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THE PHYSIOLOGICAL EFFECTS OF HEART RATE VARIABILITY BIOFEEDBACK DURING LABORATORY INDUCED COGNITIVE STRESS

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DECLARATION

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LIST OF ABBREVIATIONS

ACC	Anterior cingulate cortex
ACTH	Adrenocorticotrophic hormone
ANOVA	Analysis of variance
AVP	Arginine vasopressin
BIO group	Biofeedback intervention group
BP	Blood pressure
BRS	Baroreflex sensitivity
CAD	Coronary artery disease
CIC	Cardio inhibitory centre
COM group	Comparative intervention group
COPD	Chronic obstructive pulmonary disease
CRH	Corticotropin releasing hormone
CVLM	Caudal ventrolateral medulla
DBP	Diastolic blood pressure
ECG	Electrocardiogram
EEG	Electroencephalogram
EMG	Electromyogram
FEV1	Forced expiratory volume in 1 second
GIT	Gastrointestinal tract
GRs	Glucocorticoid receptors
HF	High frequency
HPA	Hypothalamo-pituitary-adrenocortical
HR	Heart rate
HRV	Heart rate variability
IBI	Interbeat interval
IQR	Inter quartile range
LC/NE	Locus ceruleus/nor epinephrine
LF	Low frequency
MBSR	Mindfulness based stress reduction
MI	Myocardial infarction
MRs	Mineralocorticoid receptors
MSNA	Muscle sympathetic nerve activity

NN50	Number of successive NN intervals having a difference greater than 50 ms
NTS	Nucleus tractus solitarius
pNN50	Proportion of the total number of NN intervals
PVN	Paraventricular hypothalamic nucleus
R1	First rest period
R2	Second rest period
REM	Rapid eye movement
RF	Respiratory frequency
RMSSD	Root mean square of the successive differences of the RR intervals
RR interval	Interval between peaks of the QRS complex
RSA	Respiratory sinus arrhythmia
RVLM	Rostral ventrolateral medulla
S1	First Stroop task
S2	Second Stroop task
SBP	Systolic blood pressure
SDANN	Standard deviation of the average NN interval
SDNN	Standard deviation of the normal to normal interval
SRSI3	Smith Relaxation State Inventory
STAI5	Spielberger State Anxiety Inventory
STAIT	Spielberger Trait Anxiety Inventory
TF	Total frequency
VAS	Visual Analogue Scale
VF	Ventricular fibrillation
VLF	Very low frequency
VLM	Ventrolateral medulla
VT	Ventricular tachycardia

LIST OF PUBLICATIONS AND PRESENTATIONS

Publications

The work described in this thesis has been published in or is in review with the following journals:

1. Prinsloo GE, Rauch HGL, Lambert MI, Muench F, Noakes TD, Derman WE. The effect of short duration heart rate variability (HRV) biofeedback on cognitive performance during laboratory induced cognitive stress. *Applied Cognitive Psychology* 25: 792 – 801 (2011)
2. Prinsloo GE, Derman WE, Lambert MI, Rauch HGL. The effect of a single session of short duration biofeedback-induced deep breathing on measures of heart rate variability during laboratory induced cognitive stress: a pilot study. *Applied Psychophysiology and Biofeedback* (in review, revisions requested)
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ABSTRACT

Psychosocial stress is increasingly prevalent in the world today, and can lead to anxiety, impaired cognitive function and the development of both psychological and physical disorders. As a result, it is increasingly important to find effective stress management techniques that are easy to use. Heart rate variability (HRV) biofeedback is effective in reducing stress as well as managing chronic disease. It facilitates easy manipulation of HRV, and, therefore, potentially provides a valuable intervention for altering the activity of the autonomic nervous system.

The aim of this thesis was to examine the effects of a single 10 minute episode of HRV biofeedback on measures of HRV and EEG during and immediately after the intervention, measures of HRV and cognitive performance during laboratory induced cognitive stress and subjective feelings of anxiety and relaxation states after testing.

Eighteen healthy male volunteers (34 ± 6 years) exposed to work-related stress, were randomised into an HRV biofeedback intervention (BIO) and a comparative intervention group (COM). Subjects in the BIO group used a hand-held mobile HRV biofeedback device, which measured the real-time interbeat-interval (IBI) of the heart and displayed a wave reflecting respiratory sinus arrhythmia (RSA). Using the RSA wave, users are guided to find their optimal slow respiration rate. The COM group used a device which appeared identical, but made use of a different algorithm to display a wave on the screen. Subjects were informed that the wave represented their blood density and were instructed to watch the wave whilst not thinking any stressful thoughts. They were not instructed to alter the wave in any way.

All subjects underwent a single standardised training session during the week prior to the start of their experimental trials. The experimental trial consisted of 5 consecutive time periods: a 5 minute eyes-closed rest period (Rest 1), a modified Stroop task (Stroop 1), the 10 minute intervention period, a second 5 minute eyes-closed rest period (Rest 2) and a second modified Stroop task (Stroop 2). The modified Stroop task included having to mentally count 18 white squares randomly presented between colour words. Differences in reaction time responding to colour words as well as mistakes made in responding to cues between Stroop 1 and 2 were analysed. Respiratory rate and HRV were recorded throughout testing. Time-domain variables including mean heart rate (HR), SDNN and RMSSD, spectral power in the low, high and total frequency (LF, HF and TF respectively)

bands and respiratory frequency (RF) were calculated. EEG was recorded during the intervention and during rest periods before and after the intervention. Power spectral density in theta, alpha and beta frequency bands and theta/beta ratios were calculated. The measurement of changes in HRV and EEG provides insight into the underlying physiological changes that occur during HRV biofeedback. The Spielberger Trait Anxiety Inventory (STAIT) was completed at recruitment, and the Spielberger State Anxiety Inventory (STAIS) and the Smith Relaxation States Inventory 3 (SRSI3) were completed before and after testing. Subjects rated the subjective efficacy of the intervention as well as feelings of sleepiness using a visual analogue scale (VAS) devised for this study.

Changes in cognitive performance are described in Chapter 3. While both groups improved their reaction times ($p < 0.01$), HRV biofeedback resulted in greater improvements in reaction time ($p < 0.05$) as well as greater consistency of responses from Stroop 1 to Stroop 2 ($p < 0.05$). BIO subjects also made fewer mistakes in counting squares during Stroop 2 ($p < 0.05$).

Analysis of HRV data is detailed in Chapter 4. Both groups had similar physiological responses to laboratory induced stress in Stroop 1. In Stroop 2, the COM group responded similarly to the way they did to Stroop 1: RF ($P < 0.01$) and HR ($p < 0.05$) increased; RMSSD decreased ($p < 0.05$) and HF power showed a tendency to decrease ($p = 0.07$), while LF power showed no change. However, the BIO group responded differently in Stroop 2: while RF increased ($p < 0.05$) and LF power ($p < 0.05$) decreased, HR, RMSSD and HF power showed no change. In the BIO group, RMSSD was higher in Stroop 2 compared to Stroop 1 ($p < 0.05$).

Analysis of the EEG is presented in Chapter 5. During the intervention, the BIO group had higher theta/beta at Fz ($p < 0.01$), Cz ($p < 0.01$) and Pz ($p < 0.05$), higher relative theta power at Fz ($p < 0.01$), Cz ($p < 0.05$) and Pz ($p < 0.01$), and lower fronto-central relative beta power ($p < 0.05$) than the COM group. The groups showed different responses after the intervention with increased posterior theta/beta in the BIO group ($p < 0.01$) and altered posterior relative theta ($p < 0.05$), central relative beta ($p = 0.06$) and central-posterior theta/beta ($p < 0.01$) in the post-intervention rest period.

The VAS scores revealed that the COM group felt sleepier than the BIO group after using the intervention ($p < 0.05$). After testing, while there were improvements in both groups including increases in total relaxation scores ($p < 0.001$) and decreased anxiety ($p < 0.001$), HRV biofeedback resulted in greater increases in total relaxation scores ($p < 0.05$), greater increases in the category of

mindfulness ($p < 0.05$) as well as increases in the category of energized positive feelings ($p < 0.05$). These changes are described in Chapter 6.

In conclusion, these results suggest that a single 10 minute HRV biofeedback intervention led to improved cognitive performance, HRV changes suggestive of improved vagal modulation, EEG changes suggestive of increased attention together with increased relaxation both during and after the intervention, and greater improvements in perceived anxiety and relaxation states. HRV biofeedback, therefore, provides an effective, inexpensive and time efficient tool that could be a useful aid for improving cognitive performance in the face of stress, as well as a valuable component in the management of stress and anxiety, both for the clinician and in the work place.

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CHAPTER 1

LITERATURE REVIEW: PRIOR RESEARCH AND CLINICAL APPLICATIONS

1.1 INTRODUCTION AND SCOPE OF THESIS

Psychosocial stress is increasingly prevalent in the world today. A third of people in the U.S. reported experiencing 'extreme levels of stress' in a poll conducted by the American Psychological Association in 2007, and a fifth experienced high levels of stress a minimum of 15 days a month ¹. Extreme or chronic stress leads to emotional distress, impaired cognitive function and increased disease.

A very common and normal reaction to stress is anxiety ². From 2001 to 2003, 18.1% of the US population experienced ongoing anxiety, 22.8% of which were classified as severe ³. Chronic psychological stress plays an integral role in the development of both psychological and physical disorders including depression ⁴⁻⁶, cardiovascular disease ⁷⁻⁹, metabolic syndrome ^{8;10} and possibly chronic respiratory disease ¹¹. In fact, in the development of cardiovascular disease, psychological stress has been shown to be a risk factor of comparable or greater importance than elevated cholesterol ⁹.

The World Health Organization reports that chronic diseases related to lifestyle, including predominantly cardiovascular disease, diabetes, cancer and chronic respiratory disease, are currently the leading cause of death globally, and are projected to increase by 15% between 2010 and 2020 ¹². As the burden of chronic disease grows, it becomes increasingly important to effectively manage all risk factors including psychosocial stress. In addition to ill health, stress and anxiety result in a large financial burden from medical expenses as well as from loss of productivity and absenteeism. While there are many factors that contribute to the stress load of each person, a large component is formed by work related stress.

The assessment and management of psychosocial stress can be complex and is often one of the most challenging aspects for the clinician. Part of the challenge is the difficulty in quantifying stress. The measurement of heart rate variability (HRV) is a potentially valuable non-invasive tool in this regard as it provides a valuable quantitative marker of the effect of the autonomic nervous system

on the heart ¹³⁻¹⁵. Techniques to increase HRV may be effective in reducing stress as well as managing chronic disease. HRV biofeedback facilitates easy manipulation of HRV, and, therefore, potentially provides a valuable intervention for altering the activity of the autonomic nervous system.

As a result of the high prevalence of stress and anxiety, many forms of stress management are available. However, many of these are lengthy, time consuming, expensive and/or require the involvement of a professional. Therefore, there is a need to find an effective, short duration, easily accessible method of managing stress that is easy to use and can be self applied. Heart rate variability (HRV) biofeedback shows potential as an effective stress management tool that fulfils these criteria.

This literature review is divided into 4 main sections. First there is a description of stress: the physiology of stress, the impact of stress on disease and cognitive performance, and an overview of stress management. Secondly, there is a description of HRV and HRV biofeedback. This includes a description of the different forms of measurement as well as a description of the physiology involved in the control of heart rate, blood pressure, respiration and HRV. In addition, factors modulating HRV in health and changes in HRV in stress, disease and cognitive performance are described. A final element of this section provides a description of HRV biofeedback, as well as the effect of HRV biofeedback on HRV, disease and cognitive performance. The third main section of this chapter is a brief review of spectral analysis of EEG. This is important as it provides insight into the mechanisms by which HRV biofeedback might improve performance and reduce stress and anxiety. This section includes an interpretation of theta, alpha and beta frequency bands, and a description of the changes in EEG that occur during cognitive performance, stress, anxiety, relaxation, meditation and HRV biofeedback. Finally, a concise summary of the literature leading to the objective of the thesis is provided.

1.2 PSYCHOSOCIAL STRESS

Stress is defined as 'a real or implied threat to the psychological and physiological integrity' of an individual^{16;17}. It refers to a combination of 'an external stimulus called a stressor and the emotional and physical response to that stimulus'¹⁸. While physical challenges can be stressors, psychological factors may be even more powerful¹⁷. Therefore, most sources use the term stress to refer to psychological and emotional strain. In this review the term 'stress' will be defined as 'a state of mental or emotional strain or tension resulting from adverse or demanding circumstances' as described by the Oxford online dictionary¹⁹.

The American Psychological Association has identified 3 forms of stress: acute stress, episodic acute stress and chronic stress²⁰. Acute stress occurs in response to past and future demands and is commonly experienced by everyone. Episodic acute stress occurs when an individual repeatedly experiences acute stress, and chronic stress occurs in response to ongoing high pressures.

The healthy body is able to adapt in response to an acute stressor²¹. This is beneficial in many situations. However, when stress is chronic, the body loses its ability to adapt and physiological responses become out of proportion to stressors²¹. Damage or disease occurs in chronic stress or when an appropriate acute stress response is ongoing²¹. In addition to the specific responses which may occur in response to different stressors, stress also results in a nonspecific generalised response that aims to prepare the body for fight or flight. Hans Selye named this the general adaptation syndrome²² and he described it as having 3 stages including the 'general alarm reaction', 'adaptation' and when the stress is ongoing, 'exhaustion'.

There is considerable variation in how different individuals perceive and respond to potentially stressful situations. Some people may experience a particular incident as stressful while others may not. People may also have different physiological responses to stressors. These different responses are influenced by genetics, past experiences, society and psychological factors such as anxiety²³.

Common symptoms of stress include the symptoms of increased sympathetic activation²⁴ which will be described below, as well as emotional distress including anxiety, anger or frustration and depression²⁰.

1.2.1 Physiology of the stress response

There are 2 main systems that generate the stress response: the sympathetic component of the autonomic nervous system and the hypothalamo-pituitary-adrenocortical (HPA) axis.

1.2.1.1 The sympathetic component of the autonomic nervous system

This is the main system activating the body in response to acute stressful incidents²⁵. Information regarding stressors is relayed via the sensory and visual afferents of the peripheral nervous system to the central nervous system. The locus ceruleus-norepinephrine (LC/NE) system in the pons and medulla is the main control centre for the efferent sympathetic/adrenomedullary system²⁵. In addition to sending impulses to the periphery, the LC/NE system releases epinephrine directly into the brain regulating arousal and attention²⁶⁻²⁹, increasing alertness and decreasing neurovegetative functions²⁵.

Efferent impulses stimulate the adrenal medulla to release epinephrine and norepinephrine. These hormones reinforce the direct actions of the sympathetic nervous system. Epinephrine and norepinephrine bind to alpha and beta adrenergic receptors and thereby influence target organs. Activation of the sympathetic nervous system results in increased arousal, increased sweat secretion, pupil dilation, bronchiolar dilation, increased rate and force of cardiac contraction, blood vessel constriction and therefore increased blood pressure, increased catabolism and redirection of blood flow to the muscles, heart and brain, as well as decreased gastrointestinal tract (GIT) motility and relaxation of the gallbladder and urinary bladder²⁴.

1.2.1.2 The hypothalamo pituitary adrenal (HPA) axis

The main control centre for the HPA axis is the paraventricular hypothalamic nucleus (PVN)²⁵. The hypophysiotropic neurons in the medial parvocellular division of the PVN produce adrenocorticotrophic hormone (ACTH) releasing factors^{30;31} including corticotropin releasing hormone (CRH) and arginine vasopressin (AVP). AVP acts synergistically with CRH to stimulate the release of ACTH from the anterior pituitary gland³⁰ into the systemic circulation. ACTH then stimulates the release of cortisol from the zona fasciculata and zona reticularis of the adrenal cortex.

Under normal non-stressful conditions both CRH and AVP are released in pulses every 20 to 30 minutes³². The amplitude of these pulses increases in the morning resulting in a diurnal circadian rhythm with peak glucocorticoid secretion at 9 am^{33;34}. Under stressful conditions such as the

disruption of homeostasis or in anticipation of a stressful event, the pulsatile release of CRH and AVP increases in frequency and amplitude resulting in increased secretion of ACTH and increased release of adrenal corticosteroids^{35;36}.

Cortisol crosses the blood brain barrier and stimulates glucocorticoid (GRs) and mineralocorticoid receptors (MRs) within the brain^{37;38}. MRs have a high affinity for glucocorticoids³⁹, while GRs have a low affinity⁴⁰⁻⁴². During the circadian trough cortisol occupies mainly the MRs, while during the circadian peak and in times of stress, MRs are saturated and most of the GRs are occupied³⁹⁻⁴². This is relevant in understanding the impact of different levels of stress on memory as will be described below. Activation of MRs provides negative feedback resulting in inhibition of the PVN, while activation of GRs after stress inhibits the effect of the MRs and therefore activates the PVN⁴².

The effects of cortisol tend to restore homeostasis but are generally catabolic in nature³⁶. Fuel stores are mobilised resulting in an increase in blood glucose, amino acid and fatty acid concentrations, bone and muscle growth is inhibited, immunity and reproductive function suppressed and sympathetic mediated vasoconstriction increased^{24;43;44}. These changes in response to stress differ depending on both age⁴⁵ and sex^{46-48;48-53}.

1.2.2 The effect of stress on disease

Adverse psychological stress plays an integral role in the development of both psychological disorders such as depression⁴⁻⁶ and negative mood⁵⁴, and physical disorders. Physical disease states associated with increased psychological stress are shown in Table 1.1 below. To date, cardiovascular disease has been the most extensively studied.

Adverse psychological stress leads to increased risk of cardiovascular disease and mortality both directly⁵⁵⁻⁵⁸ and indirectly as a result of increased unhealthy behaviours⁵⁹. Chronic stress is a risk factor for the development of hypertension^{8;60;61} and coronary artery disease (CAD)^{62;63}, as well as a trigger for myocardial ischaemia⁶⁴⁻⁶⁸ and infarction^{56;68-71}. Ischaemia induced by mental stress generally leads to higher rates of subsequent fatal cardiac events^{72;73}. The acute increase in blood pressure seen in response to mental stress^{54;60;65;74} is similar to that caused by exercise⁶⁵, and the impact of stress on ischaemic events may be comparable to the impact of strenuous physical exercise^{68;75}. Mental stress leads to accelerated atherosclerosis⁸, arterial vasoconstriction in

diseased coronary vessels ⁷⁶ and abnormal ventricular wall motion in patients with CAD ⁶⁵. It also causes increased myocardial oxygen demand and increased systemic vascular resistance ⁷⁷.

Table 1.1 Physical disease states that are associated with increased psychological stress

Disease states	
Cardiovascular disease	Hypertension ^{8;60;61} Coronary artery disease ^{62;63;76} Accelerated atherosclerosis ⁸ Abnormal ventricular wall motion in patients with CAD ⁶⁵ Increased myocardial oxygen demand ⁷⁷ Increased systemic vascular resistance ⁷⁷ Myocardial ischaemia ⁶⁴⁻⁶⁸ and infarction ^{56;68-71} Takotsubo or stress cardiomyopathy ⁷⁸⁻⁸⁵ Atrial fibrillation ⁸⁶ Ventricular tachyarrhythmia ⁸⁷ Ventricular fibrillation ^{88;89}
Metabolic Syndrome ^{8;10}	Hyperlipidaemia ⁹⁰ (effect of high cortisol) Abdominal fat deposition ⁹¹ (effect of high cortisol) Risk of diabetes ⁹⁰ (effect of high cortisol)
Chronic respiratory disease	Asthma ¹¹
Neurological disease	Neurodegenerative diseases ⁹²
Endocrine disease	Suppression of growth hormone ²⁴
	Suppression of sex steroids ²⁴

Psychological stress may precipitate a cardiomyopathy known as a Takotsubo or stress cardiomyopathy ⁷⁸⁻⁸⁵. This consists of a reversible ^{80;83;85} left ventricular apical wall motion abnormality in the absence of underlying coronary artery disease. It is thought that the primary cause is a catecholamine surge which leads to myocardial stunning ⁸³. Samuels suggests that severe cardiac arrhythmias may be caused by similar, but less severe, cardiac damage which is undetected ⁹³.

Arrhythmias including atrial fibrillation⁸⁶, ventricular tachycardia (VT)⁸⁷, and potentially lethal ventricular fibrillation (VF)^{88;89} are commonly triggered by psychological stress. In fact, the major mechanism of sudden cardiac death after acute emotional stress may be related to arrhythmias following subendocardial myofibrillar degeneration⁹³. Patients with idiopathic QT prolongation are particularly sensitive to these life threatening stress induced arrhythmias⁹⁴.

Chronic work stress is a risk factor for metabolic syndrome^{8;10}, both as an independent risk factor¹⁰ and by leading to increased unhealthy lifestyle choices^{95;96}. Furthermore, high cortisol levels have been shown to lead to hyperlipidaemia⁹⁰, increased abdominal fat deposition⁹¹ and increased risk of diabetes⁹⁰.

Psychological stress has a negative impact on asthma¹¹, however the exact mechanisms are not currently known^{97;98}. Chronic stress also results in increased development of neurodegenerative diseases⁹². It leads to suppression of growth hormone and sex steroids²⁴, and excessive glucocorticoid secretion has been identified as a major factor in the ageing process^{99;100}. While the immune system is activated during acute stress^{17;101-104}, it is suppressed in response to chronic stress¹⁰⁴⁻¹⁰⁷.

1.2.3 The effect of stress on cognition and performance

While it is easy to investigate the effect of acute stress on cognition in humans, it is not ethical to induce chronic stress. Thus most studies exploring chronic stress in humans have evaluated groups of people who have been exposed to high levels of cortisol over time. High levels of stress and glucocorticoids have a large impact on memory as well as other components of cognition. For a full review of the effect of glucocorticosteroids on cognition see Belanoff et al¹⁰⁸.

High levels of cortisol have been shown to impair cognitive function¹⁰⁹⁻¹¹¹, attention^{112;113} and learning^{114;115}. Lupien and McEwen¹¹⁶ describe the relationship between plasma glucocorticoids and memory performance as an inverted U-shaped dose-response curve. Low and moderate levels of glucocorticoids^{117;118} together with high catecholamines result in increased memory formation¹¹⁹⁻¹²¹ while high or chronically increased levels inhibit memory^{17;116;122}.

Studies on stress have also shown a dose related response. Acute stress and low levels of ongoing stress result in improved memory formation^{119;123} and recall^{120;124;125} mediated through

catecholamines and glucocorticoids^{119;124}. However, this usually only occurs when the material to be remembered is directly related to the stressful stimulus¹²⁶⁻¹²⁸. In addition, the action of norepinephrine enables the individual to focus their attention more clearly¹²⁹.

Conversely, acute and chronic stress have been shown to impair cognitive function¹³⁰⁻¹³², with impaired memory^{45;114;115;117;118;124;130;133-144}, including working memory¹⁴⁵, impaired set shifting¹⁴⁶ and cognitive flexibility¹⁴⁷, and impaired attention¹⁴⁸ suggestive of frontal cortex dysfunction¹⁴⁹. In addition, people tend to work more slowly and make more errors¹⁵⁰ and have increased error related brain activity¹⁵¹. Other studies have shown no influence on memory^{120;124;128;152-155}. Fortunately, the memory impairment caused by acute stress is short term and reversible¹⁷, and bringing glucocorticoid levels back to normal improves cognition^{122;156;157}.

1.2.4 Stress management

Given the high prevalence of stress, the severity of the associated diseases and the cost of disease^{697;698;699;701} and associated lack of productivity⁷⁰⁰, it is important to find methods to manage stress effectively. There are many different stress management techniques and each person needs to find the method that is right for him/her. Effective stress management involves techniques that reduce the stressors to which one is exposed, as well as techniques that increase our ability to manage or cope with the unavoidable stressors.

Reducing stressors by learning life skills such as good planning and time management, financial planning and management, and conflict resolution, leads to a reduction in stress¹⁵⁸. However, nowadays much stress is unavoidable and so it is particularly important to find effective tools to manage stress. Many people use allopathic or natural medication to manage the associated anxiety or depression and to improve sleep. Cognitive therapy^{159;160}, relaxation training^{161;162}, body therapy such as massage^{163;164}, exercise¹⁶⁵ and yoga^{160;166} are also used by many people to manage stress. Additionally, hobbies such as listening to music, reading, art or spending time in nature can be effective. Listening to relaxing and classical music has been shown to decrease state anxiety^{167;168} and increase feelings of relaxation¹⁶⁹.

Meditation is also commonly used as a stress management technique and can include both relaxation training and specific breathing techniques. There are two main styles of meditation, concentrative and mindfulness meditation, and most techniques contain varying components of

both ^{170;171}. Concentrative meditation includes forms of yogic and Buddhist meditations and, in modern medicine, transcendental meditation ^{170;172}, while mindfulness meditations include Zen, Vipassana and, in modern medicine, mindfulness-based stress reduction (MBSR) ^{170;172}. The main psychological parameter affected by meditation is attention ¹⁷³. Providing a single focus of attention has been shown to be the most common way to relax ¹⁷⁴. Meditation decreases experienced stress ¹⁷⁵⁻¹⁸⁴, decreases sympathetic activity ¹⁸⁵⁻¹⁹³ and increases parasympathetic activity ^{193;194}. In addition, it results in decreased anxiety experienced in anxiety disorders ¹⁷² and increased cognitive performance ¹⁹⁵.

Relatively recently, biofeedback has been used in the management of insomnia, anxiety and stress. Specifically, HRV biofeedback shows promise in the management of stress ¹⁹⁶ and anxiety ^{195;197-199}. HRV biofeedback is similar to a concentrative meditation in that it is focused on a specific sensory activity ¹⁷⁰. However, it is different from a concentrative meditation in that in addition to observing, one is actively controlling the breath in response to an external biofeedback stimulus.

Most relaxation techniques result in a non-specific relaxation characterised by decreased sympathetic arousal ²⁰⁰ and lead to a reduction of stress and anxiety ^{177;201;202}. However, different techniques may produce different specific effects ^{203;204}. Davidson has differentiated between cognitive and somatic relaxation effects ²⁰⁵, while Smith has identified 4 different relaxation states including mindfulness, energized positive feelings, basic relaxation and transcendence ²⁰⁶.

The next section of this chapter will discuss HRV leading up to the use of HRV biofeedback in the management of stress.

1.3 HEART RATE VARIABILITY

Heart rate variability is the cyclical change in heart rate over time²⁰⁷. As heart rate is regulated by the parasympathetic and sympathetic components of the nervous system, measurement of HRV provides a valuable quantitative marker of the effect of the autonomic nervous system on the heart^{13-15;208}. It is therefore a useful tool in the measurement of the physiological effect of stress and relaxation.

Observation of HRV was first documented in the mid-1800s and observation of respiratory sinus arrhythmia (RSA), which is the cyclical change in heart rate that occurs in synchrony with respiration, in the mid-1900s²⁰⁹. However, research in HRV only started in the 1960s²¹⁰, most likely as a result of technical advances which allowed accurate and reliable measurement of cardiac electrical activity. At the time, while many researchers viewed HRV as an error as a result of poor experimental technique²⁰⁹, others had identified the importance of its clinical application¹⁵. Research on HRV was being conducted in cardiology and obstetrics in the USA²⁰⁹, and in HRV regulation through biofeedback in Russia²¹⁰. Technical advances continued, and power spectral analysis of HRV started in the late 70s and early 80s^{207;211}.

Recently, there has been an exponential increase in research on the physiology of HRV, the changes in HRV in health and disease, as well as the modification of HRV with biofeedback and the application of HRV biofeedback. While recording HRV is uncomplicated and non-invasive, there is still much debate regarding the interpretation of the autonomic effect on the different measures of HRV. Therefore, it is perhaps important to understand these limitations when the literature is reviewed and interpreted.

1.3.1 Measurement of HRV

Oscillations in HRV can be quantified using both time and frequency domain measures. These different measures reflect changes in different aspects of the underlying neural regulation²¹²⁻²¹⁴. The Task Force of the European Society of Cardiology and the North America Society of Pacing and Electrophysiology have published a comprehensive guideline document on the measurement and interpretation of HRV¹⁵. For both time and frequency domain measurements, it is important that recording segments of similar length are compared as the total variability of changes in heart rate increases as the length of the analysed segment increases²⁰⁸.

1.3.1.1 Time domain measures

Commonly used time domain variables include SDNN, SDANN, RMSSD, NN50 and pNN50. SDNN is the standard deviation of the NN interval or normal-to-normal RR interval. It 'reflects all the cyclic components responsible for variability in the period of recording'¹⁵ and is mathematically equal to the total spectral power¹⁵. As the length of recording decreases, SDNN reflects higher frequencies. SDANN is the standard deviation of the average NN interval which has been calculated over short periods. This is typically done using periods of 5 minutes over a 24 hour recording, and it provides an estimate of longer cycles in HRV¹⁵.

RMSSD is the root mean square of the successive differences of the RR intervals and reflects the variability in the change in NN interval¹⁵. High frequency oscillations will cause NN to change faster resulting in greater changes in RMSSD, while low frequency oscillations will result in slower changes in NN and thus less change in RMSSD. Therefore, while RMSSD is affected by all oscillations at all frequencies²¹⁵, higher frequencies will have a greater impact^{15;216-218}. This is the reason why many studies have shown a high correlation between RMSSD and high frequency power in the cardiac spectrogram^{15;209;215;219} and suggest that RMSSD is a good indicator of cardiac vagal control^{15;209;219}. However, as RMSSD reflects all frequencies it may also reflect sympathetic influences²¹⁵ and therefore not be a pure index of vagal cardiac control. While RMSSD is less sensitive to variations in respiratory patterns²²⁰, it is more reliable to compare data at similar respiratory frequencies.

The NN50 is the number of successive NN intervals which have a difference of greater than 50ms and the pNN50 is the NN50 as a proportion of the total number of NN intervals¹⁵. Both of these correlate highly with HF cardiac spectral power¹⁵.

1.3.1.2 Frequency domain measures

Elghozi et al²²¹ classified oscillations in HRV into 7 broad groups ranging from the largest oscillations to the smallest: age related, seasonal changes, circadian rhythms, hourly rhythms, minute changes (also called very low frequency (VLF)), low frequency (LF) fluctuations and high frequency (HF) fluctuations.

The power spectral density of HRV in short term recordings (2 – 5 minutes) consists of the last 3 of these spectral components: VLF (<0.04 Hz), LF (0.04 to 0.15 Hz) and HF (0.15 to 0.4 Hz) oscillations²⁰⁸. Total frequency (TF) is the sum of these 3 frequencies.

While VLF appears to be related to the control of temperature and vascular tone^{208;222;223}, it is also affected by the renin-angiotensin-aldosterone system^{207;224}, and can be influenced by both sympathetic²⁰⁹ and parasympathetic²²⁴ activity. While some studies do measure VLF, the physiological explanation is not well understood and so VLF is generally not interpreted²⁰⁸ and will not be reported in this thesis.

Therefore, the two main frequency bands in short-term recordings include the LF and HF bands. HF is often referred to as respiratory frequency, as the predominant HF peak occurs at the same frequency as respiratory frequency^{209;225;226}. HF HRV is also referred to as RSA and thus HF spectral power is commonly used as a tool to measure RSA²²⁷. However, while the average respiratory frequency of normal resting adults is within the HF band, there are instances, especially during controlled breathing, when people breathe in the LF band. RSA can, therefore, affect both HF and LF HRV²²⁸.

Another measure of HRV based on frequency domain measures is the LF/HF ratio which has been suggested to represent the sympathovagal balance²⁰⁸. HF power reflects cardiac parasympathetic activity^{225;229;230}, and initially it was believed that LF power represented sympathetic activity exclusively^{213;225;231-234}. Thus many researchers used the LF/HF ratio to give an indication of sympathovagal balance, thinking that as one was active the other would be inhibited^{225;235}. However, as LF can be affected by sympathetic and vagal activity either directly or indirectly as described below, this interpretation of the LF/HF ratio has been questioned²³⁶. Simultaneous analysis of respiratory frequency reduces the error in the interpretation of the LF/HF ratio^{228;237}; however results should still be interpreted with caution.

1.3.2 Control of heart rate, blood pressure and respiration

Heart rate variability is affected by factors regulating heart rate, including changes in blood pressure and respiration.

1.3.2.1 Heart rate and blood pressure

In the healthy human, heart rate is determined by the automatic firing frequency of the sinoatrial node in the right atrium. This is modulated by the balance between efferent sympathetic and parasympathetic (vagal) flow to the heart²³⁸. Autonomic flow to the heart is mainly regulated by control centres in the medulla, but is also affected by peripheral oscillations²²⁵.

The most important peripheral oscillator which acts via the medullary centres is the baroreflex system. This is a resonant²³⁹, closed loop system^{240;241} which maintains blood pressure homeostasis by altering the sympathetic flow to the vasculature and the vagal flow to the heart²⁴²⁻²⁴⁴. Arterial baroreceptors in the walls of the aortic arch and carotid arteries contain stretch receptors which respond to changes in arterial pressure. Afferent impulses then travel in the vagus and glossopharyngeal nerves to the nucleus tractus solitarius (NTS)²⁴⁵.

There are two components of the baroreflex system, one regulating vascular tone and one heart rate^{246;247}. The vasomotor centre or medullary sympathetic centre regulates changes in the sympathetic outflow to the vasculature^{246;248;249} controlling vasomotor tone^{250;251}. This centre consists of a depressor area in the caudal ventrolateral medulla (CVLM) and pressor area in the rostral ventrolateral medulla (RVLM). The RVLM contains sympathoexcitatory neurons which maintain tonic sympathetic vasomotor activity and resting arterial pressure²⁵². Stimulation of the arterial baroreceptors causes stimulation of the NTS, which stimulates the depressor area in the CVLM. This in turn inhibits the pressor area in the RVLM, resulting in an inversely proportional change in vascular sympathetic firing²⁵³⁻²⁵⁵. Increased baroreflex stimulation results in slow sympathetic withdrawal of 3-10 s to the blood vessels²⁴⁶ and, therefore, a decrease in vascular tone²⁵⁶, while decreased baroreflex stimulation results in increased sympathetic activity and vasoconstriction^{250;251}.

In response to increased baroreceptor activation, the NTS also stimulates the medullary parasympathetic centre or cardio inhibitory centre (CIC)²⁵⁷. This centre is the origin of the vagus nerve which supplies the parasympathetic fibres to the heart. These arise largely from the nucleus ambiguus, but also from the dorsal motor nucleus of the vagus²⁵⁷. Stimulation of the baroreceptors results in a rapid increase in cardiac vagal flow taking less than 1 second²⁴⁶ and resulting in a baroreflex mediated decrease in heart rate and increase in HRV^{258;259}. The cardiac accelerator centre in the RVLM regulates the sympathetic flow to the heart²⁶⁰. This centre is activated by higher centres in response to stress or exercise²⁶⁰.

The relationship between oscillations in heart rate and blood pressure reflects the baroreflex action^{226;246;247;261;262}. Baroreflex sensitivity (BRS) gives an indication of the ability of the baroreflex to respond to changes in blood pressure, and is expressed as the change in heart rate that occurs as a result of a change in blood pressure (interbeat interval (ms) per mm Hg change in BP)^{263;264}.

1.3.2.2 Respiration

The main respiratory centres are also situated in the medulla. The medullary respiratory centre is located in the ventrolateral medulla (VLM). Inspiration activates pulmonary stretch receptors. Afferent flow from these receptors travels via the vagal nerve to the nucleus tractus solitarius which then inhibits the medullary respiratory centre. Efferent flow via the phrenic and intercostal nerves decreases, inhibiting inspiration. Simultaneously, inspiration results in inhibition of the cardio inhibitory centre via the respiratory centre²⁶⁵, thus resulting in decreased vagal flow to the sinus node²⁶⁶.

While the medulla contains the primary control centres that govern respiration, heart rate and vasomotor tone, these are modified by higher centres. In addition to the afferent nerve impulses from arterial baroreceptors, pulmonary stretch receptors and chemoreceptors, impulses from higher centres converge on the NTS²⁶⁰. For example, the NTS receives input from the dorsomedial hypothalamic nucleus in response to acute stress activation of the amygdala.

1.3.3 Control of HRV

A summary of the regulation of the low and high frequency components of HRV is shown in Figure 1.1 below.

LF oscillations in HRV are primarily generated by resonance in the arterial baroreflex loop^{226;246;261;267}. Perturbations of blood pressure stimulate the arterial baroreceptors in the aortic arch and carotid sinus. Afferent impulses from these receptors converge together with impulses from higher centres on the nucleus tractus solitarius in the medulla²⁴⁵. Increased blood pressure results in inhibition of the tonically active sympathetic outflow from the medullary vasomotor centre to the vasculature²⁵³⁻²⁵⁵, decreasing vasomotor tone²⁵⁶ and blood pressure. Simultaneously, the medullary cardio inhibitory area is activated, increasing vagal flow to the heart²⁴⁶, decreasing heart rate and increasing HRV^{258;259}. The time delay between the initial increase and the resulting change in blood pressure sets up a new blood pressure oscillation. When the initial and resultant blood pressure oscillations are in phase, resonance occurs^{241;248;268}. This resonant oscillation is known as the Mayer wave²¹¹ and in humans is most commonly seen at 0.1Hz^{246;248;261;269} forming the main component of the LF band of blood pressure. Mayer waves stimulate the baroreflex causing vagally mediated LF oscillations in the cardiac spectrogram at the same frequency^{246;248;251;269-275}. Vagally mediated

decreases in heart rate lower the cardiac output which, together with decreased vasomotor tone, alters blood pressure, stimulating the baroreceptors and beginning the cycle again.

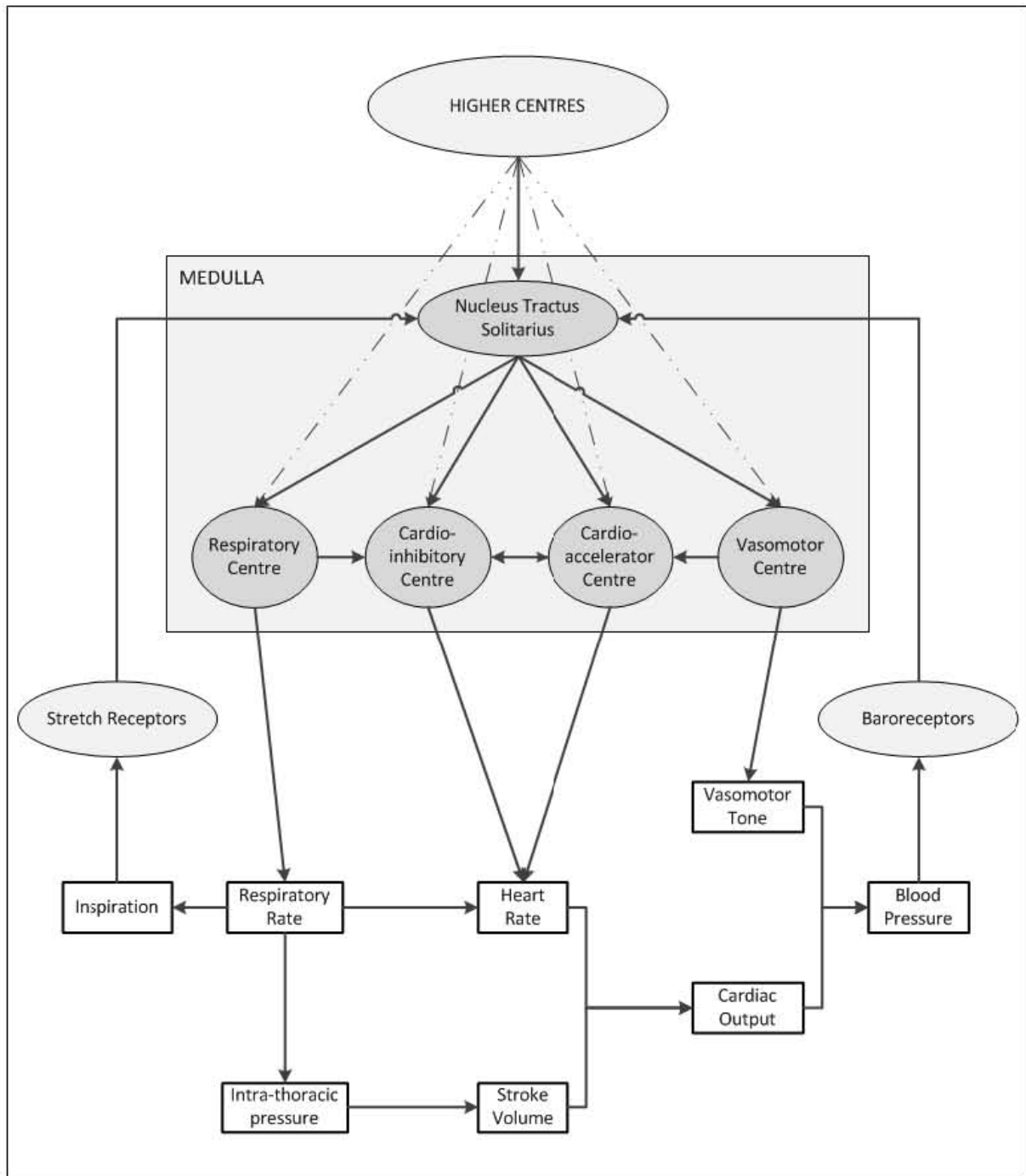


Figure 1.1 Schematic summary of the key factors regulating low and high frequency heart rate variability

Alterations in vasomotor tone and LF blood pressure variability are directly regulated by the sympathetic nervous system²⁷⁰⁻²⁷³, while LF HRV at rest is influenced directly by the parasympathetic system^{207;224;274;276-278} and indirectly rather than directly^{207;224;251;271;277} by the sympathetic system. Therefore LF cardiac spectral power reflects both sympathetic and parasympathetic influences^{15;207;209;233;246;271;276;279-285}.

Respiratory sinus arrhythmia (RSA), the cyclical change in heart rate that occurs in synchrony with respiration, affects both HF and LF HRV oscillations depending on the frequency of respiration. Respiration at a rate of about 6 breaths per minute or 0.1 Hz^{14;223;226;246;262;286} results in resonance between the respiratory and intrinsic baroreflex oscillations²⁸⁷ and is known as resonance frequency. When this occurs, RSA is maximal¹⁴ and forms the major component of the HRV spectrogram²⁸⁸. Peak RSA occurs at different respiratory rates in different individuals²⁸⁸ with resonance frequency occurring in a range from 4.5 to 6.5 breaths/min²⁸⁸.

At resonance frequency, respiration leads to changes in HRV in the LF range. RSA is mediated by gating of preganglionic vagal cardiac neural activity²⁸⁹ in response to central oscillations²⁹⁰, pulmonary and atrial stretch reflexes^{237;272} and the arterial baroreflex^{246;274;291-293}. In addition, it is affected by the intrinsic mechanical myocardial stretch in response to respiration²⁹⁴. Inspiration stimulates stretch receptors resulting in inhibition of the medullary respiratory centre and inhibition of the cardio inhibitory centre decreasing cardiac vagal flow²⁶⁶, and mechanical stretch directly stretches the right atrium affecting the SA node²⁹⁵ causing around 4% of RSA in healthy people²⁹⁶. In both cases, inspiration results in an increase in heart rate and increased RSA^{266;296}.

In addition, inspiration decreases intrathoracic pressure²⁰⁹, which increases venous return and atrial filling^{226;246}, stroke volume^{297;298} and cardiac output leading to increased arterial pressure^{267;298}. This results in decreased heart rate and vascular tone via the baroreflex. At resonance frequency, respiratory rate and heart rate oscillate in phase, while heart rate and blood pressure are 180° or half a cycle out of phase^{223;299}. Because of this time delay between the increase in blood pressure and heart rate, the heart rate will increase in response to decreased intrathoracic pressure at the same time as the increase in heart rate in response to activation of the stretch receptors and mechanical stretch, resulting in maximal RSA at resonance frequency¹⁴.

HF HRV oscillations are regulated by efferent vagal flow^{207;224;225;229;230;262;274;276;278;300} and are not directly affected by sympathetic stimulation³⁰¹ as the cardiac response to sympathetic nervous

stimulation is too slow²⁶². Similarly, sympathetic activity has an indirect^{294;302} rather than direct^{207;233;276;277;303;304} effect on RSA. Cyclical vagal discharge from the medulla^{207;229;233;276;277;300;303-308} is the final generator of RSA, and contributes to the generation of LF oscillations when breathing at resonance frequency and HF oscillations when breathing is faster than 9 breathes/minute. The magnitude of RSA gives an indication of cardiac vagal activity or tone^{207-209;229;230;276;304;309-317}. RSA increases as cardiac vagal activity increases^{229;230} and decreases as vagal activity decreases^{207;229;230;272;276;300;306;318}.

While the vagus regulates both heart rate and RSA³⁰⁴, there are times when they do not co-vary. In fact, large RSA amplitude is healthy while severe bradycardia is potentially lethal. Porges has called this the 'vagal paradox'³¹⁹ and has explained it by suggesting that there are 2 branches to the vagus, one causing RSA and the other bradycardia³¹⁹. This 'polyvagal theory'³¹⁹ identifies 3 different subsystems of autonomic control. The first is related to social communication, and consists of the myelinated vagus which originates in the nucleus ambiguus and causes RSA. This system inhibits the sympathetic influence on the heart and dampens the HPA axis. The second is responsible for mobilization of the body and depends on the sympathetic system. The third results in immobilization and consists of the unmyelinated vagus originating in the dorsal motor nucleus. These 3 subsystems are recruited in order of hierarchy. When the environment is safe, the social communication system is active. In danger, if the social communication system is ineffective, the mobilization system is activated. Finally, the primitive immobilization system is activated.

Finally, central oscillations in the respiratory and cardiovascular medullary regulatory centres contribute to both low^{207;225;301;320;321} and high frequency^{225;322} oscillations in HRV. In conclusion, the regulation of HRV is complex and depends on both peripheral and central factors^{226;246;261}. HRV reflects the ability of the cardiovascular system to adapt to both internal and external demands and increased variability is a sign of good health^{323;324}.

1.3.4 Modulators of HRV in health

HRV is modulated by many factors including age, sex, physical position, sleep and exercise. It has been shown to decrease with increasing age^{325;326} although most studies have found that the decline levels out after 40 years³²⁶⁻³²⁹. This decrease shows different patterns for different measures^{328;330}. HF power decreases linearly from 9 to 28 years³²⁸ and then remains stable³²⁶, while LF power decreases after age 50³²⁶, together resulting in a progressively increasing LF/HF ratio with age³²⁶.

RSA increases up to early adulthood and then also decreases with increasing age³³¹. Baroreflex function is also negatively correlated with age³³². These findings may be explained as with increasing age, muscle sympathetic nerve activity (MSNA) increases³³³, cardiac vagal tone changes³³⁴ and HRV responsiveness to parasympathetic stimulation decreases³³⁵.

HRV shows sex specific variations which are also modulated by age. Women under the age of 30 have lower SDNN and RMSSD than men, and the differences slowly decrease until none are evident after 50 years of age³³⁰. However, when examining LF and HF power, women around the age of 50 have lower LF and higher HF power than men³³⁶. Furthermore, MSNA is lower in women under 50 years and similar between men and women 50 years and older³³³.

The position of the body also influences HRV. RR intervals^{224;337}, HF power^{212;337}, RSA^{233;276} and baroreflex gain²¹² all decrease, while LF power^{212;225;332} and the LF/HF ratio²¹² increase with increasing tilt angle and in the upright position. In supine rest, baroreflex induced vagal flow accounts for most of the LF heart rate oscillations²⁷⁵. However as the body becomes more upright, sympathetic flow increases^{262;337-339} and vagal flow decreases³³⁷. In the upright position, the increased sympathetic flow overrides the respiratory gating of the cardiac inhibitory centre and so RSA decreases. Even so, HF power is greater than LF power when breathing in the HF range³³⁷.

HRV during REM sleep is similar to during waking³⁴⁰. However, during non-REM sleep, RR amplitude³⁴¹ and HF power^{340;341} increase and LF power decreases³⁴⁰. This possibly occurs as sympathetic activity is greater during both REM sleep and waking³⁴⁰. While the increase in RR amplitude is seen in all ages, the increase in HF power is seen mainly in young subjects³⁴¹.

Extensive reviews have been conducted on the changes in measures of HRV during acute exercise, as a result of exercise training and in overtraining, and all agree that results are conflicting and inconclusive³⁴²⁻³⁴⁴. While measures of HRV are valuable indicators of the autonomic control of the heart at rest, they do not behave as expected during exercise³⁴². Furthermore, spectral analysis requires stationary data which is not possible during exercise^{343;345} making interpretation difficult and misleading especially during high exercise intensities³⁴². It is concluded that analysis of HRV, especially spectral analysis, during exercise is inaccurate and unreliable, and should not be used^{342;343}.

While most cross-sectional studies show higher HRV in trained subjects^{342;344} indicating greater cardiac vagal tone³⁴³, results from both cross-sectional and longitudinal studies are conflicting³⁴²⁻³⁴⁴. However, in chronic disease, exercise training has been shown to increase HRV³⁴⁶⁻³⁴⁹ as well as baroreflex sensitivity³⁴⁶ at rest in patients recovering from myocardial infarction. These changes persisted for the following year³⁴⁸ and were associated with lower cardiac mortality in the following 10 years³⁴⁶. Further research is required to validate alternative forms of HRV analysis during exercise, as well as to investigate the changes in HRV after exercise training especially in patients with chronic disease.

1.3.5 Changes in HRV during stress and relaxation

Heart rate variability is also affected by stress and anxiety. Both acute and chronic psychological stress lead to decreased amplitude of the RR intervals^{212;350;351}, decreased SDNN^{62;352}, RMSSD³⁵³, RSA^{354;355} and HF power^{212;352;356-360}, and increased LF power^{212;225;352;359} and LF/HF ratios^{212;351;352;358-362}. HF power also decreases during acute³⁵⁰ and chronic anxiety^{350;363}. Both baroreflex gain^{212;364} and sensitivity^{308;316;365;366} decrease and the set point of the baroreceptor-heart rate reflex^{365;367} changes. In addition, stress leads to an increase in HR^{368;369} and BP^{368;369} including both systolic (SBP) and diastolic blood pressure (DBP)³⁵⁹.

Porges attributes the decrease in measures of HRV during stress to the alteration of the physiological responses that occurs during chronic stress³¹⁷. The decrease in HF power indicates decreased vagal activity^{352;357;358}, and the increase in HR and BP both occur as a result of increased sympathetic activity^{368;369}. Increased LF power most likely reflects both a decrease in vagal activity and increase in sympathetic activity. The hypothalamus and other higher centres modulate the baroreflex in response to stressful stimuli, potentially affecting all HRV variables²⁵⁷.

In the period immediately after acute stress, a rebound in vagal activity may cause RMSSD to increase to higher than baseline and HR and SBP to be lower³¹⁶. RMSSD is generally greatest during the first minute of recovery suggesting that HR recovery is vagally mediated³¹⁶. People with decreased HR recovery may also have decreased HR responses to stress³⁷⁰.

During relaxation, RSA³⁷¹ and baroreflex sensitivity³⁶⁵ increase and responsiveness of the end organs to norepinephrine decreases³⁷². Meditation increases HF and decreases LF power and the LF/HF ratio³⁷³. Similarly, a year-long stress management program consisting of cognitive

restructuring and mental relaxation programs reversed the increased LF and decreased HF components of HRV that were documented in response to work stress¹⁵⁸.

1.3.6 Changes in HRV in disease

Changes in HRV are seen in many disease states and are often valuable in predicting prognosis¹⁵. The association of HRV with cardiovascular disorders is the most extensively studied to date.

1.3.6.1 Cardiovascular disease

The pathophysiology of many cardiovascular diseases is related, at least in part, to low vagal tone, as healthy stable cardiac function requires adequate vagal modulation of heart rate and conduction velocity³⁷⁴. Therefore, cardiovascular disease is associated with decreases in both time and frequency domain measures of HRV. While decreases in all measures of HRV may reflect decreased cardiac vagal tone, RMSSD, pNN50 and HF spectral power are specifically indicative of vagal modulation¹⁵.

Changes in measures of HRV associated with different cardiovascular diseases are shown in Table 1.2 below. Hypertension is associated with low SDNN³⁷⁵, low RSA³⁷⁶ and abnormal baroreflex function³⁷⁷ which has been proposed as a factor in its development. Low SDNN, RMSSD, pNN50, LF and HF cardiac spectral power are all associated with increased risk of CAD and its complications^{378;379}. Specifically, low SDNN may predict the development of CAD³⁷⁹, and is associated with CAD-related sudden death³⁸⁰, while low HF power correlates with the severity of atherosclerosis³⁸¹.

Low SDNN is also associated with increased risk of ischaemia and infarction³⁸². LF and HF spectral power decrease before the onset of ischaemia⁶⁴, and are lower immediately after³⁸³ and 2 weeks after³⁸⁴ myocardial infarction. HF power is particularly low when ischaemia follows high mental activity⁶⁴. When spectral components are expressed as normalised units, the percentage of LF power is higher and HF power lower 2 weeks after MI³⁸⁵. Both HF and LF power recover maximally but not completely over the following year³⁸⁴⁻³⁸⁶.

After myocardial infarction, HRV can be used as a prognostic factor for risk stratification and management¹⁵. Low HRV is indicative of increased risk of cardiac mortality³⁸⁷⁻³⁹² and is related to sudden cardiac death³⁹³. The general consensus is that HRV should be measured approximately 1 week after infarction and that SDNN is the measurement of choice¹⁵. At this time, patients with a

SDNN of less than 50ms have a higher risk of mortality than those with SDNN greater than 100ms^{15;389}.

Low SDNN is associated with symptomatic patients with hypertrophic cardiomyopathy³⁹⁴, and low SDNN³⁸², TF³⁹⁵, HF and LF power^{396;397} with heart failure³⁸². Both HF and LF power are positively correlated with left ventricular ejection fraction³⁹⁶ and cardiac output³⁹⁸, and negatively correlated with increasing severity of cardiac failure³⁹⁹. Low SDNN³⁸² and low LF^{395;400} power are indicators of poor prognosis, with an SDNN lower than 100 ms indicating increased mortality⁴⁰⁰.

Furthermore, low HRV is associated with increased risk of arrhythmias as well as increased mortality. Low SDNN and HF power are seen prior to the onset of sustained VT and VF⁴⁰¹ as well as atrial flutter⁴⁰² supporting the suggestion that decreased vagal stimulation results in 'cardiac electrical instability' which increases the risk of arrhythmias¹⁵. Low SDNN, pNN50, LF and HF power are risk factors for sustained VT^{380;394;401} as well as death from cardiovascular disease^{379;382;403}, and low SDNN, LF and HF power are risk factors for non-cardiac death⁴⁰³.

1.3.6.2 Metabolic syndrome

Changes in HRV associated with metabolic syndrome are shown in Table 1.2. Metabolic syndrome is associated with decreased HRV including low SDNN, HF and LF spectral power⁴⁰⁴⁻⁴⁰⁶ independent of fasting glucose levels⁴⁰⁴. As the number of metabolic components increases, HRV measures decrease⁴⁰⁵. These same HRV variables are inversely correlated with plasma glucose⁴⁰⁷, and are low in diabetes^{404;407-410}. Decreased HRV indicates abnormalities of the autonomic nervous system which may occur early in diabetes⁴¹¹ and is associated with a high risk of morbidity and mortality^{14;412-415}. Low HRV may also precede the clinical expression of autonomic neuropathy^{216;416;417} and is therefore a useful screening tool¹⁵.

1.3.6.3 Chronic pulmonary disease

Chronic obstructive pulmonary disease (COPD) has been associated with decreased HRV including low SDNN⁴¹⁸, RMSSD⁴¹⁹ and LF and HF spectral power⁴¹⁹. This suggests abnormal cardiac autonomic modulation^{418;420} including decreased vagal activity⁴¹⁹. A correlation has been found between these measures of HRV and FEV1, suggesting that HRV may reflect the severity of disease⁴¹⁹.

Table 1.2 Changes in measures of HRV associated with cardiovascular disease states, metabolic syndrome and chronic respiratory disease states

	SDNN	RMSSD	pNN50	LF	HF	TF	RSA
Cardiovascular disease							
Hypertension	↓ ³⁷⁵						↓ ³⁷⁶
CAD	↓ ³⁷⁸⁻³⁸⁰	↓ ^{378;379}	↓ ^{378;379}	↓ ^{378;379}	↓ ^{378;379;381}		
Ischaemia	↓ ³⁸²			↓ before onset ⁶⁴	↓ before onset ⁶⁴		
Infarction	↓ ³⁸²			↓ immediately after ³⁸³ ↓ 2 weeks after ³⁸⁴	↓ immediately after ³⁸³ ↓ 2 weeks after ³⁸⁴		
Cardiomyopathy	↓ ³⁹⁴						
Heart failure	↓ ³⁸² ↓ poor prognosis ³⁸²			↓ ³⁹⁶⁻³⁹⁹ ↓ poor prognosis ^{395;400}	↓ ³⁹⁶⁻³⁹⁹	↓ ³⁹⁵	
Arrhythmias							
Ventricular Tachycardia	↓ prior to onset ⁴⁰¹ ↓ ^{380;394;401}		↓ ^{380;394;401}	↓ ^{380;394;401}	↓ prior to onset ⁴⁰¹ ↓ ^{380;394;401}		
Ventricular Fibrillation	↓ prior to onset ⁴⁰¹				↓ prior to onset ⁴⁰¹		
Atrial Fibrillation	↓ prior to onset ⁴⁰²				↓ prior to onset ⁴⁰²		
Cardiac mortality	↓ ^{379;382;389;392;403}		↓ ^{379;382;403}	↓ ^{379;382;403}	↓ ^{379;382;403}		
Metabolic Syndrome							
Diabetes	↓ ⁴⁰⁴⁻⁴⁰⁶			↓ ⁴⁰⁴⁻⁴⁰⁶	↓ ⁴⁰⁴⁻⁴⁰⁶		
	↓ ^{404;407-410}			↓ ^{404;407-410}	↓ ^{404;407-410}		
Chronic Respiratory disease							
COPD	↓ ⁴¹⁸	↓ ⁴¹⁹		↓ ⁴¹⁹	↓ ⁴¹⁹		

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; SDNN = standard deviation of the normal to normal RR intervals; ms = milliseconds; RMSSD = root mean square of successive differences of RR intervals; pNN50 = the number of successive NN intervals which have a difference of greater than 50ms as a proportion of the total number of NN intervals LF, HF and TF = power of the RR interval spectrum in low frequency, high frequency and total frequency ranges respectively; RSA = respiratory sinus arrhythmia.

1.3.6.4 Other

Changes in HRV are also seen in psychiatric and neurological diseases. Severe major depression has been associated with decreased RMSSD⁴²¹ and decreased HF power^{421;422}, as well as increased LF/HF ratios^{421;423} at rest and in response to mental stress⁴²⁴, while patients post- myocardial infarction with depression have lower LF power⁴²⁵. Patients with generalised anxiety disorder have decreased HF power⁴²⁶, and those with panic attacks lower SDANN⁴²⁷ and higher LF power⁴²² than controls. Fibromyalgia is associated with decreased HRV, higher LF and lower HF power⁴²⁸ and impaired circadian variation with increased LF at night⁴²⁹.

1.3.7 The relationship between HRV and cognitive performance

In addition to being associated with health and disease, HRV shows changes associated with cognitive performance. However, the findings are conflicting. Subjects with high HRV have shown improved executive functioning including improved working memory with more correct responses and faster reaction times to cognitive tasks^{430;431}, while decreased HRV including VLF, LF and HF power and RMSSD has been associated with cognitive impairment⁴³². However, other studies show no relationship between HRV and cognitive impairment⁴³³.

In contrast, Morgan et al suggest that decreased HF power predicts improved performance⁴³⁴. However, whilst the authors suggest that the performance measure used assessed elements of cognitive executive functioning, the relationship to traditional measures of performance is not known⁴³⁴. Nevertheless, the capacity to suppress vagal tone indicates increased ability to sustain attention⁴³⁵ and is associated with adaptive cognitive function⁴³⁶ and enhanced cognitive performance in conditions of high stress⁴³⁴. It is possible that this conflicting finding occurs when cognitive function is tested in stressful conditions because of the reduction in HRV caused by stress as described above. Supporting this idea, the Stroop task⁴³⁷ which tests cognitive function and has been shown to induce stress effectively⁴³⁸, results in decreased RR interval⁴³⁹, decreased HF and LF HRV power and increased HR^{438;440}.

1.3.8 HRV biofeedback

Biofeedback is a process whereby different physiological parameters are displayed to the individual in real time. The purpose is to help them to increase awareness of their bodily processes and, hopefully, to develop a degree of conscious control, thus leading to improved health and wellbeing.

There are many different kinds of biofeedback, including those that monitor muscle tension, skin conductance, EEG, EMG, temperature, heart rate and HRV. HRV biofeedback is of particular interest as it provides an economical, mobile and easy to use tool. HRV biofeedback could be a valuable method of altering autonomic activity, potentially reducing disease and improving performance.

Different HRV biofeedback devices are available ranging from small hand held devices to larger devices requiring a complex setup of equipment. Hand held devices are of particular interest, as the intention would be to find a device that could be easily used by the individual as needed throughout the day.

A typical hand held HRV biofeedback device measures the real time RR interval (Muench, 2008), and displays the data as an RSA wave. Using this wave, users are guided to find and maintain their optimal slow respiratory rates so that real-time heart rate and respiration co-varies in a perfect phase relationship. This occurs when one is breathing at resonance frequency of about 6 breaths per minute.

1.3.8.1 Effect of HRV biofeedback on measures of HRV

The use of HRV biofeedback does indeed result in changes in HRV. These are shown consistently in the short term, while long term effects are more variable⁴⁴¹. During HRV biofeedback, TF^{442;443} and LF power⁴⁴²⁻⁴⁴⁴ increase, with either no change^{442;444} or a decrease⁴⁴³ in HF power. In keeping with the increase in TF power, SDNN increases⁴⁴⁴. In addition, a non significant increase in HR has been documented⁴⁴⁴.

Many studies have looked at the impact of HRV biofeedback on baroreflex function, as changes in baroreflex sensitivity could account for the increases in LF power. Most of these studies have shown that baroreflex gain or sensitivity increases during HRV biofeedback^{443;445} or breathing at 6 breaths per minute^{268;446}, while others have shown no change⁴⁴². Wheat et al⁴⁴¹ suggest that the studies which have shown significant changes in baroreflex gain during biofeedback were methodologically strong while those that showed no change were not. It is thought that breathing at the resonance frequency 'exercises'⁴⁴³ the baroreflex resulting in improved autonomic function^{288;443}.

Increased baroreflex gain persists into the immediate post biofeedback period⁴⁴³. Respiration remains lower⁴⁴³ and SDNN higher⁴⁴⁴. Changes in LF power are variable with some studies showing

it to be increased^{443;444} even when respiration rate is accounted for⁴⁴³, and others showing no change⁴⁴². No changes in HF power⁴⁴²⁻⁴⁴⁴ are seen.

A long-term effect has been found with increased SDNN^{197;444} and LF power⁴⁴⁴ after 4 weeks of HRV biofeedback. However, no changes were found in SDNN, LF, HF or TF power after 10 weeks of intervention^{442-445;447} or at follow up^{442;448}. A combination of breathing, HR and HRV biofeedback for 6 weeks resulted in increased SDNN and RMSSD after the treatment period which were still evident 12 weeks after testing⁴⁴⁹. Studies also have mixed results regarding baroreflex gain with some showing an increase⁴⁴³, and others finding no long term change⁴⁴².

1.3.8.2 Effect of HRV biofeedback in the management of disease

Research has found HRV biofeedback to be effective in the management of anxiety, depression, cardiovascular disease, asthma, COPD, fibromyalgia, inflammation and insomnia.

Biofeedback has resulted in a reduction in symptoms of stress¹⁹⁶, anxiety¹⁹⁵, post traumatic stress disorder¹⁹⁷ and depression^{442;444} and may be effective in the treatment of major depression⁴⁴⁴. It seems that subjects who are able to use biofeedback more effectively have a greater reduction in anxiety¹⁹⁵. Biofeedback together with psychological support¹⁹⁸ and in combination with Cognitive Behavioural Therapy¹⁹⁹ resulted in decreased anxiety. The latter combination was found to be more beneficial than other relaxation techniques including meditation, yoga and unassisted breathing¹⁹⁹.

A few weeks of HRV biofeedback has been shown to be valuable in the management of hypertension, heart failure and coronary artery disease. HRV biofeedback and similar slow breathing decreased systolic blood pressure^{450;451} and increased baroreflex function⁴⁵¹ in patients with hypertension, and decreased symptoms, increased exercise tolerance and increased resting oxygen saturation in patients with heart failure^{448;452;453}. It also results in improved vagal heart rate regulation in patients with coronary artery disease¹⁹⁶.

Increased vagal activation of the heart has been found to reduce myocardial ischemia, reperfusion-induced arrhythmias and the risk of sudden death after myocardial infarction^{454;455}. Therefore, increasing cardiac vagal modulation with HRV biofeedback may reduce the morbidity and mortality associated with cardiovascular disease especially diseases related to decreased vagal stimulation such as arrhythmias¹⁵.

Ten weeks of HRV biofeedback has resulted in improvements in asthma including increased pulmonary function⁴⁴⁵ and decreased need for controller medication⁴⁵⁶. In addition, patients with COPD had an increase in RSA after treatment as well as an improvement in clinical outcome⁴⁵⁷. While HRV biofeedback has not been investigated in the management of metabolic syndrome or diabetes, it has improved the function of the autonomic nervous system which may delay the progression of these diseases as well as prevent the cardiovascular complications. Finally, HRV biofeedback has resulted in improved symptoms and function in patients with fibromyalgia⁴⁴², decreased autonomic dysfunction induced by endotoxin induced inflammation⁴⁵⁸ and an improvement in the quality of sleep⁴⁵⁹.

1.3.8.3 The effect of HRV biofeedback on cognitive performance

Only one study has examined the effect of HRV biofeedback on cognitive performance. The authors found a reduction in the errors made during a Stroop task. There was, however, no difference between the HRV biofeedback group and a non-biofeedback concentrative control group¹⁹⁵.

1.4 EEG

HRV biofeedback increases cognitive performance and reduces stress and anxiety as described above. Examining changes in EEG provides insight into the potential mechanism of these results. EEG can be measured in different ways: event related potentials or phasic frequency changes are related to specific short term tasks⁴⁶⁰, while tonic frequency changes occur over a longer time period⁴⁶⁰.

Frequency bands commonly calculated when analysing EEG include delta, theta, alpha, beta and gamma. While different researchers use different margins for each frequency band, delta is generally within 0 and 4 Hz⁴⁶¹⁻⁴⁶³, theta within 4 and 8 Hz^{194;464-467}, alpha within 7 and 14 Hz^{194;440;464;465;467-469}, beta within 13 and 30 Hz^{461;465;467}, and gamma within 30 and 70 Hz^{462;470}. These bands can also be further divided into smaller components. Delta, theta and alpha oscillations generally span large cortical areas while beta and gamma are higher frequency, lower amplitude and distributed in more limited areas⁴⁷¹.

This review focuses on the interpretation of EEG oscillations in theta, alpha and beta frequency bands.

1.4.1 Interpretation of different frequency bands

1.4.1.1 Theta

Theta oscillations reflect changes over widespread areas of the brain including the prefrontal cortex⁴⁷²⁻⁴⁷⁴, anterior cingulate cortex (ACC)⁴⁷⁵⁻⁴⁷⁷, neocortex⁴⁷⁸, limbic system^{474;479-482}, hypothalamus⁴⁷⁴ and brain stem⁴⁷⁴. This allows integration of the activity in all of these locations⁴⁸³. Frontal theta is well studied and is generated by frontal areas including the ACC^{484;485}, and medial and dorsolateral prefrontal cortex^{476;486}. Posterior theta is less well researched but is thought to reflect different functions from frontal theta⁴⁸⁷.

Theta oscillations in different areas are likely to have different roles⁴⁷⁸. While theta has been related to a range of behavioural, cognitive and emotional variables, their main function is memory and emotional regulation⁴⁷¹. As a result of the multiple different roles, increases in theta during complex tasks are non-specific^{488;489}.

Frontal theta increases may be related to memory. In particular, it increases with increased working memory^{471;475;477;490-496}, with encoding and retrieval of episodic memory^{477;496-506} and with the formation of declarative long term memory^{502;507;508}. In addition, theta increases with increased attention^{473;476;477;484;486;509;510} during both mental performance and meditative concentration^{477;511-519}.

Increases in posterior theta have been linked to perceptual processing⁵²¹ as well as greater memory based executive functions requiring visuo-motor integration⁴⁸⁵. Two different attentional networks have been described: an anterior network involving the detection of sensory stimuli and a posterior network involving orienting of sensory attention⁵²². Posterior theta has also been found during stage 1 sleep or hypnagogic states⁵²¹. However, while Schacter describes 2 different manifestations of theta: a frontal midline theta related to alert states and a posterior theta which is associated with a hypnagogic state⁵²¹, theta found during hypnagogic states is generally spread diffusely over the cortex⁵²¹.

1.4.1.2 Alpha

Alpha is the dominant frequency in the scalp EEG of adult humans. It is generated mainly over posterior brain regions^{523;524} but is also found anteriorly⁵²⁵. Alpha oscillations are associated with thalamic burst firing⁵²⁶⁻⁵²⁸ and are thought to arise from cortico-thalamic^{529;530} or cortico-cortical network activity^{531;532}. However, the exact physiological generators of alpha are not yet known⁵³³.

Alpha oscillations are maximal during an awake, restful state with eyes closed^{534;535}. They were first identified by Berger who found that alpha power decreased when eyes were opened⁵³⁶. Alpha power also decreases by at least 50 % during sleep⁵³⁹.

Alpha power increases with increased internal attention⁵⁴⁰⁻⁵⁴³ including mental calculations⁵⁴⁴ and working memory demands^{545;546}, as well as with anticipatory waiting during attentional tasks⁵⁴⁷. Increased alpha reflects active inhibition of irrelevant information, especially sensory information^{533;533;541;548-552}. This provides a top down control mechanism preventing unnecessary or conflicting information and processes from interfering with the current internal process^{460;533;533;541;548;549;553;554}. Typically a ring of inhibition (increased alpha) surrounds an area of cortical activation (decreased alpha)^{555;556}.

Generally alpha and theta oscillations respond in opposite ways⁴⁷¹. This reciprocal relationship is mediated by the prefrontal cortex⁴⁷¹.

1.4.1.3 Beta

Activity in the beta frequency band is the least understood and requires much future research. Beta activity is thought to be related to both sensorimotor⁵⁵⁷ and cognitive functions⁴⁶⁷, and its main function appears to be the maintenance of the status quo of both motor and cognitive states⁴⁶⁷.

Beta activity increases during rest and, therefore, has been suggested to represent an 'idling rhythm' in the motor system⁵⁵⁷. However, this may be an active rather than a passive process^{467;558-561}. Beta activity increases during steady state contractions and decreases during new voluntary movements⁵⁶²⁻⁵⁶⁸. Its function may be to modulate the processing of somatosensory stimuli⁵⁶⁹ and allow efficient processing of feedback⁵⁶².

Beta activity is associated with top down processing of attention^{570;571}. Engel et al⁴⁶⁷ summarise the research and propose that beta activity increases when the current cognitive state needs to be actively maintained, decreases when the current state changes, and remains unchanged if there is no alteration to the current state. Other research, however, has found that beta activity over the frontal cortex was associated with decreased sustained attention^{572;573}.

1.4.2 Impact of age and sex on EEG

Both age⁵⁷⁴ and sex⁵⁷⁴⁻⁵⁷⁷ affect the average amplitude of EEG oscillations. During adulthood alpha⁵⁷⁸ and theta remain relatively stable⁵⁷⁹. From the age of about 50, however, there is a decrease in alpha⁵⁷⁸ and increase in beta power⁵⁷⁹.

1.4.3 Effect of anxiety and relaxation on EEG

Changes in the frequency of EEG oscillations commonly occur during anxiety and relaxation. Increased frontal midline theta occurs during relaxation⁵⁸⁰⁻⁵⁸² and relief from anxiety^{194;583;584}, and indicates lower state and trait anxiety⁵⁸⁵. It has been positively correlated with HRV measures, suggesting increased parasympathetic activity^{373;586;587} and negatively with an HRV index of the sympathetic system¹⁹⁴.

Studies examining the impact of anxiety on alpha oscillations have shown conflicting results. Some show that higher alpha activity is associated with lower levels of anxiety and increased feelings of calm and positive affect⁵⁸⁸⁻⁵⁹⁰, while others indicate that alpha power is higher at baseline in anxious people^{591;592}, increases further in anxiogenic situations⁵⁹¹ and decreases in association with relaxation^{580;582}. An increase in alpha during anxiety may occur as a result of greater attention to the surrounding environment^{591;593}. The conflicting results most likely occur as a result of the complex relationship between the numerous cerebral processes that stimulate alpha oscillations.

Feelings of anxiety have also been associated with increased beta power⁵⁹⁴ while relaxation results in a decrease⁵⁸². In addition, a general increase in spectral power of all EEG bands has been described in response to anxiogenic situations⁵⁹⁵.

1.4.4 Effect of HRV biofeedback and meditation on EEG

Very little research has been done on the effect of HRV biofeedback on EEG or even the relationship between HRV and EEG. Thayer and Lane have proposed the Neurovisceral Integration Theory, which describes an integrated neural network involving cognitive, affective and autonomic regulation^{702;703}. A key component of this system is the bidirectional central autonomic network (CAN), which regulates HRV^{702;704}. Indeed, HRV has been described as providing a 'structural and functional link between the brain and the heart'⁷⁰⁵.

Increased HRV has been associated with increased activity in the prefrontal cortex^{705;706}. It has also been associated with increased working memory and increased parasympathetic activity⁷⁰⁴, both processes that are related to the prefrontal cortex⁷⁰⁶⁻⁷⁰⁹. Therefore, one might expect that increased HRV in response to biofeedback would result in increased theta oscillations, which have been associated with prefrontal cortex activity and related to increased working memory and increased parasympathetic activity. As expected, the only study on HRV biofeedback indicated that biofeedback resulted in increased overall theta and alpha power in the post-intervention period⁵⁹⁶.

Much research has, however, been done on changes in EEG during meditation. HRV biofeedback can be viewed as a form of concentrative meditation which involves focusing on specific mental or sensory activities such as the breath¹⁷⁰. However, it is different from a concentrative meditation in that in addition to observing, one is actively controlling the breath in response to an external biofeedback stimulus.

There is large variability in the literature on EEG and meditation. However, one consistent finding is that power in the theta band increases during meditation^{521;580;597-610}. While this has most commonly been seen in the frontal midline areas^{194;373;587;598;602;611;612}, global increases in theta power have also been described during a yogic breath meditation⁶⁰⁸ and in comparison to relaxation⁶¹³. Generally, increased theta has been associated with good technique^{597;600;601;606} and long term meditation experience^{597-599;602}.

Posterior theta is also seen during the first stage of sleep⁵²¹. However, previous research has shown a difference between theta associated with meditation and stage 1 sleep^{597;599;600;602;606;614;615}. Theta power during sleep typically increases globally⁵²¹. In addition, it is associated with a decrease in alpha power of about 50%⁵³⁹, while increases in theta related to meditation are generally accompanied by stable or increased alpha power⁶⁰⁸.

While there is insufficient evidence to determine the exact cause of the pattern of theta activity during meditation⁶¹⁶, similar increases in frontal midline theta power are seen during sustained attention^{473;476;477;486} as well as during relaxation as described above. Frontal midline theta has been correlated with HF HRV during meditation^{373;587} suggesting increased vagal activity.

Power in the alpha band also commonly increases during meditation^{194;373;597;599;604-606;609;613;617-624}, again largely over frontal areas^{193;373;625;626}, as well as during yogic breathing¹⁸⁷. Increased alpha power is also seen after meditation^{622;627}, and is commonly seen at rest in meditators^{597;600;601;603;606;618;619;628;629}. However, not all studies have shown an increase in alpha power during meditation^{597;630-632}. Some have found an increase only in advanced practitioners^{617;626}, and research comparing meditation and relaxation has found no increase in alpha power^{181;204;580;600;602;608;633}. In addition, a decrease in alpha power over the occipital cortex has also been seen⁶²⁶.

No research has been done on beta activity during meditation. It has, however, been shown that beta activity decreases with relaxation⁵⁸².

1.5 SUMMARY AND CONCLUSION

Stress is increasingly prevalent in the world today, and leads to anxiety, emotional distress and impaired cognitive function. Chronic psychological stress also plays an integral role in the development of both psychological and physical disorders, in particular, being a risk factor for chronic non-communicable disease.

As the burden of stress and stress-related disease grows, it is increasingly important to identify effective stress management techniques. While many forms of stress management are available, many of these are lengthy, time consuming, expensive and/or require the involvement of a professional. Therefore, there is a need to find an effective, short duration, easily accessible method of managing stress that is easy to use and can be self applied. HRV biofeedback shows potential as an effective stress management tool that fulfils these criteria.

The measurement of HRV provides a valuable quantitative marker of the effect of the autonomic nervous system on the heart. HRV decreases in stress and anxiety, and low HRV is associated with many chronic diseases. While some studies show an association between decreased HRV and impaired cognitive performance, the results are conflicting.

HRV biofeedback facilitates easy manipulation of HRV, and therefore potentially provides a valuable intervention for altering the activity of the autonomic nervous system. HRV biofeedback increases HRV during biofeedback and there is some evidence that this is maintained into the immediate post biofeedback period. However, no studies have examined changes in HRV during stress after biofeedback.

While HRV biofeedback has been shown to lead to a reduction in symptoms of stress and anxiety, no studies have examined its effect on perceived relaxation states. Only one study using a 15 minute intervention has examined the effect of HRV biofeedback on cognitive performance, showing an increase in performance which was not different from the comparative intervention.

Changes in EEG are evident in anxiety, as well as during relaxation and meditation. Only one other study has examined the effect of HRV biofeedback on EEG in the immediate post biofeedback period; however none have investigated changes in EEG during biofeedback. Observing changes in

EEG during and after HRV biofeedback may contribute to understanding the mechanisms contributing to the reduction in anxiety and improved performance that has been shown.

The majority of studies on HRV biofeedback focus primarily on clinical outcomes and, therefore, the long-term effect of HRV biofeedback over sessions, rather than the acute effects. Furthermore, most use the conventional training protocol as described by Lehrer et al ⁶³⁴. We were specifically interested in the acute effect of 10 minutes of biofeedback, as this is the period recommended by the manufacturer for clinical use. The minimum recommended time per session is 5 minutes with a goal to accumulate a total of 20 minutes per day ⁶³⁵.

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1.6 OBJECTIVES OF THE THESIS

Therefore, the objective of this thesis is to examine the effects of a single 10 minute episode of HRV biofeedback on measures of HRV and EEG during and immediately after the intervention, measures of HRV and cognitive performance during laboratory induced cognitive stress and subjective feelings of anxiety and relaxation states after testing.

The general methodology used is described in Chapter 2. Chapter 3 describes the changes in cognitive performance. Changes in measures of HRV are detailed in Chapter 4 and changes in EEG in Chapter 5, while Chapter 6 describes the changes in measures of anxiety and relaxation states. Finally, Chapter 7 concludes with a summary and clinical interpretation of the results, a description of the clinical application of HRV biofeedback as well as a description of the limitations of this study and potential future research.

CHAPTER 2

GENERAL METHODOLOGY

2.1 PARTICIPANTS

Eighteen male volunteers (34 ± 6 years) who were employed in senior managerial positions were recruited for this study. To be included, volunteers had to have been exposed to work related stress and to have subjectively rated their own perception of life stress as high. Their trait anxiety was measured using the trait component of a Spielberger State-Trait Anxiety Inventory (STAIT)⁶³⁶ which they completed online. Subjects were screened via email. On arrival before the training session a brief history was taken by a medical doctor, to confirm the responses.

A previous clinical diagnosis of anxiety-related disorders disqualified participation in the study. Further exclusion criteria included: previously diagnosed cardiac or psychiatric disorders, current use of psychotropic or heart rate altering medications or current use of stimulants or recreational drugs, as well as volunteers practicing regular meditation techniques. Volunteers were asked about their exercise practices as well as breathing and meditation practices as these would have had the greatest impact on the outcome of the intervention. Volunteers who were technically unable to use the biofeedback device or perform the modified Stroop task were excluded from the trial. This applied to 2 subjects, one of whom had chronic low circulation and so the device was unable to obtain a clear pulse reading. The other subject was excluded as, on completion of the familiarization Stroop task, he still did not understand what to do, and continued to confuse the response keys and, therefore, could not respond effectively. We elected to test only men in an attempt to limit heterogeneity because men and women respond differently to different psychological stressors^{48;53} with varied HPA axis responses^{46;48} as well as neural responses⁶³⁷ to stress.

Subjects were randomly assigned to either an HRV biofeedback (BIO) group or a comparative (COM) group using a process of stratified randomization. The initial group of subjects was matched into two groups based on age and thereafter subjects were randomly assigned to either group. Each group consisted of 9 subjects. We decided to use a single intervention and comparative group design, as a crossover design may have confounded the interpretation in the event of there being any carry over from the intervention.

The study protocol was approved by the Research and Ethics Committee of the University of Cape Town (Rec ref: 296/2005) in accordance with the Declaration of Helsinki. All subjects signed informed consent prior to participation in the study.

2.2 TRAINING AND FAMILIARIZATION PROTOCOL

Volunteers were instructed not to eat a heavy meal, ingest caffeine or alcohol, or exercise within 4 hours before arriving at the laboratory. Compliance was checked before the onset of each testing session.

All subjects underwent a single standardised training session during the week prior to the start of their experimental trials. On arrival, height was measured using a Leicester 214 Portable Stadiometer (Lifemax) and weight was measured using a TCS-A 300 kg Platform Scale (Clover Scales). Body mass index (BMI) was calculated using the formula $BMI = \text{weight (kg)} / \text{height (m)}^2$ ⁶³⁸.

A hand-held mobile HRV biofeedback device (StressEraser™, Helicor, USA) validated by Heilman et al ⁶³⁹ was used for both the training and the testing sessions in the BIO group. An infrared emitter and sensor incorporated into the device into which the subject placed their index finger, measured the real-time interbeat-interval (IBI) of the heart using finger photoplethysmography ⁶³⁵. The IBI data are transformed and displayed as a wave on a LCD screen, allowing users to see the real-time fluctuations of their pulse rates. This wave reflects respiratory sinus arrhythmia (RSA), which is the cyclical change in heart rate occurring in response to respiration. Using the RSA wave, users are guided to find their optimal slow respiration rate and to maintain a cognitive focus so that real-time heart rate and respiration co-varies in a perfect phase relationship. To achieve this, the subjects were instructed to inhale until the RSA wave reached its peak and exhale until the wave started to rise again. They were taught pursed-lips abdominal breathing and were instructed to relax and breathe comfortably without straining ⁶³⁴.

The device rewards users with points based on the wavelength for each RSA cycle. If the wavelength meets a certain threshold (10 seconds), users are given 1 point marked by three vertical squares. Two vertical squares receive .5 point and one vertical square receives no credit. The goal is to accumulate continuous points during the session. To assist users in obtaining points, the device anticipates the peak of the RSA wave based on its slope and marks the peak with a triangle. The peak

of the wave indicates the moment heart rate deceleration is to begin, indicating the parasympathetic response. Users were instructed to begin their exhalation when the triangle appears. They were instructed to extend their exhalation for as long as possible until the wave begins to rise again. Although the device offers points based on RSA wavelength, users were instructed to maximize RSA amplitude simply by following the RSA wave (e.g. inhale until the wave stopped rising and exhale until the wave stops falling). While this device does not, technically, facilitate resonance frequency breathing as time domain analysis was used rather than frequency analysis; it does functionally facilitate a similar breathing frequency.

There is a risk of adverse first session effects with a single training session of HRV biofeedback, however these may be decreased with the use of pursed-lips breathing⁶³⁴. Subjects are not familiar with the technique and so may have difficulty performing it, causing possible anxiety^{199;288}. In addition, there may be a tendency to hyperventilate^{288;640} resulting in dizziness. Only 1 out of the 9 subjects reported difficulty performing the technique during training, and no subjects reported dizziness or other adverse effects.

The device used in the COM group was also manufactured by Helicor (USA). It appeared identical to the BIO device, but made use of a different algorithm to display a wave on the screen. The algorithm that generated this wave was derived from the subject's heart rate measured by the sensor, divided by 2 plus a random number which ranged between 0 and 25 % of the heart rate/2 value. This result was then smoothed by averaging the calculation over 5 seconds. Subjects were informed that the wave represented their blood density and were instructed to watch the wave whilst not thinking any stressful thoughts. They were not instructed to alter the wave in any way.

All of the subjects were told that we were comparing the effect of 2 different devices on laboratory induced cognitive stress; therefore both groups were given the impression that their device worked. Both groups had devices that appeared identical and both were instructed to observe the wave that appeared on the screen of the device. The only difference in instructions was that the BIO group were instructed to alter their breathing in response to the wave, while the COM group were instructed to observe the wave whilst not thinking stressful thoughts. While the BIO group focused their attention on regulating their breathing, the COM group quietly watched the wave.

After subjects had received their respective instruction, they completed a formal 10 min biofeedback session with either the BIO or COM device and their scores were recorded. A score of 30 or more on the BIO device was indicative of a successful session.

2.3 EXPERIMENTAL TRIAL

The time line for the experimental trial is shown in Figure 2.1 below. On arrival at the laboratory, subjects completed the state component of a Spielberger State-Trait Anxiety Inventory (STAIS) ⁶³⁶ and the Smith Relaxation States Inventory 3 (SRSI3) ⁶⁴¹ and were reminded how to use their respective devices. Subjects then underwent a full familiarization modified Stroop task lasting 5 minutes and 24 seconds. After the familiarisation test, electrodes and transducers were applied to the subjects and connected to a Biopac MP150WSW (Biopac Systems, Goleta, CA, USA) to record electrocardiogram (ECG), respiratory rate and electroencephalogram (EEG). The Biopac MP system is a laboratory based physiological monitoring system which is commonly used as a research tool, and has been cited in numerous publications ⁶³⁹. Subjects were seated throughout the testing and were instructed to move as little as possible. Leads were taped down to prevent interference.

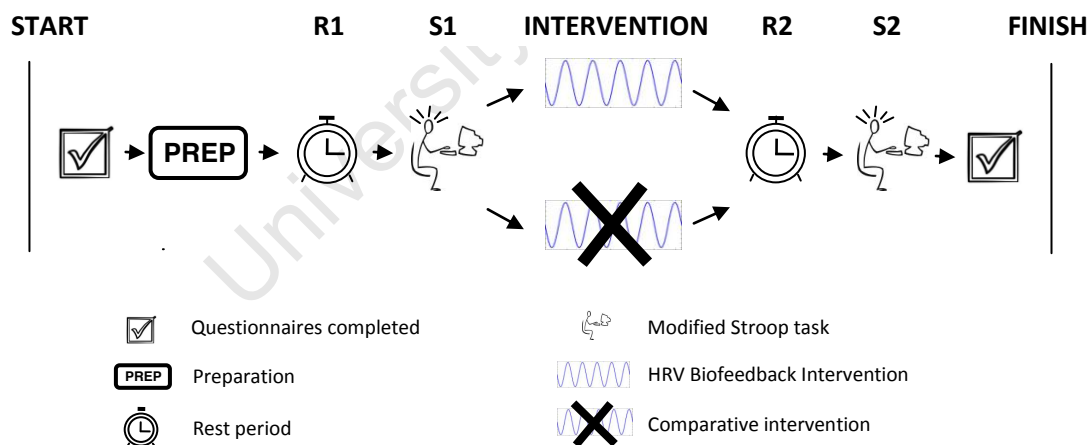


Figure 2.1 Diagram depicting the time line of the trial protocol on the day of final testing

HRV = heart rate variability; R1 = First rest period; S1= First Stroop task; R2 = Second rest period; S2 = Second Stroop task

Subjects were then instructed to relax with their eyes closed for 5 minutes (Rest 1) during which time measurements of baseline ECG, respiratory rate and EEG were recorded. Immediately after the

baseline period and without moving, subjects were instructed to open their eyes and complete the pre-intervention Stroop task (Stroop 1) which lasted 5 min 24 s in duration. Subjects then completed a 10 minute intervention with either the BIO or COM device. After the intervention, subjects completed a further 5 minute rest period (Rest 2) with their eyes closed before completing a post-intervention Stroop task (Stroop 2). ECG, respiratory rate and EEG were recorded throughout the testing.

After the final measurements, subjects completed post-testing STAIS and SRSI3 questionnaires. In addition, subjects were asked to rate the subjective efficacy of the intervention as well as feelings of sleepiness using a visual analogue scale (VAS) devised for this study. In response to each question, subjects scored from 1 to 10 with 1 being 'not at all' and 10 being 'extremely' with regard to helpfulness and sleepiness.

2.3.1 Modified Stroop Task

We modified the original Stroop task⁴³⁷ by computerising so that subjects responded by pressing keypad buttons instead of responding verbally. In addition, we added a working memory component. The colour word component was previously validated by Rauch et al⁶⁴² as follows. Twelve female subjects (students aged 18 - 25) repeated a Stroop task of about 5 minutes duration which consisted of only incongruent cues. Each task contained 72 colour words with each word being displayed for 400 ms followed by a 3.5 s response time. Five tasks were repeated one after another with a 1 min break in between each Task. Between 7 and 10 days later the subjects repeated the 5 x 5 min Stroop tasks at the same time of day (day 2).

In the current study, the modified Stroop task entailed the individual presentation of cues (2 cm in height) in the centre of a computer monitor on a black background. Cues consisted of colour-words (red, blue, green and yellow) and single white squares. Cues appeared every 3 seconds and were displayed for 400 ms after which they were replaced by a black screen which lasted for 2600 ms and which constituted the response period. The 4 colour-words were presented in 5 different colour inks: red, blue, green, yellow and grey. The colour words were either presented in grey ink or in a colour ink incongruent with the meaning of the word, i.e. red in blue colour, or green in yellow colour, but never red in red colour or blue in blue colour, etc. The subjects were asked to respond as quickly and as accurately as possible by pressing one of four response buttons to indicate either the colour of the word (if the word was written in colour ink) or the word itself (if the word was written

in grey ink). Subjects were not required to respond to the white squares other than counting the cumulative total number of squares throughout the test. They were instructed to report the total number of squares at the end of each Stroop task. This value was compared between Stroop 1 and 2. They were not told how many squares there were in the test, only that they were randomly generated. Counting squares tests the updating of working memory, while responding to the colour words tests inhibition of prepotent responses together with the delicate balancing of the speed-accuracy trade-off⁶⁴³.

Subjects used the index and middle fingers of each hand to press the response buttons (1 for red and 2 for blue with the left hand and 7 for green and 8 for yellow with the right hand) on an 8 button response box.

In total, 108 cues were randomly presented: 18 incongruent colour words in each of the 4 colours (72 incongruent words in total), 18 grey words and 18 white squares. The use of the grey words ensured that subjects had to read and recognize the colour words rather than just noticing the colours, thereby invoking the Stroop effect⁴³⁷.

2.3.2 Questionnaires used

Validated questionnaires were used to assess anxiety and relaxation states as this has been shown to increase the reliability of self-reported data⁶⁴⁴. State anxiety was assessed using the state component of the Spielberger State-Trait Anxiety Inventory (STAI-S) and trait anxiety using the trait component (STAI-T)⁶³⁶. Each component consists of 20 self-report items measured using a 4-point Likert scale ranging from 1 ('not at all') to 4 ('very much so'). This yields a total score which ranges from 20 to 80 points. The STAI-T/S is a commonly used measure of anxiety⁶⁴⁵ which shows good internal consistency and test-retest reliability across populations⁶⁴⁶.

Relaxation states were measured using the Smith Relaxation States Inventory 3 (SRSI3)⁶⁴¹. This consists of 38 self-report items measured using a 6-point Likert scale ranging from 1 ('not at all') to 6 ('maximum'), which are combined into 19 relaxation states each with a maximum score of 6. This yields a total relaxation states score which can range from 19 to 114. The 19 relaxation states are divided into 4 categories loosely based on factor analytic research⁶⁴⁷. The categories consist of mindfulness, energized positive feelings, basic relaxation and transcendence. Reliability for the SRSI3 has yet to be determined, but the previous version of the Smith Relaxation States Inventory

(excluding the 3 new subcategories of mindful acceptance, mindful centering and mindful awakening) has been shown to be reliable²⁰⁶.

2.3.3 Data recording

ECG activity was recorded from 3 electrodes (Blue Sensor, Ambu, Denmark) placed in positions representing Eindhoven's triangle: namely, sub-clavicular bilaterally and over the left anterior superior iliac crest. The skin surface was cleaned and gently abraded with an alcohol swab before electrodes were attached. Electrode cables were taped down to prevent movement artefact. ECG electrodes were connected to the Biopac ECG amplifier set to band-pass filter between 0.5 and 35 Hz (Biopac Inc. Application Note 233) and a sampling frequency of 1000 Hz. ECG recordings were analysed with AcqKnowledge for Macintosh OS X (version 3.9.0). This software used a modified Pan and Tompkins algorithm to detect QRS complexes. The filtered ECG recording tachograms were then visually inspected to determine the correct recognition of QRS complexes. Missed and ectopic beats were corrected by either adding or spacing beats. This procedure was only necessary in 2 of the 90 ECG recordings and only affected a total of 5 heart beats.

Only after each tachogram showed no spurious beats were the data analysed using HRV analysis software from the Biomedical Signal Analysis Group (Department of Applied Physics, University of Kuopio, Finland). RR interval data were transformed using Fast Fourier Transform to calculate components of spectral power within the low frequency (LF; 0.04 - 0.15 Hz), high frequency (HF; 0.15 - 0.4 Hz) and total frequency (TF; 0.005 – 0.4 Hz) bands^{15;228}. In addition, the program generated time-domain variables including mean HR, SDNN and RMSSD. The HRV power spectrum analysis during the intervention was conducted from minute 1 to minute 6 of the 10 minute session. This provided a 5 minute period as the standard time period of comparison in keeping with the recommendation that the optimal length of recording for short-term recordings is 5 minutes¹⁵.

The respiratory rate per minute was measured via a force transducer fixed to a belt placed around the chest wall. Subjects were asked to expel the air from their lungs when the transducer belt was first fitted and then instructed to breathe normally. The chest transducer was connected to an amplifier with a low-pass 10 Hz filter. Respiratory frequencies (RF), i.e. breaths per second, were calculated from the respiratory rate.

EEG was recorded from electrodes at Fp1, Fp2, Fz, Cz and Pz. A linked earlobe reference was used. EEG electrodes were connected to the Biopac EEG amplifier set to band-pass filter between 0.1 and 100 Hz and a sampling frequency of 500 Hz. EEG recordings were analysed with AcqKnowledge (Version 4.2). While EMG was not recorded, FFT of the raw data showed no peaks greater than 40 Hz suggesting that there were no large muscle contractions. Data were FIR band pass filtered using a Hamming window with a low frequency cut-off of 0.5 Hz, a high frequency cut-off of 30 Hz and the number of coefficients fixed at 4000. Eye blink/movement artefacts were identified using Fp1 and Fp2^{648;649} and the artefact-scored segments were eliminated from subsequent analysis. In addition, any segments containing voltages greater than 75 μV were rejected as artefacts and excluded as they were likely caused by spurious muscle contraction or artefact noise.

Data were excluded from two subjects, one from each group, for the duration of the testing, and from one subject from the COM group, for the intervention, as the sample lengths after artefact rejection were too short to accurately measure power in the frequency bands, and a sample size of at least 120 ms is required to measure alpha power accurately⁵⁷⁵. In addition, the Pz electrode in the data from one subject in each group malfunctioned.

Data were fast Fourier transformed using a Hamming window. Power spectral density ($\mu\text{V}^2/\text{Hz}$) in the theta (θ , 4 – 7 Hz), alpha (α , 7 – 14 Hz) and beta (β , 15 – 30 Hz) frequency bands^{465;477;650} were extracted using a Matlab program (Matlab, Mathworks, Version 7.11.0.584 (R2010b)) specifically designed for this process. There are many methods of calculating power. The calculation of power spectral density involves normalizing the data which yields absolute power values that may be lower than those found with other calculations. Relative power was calculated as it gives a better estimate of the dominant frequency changes⁴⁶⁰ as well as eliminating individual variations⁶⁵¹. It was calculated by dividing the absolute power in each band by the total power across all 3 bands and expressed as a percentage. In addition, theta/beta ratios were calculated.

2.4 STATISTICAL ANALYSIS

2.4.1 Subject characteristics

A comparison of subject characteristics between groups was analysed using an independent t – test.

2.4.2 Cognitive performance

Differences in reaction time between Stroop 1 and 2 were analysed using repeated measures analysis of variance. Specifically, differences in the main effects (group and time) and the interaction of group X time were determined. A Tukey's *post hoc* test was used to determine specific differences in the event of there being a significant main effect or interaction.

An independent t – test was used to analyse the percentage improvement in reaction time and percentage improvement in standard deviation of reaction time between Stroop 1 and 2. This last analysis was done in view of the wide range of standard deviation as a result of the different responses to different colours. This is an important finding and so it has been included; however, it is important to interpret the percentage improvement results with caution at the risk of making a type 1 error.

Levene's test of homogeneity revealed that the mistakes made in responding to cues during the Stroop task were of unequal variance, and thus non-parametric tests were used to determine differences with respect to the outcome measures. Accordingly the Friedman's analysis of variance for repeated measures was used to determine differences in values between tests. A Wilcoxon test was used to locate the specific differences when the overall value was significant and a Mann-Whitney test was used to compare values between groups.

2.4.3 HRV and respiratory data

As the sample size was relatively small and Levene's test of homogeneity revealed that the respiratory data and HRV measures were of unequal variance, non-parametric tests were used to determine differences with respect to the outcome measures. These have been described above in 2.4.2. Relationships between variability were determined by calculating Spearman's rank order correlation coefficients.

2.4.4 EEG

Data from during the intervention and during the rest periods were analysed separately, as the subject's eyes were closed during the rest periods and open during the intervention which would have altered the alpha power^{537;538} thus making comparisons misleading.

During the intervention, the comparison of absolute power, relative power and theta/beta ratios between groups were analysed using an independent t-test. Differences between relative power and theta/beta ratios during Rest 1 and Rest 2 were analysed using repeated measures analysis of variance (ANOVA). Specifically, differences in the main effects (group and time) and the interaction of group X time were determined. A Tukey's *post hoc* test was used to determine specific differences in the event of there being a significant main or interaction effect.

Levene's test of homogeneity revealed that the absolute power during Rest 1 and Rest 2 was of unequal variance; therefore non-parametric tests were used to determine differences with respect to the outcome measures. These have been described above in 2.4.2.

The relationships between the BIO intervention scores and measures of relative EEG and theta/beta ratios were determined by calculating Pearson's correlation coefficients. The relationships between BIO intervention scores and absolute EEG, between measures of EEG and measures of HRV, and between measures of EEG and respiratory frequency were determined by calculating Spearman's rank order correlation coefficients.

2.4.5 Questionnaires

Comparisons of STAIT and VAS scores between groups were analysed using an independent t – test. Differences in STAIS and SRSI3 scores between groups were analysed using repeated measures analysis of variance (ANOVA). Specifically, differences in the main effects (group and time) and the interaction of group X time were determined. A Tukey's *post hoc* test was used to determine specific differences in the event of there being a significant interaction effect.

Cohen's *d* effect sizes⁶⁵² were calculated on the STAIS, SRSI3 total scores and scores for the 4 major SRSI3 categories. Effect sizes were calculated using the formula $d = \text{mean (a)} - \text{mean (b)} / (\text{pooled variance of a and b})$. We regarded an effect size of 0.2 – 0.5 as having a small effect, 0.5 – 0.8 as

having a moderate effect and 0.8 or greater as having a large effect⁶⁵². Effect sizes of 0.5 or greater were regarded as meaningful.

Relationships between variability in the STAIT questionnaire and pre-testing STAIS questionnaire, as well as between changes in the STAIS and changes in SRSI3 scores, were determined by calculating the Pearson's correlation coefficients.

2.4.6 General

All parametric data are described as mean \pm standard deviation (SD) and non-parametric data as median and interquartile range (IQR). Correlations are expressed as r with the 95% confidence interval. A P value of < 0.05 was considered to be statistically significant. P values greater than 0.05 but approaching significance are reported as exact values.

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CHAPTER 3

THE EFFECT OF A SINGLE SESSION OF SHORT DURATION HRV BIOFEEDBACK ON COGNITIVE PERFORMANCE DURING LABORATORY INDUCED COGNITIVE STRESS

3.1 INTRODUCTION

Cognitive performance is affected by adverse psychological stress, potentially leading to decreased productivity. Chronic psychological stress leads to impaired general cognitive function^{130;131;144} specifically including impaired set shifting¹⁴⁶. Both acute¹³³ and chronic¹⁵⁷ stress result in impaired memory related to an increase in plasma cortisol concentrations^{130;131;140}. Stress impairs working memory linked to high cortisol concentrations¹⁴⁵ and has also been associated with greater error-related brain activity¹⁵¹.

Adverse chronic psychological stress also induces states of low HRV^{336;352;359;360}. While greater HRV has been associated with increased executive functioning including faster reaction times and more correct responses to cognitive tasks^{430;431}. The finding that increased HRV may be associated with improved cognitive performance, illustrates the importance of techniques which could counter the vagal lowering effects of chronic stress.

HRV biofeedback has been shown to increase HRV both during the intervention⁴⁴²⁻⁴⁴⁴ and immediately after the intervention^{443;444}, as well as decrease perceived stress¹⁹⁶. Only one study has examined the effect of HRV biofeedback on cognitive performance. The authors found a reduction in the errors made during a Stroop task, however, there was no difference between the HRV biofeedback group and a non-biofeedback concentrative control group¹⁹⁵. Therefore, the aim of this chapter was to examine the acute effect of 10 minutes of HRV biofeedback on cognitive performance during induced stress in the form of a modified Stroop task.

3.2 METHODS

The methodology for this chapter can be found in Chapter 2 . General methodology is described on pages 35 to 39, methodology regarding the modified Stroop task on pages 39 and 40, and statistics specific to cognitive performance on pages 43 and 45.

3.3 RESULTS

3.3.1 Subject characteristics

All subjects were employed at a senior to executive management level and had significant responsibility in terms of managing finances, people and/or projects. The exact nature of each job was different for each person, however, all were related to information systems, health and wellness, engineering or banking. All subjects were healthy and were not using psychotropic or heart rate altering medications, stimulants or recreational drugs.

The BIO and COM groups were similar in age (33 ± 6 vs. 34 ± 6 years respectively), body mass index (28.7 ± 6.8 vs. 27.2 ± 4.5 kg/m², respectively) and adherence to exercise training (3 ± 1 vs. 3 ± 1 units respectively) measured on a scale of 1 to 5 (1 = less than once a month, 5 = every day). There was no difference between groups in the STAIT questionnaire (48 ± 6 vs. 44 ± 7 units, BIO vs. COM).

3.3.2 Cognitive performance

Subjects were instructed to respond as fast and as accurately as possible. During any decision making task, subjects have to balance speed with accuracy (known as the speed-accuracy trade-off) and studies have shown that when subjects focus more on responding as fast as possible they make more mistakes, thereby sacrificing accuracy for speed^{642,653}.

The data from one subject in the COM group was excluded as the mistakes that he made during Stroop 2 were more than 3 standard deviations greater than the mean while all of the other subjects were within 1 standard deviation. Furthermore, he increased his reaction time more than any other subject and in response to some colours more than 2 standard deviations from the mean. This suggests that he was not as focused on minimising mistakes as the other subjects were, and thus was not performing optimally in the Stroop tasks. All of his Stroop data were excluded as the

changes in reaction time would have an impact on changes in his accuracy, since subjects balance speed and accuracy⁶⁴³. The data from 2 other subjects (one from each group) were missing as a result of failure of the recording equipment.

3.3.2.1 Mistakes made

A detailed analysis of the mistakes made by the subjects in the BIO and COM groups during the modified Stroop tasks before and after intervention is shown in Figure 3.1 below.

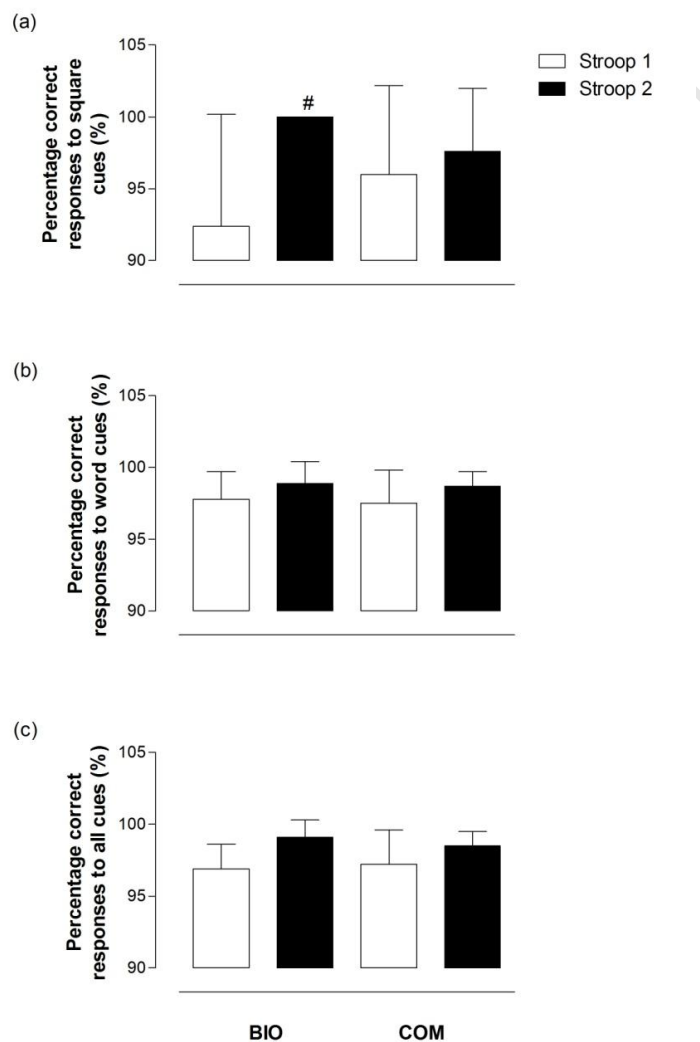


Figure 3.1 The percentage of correct responses to squares cues (a), word cues (b) and total cues (c) during the first and second modified Stroop tasks in the BIO and COM groups

BIO, biofeedback group; COM, comparative group

$P < 0.05$

BIO square mistakes Stroop 2 vs. BIO square mistakes Stroop 1

There were no differences in the total mistakes made in either group in identifying the 108 cues over time. By differentiating the mistakes made on identification of colour words from the mistakes made while counting the total number of squares it was determined that word mistakes were not significantly different pre- vs. post-intervention in either group. However, there was a significant difference in mistakes made in responding to squares. After the intervention no subject in the BIO group missed any squares (1 ± 1 vs. 0 squares missed, Stroop 1 vs. Stroop 2, $p < 0.05$), while subjects in the COM group missed as many squares after the intervention as they did before (1 ± 1 vs. 0 ± 1 squares missed, Stroop 1 vs. Stroop 2).

3.3.2.2 Reaction time

ANOVA showed a time effect with improved reaction time to all colours (BIO group: 1.16 ± 0.15 s vs. 0.98 ± 0.13 s, pre vs. post; COM group: 1.25 ± 0.20 s vs. 1.19 ± 0.23 s, pre vs. post; $p < 0.01$) and to grey colours (BIO group: 1.30 ± 0.21 s vs. 1.14 ± 0.21 s, pre vs. post; COM group: 1.26 ± 0.17 s vs. 1.27 ± 0.23 s, pre vs. post; $p < 0.05$), as well as an interaction effect with the BIO group improving more than the COM group in response to grey colours ($p < 0.05$). Tukey's *post hoc* test showed a decrease in reaction time in response to grey colours in the BIO group from Stroop 1 to Stroop 2 ($p < 0.05$). There was no group effect.

Figure 3.2 below shows each subject's average percentage improvement in reaction time to all colours and Figure 3.3 below shows each subject's average percentage improvement in reaction time to grey colours. When looking at the percentage improvement in reaction time, the BIO group improved significantly more than the COM group when responding to grey colours ($p < 0.05$) as well as to all colours ($p < 0.05$). It is interesting to note that all 8 of the BIO subjects improved their reaction time to all colours by more than 5%, while only 3 of the COM subjects improved their reaction time by more than 5%.

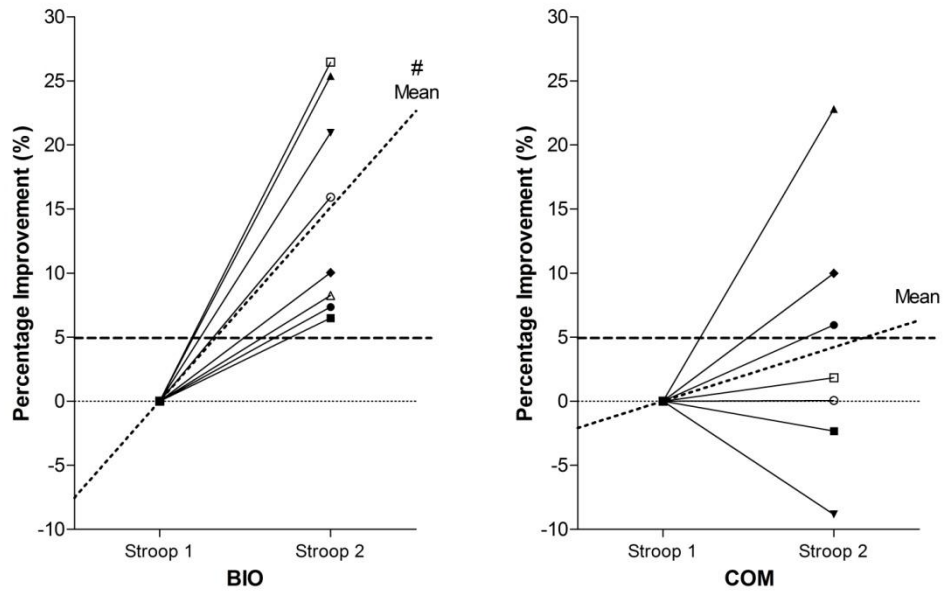


Figure 3.2 Individual subject's average percentage improvement in reaction time to all colours during the first and second modified Stroop tasks in the BIO and COM groups

BIO, biofeedback group; COM, comparative group

$P < 0.05$

BIO mean percentage improvement in reaction time vs. COM mean percentage improvement in reaction time

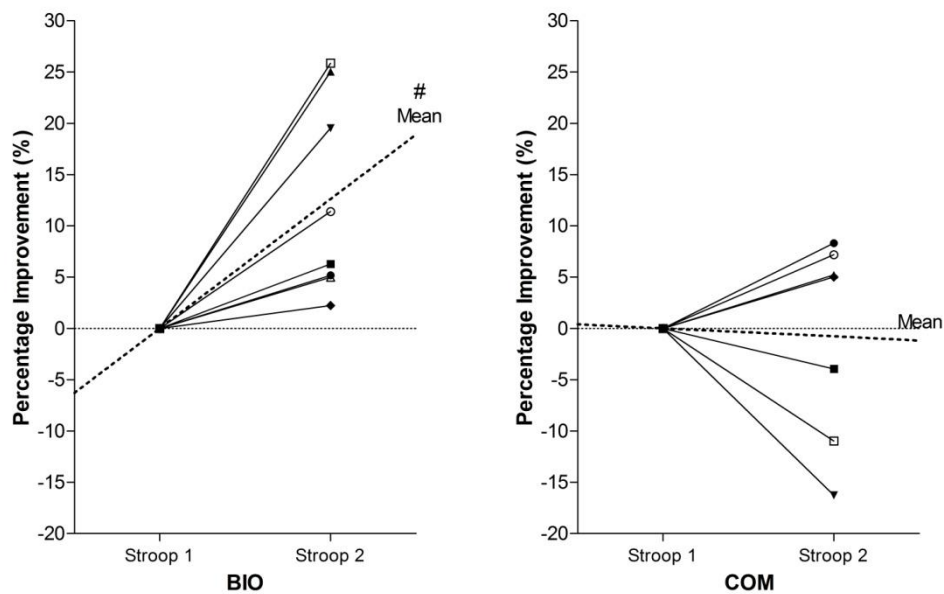


Figure 3.3 Individual subject's average percentage improvement in reaction time to grey colours during the first and second modified Stroop tasks in the BIO and COM groups

BIO, biofeedback group; COM, comparative group

$P < 0.05$

BIO mean percentage improvement in reaction time vs. COM mean percentage improvement in reaction time

Figure 3.4 below shows the percentage change in the standard deviation of the reaction time between Stroop 1 and Stroop 2. The BIO group significantly decreased the standard deviation of their reaction times to all colours compared to the COM group ($p < 0.05$). Furthermore, 7 of the BIO subjects had tighter standard deviation values in their reaction times compared to only 2 of the COM group.

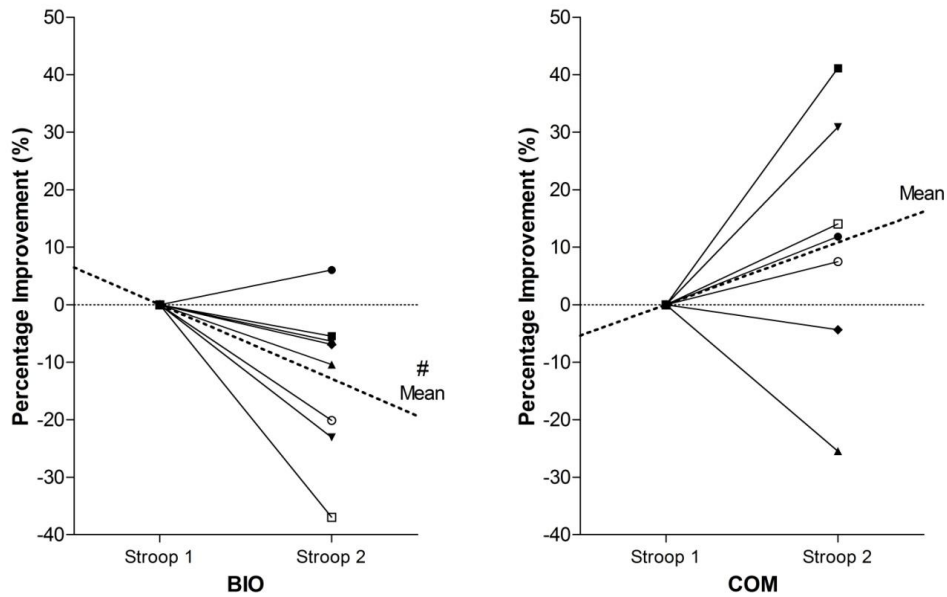


Figure 3.4 Individual subject's average percentage change in the standard deviation of their reaction time to all colours during the first and second modified Stroop tasks in the BIO and COM groups

BIO, biofeedback group; COM, comparative group

$P < 0.05$

BIO mean percentage change in the standard deviation of reaction time vs. COM mean percentage change in the standard deviation of reaction time

3.4 DISCUSSION

The key finding in this study was that the use of a short duration HRV biofeedback intervention resulted in improved cognitive performance during a modified Stroop task. This effect was not seen after the comparative intervention. Improvements in cognitive performance were evidenced by increased speed and consistency of reaction times after the intervention as well as fewer mistakes made in counting the number of square cues.

Factors influencing cognitive performance and mistakes made are complex. The modified Stroop task provided a complex cognitive challenge which included 3 elements of executive functioning: updating of working memory, mental set shifting and inhibition of prepotent responses⁶⁵⁴. Counting squares entails updating information in working memory, mental set shifting occurs when subjects shift from counting squares to responding to the colour words and inhibition of prepotent responses occurs when subjects react to the colour rather than to the word.

Both groups improved their reaction time from Stroop 1 to Stroop 2. This improvement is unlikely to be due to the learning effect of the Stroop task, as a previously completed validation trial showed a learning effect between the first and second modified Stroop task but not between the second and third⁶⁴². For this reason we used a familiarisation Stroop task as the first task. Furthermore, ANOVA showed that the BIO group improved significantly more than the COM group, reinforcing that this improvement did not result from a learning effect.

The standard deviation of the reaction time to cues in the BIO group decreased after the intervention while the standard deviation of the COM group increased. This shows that the BIO group were more consistent in their responses during the Stroop task after the intervention compared to before the intervention.

While there were no differences in mistakes made in responding to words in either group, there were differences in the mistakes made in counting squares. None of the BIO subjects missed any of the squares after the intervention resulting in a significant improvement; however, the COM subjects missed as many squares after the intervention as before. This strongly suggests working memory enhancement in the BIO, but not in the COM subjects. All of these improvements in

cognitive performance suggest that the BIO subjects were more focused, while the COM subjects may have allowed their attention to wander somewhat more.

There is a balance between speed and accuracy when responding to a Stroop task^{642;653}. In a previous validation trial Rauch et al⁶⁴² showed that some subjects were more intent on obtaining a faster reaction time while others seemed to be more concerned with accuracy and so sacrificed speed. This resulted in an inverse relationship between reaction time and number of mistakes made. Subjects were consistent in the number of mistakes that they made – whether high or low - in response to a modified Stroop task on 2 separate days. These subjects could generally tell how many mistakes they made, but they did not have a clear idea about their reaction time (unpublished observations).

In this regard, Mayes and co-workers found that 7 – 9 year old children, who were cocaine exposed prenatally, reacted significantly slower than non-drug-exposed matched controls during a Stroop task; however, they did not make more mistakes in responding to the colour words (2% vs. 3%). Thus, even though the cortical processing speed of the cocaine exposed children was impaired, they merely slowed their reaction time to keep their mistakes in line with controls⁶⁵⁵.

This study also demonstrated that the mistakes made in responding to colour words were in the range of 1 – 3 %. While most of the subjects increased their reaction time in the post-intervention Stroop task (except for 2 COM subjects), they made a similar amount of mistakes in responding to words. This suggests that there is a range of mistakes, remarkably similar throughout the above studies, that subjects are comfortable with, and that they adjust their reaction times to accommodate this range. However, it is important to note that the subjects in the BIO group decreased their reaction time more than the COM group, while not increasing the amounts of mistakes made, indicating improved cognitive performance.

The increased cognitive performance evident after HRV biofeedback may be related to improved HRV together with changes in EEG. HRV biofeedback resulted in increased HRV, which has been shown to lead to improved cognitive performance^{430;431}. Thayer and Lane describe a neurovisceral integration theory, in which HRV influences neural structures which impact cognitive performance^{702;703}. Increasing HRV would therefore lead to improved performance⁷⁰⁶. While both groups experienced vagal withdrawal in response to stress, the patterns of vagal modulation in each group were different. It is tempting to speculate that this may have contributed to the differences in

cognitive performance between groups. According to Porges' polyvagal theory, the pattern of vagal withdrawal evident in the BIO group would allow effective social engagement in a stressful environment, which increases the ability to function successfully and perform well^{319;324}. These results are described and discussed in full in Chapter 4.

EEG changes during and after HRV biofeedback were suggestive of increased attention together with increased relaxation (described in Chapter 5). It is possible that increased attention led to the improved cognitive performance seen in the BIO group. Finally, the BIO group felt alert and relaxed, and had greater increases in mindfulness and energized positive feelings (results described in Chapter 6). Increased mindfulness has been associated with a state of relaxed alertness²⁰⁰, and both mindfulness and positive emotions are associated with improved attention and cognitive performance^{675-677;683;684}.

It is of interest to note that the above cognitive improvements were witnessed after only a 10 minute intervention. We were specifically interested in the acute effect of 10 minutes of biofeedback, as this is the period recommended for clinical use. The minimum recommended time per session is 5 minutes with a goal to accumulate a total of 20 minutes per day⁶³⁵. The intention is to create a device that could be used easily for short periods of time as needed throughout the day.

Importantly, the results of this study perhaps fail to reflect the magnitude of the effect which might become evident with a longer duration intervention or indeed regular training with the intervention.

3.5 CONCLUSION

In conclusion, the use of a short duration HRV biofeedback intervention resulted in improved cognitive performance. Reaction time was improved and more consistent, and there was a reduction in mistakes made in counting squares during a modified Stroop task.

Chapter 4 will evaluate the changes in HRV that occur during HRV biofeedback, in the immediate post-biofeedback period and during the Stroop task. This provides insight into underlying physiological changes that may contribute to the improvements in cognitive performance.

CHAPTER 4

THE EFFECT OF A SINGLE SESSION OF SHORT DURATION HRV BIOFEEDBACK ON MEASURES OF HRV DURING LABORATORY INDUCED COGNITIVE STRESS

4.1 INTRODUCTION

Autonomic nervous system modulation during stress and its effect on health and disease has recently been a topic of much debate. Occupational (work related) stress decreases HRV^{212;336;352} and is associated with increased risk of chronic disease^{92;656} as well as impaired cognitive function^{130;144}. The previous chapter demonstrated that the use of HRV biofeedback-induced breathing at 0.1 Hz resulted in improved cognitive performance. There is a strong link between changes in measures of HRV and changes in cognitive performance, with high HRV correlating with improved executive functioning^{430;431}. Furthermore, HRV biofeedback has been shown to reduce stress and anxiety^{196;199}.

HRV biofeedback guides the user to breathe at the optimal respiratory frequency to maximally increase their HRV. During HRV biofeedback there is an acute increase in baroreflex gain^{443;445}, SDNN⁴⁴⁴, and TF⁴⁴²⁻⁴⁴⁵ and LF power^{442-445;456} in the cardiac spectrogram, indicative of increased vagal modulation of the heart^{443;444}.

The majority of studies focus primarily on clinical outcomes and, therefore, the long term effect of HRV biofeedback over sessions, rather than the acute effects. The few studies that have examined the short-term carry-over effect showed that the increased vagal stimulation of the heart seen during biofeedback persisted into the period immediately following the biofeedback as evidenced by an increase in SDNN⁴⁴⁴, LF power⁴⁴⁴ and baroreflex gain^{442;443}. No studies have examined changes in HRV during stress after biofeedback.

Therefore, the aim of this chapter is to examine the acute effect of 10 minutes of HRV biofeedback on measures of HRV during the use of the intervention, in the immediate post-biofeedback period and during the following laboratory induced stress.

4.2 METHODS

The methodology for this chapter can be found in Chapter 2 . General methodology is described on pages 35 to 39, methodology regarding the measurement and analysis of HRV and respiration on page 41, and statistics specific to analysis of HRV and respiration on pages 43 and 45.

4.3 RESULTS AND DISCUSSION

The novel finding of this study is the presence of a short-term carry-over effect after HRV biofeedback that modified the physiological response during both the 5 min rest period and the following 5 min laboratory induced stress. This effect was evidenced by an unchanged heart rate, RMSSD and HF power in Stroop 2 relative to the preceding rest period, indicative of maintained HF vagal control of the heart and concurrent LF vagal withdrawal when shifting from rest to stress.

HRV data during Rest 1 were compared with normative data described by Nunan et al ⁷¹⁰. The SDNN, RMSSD and absolute HF power data were within the normal range and medians were similar to the medians described ⁷¹⁰. The median of the LF data was just outside the upper limit of the normative data. A potential explanation could be that the subjects experienced psychological stress related to the upcoming Stroop task which led to an increase in LF power ^{212;225;352;359}.

4.3.1 Normal response to stress

When an individual is exposed to acute stress the sympathetic nervous system becomes more active ⁶⁵⁷. Respiratory rate ⁶⁵⁸ and heart rate increase ^{352;368}, and LF power ²¹², HF power ^{352;356}, SDNN ³⁵² and RMSSD ³⁵³ decrease.

The findings of this study were in accordance with these physiological changes. During Rest 1 prior to the first Stroop task, while RF was lower in the BIO group than the COM group ($p < 0.05$), there were no differences in HR or any of the measures of HRV. During the first Stroop task there were no differences between groups and both groups responded similarly to stress: respiratory frequency (BIO $p < 0.05$, COM $p < 0.01$) and heart rate (BIO $p < 0.05$, COM $p < 0.05$) increased, and TF (BIO $p < 0.05$, COM $p < 0.05$) and LF power (BIO $p < 0.05$, COM $p < 0.05$) decreased. HF power decreased in both groups with the BIO group attaining statistical significance (BIO $p < 0.05$, COM $p = 0.08$), and RMSSD decreased in both groups with the COM group attaining significance (COM $p < 0.05$, BIO $p = 0.05$).

SDNN reflects all cyclic components responsible for the variability during the recording¹⁵, therefore as TF power decreased one would have expected SDNN to decrease. While SDNN did decrease in both groups, this decrease did not reach significance due to the large inter-subject variability. These results are shown in the first 2 data columns of Table 4.1, and the changes in RMSSD are further elaborated in Figure 4.1 and TF, HF and LF power in Figure 4.2.

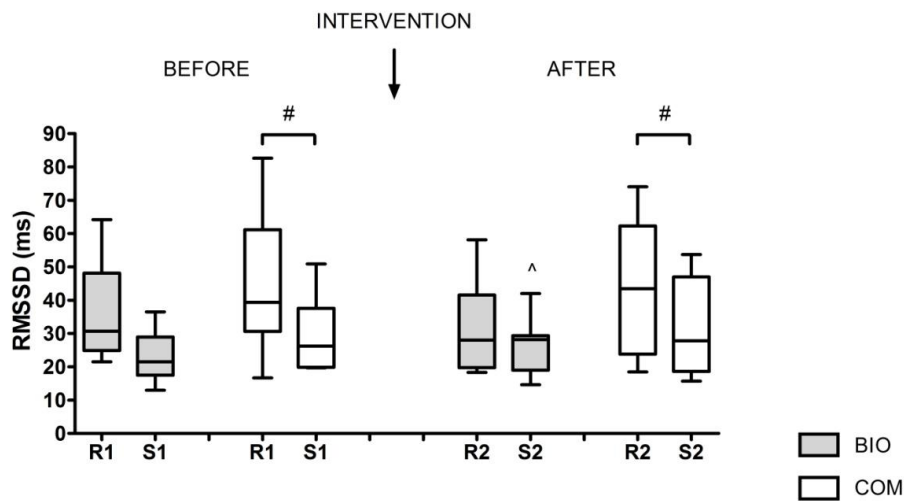


Figure 4.1 RMSSD during Rest 1 (R1) and Stroop 1 (S1) (before the intervention) and during Rest 2 (R2) and Stroop 2 (S2) (after the intervention) in the BIO (n=9) and COM (n=9) groups

BIO = biofeedback group; COM = comparative group; RMSSD = root mean square of the successive differences; ms = milliseconds

Time effect between Rest 1 and Stroop 1 (Wilcoxon): # $P < 0.05$ COM RMSSD
Time effect between Rest 2 and Stroop 2 (Wilcoxon): # $P < 0.05$ COM RMSSD
Time effect between Stroop 1 and Stroop 2 (Wilcoxon): ^ $P < 0.05$ BIO RMSSD

Table 4.1 Respiratory frequency, heart rate and heart rate variability measures throughout testing in the BIO (n = 9) and COM (n = 9) groups. Data are expressed as medians with interquartile ranges in brackets.

Variable	Group	Rest 1	Stroop 1	Intervention	Rest 2	Stroop 2
RF (Hz)	BIO	0.16 (0.14 – 0.20) *	0.34 (0.30 – 0.38) #	0.10 (0.10 – 0.12) ***,#	0.14 (0.12 – 0.18) **,#	0.33 (0.28 – 0.39) #
	COM	0.27 (0.20 – 0.29)	0.33 (0.28 – 0.33) ##	0.27 (0.23 – 0.29)	0.25 (0.23 – 0.29)	0.32 (0.30 – 0.33) ##
HR (b/min)	BIO	68 (67 – 76)	79 (71 – 81) #	73 (70 – 78) #	68 (66 – 75) ##	68 (66 – 77) ^^
	COM	68 (60 – 70)	74 (73 – 76) #	67 (60 – 69)	66 (59 – 68) #	67 (63 – 73) #, ^^
TF (ms²)	BIO	2636 (1851 - 4314)	957 (822 – 1534) #	5834 (2971 – 7479) *	2344 (1713 – 3626) #	1353 (1124 – 1549) #
	COM	2415 (1825 – 3021)	1437 (636 – 1690) #	2381 (943 – 3552)	2428 (1443 – 3704)	2053 (606 – 2336) #
HF (ms²)	BIO	543 (172 - 708)	161 (116 – 213) #	195 (100 – 342) #	162 (114 – 301)	196 (167 – 227)
	COM	556 (306 – 744)	172 (156 – 392)	344 (241 – 491)	437 (217 – 1021)	451 (178 – 548)
LF (ms²)	BIO	1301 (889 – 1721)	399 (350 – 686) #	5159 (2719 – 7009) ***,#	1132 (669 – 2679) ##	532 (482 – 667) #
	COM	1013 (975 – 1867)	320 (229 – 766) #	863 (540 – 1037)	807 (623 – 1303)	740 (254 – 1361)
SDNN (ms)	BIO	55.6 (47.7 – 57.8)	48.7 (42.0 – 50.6)	74.8 (58.9 – 92.8) *	48.4 (44.6 – 65.0) #	42.9 (38.7 – 49.7)
	COM	51.5 (47.7 – 72.6)	41.0 (33.4 – 61.1)	48.8 (35.7 – 58.9)	50.5 (49.0 – 65.3)	46.0 (34.0 – 60.2)
RMSSD (ms)	BIO	30.7 (27.3 – 47.2)	21.5 (18.8 – 28.5)	40.0 (28.5 – 57.1)	28.0 (19.9 – 38.1) #	28.2 (22.4 – 28.9) ^
	COM	39.4 (33.4 – 53.4)	26.2 (19.9 – 34.6) #	30.5 (26.1 – 58.1)	43.4 (25.4 – 58.5)	27.8 (19.0 – 42.2) #

BIO = biofeedback group; COM = comparative group; RF = respiratory frequency; Hz = Hertz; HR = heart rate; b/min = beats per minute; TF, HF and LF = power of the RR interval spectrum in total frequency, high frequency and low frequency ranges respectively; ms² = milliseconds squared; SDNN = standard deviation of the normal to normal RR intervals; ms = milliseconds; RMSSD = root mean square of successive differences of RR intervals.

Time effect between Rest 1 and Stroop 1 (Wilcoxon)

$P < 0.05$ BIO RF, BIO HR, COM HR, BIO TF, COM TF, BIO HF, BIO LF, COM LF, COM RMSSD

$P < 0.01$ COM RF

Time effect between Rest 1 and Intervention (Wilcoxon)

$P < 0.05$ BIO RF, BIO HR, BIO HF, BIO LF

Time effect between Intervention and Rest 2 (Wilcoxon)

$P < 0.05$ BIO RF, COM HR, BIO TF, BIO SDNN, BIO RMSSD

$P < 0.01$ BIO HR, BIO LF

Time effect between Rest 2 and Stroop 2 (Wilcoxon)

$P < 0.05$ BIO RF, COM HR, BIO TF, COM TF, BIO LF, COM RMSSD

$P < 0.01$ COM RF

Time effect between Stroop 1 and Stroop 2 (Wilcoxon)

^ $P < 0.05$ BIO RMSSD

^^ $P < 0.01$ BIO HR, COM HR,

Group effect (Mann-Whitney)

* $P < 0.05$ BIO Rest 1 RF vs. COM Rest 1 RF, BIO Intervention TF vs. COM Intervention TF, BIO Intervention SDNN vs. COM Intervention SDNN

** $P < 0.01$ BIO Intervention LF vs. COM Intervention LF, BIO Rest 2 RF vs. COM Rest 2 RF

*** $P < 0.0001$ BIO Intervention RF vs. COM Intervention RF

(Time effects between Rest 1 and Stroop 2, Stroop 1 and Intervention, Stroop 1 and Rest 2, and Intervention and Stroop 2 are not shown as they are not relevant to our interpretation.)

4.3.2 Effects of intervention

Respiration causes a corresponding cyclical change in heart rate that is known as respiratory sinus arrhythmia (RSA) ^{659;660}. The amplitude of RSA is maximal when there is resonance between the respiratory oscillations and the baroreflex induced Mayer wave oscillations ¹⁴. The frequency at which this occurs is known as resonance frequency ²⁸⁷ and generally occurs at about 0.1Hz or 6 breaths/minute ^{226;299} which is the respiratory frequency seen in response to biofeedback in this study. RSA is thought to be mediated almost exclusively by parasympathetic activity ^{229;306}, and increases as a result of increased cardiac vagal stimulation ^{229;230}.

Previous studies have shown that HRV biofeedback-induced breathing at around 0.1Hz results in an increase in LF power, TF power ⁴⁴²⁻⁴⁴⁴ and SDNN ⁴⁴⁴, with either no change ^{442;444} or a decrease ⁴⁴³ in HF power. In addition, a non-significant increase in HR has been documented ⁴⁴⁴.

The changes observed in the BIO group were in keeping with these findings. Compared to Rest 1, RF decreased ($p < 0.05$) to 0.1 Hz during the intervention, and LF power increased ($p < 0.05$), TF power increased approaching significance ($p = 0.09$) and HR increased ($p < 0.05$), while HF power decreased ($p < 0.05$). Both SDNN and RMSSD increased but did not reach significance due to the large inter-subject variability. Similar changes were observed in comparison to the COM group. The BIO group had a lower respiratory frequency ($p < 0.001$) and higher LF power ($p < 0.01$), TF power ($p < 0.05$) and SDNN ($p < 0.05$) than the COM group. No differences were found in HR, HF power or RMSSD between groups, and the COM group showed no change from Rest 1. It is worth noting that despite the decrease in respiratory frequency, the BIO subjects were able to maintain vagal activity in the HF range. These results are shown in the 3rd data column in Table 4.1.

The RSA-induced increase in LF power during biofeedback reflects increased direct cardiac parasympathetic activity ^{271;276}. RMSSD also reflects the degree of cardiac vagal control and has a high correlation with HF power in the cardiac spectrogram ^{15;215}. It is therefore interesting that the RMSSD tended to increase while the HF power decreased.

4.3.3 Rest after intervention

After the HRV biofeedback intervention we found a carry-over effect with a trend to greater vagal withdrawal in Rest 2 in comparison to Rest 1 as well as in comparison to the COM group in Rest 2. The results during Rest 2 are shown in the 4th data column of Table 4.1. In comparison to the

preceding intervention, in the BIO group respiratory frequency ($p<0.05$) increased, and HR ($p<0.01$), LF power ($p<0.01$), TF power ($p<0.05$) and SDNN ($p<0.05$) decreased. Furthermore, it is interesting that while HF power remained unchanged, RMSSD decreased ($p<0.05$). This illustrates that while RMSSD is more sensitive to changes in HF power, it is also impacted by large changes in LF power. The COM group showed no change from the intervention to Rest 2.

Respiratory frequency, HR and all measures of HRV in both groups during Rest 2 were not different from Rest 1, except for a strong trend for RMSSD to be lower after the intervention in the BIO group ($p=0.05$). There was also a strong trend for HF power to be lower in the BIO than in the COM group ($p=0.06$) after the intervention, both indicative of a shift in vagal modulation from HF to LF in the BIO group. The ability to effectively withdraw cardiac vagal activity is known as the vagal brake³²⁴ and allows healthy adaptive flexible behaviour³²³. Lastly, respiratory frequency was lower in the BIO group than in the COM group ($p<0.01$) while no other changes were evident between groups.

Studies have shown that the increase in baroreflex gain seen during HRV biofeedback persists into the immediate post biofeedback period⁴⁴³ resulting in increased LF power and increased SDNN⁴⁴⁴ even when respiration rate is accounted for⁴⁴³. However, in keeping with our study, others have shown no carry over effect with respect to LF, HF or TF power⁴⁴².

4.3.4 Response to cognitive stress after the intervention

The results from Stroop 2 are shown in Table 4.1, Figure 4.1 and Figure 4.2. While there were no differences between groups in RF, HR or any measures of HRV during Stroop 2, there was evidence for a carry-over effect when these groups are assessed over time and intervention.

During Stroop 1, RF and HR increased, TF and LF power decreased, and RMSSD and HF power either decreased or showed a strong trend to decrease in both groups. After the intervention during Stroop 2, the COM group responded similarly with an increase in RF ($p<0.01$) and HR ($p<0.05$), a decrease in TF power ($p<0.05$) and RMSSD ($p<0.05$) and a trend towards a decrease in HF power ($p=0.07$), however there was no change in LF power. In the BIO group, RF increased ($p<0.05$), TF power ($p<0.05$) and LF power decreased ($p<0.05$), however, HR, RMSSD and HF power remained unchanged.

These findings indicate that while both groups experienced vagal withdrawal in response to stress, there was evidence for different patterns of vagal modulation in each group. It is possible that these different patterns occur as a result of different physiological pathways. Porges³¹⁹ has identified 2 different branches of the vagus which have different physiological effects on the heart: a myelinated branch originating from the nucleus ambiguus which is important in social communication and is highest in the phylogenetic hierarchy, and an unmyelinated branch originating in the dorsal motor nucleus of the vagus which causes immobilization. Inhibition of the myelinated branch causes increased HR and decreased HF without change in LF (similar to the pattern seen in the COM group), while inhibition of the unmyelinated path may reduce LF with no change to HF power (similar to the pattern seen in the BIO group)³¹⁹.

Importantly the carry over effect seen during Stroop 2 in the BIO group occurs in part as a result of a relatively greater vagal withdrawal in Rest 2 as discussed above. In comparison to Stroop 1, HR was lower in both groups (BIO $p < 0.01$, COM $p < 0.01$) and RMSSD higher in the BIO group only ($p < 0.05$). This suggests less HF vagal withdrawal during stress after the intervention²²⁰ in the BIO group and, in effect, a reverse of the shift in vagal modulation seen in Rest 2 from LF back to HF.

Breathing at 0.1 Hz leads to increased HRV as a result of a combination of mechanisms including gating of preganglionic vagal cardiac neural activity²⁸⁹ in response to central oscillations²⁹⁰, pulmonary and atrial stretch reflexes^{237;272} and resonance with the arterial baroreflex loop^{246;274;291-293}. One might speculate that activation of these mechanisms led to changes in the central structures involved in the autonomic regulation of HRV, which persisted into the post-intervention periods. This may have accounted for the proposed shift in activity from the unmyelinated vagus to the myelinated vagus, resulting in increased autonomic flexibility and increased ability to adapt and respond to environmental demands such as the Stroop task.

The neural structures involved in the autonomic regulation of HRV are linked together with structures involving cognitive and affective regulation^{702;704;705}. Through this bidirectional system, improved regulation of HRV could result in improved cognitive performance⁷⁰². It is, therefore, tempting to speculate that the different patterns of vagal withdrawal in each group may have contributed to the differences in cognitive performance between groups demonstrated in Chapter 3, as well as the differences in alertness between groups demonstrated in Chapter 6.

4.4 CONCLUSION

A single episode of short duration biofeedback resulted in a short term carry-over effect after biofeedback that modified the physiological response during both the 5 min rest period and the following laboratory induced stress. While both groups demonstrated evidence for vagal withdrawal in response to induced stress, the pattern of vagal modulation in each group differed. The BIO group maintained HF power and RMSSD in Stroop 2 relative to the preceding rest period despite decreased TF and LF power, while the COM group maintained LF power despite decreased TF and HF power.

Chapter 5 examines the changes in EEG that occur during and immediately after HRV biofeedback.

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CHAPTER 5

THE EFFECT OF A SINGLE SESSION OF SHORT DURATION HRV BIOFEEDBACK ON EEG

5.1 INTRODUCTION

Extreme and chronic stress leads to increased anxiety⁶⁶¹. Changes in EEG are evident in anxiety, as well as during relaxation and meditation. Frontal theta power reflects alterations in autonomic nervous system activity^{194;373;586;597}, and increases with relaxation⁵⁸⁰⁻⁵⁸² and decreased anxiety^{194;583-585}. In addition, relaxation causes a decrease in beta power⁵⁸². During meditation, theta power also increases both in the frontal midline areas^{194;598;602}, and globally⁶⁰⁸. While many studies have shown an increase in alpha power^{373;598;619;620}, others have found this only in advanced practitioners^{600;617;626}.

HRV biofeedback can be viewed as a form of concentrative meditation, which involves focusing on specific mental or sensory activities¹⁷⁰, in this case the breath. However, biofeedback is different in that in addition to observing the breath, one is actively controlling it in response to an external biofeedback stimulus. One of the key psychological factors contributing to successful meditation is attention^{173;613}. Two different attentional networks have been described: an anterior network involving the detection of sensory targets and a posterior network involving the orienting of sensory attention⁵²². Changes in EEG theta, alpha and beta power, and theta/beta ratios reflect these changes in attention and relaxation.

Observing changes in EEG during and after HRV biofeedback may contribute to understanding the mechanisms contributing to the improved performance shown in Chapter 3, the changes in HRV shown in Chapter 4 and the reduction in anxiety and increased perceived relaxation shown in Chapter 6. While the majority of HRV biofeedback studies use the conventional training protocol as described by Lehrer et al⁶³⁴, the aim of this chapter is to examine the acute effect of a single 10 minute HRV biofeedback intervention on power in the theta, alpha and beta frequency bands and theta/beta ratios during the use of the intervention, and in the immediate post-biofeedback period.

5.2 METHODS

The methodology for this chapter can be found in Chapter 2 . General methodology is described on pages 35 to 39, methodology regarding the measurement and analysis of EEG on page 42, and statistics specific to the EEG analysis on pages 44 and 45.

5.3 RESULTS

5.3.1 BIO intervention scores

During the training session, scores for the BIO intervention were 41 ± 7 points, with 8 of the 9 subjects having a score above 30 and a lowest score of 29. During testing the scores were 46 ± 5 points with all scores above 30 and a lowest score of 38. A score of 30 or more is indicative of a successful session.

5.3.2 EEG measures

5.3.2.1 Intervention

There were no differences in absolute power between groups during the intervention (Table 5.1).

Table 5.1 Absolute power in theta, alpha and beta EEG bands at Fz, Cz and Pz during the intervention in the BIO and COM groups (n = 8 in each group at Fz and Cz, n = 7 in each group at Pz). Data are expressed as medians with interquartile ranges in brackets.

Variable	Position	BIO	COM
Theta power ($\mu\text{V}^2/\text{Hz}$)	Fz	0.046 (0.038 – 0.049)	0.047 (0.024 – 0.053)
	Cz	0.045 (0.037 – 0.049)	0.044 (0.026 – 0.052)
	Pz	0.038 (0.032 – 0.040)	0.046 (0.029 – 0.048)
Alpha power ($\mu\text{V}^2/\text{Hz}$)	Fz	0.064 (0.053 – 0.070)	0.076 (0.047 – 0.088)
	Cz	0.065 (0.057 – 0.074)	0.085 (0.046 – 0.094)
	Pz	0.063 (0.056 – 0.074)	0.104 (0.059 – 0.119)
Beta power ($\mu\text{V}^2/\text{Hz}$)	Fz	0.067 (0.056 – 0.074)	0.086 (0.063 – 0.090)
	Cz	0.074 (0.057 – 0.083)	0.082 (0.064 – 0.097)
	Pz	0.064 (0.050 – 0.081)	0.086 (0.064 – 0.091)

BIO = Biofeedback group; COM = comparative group; $\mu\text{V}^2/\text{Hz}$ = microvolt squared per Hertz.

Differences in relative power and the theta/beta ratio in the different frequency bands are shown in Figure 5.1. During the intervention relative theta power was higher in the BIO group than the COM group at Fz ($p < 0.01$), Cz ($p < 0.05$) and Pz ($p < 0.01$). There were no differences in relative alpha power. Relative beta power was lower in the BIO group at Fz ($p < 0.05$) and Cz ($p < 0.05$), with no difference at Pz. In addition, the theta/beta ratio was higher in the BIO than the COM group at Fz ($p < 0.01$), Cz ($p < 0.01$) and Pz ($p < 0.05$).

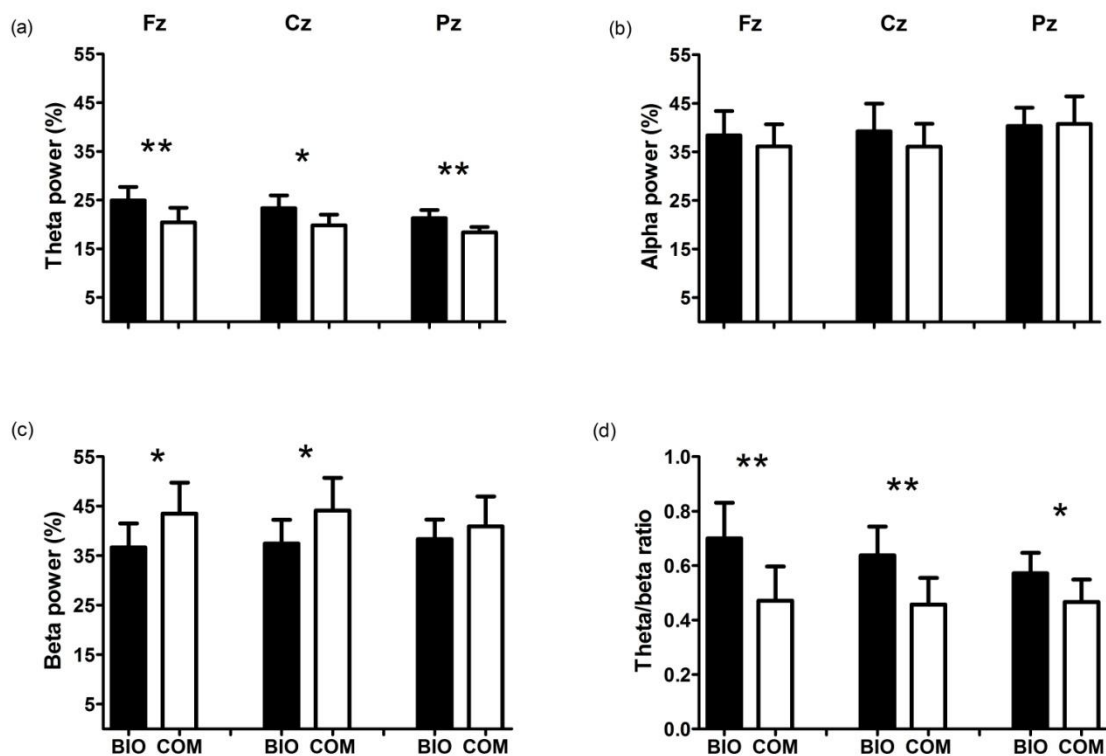


Figure 5.1 Relative theta (a), alpha (b) and beta power (c) and theta/beta ratios (d) at Fz, Cz and Pz during the intervention in the BIO and COM groups (n = 8 in each in group at Fz and Cz, n = 7 in each group at Pz)

BIO = biofeedback group; COM = comparative group; % = percentage.

* $P < 0.05$ BIO Cz theta power vs. COM Cz theta power, BIO Fz beta power vs. COM Fz beta power, BIO Cz beta power vs. COM Cz beta power, BIO Pz theta/beta ratio vs. COM Pz theta/beta ratio

** $P < 0.01$ BIO Fz theta power vs. COM Fz theta power, BIO Pz theta power vs. COM Pz theta power, BIO Fz theta/beta ratio vs. COM Fz theta/beta ratio, BIO Cz theta/beta ratio vs. COM Cz theta/beta ratio

During the intervention RF correlated negatively with % theta at Fz ($r=-0.79$ (-0.93 to -0.45), $p<0.001$), Cz ($r=-0.76$ (-0.92 to -0.40), $p<0.005$) and Pz ($r=-0.73$ (-0.92 to -0.28), $p<0.01$), as well as with theta/beta ratios at Fz ($r=-0.66$ (-0.88 to -0.2), $p<0.01$), Cz ($r=-0.72$ (-0.90 to -0.32), $p<0.01$) and Pz ($r=-0.58$ (-0.86 to -0.02), $p<0.05$). RF correlated positively with % beta at Fz ($r=0.54$ (0.02 to 0.83), $p<0.05$) and Cz ($r=0.53$ (0.01 to 0.83), $p<0.05$). Both LF and TF power correlated positively with Pz % theta ($r=0.59$ (0.03 to 0.87), $p<0.05$, and 0.57 (0.11 to 0.86), $p<0.05$, respectively). In the BIO group, the BIO intervention score correlated positively with the Fz % theta ($r=0.77$ (0.14 to 0.96), $p<0.05$).

5.3.2.2 Rest 1 vs. Rest 2

Absolute power values during Rest 1 and 2 are shown in Figure 5.2 below. While there were no differences between groups in Rest 1, during Rest 2 Fz beta tended to be lower in the BIO than the COM group ($p=0.06$). There were no differences in any of the absolute power values between Rest 1 and Rest 2 in the BIO group, while in the COM group all values increased ($p<0.05$).

Differences in relative power are shown in Table 5.2 below. There were no differences in either of the 2 main effects (group and time) for any variable. There was an interaction effect (group x time) in relative theta power at Pz ($p<0.05$) suggesting that the two groups responded differently over time. The Tukey's *post hoc* test, however, failed to detect any specific differences. In addition, there was an interaction effect (group x time) in relative beta power at Cz that approached significance ($p=0.06$). No differences were found in relative theta power at Fz or Cz, in relative alpha power at any location, or in relative beta power at Fz or Pz for any main effect or interaction.

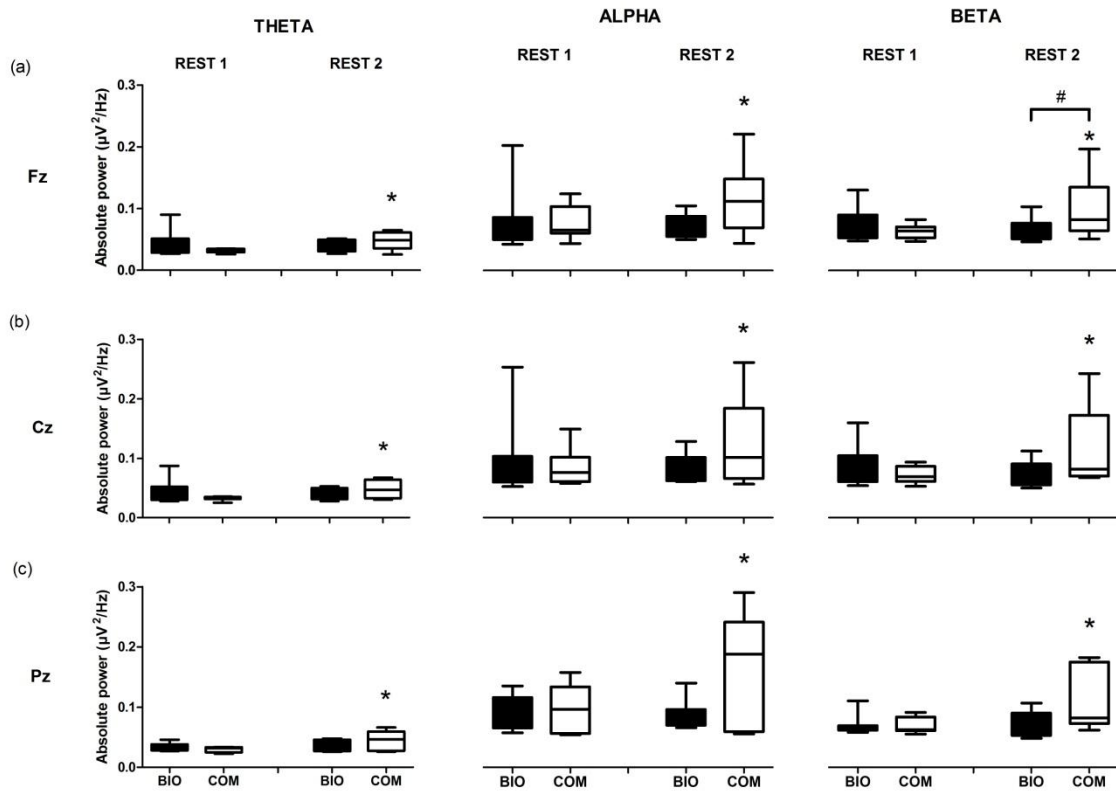


Figure 5.2 Absolute theta, alpha and beta power during Rest 1 and Rest 2 at Fz (a), Cz (b) and Pz (c) in the BIO and COM groups (n = 8 in each group at Fz and Cz, n = 7 in each group at Pz)

BIO = biofeedback group; COM = comparative group; $\mu\text{V}^2/\text{Hz}$ = microvolt squared per hertz.

Time effect between Rest 1 and Rest 2 (Wilcoxon)

* $P < 0.05$ COM Fz theta, COM Fz alpha, COM Fz beta, COM Cz theta, COM Cz alpha, COM Cz beta, COM Pz theta, COM Pz alpha, COM Pz beta.

Group effect (Mann-Whitney)

$P = 0.06$ BIO Rest 2 Fz beta vs. COM Rest 2 Fz beta

Table 5.2 Relative power in theta, alpha and beta EEG bands at Fz, Cz and Pz during Rest 1 and Rest 2 in the BIO and COM groups (n = 8 in each group at Fz and Cz, n = 7 in each group at Pz)

Variable	Group	Rest 1	Rest 2
Relative Theta power (%)			
Fz	BIO	22.7 ± 2.3	22.9 ± 2.4
	COM	19.6 ± 3.5	19.5 ± 4.2
Cz	BIO	20.9 ± 2.4	21.4 ± 2.5
	COM	18.7 ± 3.5	18.7 ± 4.2
Pz	BIO	18.0 ± 2.4	19.2 ± 2.9
	COM	16.5 ± 3.3	16.1 ± 4.2
Relative Alpha power (%)			
Fz	BIO	40.4 ± 5.3	40.6 ± 6.5
	COM	43.4 ± 7.0	42.8 ± 7.2
Cz	BIO	41.9 ± 5.8	42.1 ± 7.3
	COM	43.4 ± 7.4	42.0 ± 7.1
Pz	BIO	46.5 ± 7.1	45.3 ± 8.4
	COM	47.9 ± 8.6	47.9 ± 9.6
Relative Beta power (%)			
Fz	BIO	37.0 ± 5.1	36.5 ± 6.2
	COM	37.1 ± 5.5	37.8 ± 5.6
Cz	BIO	37.2 ± 4.9	36.5 ± 6.2
	COM	37.9 ± 6.0	39.3 ± 6.2
Pz	BIO	35.5 ± 5.4	35.5 ± 6.2
	COM	35.7 ± 6.6	36.0 ± 6.6

% = percentage; BIO = biofeedback group; COM = comparative group.

* $P < 0.05$ Interaction effect: Pz relative theta (group x time)

$P = 0.06$ Interaction effect: Cz relative beta (group x time)

Differences in theta/beta ratios are shown in Figure 5.3. While there was no significant difference in theta/beta ratio at Fz, interaction effects (group x time) were found at both Cz ($p < 0.01$) and Pz ($p < 0.01$). Tukey's *post hoc* test revealed a significant increase in theta/beta ratio at Pz from Rest 1 to Rest 2 in the BIO group ($P < 0.05$), while at Cz it failed to detect any specific differences.

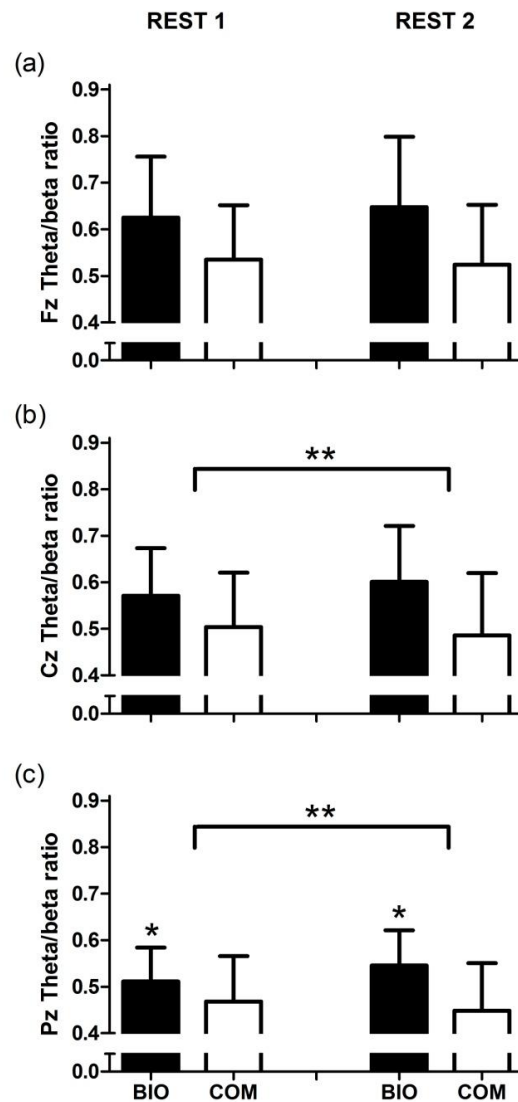


Figure 5.3 Theta/beta ratios at Fz (a), Cz (b) and Pz (c) during Rest 1 and Rest 2 in the BIO and COM groups (n = 8 in each group at Fz and Cz, n = 7 in each group at Pz)

BIO = biofeedback group; COM = comparative group.

* $P < 0.05$ Rest 1 BIO Pz theta/beta ratio vs. Rest 2 BIO Pz theta/beta ratio

** $P < 0.01$ Interaction effect: Cz theta/beta ratio (group x time), Pz theta/beta ratio (group x time)

5.4 DISCUSSION

The main finding of this study is that a single short duration episode of HRV biofeedback resulted in EEG changes suggestive of increased attention as well as increased relaxation and reduced anxiety both during and after the intervention, while the comparative intervention resulted in changes suggestive of increased mental effort and anxiety.

5.4.1 EEG changes during the intervention

During the intervention, relative theta power was higher in the BIO group than the COM group at all 3 electrodes suggesting increased internal attention^{476;477;516;608} both in the anterior and posterior networks⁵²². Activity in the anterior network commonly increases during meditation^{662;663}, while activation of the posterior attention network increases as subjects actively regulate their breath in response to biofeedback increasing posterior visuo-motor integration⁴⁸⁵.

In addition, the BIO group experienced EEG changes suggestive of increased relaxation, decreased anxiety and decreased mental effort. The higher frontal relative theta power seen in the BIO group is associated with activation of the parasympathetic nervous system^{373;586;597}, while both the higher theta and lower fronto-central relative beta power suggest increased relaxation^{580-582;582}. Higher frontal theta is also associated with decreased anxiety^{194;583;585}, and the higher theta/beta ratios seen in the BIO group at all 3 electrodes suggest decreased mental effort⁴⁶⁵.

These findings are in keeping with other studies which show that some forms of meditation result in concurrent increased internal attention and relaxation^{662;664} causing a state in which the brain is 'calm and relaxed, yet awake and alert'⁶⁶². While no other studies have evaluated changes in EEG during HRV biofeedback, similar changes are seen during meditation. Theta power increases both in the frontal midline area^{194;598;602} and globally^{608;662}, and theta/beta ratios increase globally suggesting increased attention and visual imagery⁶⁶⁵.

Subjects achieved sufficient StressEraser scores both during training and during the intervention to indicate adequate mastery of the biofeedback requirements. This suggests that despite the short duration of the intervention and the single training session, subjects used the device effectively. Furthermore, the average respiratory frequency of the BIO group during the intervention was $0.10 \pm$

0.01 Hz, suggesting that they achieved a similar frequency as targeted in traditional HRV biofeedback using frequency analysis.

All of the EEG changes observed during HRV biofeedback are correlated with decreased respiratory frequency. The HRV biofeedback device guides subjects to find their optimal slow respiration rate⁶³⁵ and as a result the BIO group had a lower respiratory frequency than the COM group. Furthermore, there was a dose effect with the subjects who had higher HRV biofeedback intervention scores having increased frontal relative theta power. This suggests that those who used the intervention more effectively experienced greater internal attention and relaxation.

EEG was also correlated with HRV. The only other study to examine the relationship between HRV and EEG showed a positive correlation between HF HRV power and frontal midline theta power during meditation which was most likely mediated by increased activation of the parasympathetic nervous system⁵⁸⁷. While we did not find a correlation between EEG and HF power, we did find that both LF and TF HRV power were positively correlated with posterior relative theta power. We do not know the explanation for the association between these variables, however, both are related to breathing. LF and TF power increase when one breathes at 0.1 Hz during HRV biofeedback⁴⁴³, and posterior theta power increases with increased posterior visuo-motor integration⁴⁸⁵ as subjects regulate their breath during biofeedback.

The comparative intervention resulted in higher fronto-central relative beta power as well as lower theta/beta ratios at all 3 electrodes, both suggestive of increased mental effort^{666;465}. This intervention required a constant cognitive state potentially contributing to the increase in beta activity⁴⁶⁷. Increased mental effort may have been required to maintain this constant cognitive state.

No differences were found in alpha power between groups during the intervention. This is in keeping with other studies which have found no difference when comparing meditation with relaxation^{204;608;633}, as both biofeedback and the comparative intervention could be considered forms of meditation and both resulted in relaxation as indicated by the questionnaire results. Furthermore, the subjects in this study had no prior experience of meditation.

5.4.2 EEG changes in the immediate post intervention period

In the BIO group, increased posterior relative theta power, decreased central relative beta power and increased central and posterior theta/beta ratios suggest that HRV biofeedback resulted in increased internal attention in the posterior network^{522;608} together with increased relaxation⁵⁸² which persisted after the intervention. This is in keeping with questionnaire results, reported in Chapter 6, which indicated that the BIO subjects felt alert and relaxed. The BIO group were most likely still focused on and aware of the sensation of their breath, resulting in increased sensory attention and, therefore, increased posterior relative theta power⁵²².

EEG changes in the COM group suggest increased mental effort and anxiety. Increased central beta power suggests that the subjects experienced greater mental effort⁶⁶⁶. After the comparative intervention, subjects felt sleepy and relaxed (results shown in Chapter 6) and as a result possibly needed to exert increased mental effort to maintain a constant cognitive state. In addition, they may have felt some anxiety⁵⁹⁴ as they knew that they were not supposed to fall asleep. Furthermore, absolute power in all frequency bands at all 3 electrodes increased in the COM group relative to the first rest period. A global increase in EEG power has previously been described in response to anxiogenic situations⁵⁹⁵, but could conceivably be caused by electrical interference created by low grade EMG activation likely resulting from anxiety.

The only other study to examine the effects of HRV biofeedback on changes in EEG used a similar protocol but with a 15 minute intervention⁵⁹⁶. The authors found that biofeedback resulted in increased theta and alpha power after the intervention, while no differences in beta power were found⁵⁹⁶. It is possible that the extra 5 minutes of intervention provided enough additional stimulus to increase the alpha power at rest. It is, however, difficult to make a direct comparison as the authors state an overall power value obtained from 19 electrodes in a 10-20 montage and don't state specific findings at Fz, Cz or Pz. In addition, subjects in their study had open eyes and in ours closed eyes, possibly affecting the alpha power^{537;538}.

A single episode of 10 minutes of HRV biofeedback has proven to be beneficial; however the EEG changes found in this study differ slightly to those found in response to a similar intervention of longer duration⁵⁹⁶. It would therefore be beneficial to measure the effect of varying durations of a single episode intervention. In addition, the benefit of the conventional training protocol⁶⁶⁷ as well

as long term use is unknown. In particular, as users achieve mastery of the HRV biofeedback one might expect to see changes in alpha power^{600;617;626}.

One of the limitations of the interpretation of EEG and, specifically, EEG frequency analysis is that the underlying mechanisms are not yet completely understood. A single oscillation can reflect many different processes and be generated in many different areas^{478;471}. As a result, changes that occur during complex tasks may be non-specific^{488;489} and, therefore, difficult to interpret. Furthermore, some of these processes and underlying neural networks have been identified, while many have not. One might, therefore, interpret EEG according to the current understanding, however, there may be additional relevant associations that have not yet been described.

5.5 CONCLUSION

In conclusion, a single episode of short duration HRV biofeedback induced relative EEG changes during the intervention compared to the comparative intervention. While the absolute power was similar in the two groups, HRV biofeedback resulted in higher relative theta power and theta/beta ratios at Fz, Cz and Pz, and lower fronto-central relative beta power in comparison to the control. In the post intervention rest period, the COM group had increases in absolute power over all frequencies at Fz, Cz and Pz, while the BIO group showed no change in absolute power relative to the first rest period. In addition, the groups showed different responses to the intervention with changes in posterior theta, central beta and central-posterior theta/beta, and the posterior theta/beta ratio increased in the BIO group from Rest 1 to Rest 2.

These findings suggest that HRV biofeedback resulted in increased attention together with increased relaxation during the intervention persisting into the post intervention period. Furthermore, those who used the intervention more effectively experienced greater internal attention and relaxation. In contrast, the comparative intervention caused increased mental effort possibly in response to the need to maintain a constant cognitive state both during and after the intervention, as well as possible anxiety in the post intervention period.

Chapter 6 describes the changes in measures of perceived anxiety and relaxation states after testing.

CHAPTER 6

THE EFFECT OF A SINGLE SESSION OF SHORT DURATION HRV BIOFEEDBACK ON MEASURES OF ANXIETY AND RELAXATION STATES

6.1 INTRODUCTION

As a result of the high prevalence of stress and the growing burden of stress-related anxiety^{20;661} and disease⁸⁻¹², it is increasingly important to identify effective stress management techniques. Interventions that are commonly used to reduce stress and anxiety include techniques such as progressive muscle relaxation^{161;162}, listening to relaxing and classical music^{168;169}, cognitive behavioural interventions¹⁵⁹ and meditation^{176;177;179}. Heart rate variability biofeedback is another intervention which has recently shown promise^{195;196}.

Most relaxation techniques result in a non-specific relaxation characterised by decreased sympathetic arousal²⁰⁰ and lead to a reduction of stress and anxiety^{177;201;202}. However, different techniques may produce different specific effects^{203;204}. Davidson has differentiated between cognitive and somatic relaxation effects²⁰⁵, while Smith has identified 4 different relaxation states including mindfulness, energized positive feelings, basic relaxation and transcendence²⁰⁶.

Mindfulness is a quality of attention rather than a technique⁶⁶⁸ and is characterised by a combination of complete awareness of internal and external stimuli together with non-judgement⁶⁶⁹⁻⁶⁷¹. It has been shown to increase as a result of meditation^{668;672;673} as well as in response to HRV biofeedback in combination with mindfulness training⁶⁷⁴. It induces a state of relaxed alertness²⁰⁰ and is associated with decreased anxiety⁶⁶⁸, increased well being⁶⁷², EEG changes suggestive of increased positive emotions⁶⁶² as well as increased cognitive performance⁶⁷⁵⁻⁶⁷⁷.

The category of energized positive feelings includes the subcategories of feeling energized, as well as positive emotions or states of mind including happiness, hope, optimism, love and thankfulness. While no studies have examined the effect of HRV biofeedback on any of these emotions or states, other relaxation techniques have been associated with increased feelings of happiness⁶⁷⁸ and joy⁶⁷⁹. Positive emotions lead to increased emotional well being⁶⁸⁰ and reduced anxiety⁶⁸¹, and improve

the ability to manage stress⁶⁸² and stress related health problems⁶⁸¹. Furthermore, they contribute to improved cognitive performance^{683;684}.

The category of basic relaxation reflects the non-specific relaxation seen in response to most relaxation techniques²⁰⁰ and consists of both physical and mental relaxation. While no studies have evaluated the effects of HRV biofeedback on feelings of relaxation, it has been shown to increase cardiac parasympathetic activity⁴⁴⁴. The final category of transcendence includes the feelings of awe and wonder, prayerfulness, deep mystery and timelessness. Transcendence is defined as the ability to move beyond 'self-centred consciousness' taking on a broader, clearer perspective⁶⁸⁵⁻⁶⁸⁷ and has been positively associated with emotional wellbeing⁶⁸⁸. The practice of Zen meditation has been associated with increased prayerfulness⁶⁸⁹, however no studies have investigated the effect of HRV biofeedback on forms of transcendence.

The aim of this chapter is to conduct a detailed analysis of these attributes and determine the effects of a single episode of short duration HRV biofeedback on feelings of anxiety and different relaxation states.

6.2 METHODS

The methodology for this chapter can be found in Chapter 2 . General methodology is described on pages 35 to 39, methodology regarding the questionnaires on pages 40 and 41, and statistics specific to the analysis of the questionnaire data on pages 44 and 45.

6.3 RESULTS

6.3.1 STAIT and STAIS

There was no difference between groups in the STAIT questionnaire (48 ± 6 vs. 44 ± 7 units, BIO vs. COM), and no correlation between trait anxiety (STAIT) and pre-testing state anxiety (STAIS) was found. Results from the STAIS are shown in Figure 6.1 below. Analysis revealed a time effect ($p < 0.001$), with no group or interaction (group x time) effects. Effect sizes were -1.17 for the BIO group and -0.72 for the COM group. Normative data for the STAIT/S indicate that values between 20 to 30 are regarded as normal and anxiety free, while values of more than 30 are associated with various degrees of anxiety⁶³⁶. Scores for the STAIT and pre-testing STAIS for both BIO and COM groups were associated with anxiety, while the scores for the post-testing STAIS were on the margin of normal. Changes in STAIS from pre- to post-testing correlated negatively with change in the SRSI3 total relaxation scores ($r = -0.58$ (CI 95% -0.83 to -0.13), $p < 0.05$) as well as with change in the SRSI3 basic relaxation scores ($r = -0.66$ (CI 95% -0.86 to -0.26), $p < 0.01$).

6.3.2 SRSI3

SRSI3 total relaxation state scores and scores for the main categories are shown in Figure 6.1 below. Comparison of the total relaxation state scores before and after testing revealed both an interaction (group x time) ($p < 0.05$) and a time ($p < 0.001$) effect, with no group effect. Tukey's *post hoc* test showed an increase in total score in the BIO group ($p < 0.001$) from pre to post testing. Effect sizes were 1.14 for the BIO group and 0.40 for the COM group.

The SRSI3 total score is divided into 4 main categories: mindfulness, energized positive feelings, basic relaxation and transcendence. Analysis of these categories revealed interaction (group x time) effects for mindfulness ($p < 0.05$) and energized positive feelings ($p < 0.05$) from pre- to post-testing. Tukey's *post hoc* test revealed that the BIO group increased their scores for both mindfulness

($p < 0.01$) and energized positive feelings ($p < 0.05$). In addition, there was a time effect for mindfulness ($p < 0.01$), basic relaxation ($p < 0.001$), and transcendence ($p < 0.05$). Effect sizes were also calculated for each category. In the category of mindfulness the effect size was 1.21 for the BIO group and 0.67 for the COM group, energized positive feelings showed an effect size of 0.86 for the BIO group and -0.12 for the COM group, basic relaxation 1.21 for the BIO group and 0.67 for the COM group, and for transcendence 0.56 for both the BIO and COM groups.

Subcategory scores are shown in Table 6.1 below. In the first category of mindfulness, there were interaction effects for mindful quiet ($p < 0.05$) and innocence ($p < 0.05$). Tukey's *post hoc* test revealed that the BIO group increased their scores for both mindful quiet ($p < 0.001$) and mindful innocence ($p < 0.01$). In addition, there were time effects for mindful quiet ($p < 0.0001$), mindful innocence ($p < 0.01$), mindful acceptance ($p < 0.05$) and mindful centering ($p < 0.01$), and a group effect for mindful awareness ($p < 0.05$). No group, time or interaction (group x time) effects were found for mindful awakening.

In the category of energized positive feelings, there was a time effect ($p < 0.05$) for the category of energized. No group, time or interaction (group x time) differences were found for optimism/hope/trust, happiness or feeling thankful and loving.

In the category of basic relaxation, there was an interaction effect for feeling rested and refreshed ($p < 0.05$). Tukey's *post hoc* test revealed that the BIO group felt more rested and refreshed after than before testing ($p < 0.01$). In addition, there were time effects for rested and refreshed ($p < 0.01$), disengagement ($p < 0.01$), physical relaxation ($p < 0.001$) and mental relaxation ($p < 0.01$). No group, time or interaction (group x time) effects were found for sleepiness before and after testing.

Finally in the category of transcendence, no group, time or interaction (group x time) differences were found for awe and wonder, feeling prayerful, deep mystery or feeling timeless/boundless/infinite.

6.3.3 Scores for helpfulness and sleepiness

There were no differences in scores for helpfulness of the device (7 ± 1 vs. 6 ± 2 units, BIO vs. COM) or sleepiness after 5 (4 ± 3 vs. 6 ± 3 units, BIO vs. COM) or 10 (5 ± 3 vs. 7 ± 2 units, BIO vs. COM)

minutes of using the device, however the COM group felt more sleepy than the BIO group (5 ± 3 vs. 7 ± 2 units, BIO vs. COM, $p < 0.05$) during the rest period after the intervention (Rest 2).

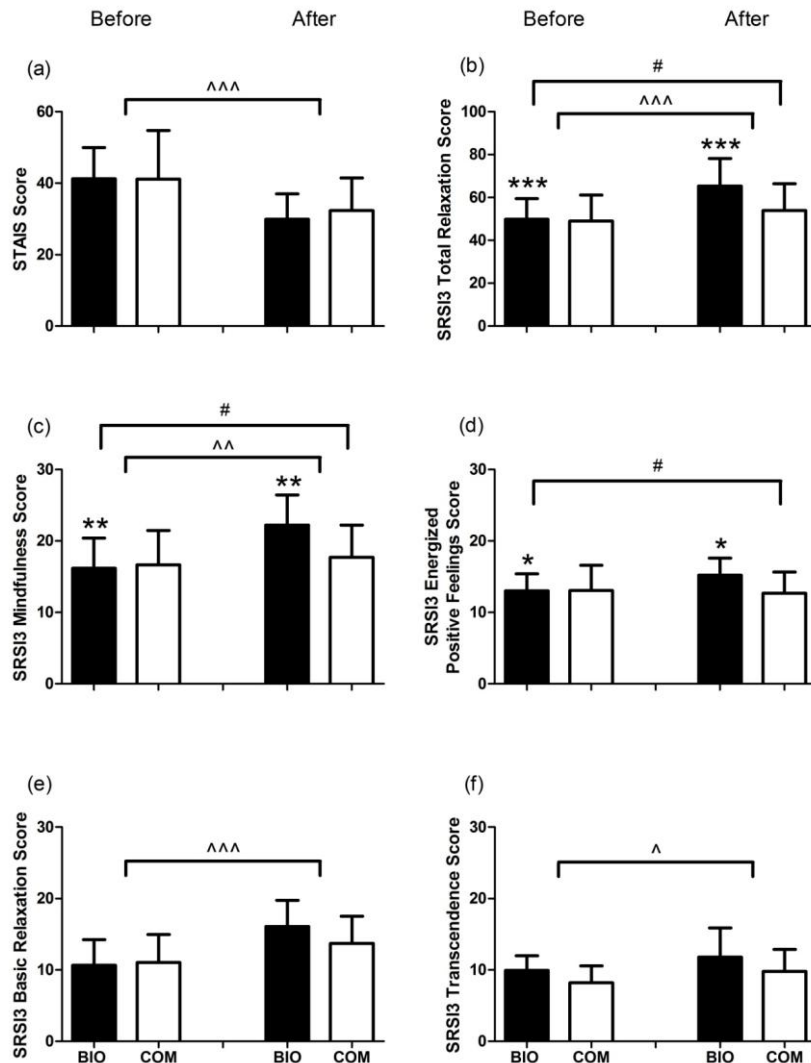


Figure 6.1 Scores for STAIS (a), SRSI3 Total Relaxation States (b), SRSI3 Mindfulness (c), SRSI3 Energized Positive Feelings (d), SRSI3 Basic Relaxation (e) and SRSI3 Transcendence (f) before and after testing in the BIO (n=9) and COM (n=9) groups

BIO = biofeedback group; COM = comparative group; STAIS = Spielberger State Anxiety Inventory; SRSI3 = Smith Relaxation States Inventory 3.

- * $P < 0.05$ Positive feelings BIO pre vs. BIO post
- ** $P < 0.01$ Mindfulness BIO pre vs. BIO post
- *** $P < 0.001$ Total score BIO pre vs. BIO post
- # $P < 0.05$ Interaction (group x time) effect: Total score, Mindfulness, Positive feelings
- ^ $P < 0.05$ Time effect: Transcendence
- ^^ $P < 0.01$ Time effect: Mindfulness
- ^^^ $P < 0.001$ Time effect: STAIS, Total score, Basic relaxation

Table 6.1 Scores for each individual subcategory in the Smith Relaxation States Inventory 3 before and after testing in the BIO (n=9) and COM (n=9) groups

Variable	Group	Before	After	Group	Time	Interaction
MINDFULNESS						
Mindful quiet	BIO	2.22 ± 1.25 **	4.28 ± 0.87 **	NS	P<0.0001	P<0.05
	COM	2.67 ± 1.27	3.56 ± 1.10			
Mindful innocence	BIO	1.44 ± 0.53 *	2.44 ± 1.01 *	NS	P<0.01	P<0.05
	COM	1.44 ± 0.53	1.56 ± 0.73			
Mindful acceptance	BIO	3.39 ± 1.11	4.11 ± 1.11	NS	P<0.05	NS
	COM	3.35 ± 1.41	3.56 ± 1.01			
Mindful centering	BIO	2.89 ± 0.93	3.94 ± 0.95	NS	P<0.01	NS
	COM	3.06 ± 0.92	3.61 ± 1.19			
Mindful awareness	BIO	4.00 ± 1.22	4.67 ± 0.71	P<0.05	NS	NS
	COM	3.44 ± 1.13	3.11 ± 1.36			
Mindful awakening	BIO	2.22 ± 1.39	2.78 ± 1.56	NS	NS	NS
	COM	2.67 ± 1.41	2.33 ± 0.87			
ENERGIZED POSITIVE FEELINGS						
Energized	BIO	2.56 ± 1.24	3.89 ± 0.93	NS	P<0.05	NS
	COM	3.00 ± 1.41	3.11 ± 1.27			
Optimism/hope/trust	BIO	4.00 ± 1.22	4.22 ± 1.20	NS	NS	NS
	COM	3.33 ± 1.32	3.33 ± 0.87			
Happy	BIO	3.28 ± 0.67	3.67 ± 0.56	NS	NS	NS
	COM	3.61 ± 0.89	3.39 ± 0.93			
Thankful and loving	BIO	3.17 ± 0.87	3.44 ± 0.73	NS	NS	NS
	COM	3.11 ± 1.02	2.83 ± 0.75			
BASIC RELAXATION						
Rested/refreshed	BIO	2.22 ± 1.39 *	4.00 ± 0.87 *	NS	P<0.01	P<0.05
	COM	2.22 ± 1.30	2.44 ± 1.42			
Disengagement	BIO	2.17 ± 1.09	3.22 ± 1.35	NS	P<0.01	NS
	COM	2.28 ± 0.83	2.67 ± 1.20			
Physical relaxation	BIO	1.77 ± 0.52	3.10 ± 0.95	NS	P<0.001	NS
	COM	1.88 ± 1.03	2.84 ± 1.06			
Mental relaxation	BIO	2.85 ± 0.98	3.55 ± 1.09	NS	P<0.01	NS
	COM	2.66 ± 1.16	3.26 ± 0.73			
Sleepiness	BIO	1.67 ± 1.27	2.22 ± 0.79	NS	NS	NS
	COM	2.00 ± 1.35	2.50 ± 1.00			
TRANSCENDENCE						
Awe and wonder	BIO	2.61 ± 0.93	3.00 ± 1.32	NS	NS	NS
	COM	1.78 ± 0.67	2.44 ± 1.01			
Prayerful	BIO	2.33 ± 1.22	3.00 ± 1.21	NS	NS	NS
	COM	2.11 ± 1.27	2.22 ± 1.09			
Deep mystery	BIO	2.56 ± 1.24	2.78 ± 1.20	NS	NS	NS
	COM	2.33 ± 1.00	2.56 ± 1.24			
Timeless, boundless, infinite	BIO	2.44 ± 0.88	3.00 ± 1.41	NS	NS	NS
	COM	2.00 ± 1.22	2.56 ± 1.13			

Interaction = (group x time); BIO = Biofeedback group; COM = Comparative group; NS = non significant.

* P < 0.01

BIO rested/refreshed before vs. BIO rested/refreshed after
BIO mindful innocence before vs. BIO mindful innocence after

** P < 0.001

BIO mindful quiet before vs. BIO mindful quiet after

6.4 DISCUSSION

The main finding of this study is that a single session of short duration HRV biofeedback resulted in large improvements in total relaxation state scores as well as in scores for mindfulness, energized positive feelings and basic relaxation from pre- to post-testing. These changes occurred despite the stress induced by the Stroop task⁴³⁸. In contrast, the comparative intervention resulted in only a small increase in overall total relaxation states scores, with a moderate improvement in basic relaxation, a small improvement in mindfulness and no improvement in energized positive feelings.

While both interventions resulted in improvement in overall mindfulness as well as several of the subcategories of mindfulness, HRV biofeedback resulted in greater improvements than the comparative intervention, both in overall mindfulness as well as in the subcategories of mindful quiet and mindful innocence. This suggests that subjects using the HRV biofeedback increased their awareness of internal and external stimuli⁶⁶⁹⁻⁶⁷¹. Increased mindfulness has been associated with decreased anxiety⁶⁶⁸ and increased well being⁶⁷², as well as with a state of relaxed alertness²⁰⁰. Furthermore, it is associated with improved ability to sustain attention⁶⁷⁷ and increased cognitive performance⁶⁷⁵⁻⁶⁷⁷. While mindfulness has been shown to increase as a result of meditation⁶⁷⁷ as well as in response to HRV biofeedback in combination with mindfulness training⁶⁷⁴, this is the first study to look at the effect of HRV biofeedback alone.

HRV biofeedback also resulted in a large increase in the overall category of energized positive feelings, while the comparative intervention showed no improvement. Both groups did, however, have increases in the subcategory of feeling energized. The increased positive emotions seen in the BIO group may be associated with the concurrent increases in mindfulness⁶⁶². Positive emotions lead to increased emotional well-being⁶⁸⁰ and reduced anxiety⁶⁸¹, and improve one's ability to manage stress and adversity⁶⁸² as well as stress-related health problems⁶⁸¹. Furthermore, positive emotions broaden attention⁶⁸³ and are associated with improved cognitive performance^{683;684}. It is tempting to speculate that the increased positive energy together with the increased mindfulness in the BIO group contributed to the increased cognitive performance during the Stroop task following the intervention (reported in Chapter 3). While other relaxation techniques have been associated with increased feelings of happiness⁶⁷⁸ and joy⁶⁷⁹, no other studies have looked at the effect of HRV biofeedback on positive energy or positive emotions.

Both interventions led to increased scores in the category of basic relaxation. This is perhaps not surprising, as both interventions involve focusing attention on a single variable, which has been shown to increase relaxation⁶⁹⁰. However, the HRV biofeedback had a large effect size and the comparative intervention a moderate effect size, suggesting that greater benefit is achieved when focused attention was combined with biofeedback-induced slow breathing. While no studies have examined the effects of HRV biofeedback on feelings of relaxation, it has been shown to increase cardiac parasympathetic activity⁴⁴⁴.

In the subcategories of basic relaxation, both groups improved physical and mental relaxation, and felt more disengaged and more rest and refreshed after testing, however the BIO group had a greater improvement in the latter. While there were no differences in sleepiness before or after testing between groups, the VAS score revealed that the COM group felt sleepier than the BIO group during the rest period immediately after the intervention. This may be suggestive of somatic relaxation in the BIO group, and both cognitive and somatic relaxation in the COM group²⁰⁵. Furthermore, this may reflect relaxed alertness associated with the increased mindfulness²⁰⁰ seen in the BIO group.

In the last category of transcendence, there was a time effect with both groups increasing their overall scores moderately; however there were no changes in the subcategories. This suggests that both groups achieved a clearer awareness⁶⁸⁶ and broader perspective⁶⁸⁷, which has been associated with emotional wellbeing⁶⁸⁸. While increased prayerfulness has been associated with the practice of Zen meditation⁶⁸⁹, no studies have looked at the effect of HRV biofeedback on forms of transcendence.

In addition to changes in relaxation states, changes in measures of anxiety were found. Both groups felt less anxious after testing as indicated by a significant time effect. While there was no interaction effect, the BIO group had a large effect size and the COM group a moderate effect size. A similar study revealed that both the HRV biofeedback and comparative intervention groups experienced decreased state anxiety, with the HRV biofeedback group having a greater decrease¹⁹⁵. The authors used a 15 minute intervention as opposed to the 10 minute intervention in this study, which could have accounted for the additional interaction effect. Other studies have also shown a reduction in state anxiety with HRV biofeedback but in combination with psychotherapy^{198;199}.

The decrease in state anxiety in both groups over testing correlated with increased total relaxation and basic relaxation scores, as one would expect ^{177;201;691}. There was no correlation between state and trait anxiety. State anxiety is the acute anxiety experienced in response to a specific stressful event ⁶⁹², while trait anxiety is ongoing anxiety which is regarded as a relatively stable personality trait ^{692;693}. While the level of state anxiety is affected by trait anxiety ⁶⁹⁴, the correlation is not direct as state anxiety is also affected by the specific stressors to which one is exposed ⁶⁹⁴.

The hand held HRV biofeedback device is easy to use, doesn't require the assistance of other individuals and can be used for short periods of time as needed throughout the day. Furthermore, benefit is derived from a single session of biofeedback and a single training session. These findings together with other research suggest that HRV biofeedback would be a valuable intervention to include in the management of stress and anxiety ^{195;196} as well as in the treatment and prevention of stress and anxiety related disorders ^{197;444}.

6.5 CONCLUSION

In conclusion, while both interventions facilitated reduced anxiety and increased scores for total relaxation states, mindfulness, basic relaxation and transcendence, HRV biofeedback had added benefit with greater increases in scores for total relaxation states, mindfulness and basic relaxation, as well as increased energized positive feelings. Further, while there was no difference in sleepiness after testing, immediately after the intervention the HRV biofeedback group felt alert, while the comparative group felt sleepy.

CHAPTER 7

SUMMARY, CLINICAL APPLICATION AND CONCLUSIONS

7.1 OVERVIEW AND CLINICAL INTERPRETATION

The objective of this thesis was to examine the effects of a single 10 minute episode of HRV biofeedback on measures of HRV and EEG during and immediately after the intervention, measures of HRV and cognitive performance during laboratory induced cognitive stress and subjective feelings of anxiety and relaxation states after testing.

The majority of research on HRV biofeedback focuses primarily on clinical outcomes and, therefore, the long term effect of biofeedback over sessions. Furthermore, most use the conventional training protocol as described by Lehrer. This thesis examines the acute effect of a single short duration HRV biofeedback intervention. While other studies have investigated the changes in HRV both during and immediately after HRV biofeedback, the effect of HRV biofeedback on changes in HRV during stress has not been previously examined. Further, no other studies have examined the effect of HRV biofeedback on EEG during biofeedback, only one other study has investigated the changes in EEG after biofeedback and only one other the effect of HRV biofeedback on cognitive performance. Finally, while other studies have examined levels of stress and anxiety in response to HRV biofeedback, none have examined changes in perceived relaxation states.

7.1.1 Chapter 3

Chapter 3 examined the effect of HRV biofeedback on cognitive performance during laboratory-induced stress. In summary, the data showed that:

1. Both groups improved their reaction times in response to cues from Stroop 1 (before the intervention) to Stroop 2 (after the intervention)
2. HRV biofeedback resulted in a greater improvement in reaction time as well as greater consistency of responses from Stroop 1 to Stroop 2 than the comparative intervention
3. All 8 of the subjects using HRV biofeedback increased their reaction times by more than 5%, while only 3 of the 8 subjects using the comparative intervention improved more than 5%
4. Fewer mistakes were made in counting squares after the HRV biofeedback intervention

In conclusion, these data suggest that while both interventions resulted in an improvement in performance, HRV biofeedback resulted in greater improvements with both greater increases in reaction time and greater reduction in mistakes made. This suggests that HRV biofeedback resulted in improved working memory as well as possible improvements in mental set shifting, suppression of prepotent responses, and increased attention and focus.

7.1.2 Chapter 4

To further understand the physiological changes underlying the effect of HRV biofeedback, measures of HRV and EEG were analysed. Chapter 4 examined the effect of HRV biofeedback on measures of HRV during and immediately after the intervention, as well as during the following laboratory induced stress. In summary, the data showed that:

During the intervention

1. In comparison to Rest 1, respiratory frequency decreased to 0.1 Hz, LF power increased, TF power increased approaching significance and HF power decreased during HRV biofeedback, while no changes were evident during the comparative intervention.
2. The BIO group had a lower respiratory frequency and higher LF power, TF power and SDNN than the COM group.

In the immediate post intervention rest period

1. In comparison to the preceding intervention, in the BIO group respiratory frequency increased, and HR, LF power, TF power, SDNN and RMSSD decreased, while HF power remained unchanged. The COM group showed no change from the intervention to Rest 2.
2. There was a trend for RMSSD to be lower after the intervention in the BIO group, as well as a trend for HF power to be lower in the BIO than in the COM group, both indicative of a shift in vagal modulation from HF to LF in the BIO group.

During Stroop 2

1. During Stroop 2, both groups had increased respiratory rates indicative of increased sympathetic activity, and decreased TF HRV power indicative of cardiac vagal withdrawal in comparison to the preceding rest period. However, the pattern of vagal withdrawal was different in each group:
 - HRV biofeedback resulted in maintained heart rate, maintained RMSSD and HF power, and decreased LF power.

- The comparative intervention resulted in increased heart rate, maintained LF power and decreased RMSSD and a trend towards a decrease in HF power.
2. In comparison to Stroop 1, HR was lower in both groups and RMSSD higher in the BIO group only.

In conclusion, HRV biofeedback resulted in a short term carry-over effect after biofeedback that modified the physiological response during both the 5 min rest period and the following laboratory-induced stress.

Porges identifies 3 different autonomic influences on the heart. The myelinated vagal system affects HF power and increases the ability to engage and communicate socially. The sympathetic nervous system results in mobilization in response to stress. Finally, the phylogenetically lowest system, the unmyelinated vagus causes immobilization and is reflected by LF HRV spectral power.

In the immediate post-biofeedback rest period there was a trend to greater HF vagal withdrawal after HRV biofeedback. Previous studies have shown that the ability to withdraw myelinated cardiac vagal activity is indicative of healthy adaptive physiology associated with adaptive cognitive function, allowing the individual to rapidly engage with the environment as needed and increase the ability to sustain attention.

While both groups demonstrated evidence for vagal withdrawal in response to induced stress, the pattern of vagal modulation in each group differed, with the BIO group maintaining HF power and RMSSD in Stroop 2 relative to the preceding rest period despite decreased TF and LF power, and the COM group maintaining LF power despite decreased TF and HF power.

Changes in response to the comparative intervention suggest withdrawal of the beneficial social engagement system and increased sympathetic activation affecting the heart and increasing respiratory rate, with no change in unmyelinated vagal activity. However, HRV biofeedback resulted in changes suggestive of maintained myelinated vagal cardiac activation, no increase in sympathetic stimulation of the heart and withdrawal of unmyelinated vagal cardiac stimulation in the face of stress. While there was no sympathetic effect on the heart, there was on respiratory rate. According to Porges' polyvagal theory, this pattern of vagal withdrawal would allow effective social engagement in a stressful environment, which increases the ability to function successfully.

7.1.3 Chapter 5

This chapter examined the effect of HRV biofeedback on measures of EEG during and immediately after the intervention. In summary, the data show that:

During the intervention

1. HRV biofeedback resulted in higher frontal, central and parietal theta/beta ratios and relative theta power, and lower frontal and central relative beta power than the comparative intervention.
2. Respiratory frequency correlated negatively with frontal central and parietal theta/beta ratios and relative theta power, and positively with frontal and central relative beta power. Posterior relative theta also correlated with LF and TF cardiac spectral power.
3. The BIO intervention score correlated positively with frontal relative theta power.

During rest immediately after the intervention

1. The HRV biofeedback and the comparative device resulted in significantly different effects on centro-parietal theta/beta ratios, parietal relative theta power and central relative beta power.
 - After HRV biofeedback, theta/beta increased posteriorly and appears to increase centrally, relative theta power appears to increase posteriorly and beta power tends to decrease centrally.
 - After the comparative intervention, theta/beta appears to decrease centrally and posteriorly, and relative beta power tends to increase centrally.
2. There was no change in absolute power after HRV biofeedback, while the comparative intervention led to increases in absolute theta, alpha and beta power at all locations. Absolute frontal beta power tended to be lower in the BIO group than the COM group.

In conclusion, these findings suggest that a single episode of short duration HRV biofeedback resulted in EEG changes suggestive of increased attention together with increased relaxation during the intervention and persisting into the post intervention period. In contrast, the comparative intervention resulted in changes suggestive of increased mental effort, possibly in response to the need to maintain a constant cognitive state, both during and after the intervention, as well as possible anxiety in the post-intervention period. It is tempting to speculate that the increased attention during rest in the HRV biofeedback group contributed to the improved cognitive performance seen during the following Stroop task described in Chapter 3.

All of the EEG changes observed during HRV biofeedback are correlated with decreased respiratory frequency which occurs during biofeedback. Furthermore, there was a dose effect suggesting that subjects who used the HRV biofeedback intervention more effectively experienced greater internal attention and relaxation.

7.1.4 Chapter 6

Finally, this chapter examined the acute effect of HRV biofeedback on feelings of sleepiness after using the intervention, as well as perceived anxiety and relaxation states after testing. The main findings were:

1. The COM group felt more sleepy than the BIO group during the rest period immediately after the intervention
2. Both groups felt less anxious after testing, with the HRV biofeedback resulting in a large effect size and the comparative intervention a moderate effect size.
3. Both groups felt more relaxed after testing with increases in total relaxation scores, increases in the categories of mindfulness, basic relaxation and transcendence, and increases in the subcategories of mindful quiet, mindful innocence, mindful acceptance, mindful centering, feeling energized, feeling rested and refreshed, disengagement, physical relaxation and mental relaxation.
4. HRV biofeedback resulted in greater increases in total relaxation scores, greater increases in the categories of mindfulness and basic relaxation, and greater increases in the subcategories of mindful quiet, mindful innocence and feeling rested and refreshed. In addition, HRV biofeedback led to increases in the category of energized positive feelings.

In conclusion, while both interventions facilitated reduced anxiety and increased perceived relaxation, HRV biofeedback had added benefit with greater increases in scores for total relaxation states, mindfulness and basic relaxation, as well as increased energized positive feelings. Increased mindfulness has been associated with decreased anxiety as well as with a state of relaxed alertness, and both mindfulness and positive emotions are associated with improved attention and cognitive performance. It is tempting to speculate that the increased mindfulness together with increased positive energy in the BIO group may have contributed to the increased cognitive performance during Stroop 2. Increased perceived relaxation would also be in keeping with the changes evident in HRV during Stroop 2 which suggest maintained myelinated vagal cardiac activation during stress.

Further, while there was no difference in sleepiness after testing, immediately after the intervention the HRV biofeedback group felt alert, while the comparative group felt sleepy. The perception of alert relaxation immediately after HRV biofeedback supports the EEG findings of concurrent increased attention and relaxation.

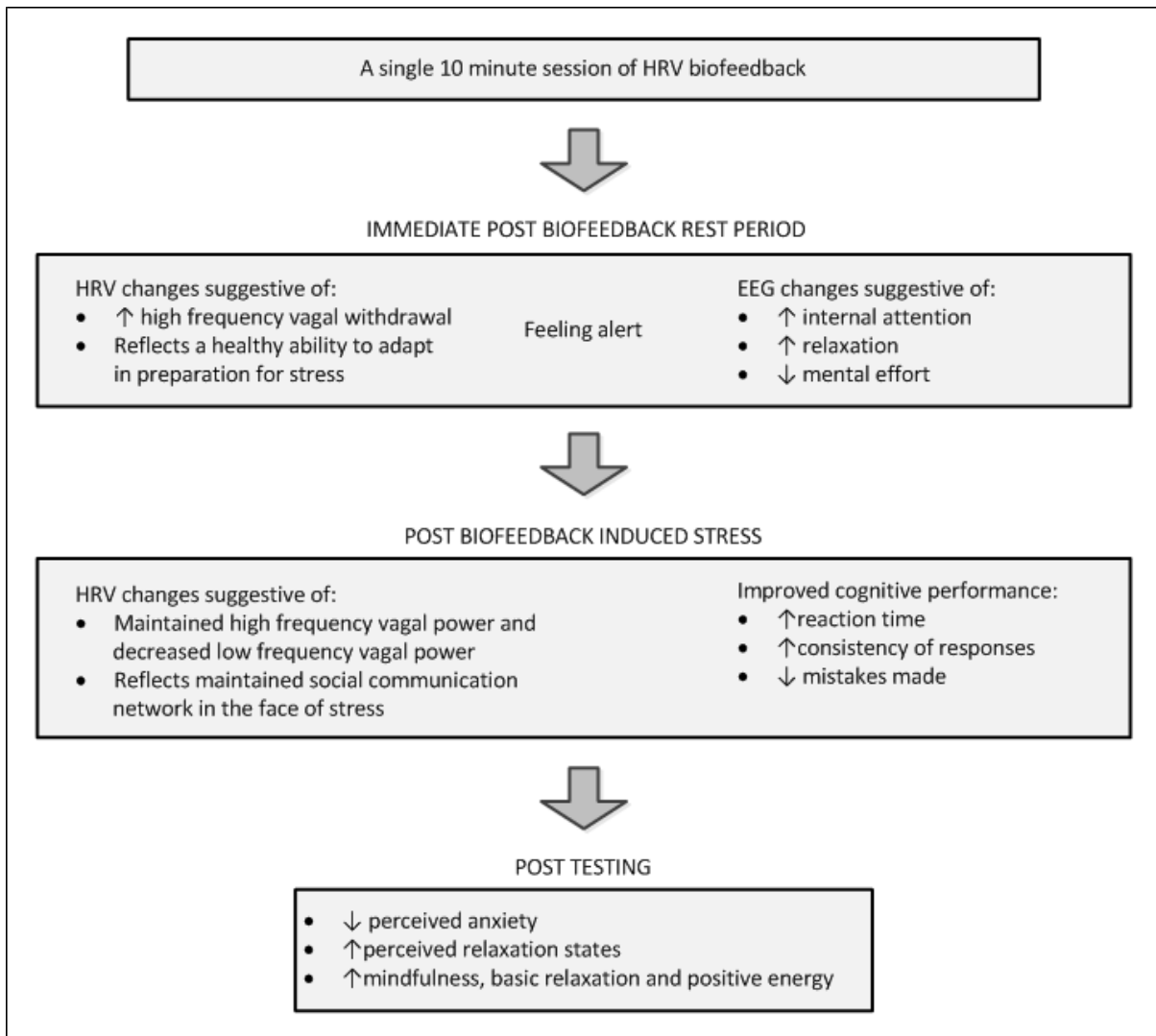


Figure 7.1 Summary of the effects of a single episode of HRV biofeedback on HRV, EEG, cognitive performance and perceived anxiety and relaxation states

In conclusion, while there is benefit to maintaining focused attention on a single variable as shown by the improvements in the comparative group, there is greater benefit in combining focused attention with HRV biofeedback. A single 10 minute HRV biofeedback intervention led to improved cognitive performance, HRV changes suggestive of improved vagal modulation, EEG changes suggestive of increased attention together with increased relaxation and greater improvements in

perceived anxiety and relaxation states. HRV biofeedback, therefore, provides an effective, inexpensive and time efficient tool that could be a useful aid for improving cognitive performance in the face of stress, as well as a valuable component in the management of stress and disease, both for the clinician and in the work place.

7.2 CLINICAL APPLICATION

The findings of this thesis offer new insight into an effective and readily accessible stress management technique. A single 10 minute HRV biofeedback intervention led to a reduction in perceived anxiety and an increase in perceived relaxation states. Furthermore, it led to HRV changes suggestive of an improved autonomic response to stress, with evidence for an increase in HRV during induced stress as indicated by the increase in RMSSD from Stroop 1 to Stroop 2.

This has important implications in the management of acute stress and anxiety, and potentially chronic stress- and anxiety-related disease. An important component of the management of chronic non-communicable disease is the assessment and management of psychosocial stress, which is often one of the most challenging aspects for the clinician. A reduction in stress will lead to improvement in many diseases, especially cardiovascular disease. Patients with uncomplicated coronary artery disease have decreased vagal drive to the heart^{400;695} which contributes to an increased risk of arrhythmia¹⁵. Increasing the vagal activation of the heart reduces myocardial ischemia, reperfusion-induced arrhythmias and the risk of sudden death after myocardial infarction^{454;455}. This study has shown an increase in vagal control of the heart following a short duration HRV biofeedback intervention in healthy subjects. A similar effect of HRV biofeedback has also been shown in patients with coronary artery disease¹⁹⁶. HRV biofeedback would therefore be a potentially valuable intervention to include in the prevention and management of patients with cardiovascular disease, as well as other stress- and anxiety-related diseases.

Furthermore, this study showed that a single HRV biofeedback intervention resulted in improved cognitive performance during stress. Cognitive function and HRV have been found to be directly correlated^{430;431} and both are negatively impacted by work related stress^{130;144;212;336}. HRV biofeedback would therefore be a valuable intervention for people to use when working in stressful environments.

HRV biofeedback is an inexpensive, time efficient and effective method of increasing HRV and increasing cardiac vagal modulation. It can be provided by hand-held portable devices such as the emWave2 or StressEraser, computer based interactive programs such as emWave desktop, Journey to the Wild Divine: Wisdom Quest or Relaxing Rhythms or with professional recording equipment such as Biograph Infiniti with Cardiopro. The advantage of a portable device is that it can be carried

at all times and so is available whenever needed such as before stressful situations or during moments of anxiety.

7.3 LIMITATIONS

A limitation of this study is that it may not be representative of the entire population. We elected to test only men in an attempt to limit heterogeneity as men and women have different responses to stress^{48,637}. Further research needs to be done to examine the benefit of HRV biofeedback for women. This sample also specifically evaluated men in senior managerial positions, and so may not be representative of all job descriptions. Furthermore, while the Stroop task has been shown to be an effective stressor⁴³⁸, it may not be representative of stress induced outside the laboratory.

Subjects received training with their respective devices without prior baseline physiological recording. As a result of this, the respiratory rate in the BIO group during baseline testing in Rest 1 was lower than the COM group. It is most likely that this group difference was caused by the prior training as the subjects in this study were randomised which should remove any group difference. In addition, other studies have shown a tendency for subjects to breathe more slowly during rest periods after HRV biofeedback despite instructions not to⁴⁵⁸. There were no other group differences during Rest 1. In hindsight, it would be better to take baseline physiological recordings prior to training. Finally, it would also be advisable to record EMG of shoulder, neck and jaw musculature to enable complete removal of all muscle tension artefacts when analysing EEG data.

7.4 FUTURE RESEARCH

This thesis was specifically interested in the acute effect of 10 minutes of biofeedback, as this is the period recommended for clinical use. The minimum recommended time per session is 5 minutes with a goal to accumulate a total of 20 minutes per day⁶³⁵. While the benefits described in this thesis were achieved with only 10 minutes of intervention, greater benefits may be achieved with a longer duration of intervention as described by Sherlin et al¹⁹⁵, as well as with regular training, as often major improvements in relaxation states occur only after a few weeks of training⁶⁹⁶. It would therefore be beneficial to investigate the effect of varying durations of a single episode of biofeedback to determine the optimal period of use.

While there is benefit in the use of a single episode of biofeedback, there may be greater benefit with regular training such as with the conventional HRV biofeedback training protocol as described by Lehrer. Long-term meditation is effective in reducing anxiety, improving attention and preventing age-related reduction in grey matter volume, thus one could postulate that long term HRV biofeedback could have similar effects resulting in reduced anxiety and increased performance. Furthermore, relaxation states show greater improvements after several weeks of intervention.

It would be beneficial to investigate the effect of HRV biofeedback on women, and on people of different ages as well as different occupations. While we decided to use a single intervention and comparative group design, as a crossover design may have confounded the interpretation in the event of there being any carry over from the intervention; it would be useful to redesign the study to include a crossover design effectively.

Finally, additional future research could include measurement of the biochemical markers of stress during and after biofeedback and analysis of EEG during the Stroop task after biofeedback.

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Appendix A - Explanation of authorship for each publication

1. Prinsloo GE, Rauch HGL, Lambert MI, Muench F, Noakes TD, Derman WE. The effect of short duration heart rate variability (HRV) biofeedback on cognitive performance during laboratory induced cognitive stress. *Applied Cognitive Psychology* 25: 792 – 801 (2011)
2. Prinsloo GE, Derman WE, Lambert MI, Rauch HGL. The effect of a single session of short duration biofeedback-induced deep breathing on measures of heart rate variability during laboratory induced cognitive stress: a pilot study. *Applied Psychophysiology and Biofeedback* (in review, revisions requested)
3. Prinsloo GE, Rauch HGL, Karpul D, Derman WE. The effect of a single session of short duration heart rate variability biofeedback on EEG: a pilot study. *Applied Psychophysiology and Biofeedback* (accepted for publication)
4. Prinsloo GE, Derman WE, Lambert MI, Rauch HGL. The effect of a single episode of short duration heart rate variability biofeedback on measures of anxiety and relaxation states. *International Journal of Stress Management* (in review, revisions requested)

For each study, I was involved in developing the study concept and design, collected and analysed the data, and completed the statistical analysis of the data. I interpreted the data and wrote the initial drafts of the papers as well as integrating all comments and completing the final drafts.

Prof Derman was my primary supervisor. As such he was involved in developing the study concept and design, as well as providing a detailed critical revision of each of the manuscripts.

Dr Rauch was my second supervisor. He was involved in developing the study design and concept. In addition, he provided guidance in the analysis and interpretation of data, especially the HRV and cognitive performance data, as well as providing a detailed critical revision of each of the manuscripts.

Prof Lambert provided guidance in the statistical analysis of the cognitive performance, HRV and questionnaire data as well as detailed critical revisions of those three papers.

Dr Muench was involved in developing the study concept and design, as well as providing a detailed critical revision of the cognitive performance paper.

Mr Karpul was involved the complex analysis of the EEG data and provided a detailed critical revision of the EEG paper.

Prof Noakes was involved in developing the study concept and was consulted in the compilation of the final manuscript.

We confirm that this is an accurate description of our respective contributions to the various studies:

Prof W Derman _____ Date 31/08/12

Dr I Rauch _____ Date 03 August 2012

Prof M Lambert _____ Date 3/8/2012

Dr F Muench _____ Date 8.23.12

Mr D Karpul _____ Date 03/08/2012

Prof T Noakes _____ Date 7.8.2012

Appendix B - Copyright clearance

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Appendix C - Informed consent

INFORMED CONSENT DECLARATION

STUDY ON BIOFEEDBACK AND LIFESTYLE INDUCED STRESS

As part of a research project that aims to understand the physiological benefits of a biofeedback (applied psychophysiology) technique in reducing your stress levels, you are invited to complete the attached questionnaires (describing your subjective perception of your levels of stress) and at a later stage to participate in the on-screen cognitive tests during which physiological changes in brain waves, respiration, skin conductance, muscle activity and heart rate will be measured. The anticipated time required to complete these tests is approximately 60 minutes. Testing is not invasive and the methodology should not expose you to any risk.

Participation in this study is completely voluntary, and you are free to choose not to complete the questionnaire, or *opt out* of the research at any stage. However you are kindly requested to participate as the study stands to enhance the understanding of the benefit of a biofeedback technique in reducing unhealthy levels of psychological stress. This psychological stress, if addressed, may result in a lowered risk of developing physiological disorders. Your answers and individual identity will be kept strictly confidential.

Date _____

Name _____

I hereby consent to participate in this research study with full knowledge and understanding of the nature of the research project and what is expected of me.

Signature _____

Appendix D - Intake information

Date of Birth:	Nationality:
<input type="checkbox"/> Male <input type="checkbox"/> Female	Ethnicity:
Highest level of education completed: <input type="checkbox"/> Did not complete high school <input type="checkbox"/> High school diploma or GED <input type="checkbox"/> Some college or associates degree <input type="checkbox"/> Bachelors degree <input type="checkbox"/> Masters, doctoral or other professional degree	Marital status: <input type="checkbox"/> Single <input type="checkbox"/> Live-in partner <input type="checkbox"/> Married <input type="checkbox"/> Separated <input type="checkbox"/> Divorced <input type="checkbox"/> Widowed Number of children: <input type="checkbox"/> 0 <input type="checkbox"/> 3 <input type="checkbox"/> 6 or more <input type="checkbox"/> 1 <input type="checkbox"/> 4 <input type="checkbox"/> 2 <input type="checkbox"/> 5
How often do you exercise: <input type="checkbox"/> Less than once a month <input type="checkbox"/> Once or twice a month <input type="checkbox"/> Once a week <input type="checkbox"/> A few times a week <input type="checkbox"/> Every day	

University of Cape Town

Appendix E.2 - Spielberger Trait Anxiety Inventory

Patient Name _____
 Patient No. _____

Date _____

SPIELBERGER STATE-TRAIT ANXIETY INVENTORY (STAI-T) Self-Evaluation Questionnaire

Directions:

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate answer to indicate how you generally feel. There are no right or wrong answers. Do not spend too much time on any one statement, but give the answer which seems to describe how you generally feel.

	Almost Never	Sometimes	Often	Almost Always
1. I feel pleasant	1	2	3	4
2. I feel nervous and restless	1	2	3	4
3. I feel satisfied with myself	1	2	3	4
4. I wish I could be as happy as others seem to be	1	2	3	4
5. I feel like a failure	1	2	3	4
6. I feel rested	1	2	3	4
7. I am "calm, cool, and collected"	1	2	3	4
8. I feel that difficulties are piling up so that I cannot overcome them	1	2	3	4
9. I worry too much over something that really doesn't matter	1	2	3	4
10. I am happy	1	2	3	4
11. I have disturbing thoughts	1	2	3	4
12. I lack self-confidence	1	2	3	4
13. I feel secure	1	2	3	4
14. I make decisions easily	1	2	3	4
15. I feel inadequate	1	2	3	4
16. I am content	1	2	3	4
17. Some unimportant thought runs through my mind and bothers me	1	2	3	4
18. I take disappointments so keenly that I can't put them out of my mind	1	2	3	4
19. I am a steady person	1	2	3	4
20. I get in a state of tension or turmoil as I think as I think over my recent concerns and interests	1	2	3	4

Appendix E.3 - Spielberger State Anxiety Inventory

Patient Name _____
 Patient Nr. _____

Date _____

SPIELBERGER STATE-TRAIT ANXIETY INVENTORY (STAI-S)

Self-Evaluation Questionnaire

Instructions:

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you feel right now, that is, at this moment. There are no right or wrong answers. Do not spend too much time on any statement, but give the answer which seems to describe your present feelings best.

	Not at all	Somewhat	Moderately so	Very much so
1. I feel calm.	1	2	3	4
2. I feel secure.	1	2	3	4
3. I am tense.	1	2	3	4
4. I feel strained.	1	2	3	4
5. I feel at ease.	1	2	3	4
6. I feel upset.	1	2	3	4
7. I am presently worrying over possible misfortune.	1	2	3	4
8. I feel satisfied.	1	2	3	4
9. I feel frightened.	1	2	3	4
10. I feel comfortable.	1	2	3	4
11. I feel self-confident.	1	2	3	4
12. I feel nervous.	1	2	3	4
13. I am jittery.	1	2	3	4
14. I feel indecisive.	1	2	3	4
15. I am relaxed.	1	2	3	4
16. I feel content.	1	2	3	4
17. I am worried.	1	2	3	4
18. I feel confused.	1	2	3	4
19. I feel steady.	1	2	3	4
20. I feel pleasant.	1	2	3	4

Appendix E.4 - Smith Relaxation States Inventory

HOW DO YOU FEEL RIGHT NOW? PLEASE CHECK ALL THE ITEMS USING THIS KEY.

RIGHT NOW, I FEEL LIKE THIS

①	②	③	④	⑤	⑥	
Not at All	A Little	. . Moderately . .		A Lot	Maximum	
①	②	③	④	⑤	⑥	1. My mind is SILENT and calm (I am not thinking about anything).
①	②	③	④	⑤	⑥	2. My muscles feel TIGHT and TENSE (clenched fist or jaws; furrowed brow).
①	②	③	④	⑤	⑥	3. I feel AT PEACE.
①	②	③	④	⑤	⑥	4. I feel DROWSY and SLEEPY.
①	②	③	④	⑤	⑥	5. Things seem AMAZING, AWESOME and EXTRAORDINARY.
①	②	③	④	⑤	⑥	6. Right now I recognize the wisdom of sometimes ACCEPTING things as they are.
①	②	③	④	⑤	⑥	7. My muscles are SO RELAXED that they feel LIMP.
①	②	③	④	⑤	⑥	8. I am HAPPY.
①	②	③	④	⑤	⑥	9. I am WORRYING.
①	②	③	④	⑤	⑥	10. I feel AT EASE.
①	②	③	④	⑤	⑥	11. I feel DISTANT and FAR AWAY from my cares and concerns.
①	②	③	④	⑤	⑥	12. I feel ENERGIZED, CONFIDENT and STRENGTHENED.
①	②	③	④	⑤	⑥	13. I am DOZING OFF or NAPPING.
①	②	③	④	⑤	⑥	14. I feel THANKFUL.
①	②	③	④	⑤	⑥	15. I feel like I am fully and SIMPLY in the PRESENT, not distracted by past or future concerns.
①	②	③	④	⑤	⑥	16. Things seem TIMELESS, BOUNDLESS, or INFINITE.
①	②	③	④	⑤	⑥	17. I feel IRRITATED or ANGRY.
①	②	③	④	⑤	⑥	18. I feel JOYFUL.
①	②	③	④	⑤	⑥	19. I feel SAD, DEPRESSED, or BLUE.
①	②	③	④	⑤	⑥	20. I feel AWARE, FOCUSED, AND CLEAR.
①	②	③	④	⑤	⑥	21. My hands, arms, or legs are SO RELAXED that they feel WARM and HEAVY.
①	②	③	④	⑤	⑥	22. I feel INNOCENT and CHILDLIKE.
①	②	③	④	⑤	⑥	23. My BREATHING is NERVOUS and UNEVEN (Or shallow and hurried).
①	②	③	④	⑤	⑥	24. I feel LOVING.
①	②	③	④	⑤	⑥	25. Things seem FRESH and NEW, as if I am seeing them for the first time.
①	②	③	④	⑤	⑥	26. I feel INDIFFERENT and DETACHED from my cares and concerns.
①	②	③	④	⑤	⑥	27. I feel PRAYERFUL or REVERENT.
①	②	③	④	⑤	⑥	28. I feel PHYSICAL DISCOMFORT or PAIN (backaches, headaches, fatigue).
①	②	③	④	⑤	⑥	29. My mind is QUIET and STILL.
①	②	③	④	⑤	⑥	30. I feel ANXIOUS.
①	②	③	④	⑤	⑥	31. I sense the DEEP MYSTERY of things beyond my understanding.
①	②	③	④	⑤	⑥	32. I feel RESTED and REFRESHED.
①	②	③	④	⑤	⑥	33. I feel CAREFREE.
①	②	③	④	⑤	⑥	34. TROUBLESOME THOUGHTS are going through my mind.
①	②	③	④	⑤	⑥	35. My body is PHYSICALLY RELAXED.
①	②	③	④	⑤	⑥	36. Presently I feel there's no need to try to change things that simply can't be changed.
①	②	③	④	⑤	⑥	37. I feel fully focused and ABSORBED in what I am doing.
①	②	③	④	⑤	⑥	38. I feel OPTIMISTIC, HOPEFUL, or TRUSTING that I can rely on someone or something.

Your age: _____ Gender: M F

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Appendix F - Post test recording forms

SE device history

How many points did the participant get? _____

Exactly how long did they use the device for? _____

Did the participant have difficulty learning to use the device? Yes No

If yes, please describe here:

Control device history

Exactly how long did they use the device for? _____

How much Quality Time? _____

Breathe Power? _____

Average Wavelength _____

Please write down anything that may have affected the study results with this participant.

Adverse Events

Did the subject experience any adverse events? Yes No

Event: Specify	Start date: Stop date:	Time elapsed	Severity: 1 Very mild 2 Mild 3 Moderate 4 Severe	Relationship to treatment: 1 Unrelated 2 Probably not 3 Possibly 4 Probably 5 Definitely