA: Negative Affectivity Subscale, PA: Positive Affectivity Subscale (PANAS), AUDIT: Alcohol Use Disorders Identification Test; COVID: COVID-19 Stress Questionnaire.

6.4.2 Intervention Effects:

6.4.2.1 2 x 2 Repeated Measures ANOVA - HRV:

There was a significant main effect for pre-intervention, post-intervention, and recovery RMSSD ($F_{(2,110)} = 16.65$, $p < .001$, $n^2_p = .23$), as well as a significant interaction by group ($F_{(2,110)} = 3.07$, $p = .05$, $n^2_p = .05$). Bonferroni corrected post-hoc comparisons for Group * RMSSD found significant increase in HRV in pre-intervention vs BFB post-intervention ($t_{(1,55)} = -4.34$, $p < .001$), as well as pre-intervention and recovery ($t_{(1,55)} = -5.01$, $p < .001$). For the PMR group, RMSSD was significantly higher for recovery than pre-

intervention ($t_{(1,55)}$ = 3.07, p = .05). No other pairwise comparisons were significant (p's > .05).

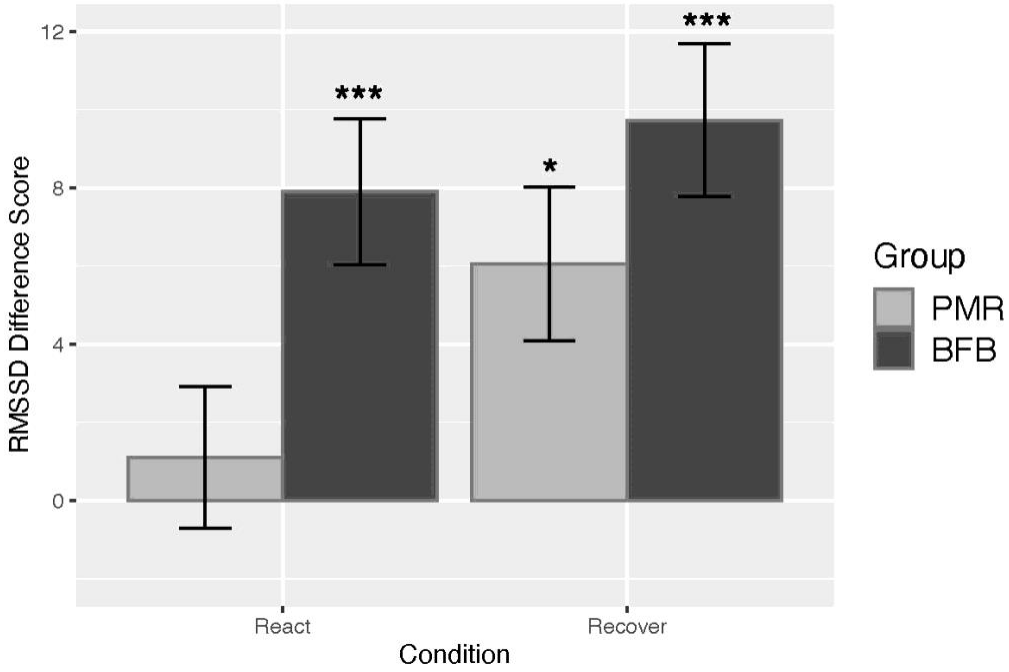

Figure 19: RMSSD difference scores and standard errors for post-intervention – pre-intervention baseline (React) and recovery – pre-intervention baseline (Recover) for BFB and PMR groups. *p < .05, *** p < .001.

6.4.6.2 2 x 2 Repeated Measures ANOVA – BMIS:

There was a significant main effect for BMIS pre- and post-intervention ($F_{(1,55)}$ = 28.91, p < .001, n^2_p = .35). No significant interaction was found for Group (BFB vs. PMR) or Mood pre- and post-intervention was found (p's > .05). Bonferroni corrected post-hoc comparisons for changes in mood found significant increases in mood post-intervention in both BFB ($t_{(1,55)}$ = 4.34, p < .001) and PMR ($t_{(1,55)}$ = 3.27, p = .011).

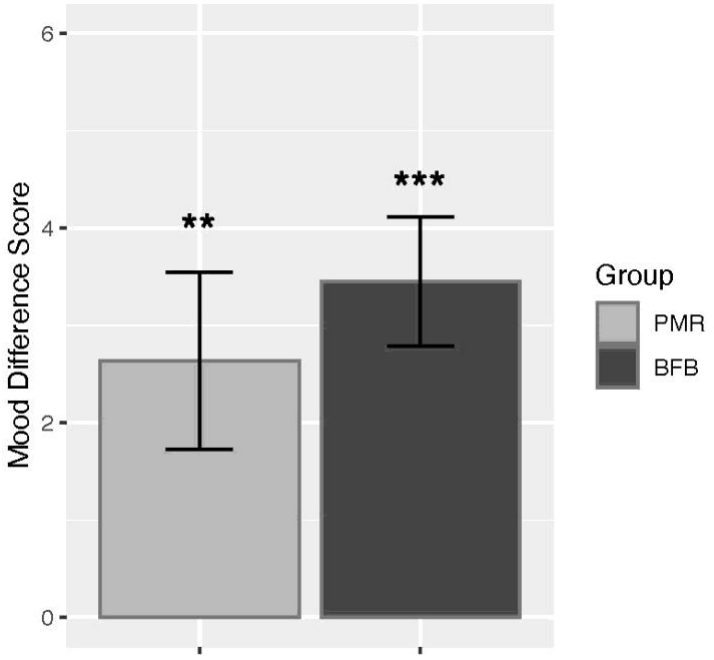

Figure 21: Mood (BMIS) difference scores and standard errors for post-intervention – pre-intervention baseline for BFB and PMR groups. ***p < .001, **p < .01.

6.4.6.3 2x2 Repeated Measures ANOVA – P-Err:

There was a significant main effect for preservative errors pre- and post-intervention ($F_{(1,55)} = 17.38$, .p < .001, $n^2_p = .24$). A significant interaction was also found for Group (BFB vs. PMR) and preservative errors pre- and post-intervention was also found ($F_{(1,55)} = 4.63$, p = .036, $n^2_p = .078$). Post-hoc comparisons for Group * P-Err found significant decrease in preservative errors in the BFB pre-intervention vs BFB post-intervention ($t_{(1,55)} = -4.51$, p <.001). No other pairwise comparisons were significant (p's > .05).

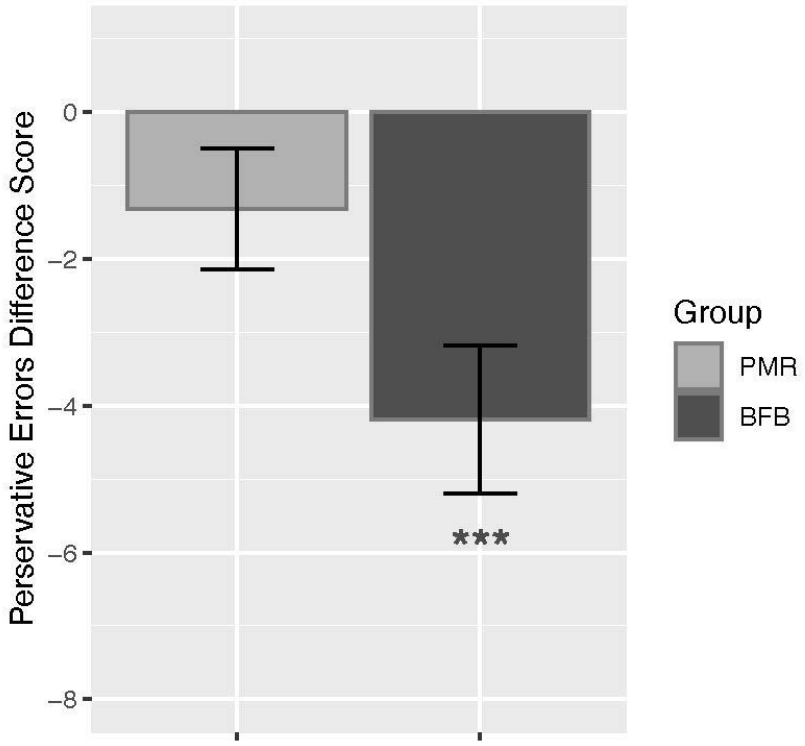

Figure 22: Berg's Card Task preservative errors difference scores and standard errors for post intervention – pre-intervention baseline for BFB and PMR groups. *** $p < .001$.

6.4.3 VMWT:

6.4.3.1 VMWT and baseline measures:

Significant relationships were found between VMWT phase trials-to-criteria and baseline HRV and baseline questionnaire ratings. Baseline RMSSD was positively related to PA ($r_{(57)} = .36$ $p = .006$) and negatively correlated with NA ($r_{(57)} = -.313$, $p = .01$). PA was positively correlated with P6 trials-to-criteria ($r_{(38)} = .377$, $p = .01$). Higher BAI scores were correlated with higher P2 trials to criteria ($r_{(55)} = .32$, $p = .02$) and P4 trials to criteria ($r_{(54)} = .29$, $p = .04$). All other correlations between VMWT, baseline HRV, and baseline questionnaire scores did not reach significance (p's > .05) (Table S1).

6.4.3.2 Group Differences in Performance on VMWT:

There were no significant intervention group differences in completion of the VMWT ($X^2_{(1)}$ = .88, p > .05). No association between intervention group and VMWT was observed.

6.4.3.3 VMWT and pre/post Mood, HRV, and WCST, by Intervention Group:

Pearson correlations were run to investigate the relationship between VMWT performance by phase and pre/post intervention mood, HRV, and WCST preservative errors separately for the PMR and BFB groups. Mood and HRV were positively correlated with one another in the BIO group (BMIS-Pre & RMSSD-Post ($r_{(29)}$ = .40 p <.001), BMIS-Post & RMSSD-Base ($r_{(29)}$ = .38, p = .04), RMSSD-Post ($r_{(29)}$ = .49, p = .009). No significant relationship was found between HRV or Mood with VMWT phase performance (p's > .05). No significant relationships were found for HRV and Mood measures for PMR (p's > .05). Phase trial-to-criteria only correlated during P4 to BMIS pre-intervention in the Relax group ($r_{(23)}$ = -.59, p = .002). All other VMWT phase measures were not significantly correlated with mood and HRV measures (Table S2 and S3).

6.5 Aim 3 Discussion:

Mood, HRV, and set-shifting performance all significantly increased immediately following a 10-minute HRV biofeedback training session. Post-intervention HRV was significantly higher and WSCT preservative error scores were significantly lower for BFB group than pre-intervention scores in these domains. Both BFB and PMR groups exhibited an increase in BMIS scores immediately following the intervention, suggesting both

interventions increased subjective positive mood. Both BFB and PMR groups also showed increased RMSSD during the 5-minute post -VMWT recovery period.

Groups were not significantly different in proportion of completion on the VMWT. However, there were some significant correlations between affective measures, HRV, and task performance. Baseline NA and PA measures were correlated with pre- and post-intervention HRV, as well as pre- and post-intervention BMIS scores. Higher BAI scores were significantly correlated with higher trials-to-criteria in initial discrimination learning. Post-intervention BMIS score was correlated with performance on VMWT during the extra-dimensional shift. These findings suggest that both interventions may potentially be interfering with the relationship between HRV and performance on the VMWT.

CHAPTER 7:

General Discussion

Strong relationships between affect, cognitive performance, and cardiac vagal tone were found throughout the four experiments described in the previous chapters. The most pronounced associations were seen between HRV, negative affectivity, and behavioral flexibility. Baseline HRV prior to the VMWT predicted task switching performance. Negative affectivity moderated this relationship. HRV decreased as the task was performed, with lowest levels of HRV being found during the extradimensional shifting condition. Individuals who failed to complete the task showed different patterns of HRV from baseline, through the VMWT, and into the post task recovery period. The relationship between cardiac vagal tone and behavioral flexibility appears to be malleable, with HRV biofeedback improving task switching performance following a single 10-minute training. These findings provide valuable evidence of the ANS-affect-cognitive connection and suggest that biofeedback training may be quick and simple tool to improve both mood and cognitive performance through modifying vagal tone.

Aim 1 of the project sought to investigate the relationship between trait affectivity, baseline cardiac vagal tone, and cognitive performance during the attentional shifting variant of the VMWT. In Experiment 1.1 and Experiment 1.2 robust relationships were found with negative affectivity, cognitive performance on the VMWT, and ANS measures. In Experiment 1.1, a significant relationship between negative affectivity and behavioral flexibility in the virtual spatial learning environment was found. Regression models identified higher levels of trait negative affectivity were significantly related to higher trials-

to-criteria during the set shifting conditions. Higher levels of trait negative affectivity, anxiety, and depression were observed in participants who failed to meet criteria for set-shifting and this effect was more pronounced in males**.** In Experiment 1.2, individuals who successfully completed the VMWT had significantly higher HRV than those that failed learning and failed shifting conditions. During the extradimensional shift condition, there was a significant negative relationship between HRV and performance on the task. Higher RMSSD was related to lower trials-to-criteria during this set-shifting phase. The effect was moderated by NA, with H-NA negating the relationship between HRV and extradimensional set-shifting performance. High NA reduces the positive relationship between higher HRV and improved behavioral flexibility.

Aim 2 investigated how performance of a complex cognitive task influenced vagal response. In Experiment 2, HRV measures were collected at 5-minute baseline, during the VMWT, and during a 5-minute recovery period for a subset of the participants in Experiment 1.2. Changes in RMSSD, HF-HRV, LF-HRV, and HR were studied by completion of task (Complete, Failed Learning, Failed Shifting), and by phase for those that completed all 6 phases of the VMWT. Vagal HRV decreased during VMWT and stayed lower than baseline HRV in the Complete group. These task effects were not found for Failed Learning or Failed Shifting groups, suggesting failure to regulate in the ANS is related to failing performance on the task. When investigating HRV through the phases of the VMWT for the those that fully completed the task, there was a significant decrease in RMSSD and HF-HRV from baseline to the extradimensional shifting phase. These findings suggest that HRV decline is strongly related to performing task switching during the VMWT.

In the final experiment (Experiment 3/Aim 3), malleability of the relationship between affect, task switching, and HRV was investigated by attempting to improve cognitive performance through HRV biofeedback training. Participants were placed in groups that received either a 10-minute HRV biofeedback training (BFB) session or a control group that received a 10-minute Progressive Muscle Relaxation (PMR) session. Mood, HRV, and task switching performance were compared pre- and post- intervention for the two groups. HRV immediately increased after HRV Biofeedback training. This was not seen in the PMR group. Both groups reported significantly higher mood after intervention. Preservative errors during the WCST significantly decreased following HRV biofeedback training, signifying increased behavioral flexibility post intervention. These findings provide evidence of plasticity in the connection between affect, behavioral flexibility, and cardiac vagal tone and show that changing HRV can have an immediate effect on both mood and cognitive performance during a set shifting task.

7.1 Affect and set-shifting in the VMWT:

Patients with anxiety disorders and clinical depression consistently show deficits in executive function as well as lower HRV than control groups (Bunce et al., 2008; De Lissnyder et al., 2010; Gustavson et al., 2017; Murphy et al., 2012; Waldstein et al., 1997), and the present findings indicate detrimental effects of negative affect n a healthy control population. In Experiment 1.1, a linear relationship between negative affectivity and flexibility was observed for intradimensional shifting as well as extradimensional shifting. Participants who failed to meet criteria in shifting conditions had significantly higher anxiety, depression, and general negativity scores compared to individuals who met criteria.

Holtzheimer and Mayberg (2011) hypothesized these set-shifting deficits in depression are best characterized by the patient's failure to disengage from negative emotional states, while also having the inability to regulate states appropriately. Deficits in regulatory ability could present in individuals with higher levels of negative affectivity, even if not at pathological levels. Relationships between affectivity and behavioral flexibility could be associated with individual differences in the prefrontal cortex (PFC) and other functional neuroanatomy underlying attentional shifting and executive function. Impaired cognitive control, inability to inhibit responses, and set-shifting problems are consequences of damage to PFC (Monsell, 2003b; A. C. Roberts, 2000; Rogers, 1998). Underactivation in these regions and overactivation in the amygdala is common in clinical depression, both at rest (Drevets et al., 1997) and during reversal learning tasks (Taylor Tavares et al., 2008).

According to Eysenck's Attention Control Theory high anxiety leads to reduced cognitive load capacity due to anxieties taxing of the working memory system (Eysenck et al., 2007). This hypothesis argues that individuals with high anxiety devote resources to both task relevant and irrelevant cues, interfering with cognitive performance abilities. Given that anxiety, depression, and negative affectivity are interconnected constructs (Eysenck & Fajkowska, 2018), this theory provides a possible explanation of our findings, showing detrimental effects of increased anxiety, depression, and negative affectivity in set-shifting. Our results provide promising evidence that the Attentional Control Theory could be expanded to include other measures of negative affectivity, such as depression and trait affect, and is not specifically applicable to anxiety.

7.2 Affect and place learning in a virtual spatial environment:

In both Experiment 1.1 and Experiment 1.2 individuals who did not meet trials-to-criteria during initial learning were not significantly different on affective measures from individuals who met criteria. All failures to meet criteria were observed for initial place learning rather than cued learning. There was, however, a trend in Experiment 1.2 toward greater BAI in individuals who failed to meet criteria during initial learning. Other studies have found increased anxiety to be related to decreased performance on spatial performance tasks. Gray and McNaughton (2000) argue that the septo-hippocampal system plays a critical role in anxiety, and in animal studies anxiety is associated with impairments in the MWT and other spatial learning paradigms (Hawley et al., 2011; Herrero et al., 2006). While our findings failed to reach significance, the trend suggests an association between trait anxiety and place learning in the VMWT.

7.3 Executive function, visuospatial learning and shifting, and HRV:

A robust relationship between performance in the attentional set-shifting variant of the VMWT and HRV was found in Experiment 1.2. Individuals who failed learning and failed shifting conditions had significantly lower baseline RMSSD than those who successfully completed the task. During the extradimensional shift condition, there was a significant negative relationship between HRV and performance on the task. Higher RMSSD was related to lower trials-to-criteria during this set-shifting phase. The effect was moderated by NA, with H-NA negating the relationship between HRV and extradimensional set-shifting performance. For L-NA individuals, higher baseline RMSSD predicted fewer trials-to-

criteria and increased behavioral flexibility. High NA reduces the positive relationship between higher HRV and improved behavioral flexibility.

Previous research has found a relationship between HRV and executive function in many domains (for review see Forte et al., 2019). This study found supporting evidence, expanding on this body of research, with differences in baseline HRV being significantly associated with performance during set-shifting in a virtual environment. Individuals who failed to set-shift had significantly lower baseline RMSSD than those that completed the VMWT. Both Porges' Polyvagal Theory and the Neurovisceral Integration Model purport cardiac vagal tone to be a possible index of cognitive control (e.g., Porges, 2007; Thayer & Lane, 2000). They cite parasympathetic influences as essential for the adaptation to changing environmental demands (Porges, 2007; Reyes Del Paso et al., 2009; Thayer & Lane, 2000b, 2009). The reductions in baseline HRV found in the Failed Switch group could be an indication of reduced ability to handle changes in task demands, thus limiting the individuals' ability to set-shift.

Experiment 1.2 also found a significant relationship between place learning and HRV, with individuals who failed the initial place learning phase displaying lower baseline cardiac vagal tone. No previous studies have investigated HRV associations with place learning. Previous research has found inconsistent relationships between resting HRV and learning performance during tasks such as Rey Auditory-Verbal Learning and Picture-word Learning Tests, with some studies showing relationships between performance while others do not (Forte et al., 2019; Zeki Al Hazzouri et al., 2014). Even less research has investigated the connection between HRV and visuospatial abilities. These findings are mixed as well, out of two studies in this domain, only one showed a significant relationship between decreased

parasympathetic measures and decreased cognitive performance (Frewen et al., 2013; Shah et al., 2011). Differences in findings could be due to differences in difficulty of task. Task difficulty influences the relationship between HRV and cognitive performance, with positive relationships between found for more difficult tasks (Veltman & Gaillard, 1998; Wekenborg et al., 2018). The current study employed a more complex task than the above studies, providing a possible explanation for our significant finding. This relationship could also be specific to place learning, and not related to other learning and visuospatial domains. The current findings may also be evidence that the Neurovisceral Integration Model could be expanded to include place learning abilities, not just applicable to attention and behavioral flexibility.

7.4 Moderating effects of NA on behavioral flexibility and HRV:

There is evidence in the literature of a negative relationship between negative affectivity and HRV in both clinical and normal populations (Chalmers et al., 2014; Dux et al., 2008; Kemp et al., 2010). While no direct associations between trait negative affectivity and baseline HRV were found in the present study, a significant interaction between NA and HRV predicted extradimensional set-shifting performance. When the sample was split into high NA (H-NA) and low NA (L-NA) groups, there was a negative relationship between RMSSD and trials-to-criteria during the extradimensional set-shift phase for individuals low in NA. This association was not found in H-NA. These findings suggest that NA moderates the relationship between HRV and behavioral flexibility in the VMWT.

While results showed a connection between higher HRV and increased performance in both place learning and set shifting in the VMWT, the interaction between NA and

RMSSD effects on performance were specific to extra-dimensional shifting. This is also consistent with our findings from Experiment 1. No significant differences in place learning performance were found to be associated with affective measures, however, NA significantly predicted decreased behavioral flexibility during set-shifting conditions during the VMWT in the previous study.

This moderating effect of NA on the HRV-behavioral flexibility connection found in the current study supports the Neurovisceral Integration Model, which was first formulated to consider emotional regulation and dysregulation, then later expanded to cognitive domains. The hypothesis postulates that brain areas involved in regulation of cognition and emotion, including the amygdala, anterior insula, and orbitofrontal cortices; periaqueductal gray matter; ventral striatum; hypothalamus, and autonomic motor nuclei of the brainstem, are also involved in cardiac autonomic activity through the vagus nerve (Ellis & Thayer, 2010; Thayer et al., 2012). Studies have also found significant positive associations between resting HRV and activation of the prefrontal cortex executive brain regions (Thayer et al., 2012). Hypoactivation in these regions has been associated with decreased resting HRV (Park & Thayer, 2014; Thayer & Sternberg, 2006). Cardiac vagal control promotes effective functioning of neural circuits involved in self-regulation to promote flexibility. The current study found that the inability to regulate negative affect may interfere with this relationship. The neurovisceral perspective, in which emotional and attentional regulation are intertwined to direct self-regulation and goal-directed behaviors, provides an explanation for this interaction.

7.5 Moderating effects of NA on behavioral flexibility and PA:

In Experiment 1.2 there was evidence that positive affectivity (PA) may be associated with increased behavioral flexibility in individuals low in NA. While slope differences between H-NA and L-NA did not reach significance, higher PA did significantly predict lower trial-to-criteria during extradimensional set-shifting in the L-NA group. These findings support and expand on previous research in the field of emotion and cognition. Many studies have found that eliciting positive affect in individuals facilitates performance in attention breadth and behavioral flexibility (Ashby et al., 2002; Baumann & Kuhl, 2005; Kanske & Kotz, 2011; Wang et al., 2017; Xue et al., 2013). Others, however, have not found this effect (Dreisbach & Goschke, 2004; Nusbaum et al., 2018; Phillips et al., 2002). Our findings suggest that high trait negative affectivity may disrupt the relationship between PA and enhanced performance in this domain, with only L-NA individuals showing this positive relationship between higher PA and flexibility. The current findings supply a possible explanation for these differing findings in previous studies.

7.6 VMWT Task Effects on HRV:

While baseline (or resting) HRV has become a common area of research in autonomic regulation, less attention has been given to changes in HRV in response to cognitive tasks. A pertinent line of research has investigated HRV reductions in response to cognitive activities (Althaus et al., 1998; Duschek et al., 2009a; Van Roon et al., 2004). Ingrid and colleagues (2000) reported lowered HRV during mental arithmetic performance. HRV then increased back to baseline levels during a 5-minute recovery period immediately following the task. In a campaign of experiments, Dusckek and colleagues (Duschek et al.,

2009; Duschek & Schandry, 2007; Duschek et al., 2008) found HRV metrics related to task complexity and increased attention allocation as well as the magnitude of vagal reactivity were positively associated with task performance. They postulate that these findings reflect a pattern of cardiovascular adjustments including enhanced sympathetic and reduced vagal cardiovascular influence during cognitive task performance.

Luque-Casado et al (2016) also ran a series of tasks to test the modulation of HRV by cognitive processing. Participants completed an experiment which included the psychomotor vigilance task, a working memory task, a duration discrimination task, as well as oddball versions of the same tasks as control for stimulus duration and time on task on HRV. Cognitive workload was assessed for each task and condition. As task demands increased, HRV decreased with the working memory condition eliciting the lowest cardiac vagal response. They found a similar effect on HRV during the oddball control conditions as well as lower cognitive workload scores for the control tasks. The researchers purport that these findings are evidence that attentional demands have a more profound influence on HRV than other cognitive processes. The authors posit that these findings are indicative of support for Porges (1992) theoretical framework that stronger ANS reactivity and higher cardiac vagal tone are positively associated with individual differences in attentional mechanisms. They assumed that higher baseline levels of vagal tone induce stronger stress-induced sympathetic withdrawal and reductions in cardiovascular mechanisms controlling the vagal system (Luque-Casado et al., 2016). Our findings are consistent with this previous research. In Experiment 2 (Aim 2) task effects of the VMWT on HRV were investigated. For individuals that completed the task, HRV metrics decreased and remained lowered for a 5-minute recovery period. This pattern was not found in individuals who failed to complete the task

suggesting lack of cardiovascular adjustment in these individuals. This failure to regulate vagal tone may in turn lead to failure to complete the task.

However, when investigating task effects of individuals who completed the task on HRV by phase, the only significant decrease in HRV metrics found was during the extradimensional shifting condition. HRV then significantly increased from the extradimensional shifting phase to the recovery phase. This is evidence that reductions in HRV respond specifically to task-switching demands in the VMWT and may not elicit an equal regulatory response to other task demands such as initial learning, cognitive workload, or attentional allocation. A more recent theory, the Vagal Tank Theory (Laborde et al, 2018), may provide an explanation for this discrepancy.

The Vagal Tank Theory integrates the Neurovisceral Integration Model (Thayer et al, 2009) and the cognitive psychological perspective (Baumeister et al., 2018) to posit a theory on self-regulation of the ANS in response to environmental demands. They postulate that cardiac vagal tone is a psychophysiological index of regulatory ability that can be depleted, as well as replenished. This theory separates baseline, reactive, and recovery vagal tone levels and suggests that vagal tone decreases in the moment to react and regulate ANS responses, then increases to baseline levels to replenish the system. The authors argue that these replenishing factors might build higher long-term baseline HRV which build improved self-regulation capacity. Behavioral flexibility is closely tied to cognitive regulation (Rudebeck et al., 2013), providing an explanation for the current findings.

Measures of negative affect were associated with HRV reactivity to the VMWT in Experiment 2. These findings expanded on both Thayer (2009) and Laborde's (2017) complementary theories and incorporate effects of affectivity into the "vagal tank" self-

regulation equation. In the current experiment, higher trait NA is associated with larger negative reactions to the VMWT in the ANS regulatory system. The higher the NA, the larger the decrease in HRV in response to the task. The ANS in more negative individuals appears to react more strongly to the environmental demands in this instance. Moreover, when investigated HRV changes during the task, BAI scores are negativity related to variability of HRV during the task suggesting a reduced ability to replenish the system (or "vagal tank") is associated to levels of anxiety.

7.7 Modulation of the affect-cognitive-ANS connection using HRV biofeedback and PMR:

7.7.1 Single session HRV biofeedback training increases HRV:

While a majority of HRV biofeedback training protocols are a regimen of multiple training sessions over a series of days to increases HRV (for meta-analysis of research field see Goesll, 2017), a few studies have investigated the effects of a single session of HRV biofeedback with mixed results (Prinsloo et al., 2011, 2013; Sherlin et al., 2009. Wells et al., 2012, Mikosch et. al., 2012). Prinsloo et al (2013) conducted a single 10-minute HRV biofeedback training session with deep-breathing training on a group of 18 healthy participants. They found a significant increase in HRV measures and lower breathing rates in the experimental group. Similarly, following a 15-minute HRV biofeedback training in 43 healthy individuals, Sherlin et al (2009) found increased HRV in the biofeedback group immediately following the training session. Other studies did not find significant increases in HRV indices following a single session of HRV biofeedback training (Mikosch et al, 2010). In a group of performance musicians, Wells and colleagues (2012) found increases in HRV

measures following both HRV biofeedback and deep breathing relaxation techniques. The authors argue that a single session of slow breathing, regardless of biofeedback, is sufficient for controlling physiological arousal in anticipation of psychosocial stress. In Experiment 3, the BFB group exhibited elevated HRV immediately following a 10-minute HRV biofeedback training. This immediate elevation in HRV was not seen for the PMR group, supporting the importance of biofeedback to increasing HRV. The PMR group, did show an increase in HRV during the recovery period, however, which may suggest delayed mood effects on HRV. Also, since the current project does not include respiration measures, we were unable to explore Wells and colleagues (2012) assertation that deep breathing alone can increase HRV.

7.7.2 Mood Modulation:

One of the original uses of HRV biofeedback training was to treat anxiety and stress (for review see Goessl et al., 2017). In a metanalysis of 24 studies with a total of 484 participants, Goessl (2017) found a pre-post with-in group effect size of .81 and a between groups effect of .83 of biofeedback on anxiety/stress reduction. These effects were not moderated by sex, number of sessions, or presence of an anxiety disorder. They reported that HRV biofeedback training was followed by a large decrease in self-reported stress and anxiety. Other studies have reported clinically relevant effects of HRV biofeedback training on different populations with pre-post ratings of depression and anxiety over different training periods (Gevirtz, 2013; Kennedy & Parker, 2019; Wheat & Larkin, 2010; Yu et al., 2018).

In healthy individuals experiencing workplace stress, Prinsloo and colleagues (2013) found was a large decrease in state anxiety in the biofeedback group and moderate decrease in the control group that just performed deep breathing exercises. These findings suggest that although there was benefit to both interventions, a single episode of short duration HRV biofeedback led to greater gains and may be a valuable tool to include in the management of acute stress and anxiety. In Experiment 3, a significant increase in self-reported mood was found after a 10-minute HRV biofeedback training session, supporting previous findings in the field. The control group in Experiment 3, that received a 10-minute Progressive Muscle Relaxation (PMR) session, also exhibited a more self-reported positive mood post-intervention, suggesting that both interventions elicited beneficiary changes in mood and stress.

7.7.3 Biofeedback training effects task-switching performance:

Effects of HRV biofeedback trainings on cognitive performance have also been investigated in a handful of small studies. Sutrarto et al. (2013) conducted a 5-week biofeedback training to operator workers. Pre-treatment and post-treatment cognitive performance were tested in multiple domains showing cognitive enhancement post biofeedback. The authors argue that this supports HRV biofeedback training as a useful tool to increase attentional performance. They also argue that increased control over HRV may inhibit arousal, which positively impacts attention and executive skills (Thayer & Lane, 2000). However, their study did not collect HRV metrics, and so a change in HRV from the intervention was not measurable.

Research has shown that even short-term biofeedback training can lead to immediate benefits to cognitive performance (Miyake et al., 2000; Prinsloo, Derman, Lambert, & Laurie Rauch, 2013; Prinsloo et al., 2011; Sherlin et al., 2009). In a sample of 18 participants reporting work-related stress from the workforce, Prinsloo and colleagues (2011) compared stress levels and performance on a modified Stroop task . Participants were placed into two groups, one received a 10-minute biofeedback training session and one group was provided a device that did not provide HRV feedback (Control). The group that received training exhibited quicker reaction times and made fewer mistakes after the intervention. They also reported feeling more relaxed.

Stroop tasks provide a complex cognitive challenge. They include three elements of executive functioning; updating of working memory; mental set shifting; and inhibition of prepotent responses (Miyake et al., 2000), making it difficult to parse apart the cognitive process that is being affected by HRV Biofeedback Training. The aforementioned study was also conducted on a small sample of men experiencing workplace stress, which is a very specialized sample that may not transfer over to other groups of individuals. Also, previous research has shown relaxation levels and mood influences cognitive performance (Dreisbach & Goschke, 2004; Prinsloo, Derman, Lambert, & Rauch, 2013). This study does not control for these effects with their control group adding a confounding variable to their experiment. In Experiment 3, we investigate the effects of a 10-minute Biofeedback Training Session on task-switching performance, in a group of normal participants with a larger variability in age, anxiety, and sex. To control for relaxation/mood effects on the relationship, PMR was used as the control group intervention. Individuals in the HRV biofeedback training group had significantly fewer preservative errors during the WCST post-intervention. This

difference was not seen in the PMR group, supporting the importance of HRV in task switching enhancement. These findings provide some support for the Neurovisceral Integration Theory (Thayer et al., 2009), as well as the Vagal Tank Theory (Laborde et al., 2018). The Neurovisceral Integration Theory posits cardiac vagal tone to be a direct index of regulatory abilities. In Experiment 3, behavioral flexibility performance significantly improved after increasing HRV using biofeedback training. This supports Thayer's model and while also showing the malleability of this relationship. Our findings suggest that HRV biofeedback may be a potential way to replenish cardiac vagal tone. The immediate feedback from biofeedback training may help individuals gain voluntary control over the respective physiological processes and induce favorable changes that increase regulation ability. This could be evidence supporting Laborde's Vagal Tank Theory (2018).

7.7.4 VMWT:

There were no significant differences between intervention groups in completion of the VMWT. Further, no significant relationships were found between trials to criteria by phase and HRV, or affectivity measures when participants completed the VMWT following interventions. These null findings could be due to both HRV biofeedback training and PMR interfering with the ANS-affect-cognition connection. While only biofeedback training increased HRV immediately, both interventions increased mood with both groups showing significant increase in mood post-intervention. Interestingly, HRV did significantly increase in both groups during the final recovery period following the VMWT. Emotion modulation has been found to influence cognitive performance in task switching and attentional paradigms (Baumann & Kuhl, 2005; Kanske & Kotz, 2011; Xue et al., 2013). When inducing

positive affect, researchers have increased flexibility during flanker and Simon tasks. Wang, Chen, and Yu (2017) investigated switch costs during a Stroop-like set-shifting task after mood induction using emotional pictures. They found lower switch costs in the positive condition compared to negative and neutral conditions. The increase in affectivity from our interventions may be influencing performance on the VMWT and the relationship between vagal indices and task-switching performance. This task was only performed following biofeedback training and PMR, so we are not able to examine the change in performance before and after intervention completion for this specific task. The finding of increased recovery HRV in both groups may also provide evidence that the connection between ANS, affect, and cognitive may be affected by both PMR (eventually) and BFB, even if it was not apparent in the intervention behavioral flexibility task.

7.8 Sex Differences:

The findings in this dissertation show conflicting evidence for sex differences in in the relationship between negative affectivity and behavioral flexibility. In Experiment 1.1, sex differences appear to play a role the relationships between negative affectivity and behavioral flexibility, as all relationships were observed in male but not female participants. This finding was not replicated in Experiment 1.2. Previous studies have investigated sex differences in VMWT performance with males outperforming females (Astur et al., 1998; Ferguson et al., 2019; Sneider et al., 2015). Males and females have the tendency to use difference strategies, with females employing stimulus-based strategies and males more likely to employ spatial strategies (Ferguson et al., 2019). Thoresen et al (2016) found that in males, trait anxiety negatively affected performance in participants with low (but not high) mental rotation ability. In the Experiment 1.1 we found that a smaller percentage of males

failed to meet trials-to-criteria in the set-shifting task, and all males met criteria in the initial place learning task. We found the same pattern in completion of the VMWT in Experiment 1.2, with only one male failing to meet criteria in the initial learning phase. Therefore, the significant relationships between negative affectivity and behavioral flexibility observed in males cannot be attributed to general deficits in learning.

7.9 Limitations and future directions:

Sample size and sample characteristics are limitations of the current study. For the majority of experiments, the participants consisted of university students enrolled in undergraduate psychology courses. These students are skewed towards younger adult ages (18-21) and were predominately female. Therefore, exhaustedly investigating age and sex differences is out of the scope of the current study. The current study included sex in the statistical models to attempt to control for this limitation and found no significant effects. In a subset of the statistical models, groups also had unequal sizes with failed groups being much smaller than the complete group This is due to participants being grouped by performance after completion of the task rather than randomly assigning groups pre-task. The groups naturally arose from the experiment and internal variances are equal between the groups. The authors believe the differences in groups are robust and could be informative to the field of cognition and emotion. To minimize this limitation, effect sizes are reported, and Pillai's V is utilized. Further investigations could be conducted on different populations to investigate these relationships between HRV, NA, and performance. These limitations should be considered when interpreting the results of this study.

The current dissertation investigated increasing cognitive performance through biofeedback training but did not investigate if it is possible to decrease cognitive performance through modulating mood or vagal tone. Mood induction has been shown to be impactful in many cognitive domains, such as learning, memory, executive function, and attention (Laborde et al., 2018). Neural indices of this relationship could also be investigated using techniques such as EEG and fMRI to fully examine the effect of NA on the HRV and cognitive flexibility connection in the central nervous system. The use of different to study this connection would also be of interest. The set-shifting variant of the VMWT is not ideal task for studying time on task as the participants behavior has a direct effect on time spent in the different phases.

7.10 Conclusions:

The current findings support and extend on previous research delving into the role of the NA in the ANS-cognition connection. In experiments investigating Aims 1 and 2 of this dissertation, individuals who failed during initial place learning, as well as those that failed during shift conditions, exhibited lower baseline RMSSD than those that completed the task. In Experiment 1.2, baseline HRV significantly predicted performance on the VMWT, with higher HRV being associated with superior extra-dimensional set-shifting. This effect was moderated by NA, and only found in individuals with low trait negative affect, suggesting that high NA interferes with the HRV-cognition connection. High NA also interferes with PA's faciliatory effect on extra-dimensional set-shifting, with significant associations between PA and performance only being found in low NA individuals. This extension of the neurovisceral integration model to cognitive domains of place learning and behavioral

flexibility, as well trait affect influences, can improve the understanding of the relationship between the ANS and cognitive functioning.

Aim 2 extended on the first two experiments of the dissertation and investigated the relationship between VMWT task effects and cardiac vagal tone. In Experiment 2, decreases in HRV while performing the VMWT were found in the group that completed the task. Those who failed to complete this task did not exhibit significant decreases in HRV indices, signifying a potential for underregulation in cardiac vagal tone attributing to failure to perform the task. Experiment 2 also provided evidence that reductions in HRV respond specifically to task-switching demands in the VMWT and may not elicit an equal regulatory response to other task demands such as initial learning, cognitive workload, or attentional allocation. The Vagal Tank Theory may provide an explanation for these findings.

The final aim of this dissertation (Aim 3) attempted to examine this relationship between affect, HRV, and behavioral flexibility by using a single 10-minute HRV biofeedback training session. The BFB group exhibited significant increases in mood, HRV, and behavioral flexibility post-intervention session while the PMR control group only showed increased mood effects post-intervention. This suggests that changes in cardiac vagal tone, regardless of changes in affect, lead to alterations in behavioral flexibility immediately following a single session of biofeedback training. These findings, along with the results from the previous aims, elucidate the relationship between affect, cognition and the autonomic nervous system. The outcome of this aim also provides evidence of biofeedback training's efficacy outside clinical and emotional applications and expands its utilization to improving cognitive performance. The results from the three aims of this project taken together provide valuable evidence of the ANS-affect-cognitive connection and support HRV

biofeedback training as a quick and simple tool to improve both mood and cognitive performance through modifying cardiac vagal tone.

Appendix

		Base HRV	COVID	BAI	PA	NA	AUDIT	P1	P2	P3	P4	P5	P6
Base HRV	Pearson Correlation	--											
	N	57											
COVID	Pearson Correlation	0.012	--										
	Sig. (2-tailed)	0.932											
	N	57	60										
BAI	Pearson Correlation	-0.146	0.036	--									
	Sig. (2-tailed)	0.278	0.785										
	N	57	60	60									
PA	Pearson Correlation	.357**	-0.038	-0.034	--								
	Sig. (2-tailed)	0.006	0.775	0.799									
	N	57	60	60	60								
NA	Pearson Correlation	-.313*	0.218	0.05	-.406**	--							
	Sig. (2-tailed)	0.018	0.094	0.703	0.001								
	N	57	60	60	60	60							
AUDIT	Pearson Correlation	0.152	0.249	-0.118	0.089	-0.049	--						
	Sig. (2-tailed)	0.26	0.055	0.368	0.497	0.711							
	N	57	60	60	60	60	60						
P1	Pearson Correlation	-0.004	0.092	0.259	-0.115	-0.007	-0.149	--					
	Sig. (2-tailed)	0.977	0.496	0.051	0.394	0.96	0.27						
	N	57	57	57	57	57	57	57					
P2	Pearson Correlation	0.109	0.093	.316*	0.041	-0.137	0.109	.533**	--				
	Sig. (2-tailed)	0.418	0.49	0.017	0.765	0.311	0.42	<.001					
	N	57	57	57	57	57	57	57	57				
P3	Pearson Correlation	-0.09	0.163	0.02	-0.134	-0.036	0.261	0.251	.530**	--			
	Sig. (2-tailed)	0.512	0.23	0.882	0.326	0.789	0.052	0.062	<.001				
	N	56	56	56	56	56	56	56	56	56			
P4	Pearson Correlation	0.051	0.145	.287*	-0.17	0.173	-0.023	.321*	0.083	.677**	--		
	Sig. (2-tailed)	0.715	0.294	0.035	0.22	0.211	0.868	0.018	0.552	<.001			
	N	54	54	54	54	54	54	54	54	54	54		
P5	Pearson Correlation	-0.069	0.169	0.148	-0.009	0.001	0.007	-0.139	0.166	-0.204	-0.167	0.259	
	Sig. (2-tailed)	0.624	0.227	0.289	0.951	0.992	0.959	0.322	0.234	0.143	0.232	0.102	
	N	53	53	53	53	53	53	53	53	53	53	53	
P6	Pearson Correlation	0.007	0.244	0.166	.377*	-0.252	0.249	-0.106	0.05	-0.022	-0.038	--	--
	Sig. (2-tailed)	0.966	0.125	0.3	0.015	0.112	0.116	0.51	0.756	0.891	0.813		
	N	41	41	41	41	41	41	41	41	41	41	41	41

S1. Pearson correlations for VMWT phase trials-to-criteria and baseline HRV and baseline questionnaire ratings.

		RMSSD-Pre	RMSSD-Post	RMSSD-Recover	BMIS-Pre	BMIS-Post	P1	P2	P3	P4	P5	P6
RMSSD-Pre	Pearson Correlation	--										
	N	29										
RMSSD-Post	Pearson Correlation	.964**	--									
	Sig. (2-tailed)	<.001										
	N	29	29									
RMSSD-Post	Pearson Correlation	.944**	.953**	--								
	Sig. (2-tailed)	<.001	<.001									
	N	29	29	29								
BMIS-Pre	Pearson Correlation	0.346	.389*	0.362	--							
	Sig. (2-tailed)	0.066	0.037	0.054								
	N	29	29	29	29							
BMIS-Post	Pearson Correlation	.380*	.478**	.418*	.768**	--						
	Sig. (2-tailed)	0.042	0.009	0.024	<.001							
	N	29	29	29	29	29						
P1	Pearson Correlation	-0.309	-0.356	-0.304	-0.355	-0.332	--					
	Sig. (2-tailed)	0.103	0.058	0.109	0.059	0.079						
	N	29	29	29	29	29	29					
P2	Pearson Correlation	-0.191	-0.156	-0.182	-0.036	-0.183	0.249	--				
	Sig. (2-tailed)	0.322	0.421	0.344	0.853	0.343	0.194					
	N	29	29	29	29	29	29	29				
P3	Pearson Correlation	-0.183	-0.166	-0.137	-0.081	-0.105	0.203	.555**	--			
	Sig. (2-tailed)	0.342	0.388	0.479	0.676	0.589	0.292	0.002				
	N	29	29	29	29	29	29	29	29			
P4	Pearson Correlation	-0.025	-0.072	0.021	-0.104	-0.075	.556**	0.033	.767**	--		
	Sig. (2-tailed)	0.901	0.716	0.917	0.599	0.703	0.002	0.867	<.001			
	N	28	28	28	28	28	28	28	28	28		
P5	Pearson Correlation	0.148	0.176	0.206	0.211	0.34	-0.296	-0.012	-0.24	-0.249	--	
	Sig. (2-tailed)	0.463	0.379	0.302	0.291	0.083	0.134	0.951	0.228	0.21		
	N	27	27	27	27	27	27	27	27	27	27	
P6	Pearson Correlation	0.075	-0.027	0.111	0.363	0.173	-0.309	-0.278	-0.103	0.152	0.253	--
	Sig. (2-tailed)	0.74	0.905	0.622	0.097	0.44	0.161	0.211	0.648	0.499	0.256	
	N	22	22	22	22	22	22	22	22	22	22	22

S2. Pearson correlations for BFB for VMWT Phases and pre-/post intervention measures.

		RMSSD-Pre	RMSSD-Post	RMSSD-Recover	BMIS-Pre	BMIS-Post	P1	P2	P3	P4	P5	P6
RMSSD-Pre	Pearson Correlation	--										
	N	28										
RMSSD-Post	Pearson Correlation	.916**	--									
	Sig. (2-tailed)	<.001										
	N	28	28									
RMSSD-Post	Pearson Correlation	.905**	.894**	--								
	Sig. (2-tailed)	<.001	<.001									
	N	28	28	28								
BMIS-Pre	Pearson Correlation	0.24	0.226	0.225	--							
	Sig. (2-tailed)	0.218	0.247	0.25								
	N	28	28	28	28							
BMIS-Post	Pearson Correlation	0.058	0.101	0.1	.827**	--						
	Sig. (2-tailed)	0.771	0.61	0.614	<.001							
	N	28	28	28	28	28						
P1	Pearson Correlation	0.328	0.179	0.258	0.23	0.136	--					
	Sig. (2-tailed)	0.088	0.361	0.185	0.24	0.489						
	N	28	28	28	28	28	28					
P2	Pearson Correlation	0.373	0.158	0.291	0.167	0.044	.632**	--				
	Sig. (2-tailed)	0.05	0.421	0.133	0.395	0.825	<.001					
	N	28	28	28	28	28	28	28				
P3	Pearson Correlation	0.038	0.027	0.107	-0.052	0.136	0.306	.507**	--			
	Sig. (2-tailed)	0.849	0.895	0.595	0.796	0.497	0.121	0.007				
	N	27	27	27	27	27	27	27	27			
P4	Pearson Correlation	0.204	0.168	0.229	-.590**	-0.352	-0.007	0.191	.488*	--		
	Sig. (2-tailed)	0.318	0.413	0.261	0.002	0.078	0.975	0.349	0.011			
	N	26	26	26	26	26	26	26	26	26		
P5	Pearson Correlation	-0.35	-0.317	-0.218	0.045	0.262	-0.031	0.3	-0.173	-0.118	--	
	Sig. (2-tailed)	0.08	0.115	0.285	0.828	0.196	0.882	0.136	0.399	0.567		
	N	26	26	26	26	26	26	26	26	26	26	
P6	Pearson Correlation	-0.102	-0.03	-0.058	0.181	0.216	0.102	0.417	0.076	-0.194	0.266	--
	Sig. (2-tailed)	0.678	0.904	0.813	0.458	0.374	0.678	0.076	0.756	0.427	0.271	
	N	19	19	19	19	19	19	19	19	19	19	19

S3. Pearson correlations for PMR for VMWT Phases and Pre- Post-intervention measures.

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