THE INTERACTIVE EFFECTS OF BIOFEEDBACK-ASSISTED
STRESS MANAGEMENT AND TRAINING ACQUISITION
IN PREDICTING HEALTH OUTCOMES

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May 2003

Submitted in partial requirement for the degree of
MASTER OF ARTS IN PSYCHOLOGY
Cleveland State University
May 2016
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Cary M. Sears, Date of Defense: April 6, 2016
ACKNOWLEDGEMENTS

This thesis will be in memory of Dr. Michael McKee. I wish that I could thank him for his mentorship, without which this thesis would not be possible.

I would like to acknowledge my Committee Chairperson, Christine S. Moravec with sincere gratitude for her patience, wisdom, and guidance. It is rare to encounter a mentor with both great knowledge and great generosity in sharing it.

I would also like to express my gratitude to my Committee Methodologist, Dr. Kenneth E. Vail for his valuable insights and suggestions regarding research design and data analysis.

Additionally, I would like to thank my Committee Member Conor T. McI'llenan for stepping in on very short notice, and taking time out of his busy teaching and research schedules, to attend meetings and provide beneficial feedback.

Furthermore, I would like to thank my Committee member Andrew Slifkin for making special efforts to read my thesis, attend my thesis defense, and for his valuable suggestions which helped improve the overall quality of the work.

I would like to also thank Dr. Benjamin Greenberg for his assistance while working as a Post-doctoral fellow in Dr. Moravec’s lab.

Finally, I would like to acknowledge Wendy Sweet from Dr. Moravec’s lab for her graphics and layout assistance.
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CARY M. SEARS

ABSTRACT

Thirty-seven chronic disease patients were randomized to either a biofeedback-assisted stress management (BFSM) experimental group or a usual care (UC) control condition. It was hypothesized that participants enrolled in the BFSM treatment group would demonstrate lower levels of norepinephrine and depression than those in the UC control condition. It was further hypothesized that training acquisition would modify the main effect of group assignment on depression and norepinephrine. The BFSM group demonstrated significantly lower levels of norepinephrine than the UC group. There were no main effects of BFSM on depression. The training acquisition X group assignment interaction was not significant. Results are discussed in terms of providing support for a common mechanism for the effects of BFSM on health outcomes in chronic diseases with ANS dysfunction, and the implications of assessing training acquisition in both clinical and research settings.
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CHAPTER I

INTRODUCTION

Purpose of Thesis

The two purposes of this thesis are to extend the literature regarding the health outcomes of biofeedback on patients with chronic illness, and to test the interactive effects of biofeedback-assisted stress-management (BFSM) and training acquisition in predicting health outcomes, in comparison to a usual care (UC) control group.

A number of chronic illnesses, including multiple sclerosis (MS) and coronary artery disease (CAD), involve dysregulation of the autonomic nervous system (ANS). ANS imbalance includes over-activation of the sympathetic branch and under-activation of the parasympathetic nervous system. High sympathetic nervous system arousal and low parasympathetic control are predictive of worse health outcomes in CAD (Carney et al., 2005). Autonomic dysfunction, of this type, is also observed in MS (Merico et al., 2005).

Biofeedback is a non-invasive and patient-centered self-regulatory therapy that can assist in the treatment of chronic illness, particularly those illnesses related to...
dysregulation of the ANS. This thesis aims to extend the research on biofeedback health outcomes to two less frequently studied chronic disease populations, CAD and MS, which have in common ANS dysfunction.

One mechanism by which biofeedback might exert its effects is by helping patients learn to better regulate their ANS and help restore a healthier balance of sympathetic and parasympathetic control. High plasma norepinephrine is an indicator of increased sympathetic nervous system activity (Goldstein et al., 1983). It is therefore hypothesized that participants who receive BFSM will have lower levels of plasma norepinephrine than a usual UC control group.

Patients with chronic illness tend to be more prone to depression than physically healthy individuals. Disruption of work and family life, financial concerns, uncertainty regarding prognosis or when flare-ups will occur, pain and potential disability are just some of the many issues with which patients with chronic illness may contend. High levels of depression have been observed in both CAD (Carney et al., 2005) and MS (Siegert & Abernathy, 2005). It is further hypothesized that biofeedback will decrease depression in patients with chronic illness. Specifically, it is predicted that BFSM will decrease depression, such that those in the BFSM treatment group will have lower levels of depression than those in the UC group.

A second aim of this study is to assess the interactive effects of BFSM and training acquisition on health outcomes. There is much evidence for the efficacy of biofeedback. However, the literature does contain some mixed results. Some of this variation may be due to a lack of systematically assessing whether patients were successful in learning to alter their physiology in a healthy direction as a result of
biofeedback. Therefore, a training acquisition measure was developed for this study. The training acquisition variable measures the extent to which participants are able to move their physiology in a healthy direction in the absence of feedback. It is hypothesized that training acquisition will interact with BFSM vs. UC to predict health outcomes. Specifically, it is predicted that training acquisition will moderate the relationship between group assignment (BFSM vs. UC) and norepinephrine, and depression.

Measurement of training acquisition has important implications both clinically and in research settings. Without assessing whether participants are actually able to alter their physiology as a result of learning biofeedback, it is difficult to determine whether patients actually received the intended treatment, and therefore whether results, positive or negative, are in fact due to patients actually being trained in and implementing biofeedback. Health outcomes may be better predicted by the interaction of BFSM vs. UC and the extent of individuals' ability to alter their physiology, or training acquisition. Considering the cost of chronic illness to individuals' and society and the potential of biofeedback as a cost-effective and non-invasive treatment, it is relevant to determine variables that may interact to determine successful outcomes.

Cost of Chronic Illness

Chronic illness impacts a large number of Americans and places a high burden on patients and their families in terms of quality of life and economic harm. Chronic illness also negatively impacts the overall economy in terms of lost productivity and healthcare costs. In 2012, the last year for which comprehensive data are available, 52% of Americans had at least one chronic illness (Ward et al., 2014). The economic impact of
chronic disease to the United States economy is 1.3 trillion dollars annually and growing with 1.1 trillion in lost productivity and 277 billion dollars in annual treatment costs (DeVol & Bedroussian, 2007).

**Coronary Artery Disease**

Heart disease is the number one cause of death in the United States (Heron, 2015) and coronary heart disease (CHD) or coronary artery disease (CAD) is the most prevalent form of heart disease (CDC, 2009). CAD is a progressive and chronic condition that can also have deleterious effects on patients' perceived quality of life including depression (Lee, 2010).

**Multiple Sclerosis**

Approximately 400,000 people in the United States and 2.5 million worldwide are diagnosed with Multiple Sclerosis (MS), a progressive, incurable, and often disabling inflammatory disease of the Central Nervous System (Tullman, 2013). While the symptoms and course of MS are highly variable, patients with MS often experience fatigue, movement impairments and falls, spasticity, depression, cognitive impairment, bowel and bladder dysfunction, sexual dysfunction, and issues with swallowing (Cheng et al. 2010).

**Biofeedback**

Biofeedback is a self-regulation therapy in which individuals can gain awareness and control of their physiology. Schwartz and Olson (2003) indicate that the term
“biofeedback” is shorthand for external psychophysiological feedback or physiological feedback, and is sometimes referred to as augmented proprioception. Through biofeedback individuals can become aware of physiological processes that are normally beyond their awareness, and gain control over bodily functions that are not normally under conscious control. Biofeedback falls within the larger field of applied psychophysiology (Schwartz & Schwartz, 2003).

Biofeedback instrumentation measures processes, such as ANS activity, that are normally outside of awareness and control. It is difficult to measure many of these processes directly so non-invasive technology has been developed to measure correlates (Peek, 2003). Such non-invasive technology includes electrodes on the fingers to measure skin conductance, a correlate of sweat gland activity; finger thermisters to measure digital peripheral temperature, a correlate of peripheral vasoconstriction; and photoplethysmograph to measure blood volume pulse, a correlate of heart rate. Electrocardiograms can be used to calculate heart rate variability (HRV), the variation in the beat to beat interval between heart beats, a measure of ANS regulation. Electromyography electrodes record electrical manifestations of muscle contraction indicative of surface muscle tension (Peek, 2003).

Some of these parameters, such as skin conductance and digital peripheral temperature, can be used as indications of ANS arousal. HRV can be used to assess the balance between the sympathetic and parasympathetic branches of the ANS. These parameters can also be used to detect disordered physiology, such as dysregulation of the ANS. Dysregulation of the ANS is seen in hyperarousal to stress and some disease states (Moravec, 2008, 2011).
Biofeedback instruments detect minute changes in these parameters that are normally beyond the level of conscious awareness. The signal from biofeedback instruments is processed and fed back to the individual. Historically, feedback included mechanical presentation of visual or auditory feedback on the state of the signal. Today the signal is most often feedback via a computer screen that allows for presentation of multiple channels of physiological information (McKee, 2008). Working in conjunction with a biofeedback therapist, individuals' learn to interpret the physiological feedback and to alter their physiology in a healthy direction (Yucha & Montgomery, 2008).

The ultimate goal of biofeedback is for the person to learn to self-regulate physiological processes in the absence of external feedback. The person would have learned to alter their physiology in a healthy direction on their own. Doing so is expected to lead to reductions in symptoms (Schwatz & Schwartz, 2003).

*Heart Rate Variability (HRV) Biofeedback*

HRV is used as a measure of ANS regulation. HRV is the variation in time between heartbeats. The time period between heartbeats is referred to variously as the interbeat interval or the RR interval where R refers to the R wave in the QRS complex of the electrocardiogram (ECG) and RR refers to the interval of time between successive R peaks (Bertsen et al., 1997).

Heart rate is primarily under the control of the ANS and HRV reflects the balance of the sympathetic and parasympathetic inputs to the sinoatrial node of the heart. (Malik et al., 1996; Billichick & Berger, 2006). Optimal heart rate variability reflects the ability
of the healthy heart to adapt to environmental and psychological changes and challenges and thus the adaptability or resilience of the organism (McCraty & Shaffer, 2015).

Low HRV is indicative of dysregulation of the ANS that can result from too little parasympathetic control and/or sympathetic over-activation and has been related to negative health outcomes (Odemuyiwa, 1994). Dysregulation of the autonomic nervous system is involved in the pathogenesis and course of several different chronic diseases, including those in this thesis. In HRV biofeedback patients are taught to breathe at their resonant frequency or the breaths per minute that optimizes their HRV. Breathing is paced on a computer screen and patients also receive feedback regarding their HRV. While there is individual variability in resonant frequency, a typical rate of breathing to optimize HRV is around 6 breaths per minute.

**Biofeedback Models**

Several historical tributaries feed into the river of modern biofeedback. These include, but are not limited to, behavioral psychology and learning theory, cognitive behavioral psychology and cybernetics, psychophysiology, behavioral medicine, stress research and stress management techniques. These combined with the advent of biomedical engineering made modern biofeedback possible (Schwartz & Olson, 2003).

One early stream of research biofeedback draws from is classical studies of operant or instrumental conditioning of the ANS. Initially, it was believed that the ANS could only be controlled through classical conditioning and certainly not through conscious control (Lehrer, 2003). Instrumental conditioning is still sometimes used as a model to explain how biofeedback works. In this model the signal fed back to the patient
is a reinforcer that results in operant conditioning of physiological processes beyond conscious awareness or control (Schwartz & Olson, 2003).

Several contemporary models have been constructed to account for the learning and change that occurs in biofeedback. McKee (2008) delineates two operative models: The direct feedback model and the therapeutic/stress-management/biofeedback model. In the direct feedback model patients are trained to directly alter specific physiology and it is assumed that the direct feedback enhances leaning. This relies more on cognitive behavioral approaches than classical conditioning. The therapeutic/stress-management/biofeedback model takes an individual approach, particularly with patients who have excessive arousal related to autonomic dysfunction. Stress-management techniques are used, along with measurement of arousal and recovery, and feedback is provided to the patient regarding these measurements. Biofeedback-mediated stress-management (BFSM) is an education and training protocol consisting of a biofeedback therapist educating patients regarding the link between stress, autonomic dysfunction, and disease states. The therapist assists participants with learning stress-management techniques and relating those techniques to physiological parameters illustrated by real time feedback. The individual, with coaching by the biofeedback therapist, learns to alter his/her physiology in a healthier direction with the aid of stress-management techniques and physiological feedback (Moravec, 2011).

Patients with chronic disease and autonomic dysfunction have responded favorably to various relaxation protocols including biofeedback. The common mechanism underlying these various modalities may be their effects on the autonomic nervous system, in that they induce parasympathetic control and reduce sympathetic
arousal. There has been some question given the efficacy of various relaxation modalities as to whether these are sufficient without biofeedback and if biofeedback adds anything above and beyond relaxation. After all, why add machines if one can achieve the same results using just the body and mind? In two separate studies, Blanchard et al. (1982) found that chronic headache sufferers, who did not respond to relaxation training, consisting of progressive relaxation and deep breathing, demonstrated a significant response to both EMG and thermal biofeedback. Patients receiving biofeedback were instructed to find individual self-regulation techniques that worked for them but encouraged to use relaxation and imagery. Therefore, these studies were not a direct comparison between biofeedback alone and relaxation alone but were taking groups of participants that did not respond to relaxation alone and adding biofeedback. The results indicate that for at least certain patients under certain circumstances biofeedback can add something to relaxation that produces superior outcomes to relaxation alone. One argument for the efficacy of adding biofeedback to relaxation training is that it takes away the guess work because patients know from the feedback whether they are correctly altering the physiology in a healthy direction. This increased precision shortens the learning curve over trial and error and reinforces the response making reliable learning possible. Feedback can also give the patient more confidence in both the process and their own abilities when they can actually see results in real time. Furthermore, a trained biofeedback therapist is able to assess though the instrumentation how a participant is performing and help them adjust techniques. Patients undergoing BFSM receive training in a variety of different relaxation techniques combined with physiological feedback in a working relationship with a trained biofeedback therapist. Biofeedback-assisted stress
management (BFSM) protocol may help patients better regulate their ANS through learning relaxation techniques that engage the parasympathetic branch and disengage the often overactive sympathetic nervous system. This is expected to increase balance of the ANS and lead to better health outcomes.

**Efficacy of Biofeedback**

In a comprehensive review of the literature, Yucha and Montgomery (2008) determined that biofeedback has demonstrated efficacy in the treatment of a number of diseases and conditions including anxiety, attention deficit hyperactivity disorder (ADHD), chronic pain, epilepsy, constipation, adult headache, hypertension, motion sickness, Raynaud’s disease, temporomandibular disorder (TMD), and urinary incontinence particularly in females. The authors indicated that lack of demonstrated efficacy of biofeedback, with regards to particular illnesses, should not be taken as a demonstrated lack of efficacy, because a number of the reviewed diseases included few studies, poorly designed research, and/or mixed results (Yucha & Montgomery, 2008).

**Training Acquisition**

One issue with assessing outcomes in biofeedback is that it cannot be assumed that all participants received the same “dose.” In a drug study, for example, participants receive a set measurable dose. In a biofeedback experiment, or in clinical practice, it is reasonable to believe that there are individual differences in ability, belief, amount of practice, and other such variables that would result in some people being more successful
at learning biofeedback than others. It is also reasonable to believe that these differences in learning would be related to health outcomes.

Yucha and Montgomery (2008) make a distinction between training and treatment. An individual receiving treatment, under the care of a medical professional, is often a passive recipient. Other than compliance with the treatment, such individuals are not expected to do anything in particular for the treatment to be effective. Conversely, training connotes active participation in which an individual must learn, practice, and master something. It necessarily follows that there would be individual differences in ability, motivation, practice, and subsequently success in learning and application. Biofeedback can be considered training rather than a treatment and effective biofeedback necessitates learning and skill acquisition on the part of the participant (Yucha & Montgomery, 2008).

There is evidence to support the effectiveness of biofeedback. However, there are some mixed results within the literature as well. Some of this variability may be due to researchers not taking into account the extent of training acquisition, or whether or not participants had successfully learned to alter their physiology, especially in the absence of feedback. It is one thing to be able to successfully modify one’s physiology when presented with immediate feedback and coached by a trained therapist, but quite another is to be able to draw upon a learned skill in the absence of feedback, and ultimately in real life outside of the therapy room or laboratory. Failure to assess whether or not participants are able to successfully alter their physiology after receiving a biofeedback intervention is tantamount to not assessing whether participants actually received the intended treatment or the same “dose” of the treatment. Therefore, some measurement of
training criteria indicative of meaningful physiological change or training acquisition should be included in biofeedback studies. However, this is often not the case (Yucha & Montgomery, 2008).

Current Thesis

The current work tests the effects of BFSM vs. UC on health outcomes in patients with chronic illnesses that are known to involve ANS dysregulation and higher levels of depression. It is predicted that BFSM will lead to lower levels of depression, and norepinephrine as a marker of sympathetic nervous system activity, which is known to be over-active in patients with ANS dysfunction. A measure of training acquisition was also developed. This is a continuous measure of the magnitude of change in HRV from a pre-randomization physiological monitoring period of self-relaxation without feedback, to a post intervention or usual care self-relaxation physiological monitoring period. This training acquisition measure indicates the relative extent to which participants are able to regulate their ANS in the absence of feedback. It is hypothesized that training acquisition will act as a moderator to the main effect of BFSM vs. UC in predicting the health outcomes of depression and norepinephrine levels.
CHAPTER II

METHODS

Participants

Participants were 37 chronic disease patients with either CAD or MS already receiving treatment at the Cleveland Clinic Foundation (CCF). Since these diseases both involve dysfunction of the ANS, all patients were analyzed together. Inclusion criteria included being between the ages of 18 and 90, the ability to give informed consent, no significant cognitive impairment, no pacemakers or defibrillators, and the ability to attend 10 study sessions.

Equipment

Non-invasive physiological monitoring was conducted via EKG pads placed on the forearm for use in calculating HRV. HRV was used as the primary measure of physiological arousal because it is a known measure of ANS balance.1
Norepinephrine, as a marker of autonomic activity, was assessed as an outcome variable. Venous blood was drawn for analysis of norepinephrine. Depression was also measured as an outcome variable using the Patient Health Questionnaire Depression Scale (PHQ-8). The PHQ-8 is an eight item screen for depression with demonstrated reliability and validity (Pressler et al., 2010). Four patients were excluded from the analyses utilizing norepinephrine as an outcome variable due to issues with data collection. The nurse was unable to draw blood for these patients for analysis of plasma norepinephrine. Therefore, while $N = 37$ for analysis of depression, $N = 34$ for analysis of norepinephrine.

**Design and Procedure**

The design is a randomized, controlled study of biofeedback-assisted stress management (BFSM) vs. usual care (UC) in patients with chronic disease (CAD and MS). Effects of BFSM vs. UC on depression and activity of the sympathetic branch of

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1 Other physiological measures that were recorded, but that are beyond the scope of this thesis, include respiration rate, skin conductance, digital peripheral temperature, and electromyography.

2 Other measures beyond the scope of the current work were collected including epinephrine and various inflammatory markers and other questionnaires (i.e., SF36, LET, GAD-7).

3 The study, including design and data collection, was previously conducted by the Moravec Lab at CCF. It is described here to introduce the data that will be analyzed.
the ANS were assessed. Training acquisition was tested as a moderator of the effects of BSFM vs. UC on depression and ANS function. All participants underwent an initial study visit during which they were asked to complete the PHQ-8 depression scale as well as demographic data (Table 1.) Venous blood was then drawn to measure catecholamines (i.e., norepinephrine) as a measure of ANS function, specifically activation of the sympathetic nervous system.

Following the blood draw, Non-invasive physiological monitoring of HRV was conducted, for all participants, during a five minute self-relax period. During this self-relax period patients did not receive any external feedback regarding their physiology. At the end of the initial study visit, participants were randomly assigned to either a BFSM treatment group or a UC control group. Figure 1 outlines the overall study design. Following randomization, the UC control group continued to receive their usual standard treatment from their physician(s) at the Cleveland Clinic as indicated by the standard of care for their disease and their individual condition. Participants were asked to inform research personnel if they enrolled in any other relaxation, stress management, or psychotherapy interventions including biofeedback. Zero participants in the UC control group received any type of biofeedback intervention during the course of the study.

The BFSM treatment group also continued to receive usual care from their physicians(s) at the Cleveland Clinic after randomization and for at least the duration of the study. In addition to usual care, the BFSM treatment group also received eight weekly sessions of BFSM with a board certified biofeedback therapist certified through the Biofeedback Certification International Alliance. During the 8 week BFSM
**Table 1. Demographic Data Total Sample**

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<tr>
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<td>37</td>
</tr>
<tr>
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</tr>
<tr>
<td>Race (Caucasian/total)</td>
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<tr>
<td>Age (years)*</td>
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</tr>
<tr>
<td>Disease duration (years)*</td>
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*Data presented as mean ±SD.
Figure 1. Overall Study Design
intervention patients received non-invasive physiological monitoring of digital peripheral
temperature, and Galvanic skin conductance via finger sensors; surface muscle tension
via EMG; respiration via a respiratory strain gauge; and EKG for use in calculating HRV.
Participants received visual feedback regarding these physiological parameters by
computer. Patients were educated about the connection between these physiological
parameters, the stress response, the relaxation response, the ANS, and disease symptoms
and progression. Participants were taught a number of relaxation techniques including
various breathing techniques (i.e., diaphragmatic breathing, resonant frequency
breathing), progressive muscle relaxation, guided imagery, autogenics, mindfulness,
positive affirmations, and cue-controlled relaxation as well as how these techniques relate
to the physiological feedback. Patients were coached regarding how to use the relaxation
techniques and feedback to move their physiology in a healthy direction. They were also
given a finger thermistor and instructed to practice finger warming at home. Within the
standardized protocol a lot of room was given for individual differences in instruction as
fits the BFSM model. For example, patients were trained first on the physiological
parameter that appeared most reactive and salient for each individual.

After eight weeks of either BFSM or UC, all participants in both groups returned
for a final study visit. The final study visit followed the exact same protocol as the initial
study visit with all of the same measures being assessed as before, including
questionnaires, blood draws, and physiological monitoring.
**Data Analysis**

Training acquisition was assessed by the magnitude of change in mean HRV from the initial study visit five minute self-relax period to the final study visit five minute self-relax period. This was therefore, a measure of the extent to which participants learned to regulate their physiology in the absence of feedback. HRV was measured by the Standard Deviation of the Inter-Beat Interval (SDNN) because it is a widely used measure in both the psychology and cardiology literature and due to its relative clarity of interpretation.

Data analyses were conducted using 2 (Group: BFSM, UC) X Training Acquisition (continuous) moderated multiple regression analyses for each outcome variable, depression and norepinephrine. Data collected at the final study visit for both depression and norepinephrine were used in these analysis. Methods prescribed by Aiken and West (1991) were followed to regress depression and norepinephrine on training-acquisition (continuous) X 2 (BFSM vs. UC) group. Centered training-acquisition scores and the dummy coded group variable were entered first as main effects, and their product was entered second as the interaction term.

Post hoc analysis of interactions was carried out by simple slopes analysis (Aiken & West, 1991). Simple slopes for the regression of training acquisition on both depression and norepinephrine were tested at the two different group levels: BFSM treatment group and UC control group. The relationships between group assignment and depression and group assignment and norepinephrine were assessed at different levels of the moderator variable, training acquisition. These levels included the mean level of training acquisition as well as one standard deviation above and one standard deviation below the mean.
CHAPTER III

RESULTS

Normality of the distributions of the predictor variable training acquisition and the outcome variables norepinephrine and depression were assessed graphically using histograms and P-P plots and numerically using skew and kurtosis statistics as well as the Kolmogorov-Smirnov test. Skewness and kurtosis values were converted to Z scores and tested for significance against tables of the standard normal distribution. For training acquisition, while the distribution showed evidence of negative skew (-.156) and negative kurtosis (-1.037), neither of these were significantly greater than 0. The Kolmogorov-Smirnov test further indicated that training acquisition did not deviate significantly from normal (D [33] = .104, p = .200). Norepinephrine showed evidence of slightly significant positive skew (Z=1.96, p < .05) as well as non-significant positive kurtosis (Z=.107). However, the results of the Kolmogorov-Smirnov (D [37] = .106, p = .200) indicated that norepinephrine scores did not deviate significantly from normal. Depression scores (D [37] = .197, p = .001) were significantly non-normal, showing significantly positive skew
(Z = 3.64, \( p < .05 \)) and significantly positive kurtosis (Z = 2.20, \( p < .05 \)). Due to the sample size of this study no transformations were carried out. Levine’s test was used to assess homogeneity of variance. The variances for the BFSM group and the UC group were not significantly different for norepinephrine (F [1, 3] = .007, \( p = .936 \)) or depression (F [1, 35] = .2.680, \( p = .111 \)). Predictor variables were assessed for multicollinearity. Treatment and training acquisition were not highly correlated (r = .037).

**Norepinephrine**

Replicating prior research, BFSM was associated with significantly less plasma norepinephrine in comparison to UC (t [31] = -2.485, \( \beta = -.408, p = .019 \)) (Table 2). There was not a significant main effect of training acquisition on norepinephrine (F [1, 31] = .265, \( R^2 = .008, p = .610 \)) While the model was not significant, there was a very small non-significant trend indicating that a 1 unit raw score increase in training-acquisition is associated with a 1.052 unit raw score decrease in norepinephrine or a 1 standard deviation increase in training acquisition is associated with .092 standard deviation decrease in norepinephrine (Table 2).

For norepinephrine, the training acquisition X BFSM (vs. UC) interaction was not significant (F [1, 29] = .156, \( R^2 = .004, p = .696 \)) (Table 3). As displayed in Figure 2, among those with lower (-1SD) training-acquisition, norepinephrine was lower in the BFSM condition (M = 345.048, SD = 60.084) compared to the UC condition (M = 478.659, SD = 63.853) (t [35] = 1.515, \( \beta = .343, p = .141 \)). Among those with higher (+1SD) training-acquisition, norepinephrine was lower in the BFSM condition (M = 307.840, SD = 58.803) compared to the UC condition (M = 493.374, SD = 79.410) (t [35] =
Table 2. Main Effects of BFSM vs. UC on Norepinephrine

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<td>BFSM</td>
<td>-158.64</td>
<td>63.83</td>
<td>-.41</td>
<td>.019</td>
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<tr>
<td>TA</td>
<td>-1.05</td>
<td>2.04</td>
<td>-0.92</td>
<td>.610</td>
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Table 3. Interaction of BFSM vs. UC and Training Acquisition on Norepinephrine

<table>
<thead>
<tr>
<th></th>
<th>F</th>
<th>R²</th>
<th>p</th>
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<tr>
<td>BFSM X TA</td>
<td>.156</td>
<td>.004</td>
<td>.696</td>
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Figure 2. Norepinephrine in the BFSM and UC groups at different levels of training acquisition. \( n = \) number of UC participants / number of BFSM participants.
Simple slopes analysis revealed that, in the UC condition, training acquisition was not significantly related to norepinephrine ($t[13] = .145, \beta = .039, p = .886$). A small non-significant trend indicates that for the UC group, higher levels of training acquisition are related to higher levels of norepinephrine, such that a 1 unit raw score increase in training-acquisition is associated with a .443 unit raw score increase in norepinephrine and a 1 standard deviation increase in training acquisition is associated with an increase in .039 standard deviation units on norepinephrine. In the BFSM condition, training acquisition was also not significantly related to norepinephrine ($t[19] = -.445, \beta = -.098, p = .659$). However, a non-significant trend shows that higher training-acquisition is related to lower norepinephrine, such that a 1 unit raw score increase in training-acquisition is associated with a -1.121 unit raw score decrease in norepinephrine and a 1 standard deviation increase in training acquisition.

**Depression**

As demonstrated in Table 4, there was no main effect of BFSM on depression ($F[1, 35] = 2.799, R^2 = .074, p = .103$). However, a non-significant trend indicates that a change from the UC condition to the BFSM condition is associated with a 2.690 unit raw score increase in depression or a .272 standard deviation increase in depression. Additionally, there was no main effect of training-acquisition on depression ($F[1, 35] = .041, R^2 = .001, p = .841$). However, a non-significant trend indicated that a 1 unit raw score increase in training-acquisition is associated with a .010 unit raw score increase in
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<tbody>
<tr>
<td>BFSM</td>
<td>2.69</td>
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<td>TA</td>
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Table 4. Main Effects of BFSM vs. UC on Depression
depression and a 1 standard deviation increase in training-acquisition is associated with an increase in .034 standard deviations on depression (Table 4).

For depression, the training acquisition X BFSM (vs. UC) interaction was not significant ($F_{[1, 33]} = .138, R = .004, p = .713$) (Table 5). As displayed in Figure 3, among those with lower (-1SD) training-acquisition, depression was higher in the BFSM condition ($M = 5.741, SD = 1.637$) compared to the UC condition ($M = 2.438, SD = 1.693$) ($t_{[35]} = 1.403, \beta = .334, p = .17$). Among those with higher (+1SD) training-acquisition, depression was higher in the BFSM condition ($M = 5.428, SD = 1.582$) compared to the UC condition ($M = 3.375, SD = 1.761$) ($t_{[35]} = .867, \beta = .208, p = .392$) (Figure 3). Simple slopes analysis revealed that, in the UC condition, training acquisition was not significantly related to depression ($t_{[17]} = .373, \beta = .094, p = .711$). However, there was a non-significant trend indicating that depression was higher in the UC group at higher levels of training acquisition. Among those in the UC condition, a 1 unit raw score increase in training-acquisition is associated with a .028 unit raw score increase in depression or a 1 standard deviation increase in training acquisition is associated with an increase in .094 standard deviation units on depression. In the BFSM condition, training acquisition was also not significantly associated with depression ($t_{[19]} = -.139, \beta = -.03, p = .89$). However, there was a non-significant trend indicating that in the BFSM condition, higher levels of training acquisition were associated with lower levels of depression. Among those in the BFSM condition, a 1 unit raw score increase in training-acquisition is associated with a -.009 unit raw score decrease in depression or a 1 standard deviation increase in training acquisition is associated with an decrease in -.03 standard deviation units on depression.
**Table 5.** Interaction of BFSM vs. UC and Training Acquisition on Depression

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<td>BFSM X TA</td>
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Figure 3: Depression in the BFSM and UC groups at different levels of training acquisition. \( n \) = number of UC participants / number of BFSM participants
CHAPTER IV

DISCUSSION

Norepinephrine

As predicted, BFSM was associated with significantly less norepinephrine than UC. This result is in line with previous research. Mathew et al. (1981) demonstrated significant reductions in plasma norepinephrine in a biofeedback-assisted relaxation group compared to a control group in patients with generalized anxiety disorder. Hypertensive patients treated with biofeedback-assisted relaxation showed significant reductions in plasma norepinephrine in comparison to a control group (McCoy et al., 1988).

The present study extends the literature to two diseases, CAD and MS that have been less frequently studied. Both CAD and MS are characterized by dysregulation of the autonomic nervous system (ANS). Patients with both diseases tend to have increased sympathetic nervous system activation and decreased parasympathetic nervous system activity. Autonomic dysregulation of this type is related to worse health outcomes in both CAD and MS (Carney et al., 2005; Merico et al., 2005). High levels of plasma
norepinephrine can arise from over activation of the sympathetic nervous system and is an independent predictor of negative health outcomes (Goldstein et al., 1983).

In the current study, at the first study visit assessment prior to randomization the mean level of norepinephrine for the whole sample was 393.1 picograms per milliliter (pg/ml) with a standard deviation of 195.3 pg/ml and a range of 750.0 pg/ml. At time 1 those patients eventually randomized to the UC control condition had a mean level of norepinephrine of 460.0 pg/ml with a standard deviation of 211.3 pg/ml and a range of 915 pg/ml. Those patients eventually randomized to the BFSM group stared the study with a mean level of norepinephrine 364.2 pg/ml with a standard deviation of 187.6 pg/ml and a range of 660 pg/ml. Norepinephrine levels at the final study visit (second assessment) were used in the data analysis for the current in the comparison between groups after the intervention. At this time point, the mean norepinephrine level for the entire sample (both groups) was 393.1 pg/ml with a standard deviation of 195.3 pg/ml and a range 750.0 pg/ml. The mean level of norepinephrine for the UC was 484.4 pg/ml with a standard deviation 180.0 pg/ml and a range of 607.0 pg/ml. The BFSM group had a mean norepinephrine level at time 2 of 326.0 pg/ml with a standard deviation of 182.2 pg/ml and a range of 750.0 pg/ml. The UC group had a mean increase in norepinephrine from the first study visit to the final study visit of 15.6 pg/ml with a standard deviation of 158.3 pg/ml and a range of 510 pg/ml. The BFSM group had a mean decrease in norepinephrine of 38.4 pg/ml with a standard deviation of 149.1 pg/ml and a range of 553.0 pg/ml.

Cameron et al., (1986) found a range of plasma norepinephrine in healthy unstressed participants of 150 pg/ml to 250 pg/ml over 24 hours. The authors indicated
that this in the lower end of the range of norepinephrine levels reported in the literature in healthy participants. Additionally, healthy subjects demonstrated an increase in norepinephrine of 44 pg/ml in response to laboratory stressors.

The results of the current study with regards to norepinephrine provide further support for the hypothesis that BFSM may act as a buffer to the over-activation of the sympathetic nervous system observed in diseases such as CAD and MS involving autonomic dysfunction. Demonstration of enhanced ability to regulate physiology towards better autonomic balance in both MS and CAD patients is further evidence of a common mechanism.

The common mechanism may be relaxation leading to healthier autonomic balance with increased parasympathetic control and decreased sympathetic activation as evidenced in the current study by reduced norepinephrine levels. Reduced norepinephrine has been observed in response to other stress reduction interventions other than biofeedback. In-patient heart failure patients demonstrated a mean reduction in norepinephrine of 232.4 pg/ml during a 12-minute visit with a therapy dog and 240.1 after the visit. These reductions were significant in comparison to two control groups, one receiving a 12-minute visit from a human volunteer and another group receiving usual care (Cole et al., 2007). In a randomized controlled study, meditation was shown to significantly increase subjective quality of life and decrease plasma norepinephrine in elderly patients with heart failure. The meditation group significantly decreased mean plasma norepinephrine from 677.7 pg/ml with a standard deviation of 96.6 pg/ml to 387.1 pg/ml with a standard deviation of 39.1 pg/ml. The control group decreased
norepinephrine from 491.4 with a standard deviation of 35.9 to 470.6 with a standard deviation of 31.2. This change was not statistically significant.

There is some evidence that biofeedback may provide different benefits to relaxation alone. McCoy et al., (1988) compared thermal biofeedback to progressive muscle relaxation without feedback in hypertensive individuals. Patients assigned to the biofeedback group demonstrated significant reductions in norepinephrine and mean arterial pressure, while the patients in the relaxation group did not demonstrate any significant changes on any variable. The mean pre-treatment plasma levels for the biofeedback group were 277.4 pg/ml supine with a standard deviation of 127.0 pg/ml and 589.3 pg/ml standing with standard deviation of 239.8. The mean post-treatment plasma norepinephrine levels for this group were 221.7 pg/ml supine with a standard deviation of 98.2 pg/ml and 509.0 pg/ml standing with a standard deviation of 127.6 pg/ml. For the relaxation group, the mean pre-treatment plasma norepinephrine were 224 pg/ml supine with a standard deviation of 130.0 pg/ml and 545.0 pg/ml standing with standard deviation of 280.3. The post-treatment norepinephrine levels for this group were 210.3 pg/ml supine with a standard deviation of 104.8 pg/ml and 496.5 pg/ml standing with a standard deviation of 248.1. One benefit of BFSM above and beyond other relaxation or stress management interventions is that the patient is trained to alter their own physiology in a healthy direction rather than just provided with an intervention that is done to them. In the current study, BFSM participants demonstrated significant reductions in plasma norepinephrine after being trained in various relaxation modalities augmented by feedback. The plasma norepinephrine was not drawn during a feedback session but after the 8 week intervention was completed. More studies are needed directly comparing
relaxation protocols alone to relaxation with biofeedback and investigating the mechanisms both physiological and psychological that account for successful outcomes. Patients receiving biofeedback may differentially benefit from the intervention depending on how successful they are in acquiring the ability to change their physiology in a positive direction. Individual characteristics such as motivation, ability, and amount of practice outside of biofeedback sessions are just some of the variables that could influence learning and performance differences. This leads to uncertainty that all of the participants received the exact same “dose” of biofeedback since dosing cannot be as tightly controlled as in pharmacological studies. Therefore, a training acquisition measure was introduced in this proposal.

There was no main effect of training acquisition on norepinephrine. There was however, a non-significant trend demonstrating that an increase in training acquisition is related to a decrease in norepinephrine, such that a 1 unit raw score increase in training acquisition is associated with a 1.052 unit raw score decrease in norepinephrine and a 1 standard deviation increase in training acquisition is associated with a .092 standard deviation decrease in norepinephrine. However, an effect size of .092 is miniscule and does not really reflect a meaningful effect.

The training acquisition measure was conceptualized as a measure of the relative extent to which participants are able to move their physiology in a healthy direction in the absence of feedback. It is based on how well participants were able to raise their HRV during a self-relax period without feedback. This was measured prior to and after the eight week biofeedback intervention period in both the BFSM treatment and UC control groups. The magnitude of change in HRV from pre-assessment to post-assessment was
operationalized as a measure of training acquisition. Patients being able to raise their HRV in the absence of feedback points to training transfer outside the biofeedback session and without a biofeedback therapist to coach them and is therefore indicative of physiological self-regulation. The patients in this study demonstrated a mean decrease in HRV of 1.2 ms with a standard deviation of 16.6. While the UC group demonstrated a mean decrease of 3.0, the BFSM group had a mean increase in HRV of .40 ms. Clearly, there was a lot of variability among patients in their level of training acquisition. In a comprehensive review of the literature regarding changes in HRV from exercise, drug, and biobehavioral interventions, including biofeedback, (Nolan et al., 2008) found an overall magnitude of change equivalent to an increase of 9.0 ms.

It was hypothesized that training acquisition would moderate the relationship between group assignment (BFSM vs. UC) and ANS function, as measured by norepinephrine.

There was not a significant interaction between training acquisition and group assignment. Analyzing the data at different levels (±1SD) of training acquisition demonstrated that for participants with both lower and higher levels of training acquisition, norepinephrine was lower in the BFSM condition compared to U.C., reflecting the lack of interaction and essentially recapitulating the main effect of BFSM on norepinephrine. In other words, norepinephrine was lower in the BFSM group then the UC group regardless of the effect of training acquisition.

Simple slopes demonstrated that training acquisition was not significantly related to norepinephrine in either the UC or BFSM condition. However, analysis of simple slopes revealed small non-significant trends in opposite directions among the UC and
BFWM groups. While in the UC group, higher levels of training acquisition are related to higher levels of norepinephrine, in the BFWM group higher levels of training acquisition are related to lower levels of norepinephrine. The demonstrated effects, however, are not much different from 0. For the UC group, a 1 unit raw score increase in training acquisition is associated with a .443 unit raw score increase in norepinephrine and a 1 standard deviation increase in training acquisition is associated with an increase in .039 standard deviation units of norepinephrine. For the BFWM group, a 1 unit raw score increase in training acquisition is related to a 1.121 raw score decrease in norepinephrine and a 1 standard deviation increase in training acquisition is associated with a decrease in .098 standard deviation units of norepinephrine.

Given that those in the BFWM group had significantly less norepinephrine than the UC group but training acquisition, as conceptualized in this study, did not moderate the effects of group assignment on norepinephrine, it could be that just participating in BFWM is sufficient without demonstrating training acquisition. Biofeedback could also work through mechanisms other than relaxation leading to better ANS balance. The paucity of evidence for this hypothesis could alternatively be attributed to the method in which training acquisition was measured. Future studies may consider whether there is a better way to measure a training acquisition effect.

*Depression*

CAD and MS patients tend to have higher levels of depression (Carney et al., 2005; Siegert & Abernathy, 2005). Depression is related to lower survival rates among patients with CAD (Carney et al, 205). Furthermore, depressed individuals with or
without CAD have higher levels of norepinephrine and lower HRV (Carney et al., 2005). Autonomic dysfunction is observed in depressed individuals who are physically healthy, as well as in MS and CAD patients, regardless of depression. However, patients with these types of chronic illnesses are more prone to depression than physically healthy individuals. Therefore, it is possible, but untested, that depression may compound the autonomic dysfunction already occurring in MS and CAD, leading to particularly negative health consequences. Carney et al. (2005) propose that autonomic dysregulation may mediate the link between depression and negative health outcomes in CAD. In the current study, in addition to improving autonomic nervous system balance, it was hypothesized that BFSM would lead to lower levels of depression compared with UC.

There was no significant main effect of group assignment on depression. However, a non-significant trend indicated that being assigned to the BFSM group was related to increased depression compared to being randomized to the UC group. The regression coefficients demonstrated that going from the UC condition to the BFSM condition is associated with a 2.690 unit raw score increase in depression or a .27 standard deviation unit increase in depression. Even though the main effect did not reach statistical significance, it is concerning that contrary to expectations the trend indicates that those in the BFSM group actually experienced increased depression in comparison to the UC control group. The question arises as to whether this is an accurate and meaningful effect and how to interpret this in light of the existing biofeedback literature and clinical considerations. Can biofeedback, under certain circumstances, actually lead to more negative outcomes such as increased depression?
There is an extensive literature demonstrating the positive benefits of biofeedback in the treatment of depression. Karavidas et al. (2007) conducted 10 sessions of HRV biofeedback with patients meeting diagnostic criteria for major depressive disorder (MDD). Participants demonstrated significant reductions in depression with a very large effect size $d = 3.6$. Patients also significantly increased SDNN. A limitation of this study was a lack of control group. In a comparison of depressed patients vs. healthy controls, HRV biofeedback significantly decreased symptoms of depression and anxiety, and increased HRV among depressed patients (Siepmann et al., 2008). Biofeedback has led to significant reductions in depression in a number of different patient populations, including illnesses involving autonomic dysregulation. Furthermore, HRV biofeedback appears to attenuate the effects of depression by increasing parasympathetic control. An intervention using respiratory sinus arrhythmia (RSA) biofeedback to increase parasympathetic control by increasing vagal tone decreased depressive symptoms in patients who recently underwent cardiac surgery compared to patients who received treatment as usual (Patron et al. 2013). In a pilot study conducted by Hassett et al. (2007) twelve women with fibromyalgia, an illness believed to be at least partially related to autonomic dysfunction, underwent 10 weeks of HRV biofeedback, after which they demonstrated significant decreases in depression and pain, and increased overall functioning. Patients with neurocardiogenic syncope, a syndrome characterized by autonomic dysfunction, demonstrated significantly decreased depression, headache, and loss of consciousness in comparison to a medication only control group after 10 sessions of biofeedback-assisted relaxation therapy (McGrady et al., 2003).
To this author’s knowledge, there have not been published studies demonstrating increased depression as a result of biofeedback. Taken together with the numerous published studies with positive results of biofeedback in the reduction of depression among a variety of different population leads one to question the effect observed in this study sample as being representative of a true population effect. An effect size of .27 is considered a small effect size (Cohen, 1992). Being assigned to the BFSM group as opposed to the UC group was associated with a raw score increase of 2.7. The PHQ-8 consists of 8 items with a score range of 0-24. Scores below 5 are considered as no depressive symptoms. Scores of five to nine indicate mild depression, while scores above 10 indicate moderate depression, and scores higher than 15 are indicative of clinical depression (Pressler et al., 2011). In the current study, for the total sample at the initial study visit the mean score on the PHQ-8 was 4.86 with a standard deviation of 4.93 and a range of 16. The BFSM group at time 1 had a mean score on the PHQ-8 of 6.11 with a standard deviation of 5.4 and a range of 16. The UC group at the first study visit had a mean of 3.7 with a standard deviation of 4.1 and a range of 12. The PHQ-8 administered at the final study visit was bused for comparison between the groups in this study. By the time of this final study visit, participants had been randomized to the BFSM group or the UC group and the intervention carried out. At this second administration, the mean score on the PDQ-8 for the total sample was 4.3 with standard deviation of 5 and a range of 20. The UC group at time 2 had a mean PDQ-8 score of 2.9 with a standard deviation of 3.8 and a range of 15. The BFSM group had a mean score of 5.6 with a standard deviation of 5.7 and a range of 20. Rather than concluding that BFSM increases depression compared to UC, with a non-significant p-value of .103, the more probable explanation is that the
effect was due to chance and is not representative of a true population value. Alternately, the higher levels of depression in the BFSM group as compared to the UC group at the final study visit may be due to the fact that this group had much higher depression scores at the baseline assessment. The regression analyses in this study were only carried out on time 2 values. It could be that the BFSM group was by chance more depressed coming into the study and that randomization was not entirely successful with regards to depression.

There was additionally no main effect of training-acquisition on depression. However, a non-significant trend demonstrated that an increase in training-acquisition is related to an increase in depression, such that a 1 unit raw score increase in training acquisition is associated with a .10 unit raw score increase in depression and a 1 standard deviation increase in training acquisition is associated with an increase in 0.32 standard deviation units on depression.

For depression, the interaction between group and training acquisition was also not significant. Post-hoc analysis showed that depression was higher in the BFSM condition than the UC condition among both participants with both higher (+1SD) and lower (-1SD) levels of training acquisition, again reflecting the lack of interaction.

Simple slopes demonstrated that training acquisition was not significantly related to depression in the UC or BFSM conditions. However, analysis of simple slopes indicated non-significant trends in varying directions among the UC and BFSM groups. In the UC condition depression was higher at higher levels of training acquisition. Conversely, for the BFSM condition higher levels of training acquisition were related to
lower levels of depression. For the UC condition, a 1 unit raw score increase in training-acquisition is associated with a 0.28 unit raw score increase in depression and a 1 standard deviation increase in training-acquisition is associated with an increase in 0.94 standard deviation units on depression. In the BFSM condition, a 1 unit raw score increase in training-acquisition is associated with a .009 unit raw score decrease in depression and a 1 standard deviation decrease in training-acquisition is associated with a .03 standard deviation decrease in depression. The non-significant and contrary results for training acquisition and the interaction between group and training acquisition for depression are difficult to interpret in light of the small effect sizes except to state that they are not generalizable.

Limitations of this study include a small sample size. The small sample size did not allow enough power to analyze the CAD and MS groups separately. Although, it is reasonable to assume a common mechanism for these diseases due to the commonality of ANS dysregulation, there could be differences between the groups based on differing disease profiles. Also, results from the CAD and MS patients taken together may not generalize to other chronic diseases, particularly those that do not involve ANS dysregulation. In order to study these potentially different populations, it may be necessary to use different outcome measures and training acquisition criteria that do not have an underlying assumption of working through the ANS. Different types of diseases could potentially work within models of biofeedback other than BFSM, which has an underlying assumption that learning relaxation techniques with feedback will lead to better self-regulation of the ANS and hence better health outcomes. Further research is needed with larger sample sizes and different patient groups, both with other diseases
having known ANS dysfunction, as well as those without particular ANS involvement. Further research is also needed to delineate the precise mechanisms by which biofeedback might exert an influence on the ANS, as well as other pathways that may lead to subsequent health outcomes.
REFERENCES


Carner, R.M., Freedland, K.E., & Veth, R.C. (2005). Depression, the autonomic nervous system, and coronary heart disease. Psychosomatic Medicine, 6, S29-S33.


