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Feasibility and Acceptability of Heart Rate Variability Biofeedback to Treat Fibromyalgia-Related Chronic Pain

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A dissertation submitted to the faculty of the Medical University of South Carolina in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the College of Nursing.

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.

Abstract

Background: Fibromyalgia (FM) is characterized by chronic diffuse pain, fatigue, memory problems, sleep disturbance, depression, and mobility limitations. The Department of Defense (DoD) and Department of Veterans Health Administration (VA) recognize FM as potentially connected to service in the Persian Gulf War, and the rates of FM diagnosis and disability in the VA are rising.

Purpose: The purpose of this dissertation was to assess the feasibility and acceptability of heart rate variability biofeedback (HRVB) as an intervention for the treatment of FM in Veterans.

Problem/Aims: We conducted an integrative literature review (manuscript 1) and identified a gap in the literature related to HRVB to treat FM-related chronic pain. Overall, HRVB is a promising treatment for chronic pain; however, further research is needed to evaluate the relationship between HRVB and FM pain. We found only one study evaluating HRVB for the treatment of FM, and we did not identify any studies that evaluated the recommended HRVB practice protocols, or any qualitative studies investigating the individual experience of using HRVB. The specific aims of this dissertation were:

Aim 1: Examine the feasibility of recruitment and retention of Veterans with fibromyalgia.

Aim 2: Determine the feasibility of adherence to the recommended HRVB practice protocol using the *emWave2*.

Aim 3: Examine participant acceptability and satisfaction with the intervention.

Design: We used a sequential exploratory multi-method design to determine if it is feasible for Veterans with FM to follow a twice-daily 20-minute HRVB practice protocol. We conducted a focus group post-intervention to explore the participant's experiences with HRVB.

Theoretical framework: The theory of symptom self-management guided the study; it posits that when self-directed interventions are optimized, performance outcomes will improve.

Findings: We found that it was not feasible for Veterans with FM to follow the recommended HRVB protocol. Barriers identified were conflicts with family obligations and work schedule as well as difficulties operating the HRVB device. Results from weekly questionnaires suggested an improvement in functional status and quality of life, but no change in pain levels. However, during the focus group discussion, the Veterans reported a reduction in pain levels as well as improvement in sleep, relaxation, and cognition.

Conclusion: Limitations of this study were a small size (n=10), possible self-selection bias, and the lack of a control group. While the data suggests HRVB may improve the functional status and quality of life of those with FM, more research is needed.

Keywords: fibromyalgia, chronic pain, heart rate variability biofeedback, veterans, integrative literature review, feasibility, acceptability, practice protocol.

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Introduction

Manuscript 1

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Introduction

Fibromyalgia (FM), a complex chronic pain syndrome, affects 10 million individuals in the United States (1, 2). The associated fatigue, memory problems, sleep disturbance, depression, anxiety, cognitive impairment, and mobility limitations (2, 3) contribute to 1-2% loss of national productivity (4, 5), $12-14 billion per year in national health care costs (4), and individual deficits in quality of life (6).

FM is recognized by the Department of Defense (DoD) and Department of Veterans Health Administration (VA) as potentially connected to service in the Persian Gulf War (7). The DoD and VA have linked FM to the physical and emotional trauma sustained by service members who deployed during the war as well as to the various natural and man-made environmental exposures in that region (8). Repetitive muscular injuries are attributed to service members carrying over 80 pounds of equipment daily for 6-12 months, during multiple deployments between October 2001 and the present; this has resulted in more than 50% of service members/Veterans returning from these conflicts reporting chronic pain not related to direct injuries such as shrapnel, gun shots, or blasts (8-10). The rate of diagnosis and disability of Veterans is rising at an alarming rate (11). With ongoing conflicts around the world, we do not expect the rate of FM cases to decrease. As health care providers in the VA it is our mission to fulfill President Lincoln's promise "to care for him who shall have borne the battle"(12), and to honor the VA core value of excellence by striving for the highest quality and continuous improvement in care. Thus, we chose to focus our study on the Veteran population, whom we recruited as study participants.

Because of the complexity of symptoms reported by individuals with FM, and the unclear etiology of the disease, primary care physicians and advanced practice nurses have had difficulty diagnosing and treating these patients. The diagnostic criteria for FM have changed significantly in recent years. The initial diagnostic criteria set by the American College of Rheumatology (ACR) in 1990 was determined by the number of "tender points" reported by the patient during a time-consuming, complex physical exam (13). In 2010 the ACR determined that 25% of patients with FM did not meet the "tender-point" test of FM and modified the survey to address the associated fatigue, sleep, and cognitive changes (2). "Tender-points" are subjective reports of pain or discomfort when the practitioner applies pressure specified areas of the head, neck, chest, back, and extremities (2). FM diagnosis was satisfied with one of the following 3 conditions: 1) the Widespread Pain Index (WPI) ≥ 7, the Symptom Severity Score (SS) ≥ 5, or the WPI = 36 and the SS ≥ 9; 2) symptoms present and at a similar level for at least 3 months, or 3) the patient lacked a disorder that would otherwise explain the pain (2). The initial survey was self-administered by the patient and then completed by the physician after a physical exam. Wolfe et al. (14) developed a modification of the 2010 criteria that allows complete self-administration by the patient. Primary care physicians and advanced practice nurses can give the survey to patients and easily interpret the results without a visit to a specialist, such as a rheumatologist. The developers argue this practice could decrease time to diagnosis and treatment (14). Additionally, the modified survey identifies a higher FM prevalence and a larger proportion of men with FM (15). The diagnostic sensitivity to men in the modified survey may explain the increased rate of FM diagnosis among service members and Veterans.

Individuals with FM often report symptoms that are variable and unpredictable, leading to frustrations around reporting their symptoms and often feeling as if the health care provider does not believe them (16, 17). Individuals with FM are also frustrated by the lack of clarity of a diagnosis, which leads to skepticism from family, friends, and health care professionals(16). Additionally, patients reported they are often given very little if any information about FM by their health care provider, and have to seek answers from other patients, support groups, or family members with the same diagnosis (17). FM patients are often skeptical of treatment recommendations, especially medications, because prescribing physicians have difficulty explaining how the treatment will target their symptoms or disease (17). FM patients report they are often better understood and receive more acceptable treatment from holistic providers; however, these treatments are often not covered by health insurance plans (16).

Treatment Recommendations

Health care providers agree that symptoms associated with FM are generally not demonstrated in chronic headaches, back, joint, or neck pain; thus, comparing treatment among these pain syndromes is challenging (2, 6). The VA/DoD has published clinical guidelines for chronic pain management (18). The most common published guidelines for FM treatment are from the European League Against Rheumatism (EULAR) 2016; the American Pain Society (APS) 2005; the German Association of the Scientific Medical Societies (AWMF) 2013; the Israeli Pain Society (IPS); and the Canadian Pain Society (CPS) (15, 19). Recent research and findings of the etiology and pathophysiology of FM indicate treatment must be multi-focal (15). There is a consensus among the EULAR, APS, AWMF, IPS, and CPS guidelines that effective treatment must include a

multidisciplinary approach that prioritizes nonpharmacological treatments, offers judicious pharmacological treatments (15, 19), and are based on the biopsychosocial model (15).

Pharmacological therapies. Pharmacological treatment guidelines vary greatly, which increases the difficulty in treating FM. VA/DoD treatment guidelines recommend against the use of opioids to treat FM-related chronic pain (18). EULAR and AWMF do not recommend common non-opioid analgesic treatments such as non-steroidal anti-inflammatories (NSAID) (20). There is no evidence for the effective use of acetaminophen or topical creams/ointments (1, 15, 21). Importantly, AWMF and EULAR strongly recommend against the use of opioids (15, 21). The published World Health Organization pain ladder includes opioids. However, it was designed for chronic pain related to cancer and is not appropriate for the treatment of widespread chronic pain as is seen in FM (15). The antidepressant amitriptyline has some evidence for both the treatment of neuropathic pain and sleep disturbance and received varying recommendations from all four guidelines (15). CPS guidelines recommend gabapentin and pregabalin, although EULAR gives them a weak recommendation, and AWMF recommends the use of pregabalin only if the use of amitriptyline is not possible, and does not make any decision about gabapentin (21). AWMF, CPS, and EULAR recommend serotonin-norepinephrine uptake inhibitors (SNRI) like duloxetine, which may provide some benefit (21). Milnacipran, a newer SNRI, is only recommended in the EULAR guidelines and not recommended in the AWMF guidelines (21).

Nonpharmacological therapies. All treatment guidelines agree that FM management should include a personalized graded exercise program (15, 19). A meta-

analysis of randomized controlled trials examining the effects of exercise on FM symptoms of fatigue, physical functioning, depression, and quality of life support this recommendation (22). All guidelines except EULAR include psychological treatment that includes cognitive behavior therapy a "strong recommendation" (15, 19, 20). Complementary and alternative medicines (CAM) like acupuncture, Tai Qi, and chiropractic treatments are controversial but encouraged in the CPS guidelines (15). Currently, however, there is insufficient evidence to support the use of CAM (15). The most recent VA/DoD Clinical Practice Guidelines for the treatment of chronic pain, which includes pain related to fibromyalgia, is to utilize cognitive behavior therapy, biofeedback, exercise, multidisciplinary psychosocial rehabilitation (3, 18), physical therapy, occupational therapy, acupuncture, manipulation, and CAM (9, 15). EULAR treatment guidelines only evaluated two reviews that included biofeedback as a treatment for FM (20). EULAR committee members do not recommend biofeedback, because while it is effective in reducing pain intensity it is not effective for fatigue or sleep (20). The report did not specify the type of biofeedback evaluated.

Pathophysiology of FM

The symptoms of FM - fatigue, memory problems, sleep disturbance, depression, anxiety, and cognitive impairment - are complex, and the above-referenced treatment recommendations do not address recent findings of the etiology of FM (23, 24). Research utilizing functional magnetic resonance imaging (fMRI) demonstrates that in individuals with FM, there is a disruption of pain network connectivity. Strengthened connectivity of the brain regions involved in the processing and reduced connectivity of the regions involved in pain inhibitory modulation may explain this widespread chronic pain (23).

The default mode network (DMN), a constellation of brain regions engaged in self-referential thinking, is disrupted in FM during tasks like visual attention and cognitive attention, which may explain symptoms of memory problems and cognitive impairment (24). An abnormally increased level of connectivity between the DMN and the insular cortex may also explain higher reported pain levels (25). Additionally, a dysfunction of the cardiac autonomic nervous system (ANS), characterized by higher sympathetic and lower parasympathetic cardiac autonomic modulation, is associated with incoherent heart rate variability and is related to the impact of FM on quality of life (6, 26).

Heart Rate Variability

Heart rate variability (HRV) is the time measurement of the oscillations of the R-to-R intervals (27-29) (see Figure 1). HRV reflects heart-brain interaction and ANS function (28-31) and HRV information on how the ANS interacts and functions as a whole (32). Analyzing HRV provides quantitative information about the state of the ANS (6).

Figure 1. Heart rate variability

Optimal HRV is cardiac coherence, a sine-waveform that is ordered and harmonic (33). Coherent HRV reflects a healthy functioning system, adequate physical functioning, minimal pain (28), resistance to stress, emotional adaptability (27), and self-regulation (33) (see Figure 2). Conversely, an HRV measurement that is too little or chaotic is incoherent (see Figure 2). An incoherent HRV reflects an ANS that is dysfunctional,

contributing to chronic pain, decreased physical functioning, and poor quality of life (6, 28, 31).

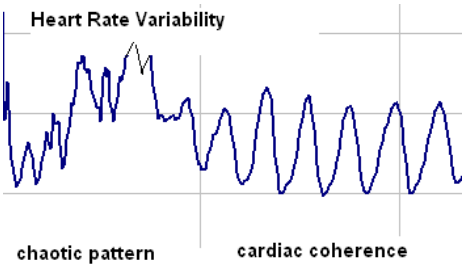

Figure 2. Heart rate variability waveform

Image retrieved from heartitelligence.com

With current technology, we can obtain HRV measurements non-invasively from an electrocardiogram, pulse wave recordings, or a plethysmographic optical sensor placed at the fingertip or on the earlobe (32). Devices that measure HRV using the fingertip or earlobe sensor are easily used by professionals and non-specialists, are relatively inexpensive, and can be used in the clinical setting as an educational tool for patients or by patients at home to regulate emotional states, stress resistance, and quality of life (32).

Heart Rate Variability Biofeedback

Heart rate variability biofeedback (HRVB) (34) is an innovative, non-pharmacological self-management strategy that uses technology to induce a vagal response as the individual slows their breathing rate to 4-6 breaths per minute (33). This technologically-guided breathing produces a maximized respiratory sinus arrhythmia, a coherent HRV (34). HRVB has the potential to improve emotion regulation, stress resistance (35-37), and quality of life (33, 37, 38). Repeated sessions of HRVB can sustain improved HRV coherence for longer periods and, with sufficient practice, can be used by individuals before, during, and after times of increased stress, thus optimizing

stress resistance and emotional adaptability to decrease pain and increase overall well-being (33, 35, 37).

Lehrer et al. (39) determined individuals cannot simply achieve and sustain an optimal breathing rate to reach HRV coherence without training with the developed HRVB protocols. HRVB training must occur gradually to adjust to the decreased rate of breathing of 4 to 6 breaths per minute (40). The *emWave2* is a handheld visual HRVB device. It is easy to use and available on the general market. A photoplethysmograph (PPG) sensor is clipped on the participant's ear and connected to the device. A blinking blue light on the device indicates the device is reading the individual's pulse (41). The strip of light fluctuates between red, blue, and green as the individual breathes rhythmically (see Figure 3). The individual is instructed to take slow, rhythmic breaths. The goal is to increase HRC and change the coherence level indicator from red (low coherence/baseline) to blue (medium coherence/improving) to green (high coherence/optimal), and to remain in the green zone as long as possible during the practice session (41). A trained registered nurse (RN) can teach a patient HRVB during a routine primary care visit, thus allowing nurse practitioners and physicians time for patient care needs that cannot be met by an RN independently (39).

Figure 3. emWave2 Heart rate variability biofeedback device.
@www.heartmath.com/emwave2

Preliminary Work

We conducted an integrative literature review to examine the relationship between HRVB and FM-related pain. We found six studies that examined the relationship between HRVB and chronic pain; only one of the studies examined FM-related pain. HRVB is a promising, effective treatment modality for chronic back pain, joint pain, neck pain, and headaches. As stated earlier, FM-related pain is complex and includes symptoms not usually seen in chronic headaches or musculoskeletal pain, and thus, treatment cannot be the same. We identified that although incoherent HRV is associated with FM-related symptoms, such as pain, mood disturbance, and fatigue, and coherent HRV is associated with normal physical function, stress resistance, and emotional stability, there is a lack of research investigating HRVB to treat FM-related chronic pain.

Theoretical Foundation

The primary complaints from those suffering from FM are symptoms of diffuse pain, fatigue, changes in mood, sleep deprivation, and brain fog (15). The Theory of Symptom Self-Management (TSSM) has been used to assist individuals in reducing, preventing, relieving, or decreasing the frequency of unpleasant symptoms like those experienced in FM, through self-management-enhancing interventions (SMI) (42, 43) like HRVB (33, 38, 44). The central tenet of TSSM that guided this study is that by optimizing self-directed SMI, such as HRVB, performance outcomes will improve. The key concepts of TSSM are: 1) perceived self-efficacy for symptom self-management (PSM), 2) symptom self-management, 3) patient characteristics, 4) symptoms, 5)

performance outcomes, and 6) perceived self-efficacy-enhancing interventions (PSI) (43). Figure 4 has been modified to illustrate the application of TSSM to HRVB.

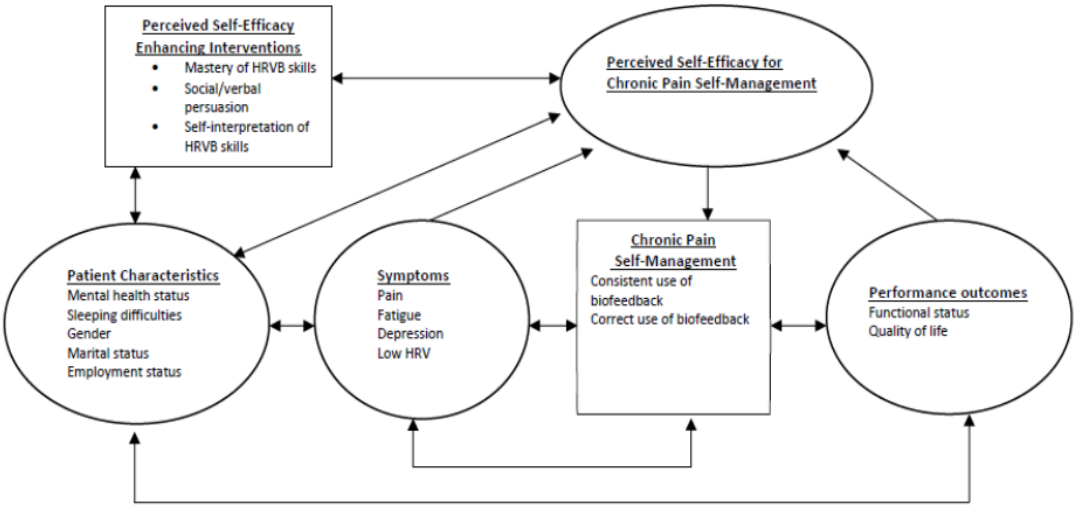

Figure 4. Theory of Symptom Self-Management model to HRVB (43)

PSM is the confidence or belief of one's own ability to implement or execute specific behaviors to attain established goals or desired outcomes (43). We asked participants if they believed HRVB would be an effective treatment before starting the study. We also asked if they believed they were successful with the prescribed protocol and if they believed they were able to affect change in their symptoms.

PSI includes self-management skills that support self-efficacy and improve self-care (43). Participants in this study implemented HRVB to self-manage their FM-related chronic pain. The participants evaluated the skill level of their self-management by reading the output (light display) on the *emWave2* device and adjusted their breathing rate until they reached their goal of "green light."

Symptom self-management encompasses self-directed active behaviors that may identify, prevent, and relieve or decrease the timing, intensity, and distress of symptoms like pain, fatigue, depression, and HRV (43). In this study, we followed the

recommendations by Lehrer et al. (39) and encouraged the participants to practice HRVB for 20 minutes, twice daily. The participants had immediate feedback regarding optimal use from the red, blue, and green display lights. Additionally, we reviewed the prior week practice schedule with the participant and helped them identify any barriers to the recommended practice schedules.

Performance outcomes are the effects of the individual's symptom self-management experience (43). The goal of HRVB is to decrease symptoms of pain, depression, fatigue, and improve cognitive and physical function. These symptoms have a direct effect on the performance outcomes of quality of life and functional status.

Methodology

We used a sequential exploratory multi-method design to assess the feasibility and acceptability of HRVB as a treatment for FM. We conducted eight individual weekly HRVB training sessions. We guided the participants' practice of HRVB breathing techniques for 20 minutes during each weekly session.

During each weekly session, we also collected and evaluated quantitative physiological data provided by the HRVB device each time the participant practiced. We collected psychometric data from the Short Form McGill Pain Questionnaire (SFMQ) and measured performance outcomes of functional status and quality of life from the Revised Fibromyalgia Impact Questionnaire (FIQR). We collected quantitative data about the acceptability of HRVB using the Credibility/Expectancy Questionnaire (CEQ). Data from the CEQ was used to explain the qualitative results obtained from focus group-driven open-ended questions post-intervention. We evaluated PSM, the Veteran's ability to adhere to a treatment protocol of 20 minutes of HRVB practice twice daily. We

evaluated PSI through the physiological measurement of HRV coherence from the *emWave2* device, as well as participant reports during the focus group discussions about the personal experience of HRVB.

Manuscripts

This dissertation consists of three manuscripts. The first manuscript, an integrative literature review, examined the relationship between HRVB and FM-related chronic pain using the Theory of Symptom Self-Management. The relationship between HRVB and FM was analyzed and evaluated based on the methodological framework proposed by Whittemore and Knafl (45). Overall the articles in this review support that HRVB is related to decreased pain. HRVB is a promising effective treatment for chronic pain. However, larger randomized controlled studies are needed to evaluate the relationship between HRVB and FM pain thoroughly.

The second manuscript details a multi-method study that examined the feasibility of recruitment and retention of Veterans with FM. We provided quantitative data from the *emWave2* HRVB device about the feasibility of the HRVB protocol recommended by Lehrer et al. (39). We also reported outcomes related to quality of life from the FIQR, pain from the SFMQ, and HRV changes pre-and-post intervention.

The third manuscript is a qualitative report of the post-intervention focus group. Eight of the ten enrolled Veterans participated in the focus group. The participants provided rich data about their experience with HRVB, their expectations before the intervention, and most importantly, their recommendations for future use.

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Review Article

Heart Rate Variability Biofeedback to Treat Fibromyalgia: An Integrative Literature Review

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ABSTRACT

Objectives: Fibromyalgia (FM) is associated with debilitating pain and a reduced heart rate variability (HRV), reflecting decreased emotional adaptability and resistance to stress. Common pharmacological treatments are ineffective, and opioids are highly addictive and cause an estimated 15,000 overdose deaths per year. Effective recommendations include patient-centered interventions like physical activity, cognitive behavioral therapy, and biofeedback. Heart rate variability biofeedback (HRVB) may be effective in improving HRV, thus increasing stress resistance and emotional adaptability and reducing pain.

Design: This integrative literature review was conducted to examine the relationship between HRVB and FM-related chronic pain using the Theory of Symptom Self-Management and to identify available HRVB technology.

Data Sources: We searched PubMed, EBSCOhost, and Google Scholar electronic databases for relevant publications. Manuscripts were selected using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses strategy, and study quality was assessed using the Critical Appraisal Skills Programme guidelines. The relationship between HRVB and FM was analyzed and evaluated based on the methodological framework proposed by Whittemore and Knafl.

Review/Analysis Methods: We reviewed 22 articles and included six in this review. Five reported HRVB as a treatment for chronic pain, and one for FM pain.

Results: Overall, the articles in this review support the claim that HRVB is related to decreased pain. The researchers evaluated five HRVB programs, three on handheld devices and two on desktop computers.

Conclusions: The reviewed studies had methodological flaws. However, HRVB is a promising treatment for chronic pain. Larger, randomized controlled studies are needed to thoroughly evaluate the relationship between HRVB and FM pain.

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Fibromyalgia (FM), a complex chronic pain syndrome, affects 10 million individuals in the United States (Center for Disease Control, 2017). Unlike other chronic pain-related conditions, FM involves an incoherent heart rate variability (HRV) and a dysfunctional autonomic nervous system (ANS) (Cohen et al., 2000; Dworkin & Fields, 2005; Martínez-Lavín & Hermosillo, 2000). HRV, the change in time intervals between heartbeats, reflects heart–brain interaction and ANS function (Cho et al., 2011; Kang, Chen, Chen, & Jaw, 2012; Meeus et al., 2013; Mostoufi, Afari, Ahumada, Reis, & Wetherell, 2012). When HRV is incoherent, chaotic, or insufficient, ANS is also dysfunctional, contributing to the chronic pain, decreased physical functioning, and poor quality of life that are associated with fibromyalgia (Cohen et al., 2000; Kang et al., 2012; Meeus et al., 2013). Optimal or coherent HRV is associated with improved physical functioning, improved stress regulation, improved emotional arousal, and improved stress resistance (De jonckheere, Ibarissene, Flocteil, & Logier, 2014; Kapitza, Passie, Bernateck, & Karst, 2010; Lehrer & Gevirtz, 2014; McCraty & Shaffer, 2015).

Heart rate variability biofeedback (HRVB), a form of cardiorespiratory feedback training (Lehrer & Gevirtz, 2014), is a self-management strategy that induces a vagal response as the individual slows their breathing rate to 4-6 breaths per minute (McCraty & Shaffer, 2015). The decreased rate of breathing during HRVB will induce a slower heart rate, allowing more time between heartbeats and an improvement in HRV coherence (McCraty & Shaffer, 2015). Additionally, repeated sessions of HRVB can sustain HRV coherence for longer periods of time (McCraty & Shaffer, 2015). It is hypothesized that routine use of HRVB can decrease pain, improve stress

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resistance and emotional adaptability, and increase overall well-being (Cohen et al., 2000; McCraty & Shaffer, 2015).

The purpose of this integrative literature review was to examine studies that reported on the relationship between HRVB and FM-related chronic pain using the Theory of Symptom Self-Management as the theoretical framework. Additionally, we sought to identify which HRVB technology has been used and any comparisons among devices. However, we were able to identify only one study devoted solely to FM-related chronic pain. To fully evaluate HRVB as a treatment for pain, we included other forms of chronic pain in our literature review.

Theoretical Framework

The Theory of Symptom Self-Management (TSSM) has been used to assist individuals to reduce, prevent, relieve, or decrease the timing of unpleasant symptoms, such as chronic pain, through self-management-enhancing interventions (Fu, LeMone, & McDaniel, 2004; Hoffman, 2013), such as biofeedback (Burckhardt, 2004; Vancleef, 2011) and HRVB (McCraty & Shaffer, 2015; Moss & Shaffer, 2017; Wheat & Larkin, 2010). The central tenet of TSSM that guided this review is that functional and cognitive performance outcomes, such as quality of life and functional status, are improved by optimizing self-directed, self-management, perceived self-efficacy (PSE)—enhancing interventions, such as HRVB (Hoffman, 2013; Lorig & Holman, 2003). The key concepts of TSSM are as follows: 1) PSE for symptom self-management, 2) actual symptom self-management, 3) patient characteristics, 4) symptoms, 5) performance outcomes and PSE-enhancing interventions (Hoffman, 2013).

Perceived Self-Efficacy for Symptom Self-Management

Self-efficacy influences how a person thinks, feels, motivates him- or herself, and performs actions (Bandura, 1994). PSE is the belief or confidence one has in oneself to perform or execute the actions required to produce the desired effects or outcomes (Bandura, 1994). PSE for symptom self-management is a patient's ability to implement specific behaviors to attain established treatment goals or desired outcomes (Hoffman, 2013).

Symptom Self-Management

Symptom self-management encompasses self-directed active behaviors that may prevent or relieve symptoms such as pain or decrease their frequency or intensity, allowing the patient to reach optimal performance outcomes (Hoffman, 2013). Self-management with biofeedback has been shown to be an effective treatment for FM pain (Macfarlane et al., 2017). The symptom self-management behaviors analyzed in this review are the consistent and correct use of biofeedback. Use is considered correct if the patient engages in HRVB as often and for as long as prescribed, following the prescribed breathing rate and depth while following along with the electronic signals emitted by the feedback device.

Patient Characteristics

Patient characteristics include the physiological and psychological factors that influence outcomes and may include severity of illness, comorbidities, age, mental state or mood status, personal beliefs, affective reaction to illness or disease, and degrees of uncertainty (Hoffman, 2013). The patient physiological and psychological characteristics analyzed in this review are mental health status, sleeping difficulties, gender, marital status, and employment status. Depression and mood disturbance, commonly seen in FM (Cohen, 2017; Macfarlane et al., 2017), are significant factors in pain management and are influencing factors on self-management (Fu et al., 2004). Fatigue or unrefreshing sleep is a hallmark symptom of FM (Wolfe et al., 2010) and can also greatly influence self-management (Cohen, 2017; Fu et al., 2004; Rosso & Maddali-Bongi, 2016). Work absenteeism and disability are considered the cause of an average of 26% of the indirect costs associated with FM and 42% of the costs of unemployment owing to FM disability (Chandran et al., 2012; Ghavidel-Parsa, Bidari, Amir Maafi, & Ghalebaghi, 2015; Schaefer et al., 2015). Women comprise 86%-96% of the population of FM patients and have a higher divorce rate when compared to those suffering from other chronic pain diseases (Wolfe, Ross, & Anderson, 1995).

Symptoms

Symptoms are the subjective experiences of a perceived threat to health or wellness, or are signs of an undesirable outcome (Hoffman, 2013). Symptoms of FM can be diffuse and multifocal, and they can wax and wane daily. The symptoms analyzed in this review are chronic pain, fatigue, depression, and low HRV. FM-related pain is often characterized as a widespread ache with multiple diffuse, exquisitely tender muscle points (Wolfe et al., 2010).

Performance Outcomes

Performance outcomes are the effects of a person's symptom self-management experience (Hoffman, 2013). Desired outcomes of self-directed behaviors, such as HRVB, include decreased symptoms of pain, depression, and fatigue, less symptom distress, and fewer symptom occurrences (Fu et al., 2004; Hoffman, 2013). These outcomes have a direct effect on quality of life (Cohen, 2017; Fu et al., 2004; Macfarlane et al., 2017), sleep (Cohen, 2017; Rosso & Maddali-Bongi, 2016), and functional status (Cohen, 2017). The performance outcomes analyzed in this review are functional status and quality of life.

Perceived Self-Efficacy—Enhancing Interventions

A patient's ability to perform PSE-enhancing interventions is developed through activity performance along with social or verbal persuasion by others, which determines how the individual will think, feel, self-motivate, and perform (Hoffman, 2013). The building blocks of PSE-enhancing interventions include mastery of the activity by performing it oneself, observing others perform the activity successfully, being persuaded by others that the activity is possible, and perceiving one's self as possessing the strength to achieve the goal (Hoffman, 2013). The following were analyzed in this review: mastery of HRVB skills via observation of trainers and frequently performing the skill oneself, being socially persuaded to perform the activity, and self-interpretation one's HRVB skills as good or adequate.

Methods

Design

This integrative review was guided by the methodological framework proposed by Whittemore & Knafl (2005). The five stages include 1) identifying a gap in the literature about HRVB as a treatment for FM-related chronic pain, 2) searching in the literature for studies supporting the use of HRVB to treat FM, 3) evaluating data using the Critical Appraisal Skills Programme (CASP) scoring system, 4) analyzing data using the TSSM as a framework, and 5) visually presenting a review matrix (Whittemore & Knafl, 2005).

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Search Methods

In September 2017, a reference librarian at an academic medical center was consulted to assist in finding the most appropriate approach in searching the literature for applicable studies. The literature was systematically selected to be included in the sample using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (see Fig. 1). We searched PubMed, EBSCOhost, and Google Scholar electronic databases for relevant publications. We searched each database for the following terms: [heart rate variability OR heart rate variability biofeedback OR heart rate coherence biofeedback OR heart rate coherence OR biofeedback] AND [fibromyalgia] AND [chronic pain]. The terms evolved from concept maps used in the development of the aims of this review. We included primary studies of any research design in the review. We reviewed reference lists from included manuscripts to identify literature not found in the initial database searches manually.

The original planned study inclusion criteria were: 1) articles that included fibromyalgia pain in the outcome measures, 2) articles reporting HRVB as an intervention, 3) peer-reviewed articles in the English language, and 4) adult participants (>17 years). Exclusion criteria were: 1) non-FM pain, 2) literature reviews, and 3) non-HRVB biofeedback. This search returned only one study. The search criteria were expanded to include other forms of chronic pain. During the review, studies involving cancer pain were eliminated; this search yielded 21 more studies. We did not set a time limit because of the novelty of the subject matter as well as an interest in historical findings.

Search Outcomes

The initial database searches yielded 22 articles. We removed 10 duplicates and reviewed the full text of the remaining 12 articles. Three of the articles eliminated were literature reviews of HRVB (Gevirtz, 2013; Moss & Shaffer, 2017; Wheat & Larkin, 2010); these were hand-searched for original studies. However, no additional studies met inclusion criteria.

The remaining nine full-text articles were then further assessed for eligibility, yielding six studies. Two of the articles eliminated reported HRVB findings, but not pain treatment (Edwards, 2014; Whited, Larkin, & Whited, 2014). The final one eliminated was an explanatory paper on how and why HRVB works (Lehrer & Gevirtz, 2014). A review of reference lists of the selected articles and the previous literature reviews did not yield any additional studies.

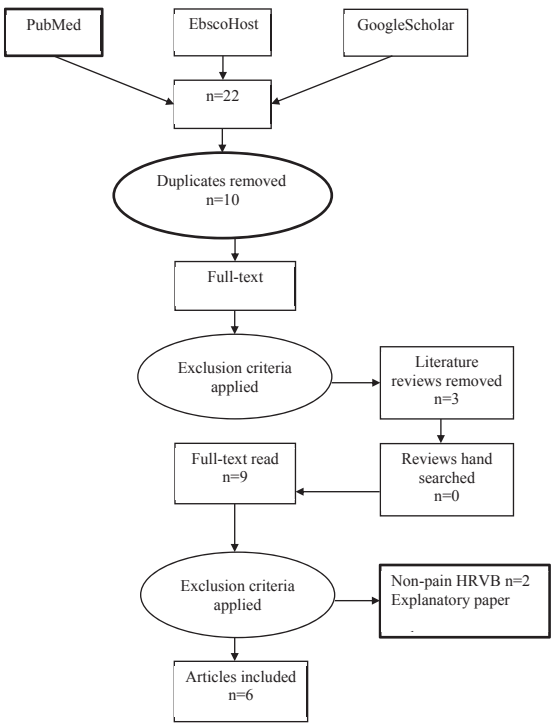

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement

Data Presentation

The resulting data were categorized and presented in table form (Table 1) by reference, interventions, biofeedback technology, population, study design, outcome measures, relevant findings, and grading. The Critical Appraisal Skills Programme (CASP) guided the grading of each randomized controlled and cohort study by addressing three broad questions: 1) Are the results of the study valid? 2) What are the results? and 3) Will the results help locally? (Critical Appraisal Skills Programme, 2018).

Results

Overview of Studies

The six articles reviewed consisted of three randomized pilot studies (Berry et al., 2014; Hallman, Olsson, von Schéele, Melin, & Lyskov, 2011; Weeks, Whitney, Tindall, & Carter, 2015) one non-randomized pilot study (Hassett et al., 2007), one retrospective archival study, (Wilson, 2017), and one retrospective cohort study (Soer, Vos, Hofstra, & Reneman, 2014). The independent variable was HRVB in all studies. The study by Hassett et al. (2007) was the only one which treated FM-related pain solely with HRVB. Hallman et al. (2011) compared two forms of treatment for neck and shoulder pain. Patients in the first group received multiple sessions of HRVB, whereas those in the second group received the same breathing protocol instructions during session one but did not receive instructions on breathing during the remaining sessions. Berry et al. (2014) added HRVB to standard care for chronic pain; however, they did not specify what this care entailed or specifics about pain location. However, they did exclude individuals with diabetes or traumatic musculoskeletal system damage. Soer et al. (2014) added HRVB to Back School, a personalized pain rehabilitation program designed to increase physical capacity and cognitive behavior interventions for chronic back pain. Weeks et al. (2015) compared faded HRVB to full HRVB in nine sessions to treat non-malignant chronic musculoskeletal pain, fibromyalgia, headache, neuropathy, and reflex sympathetic dystrophy over a 3-week period. Faded HRVB consisted of visual feedback during session 1, followed by a systematic reduction of visual biofeedback with each session so that by session nine, the participants were controlling HRV without visual feedback. The control group received visual biofeedback for nine sessions. Wilson (2017) included individuals with neuropathic pain, musculoskeletal pain, and headache. The primary outcomes measured were pain ($n = 6$), functional status ($n = 5$), depression ($n = 3$), HRV ($n = 4$), catastrophizing ($n = 1$), sleep ($n = 1$), anxiety ($n = 1$), somatization ($n = 1$), self-reported health status ($n = 1$), and biofeedback skills ($n = 1$). Only three studies reported study controls: standard care ($n = 1$), Back School ($n = 1$), and full HRVB ($n = 1$). Although none of the studies or reviews articulated the use of any theoretical framework or model, we identified some of the TSSM constructs in some of the studies (see Table 2).

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Table 1
HRVB Literature Review Outcomes

Reference	Intervention	Biofeedback Technology	Population	Design	Outcome Measures	Relevant Findings	CASP Score
Wilson. (2017)	Heart rate variability biofeedback (HRVB)	"Relaxing Rhythms" from Unyte Health Inc. finger sensor measuring skin conductance levels and HRV	N = 72; 56 F; 15 M; 1 TG	Retrospective archival study (not randomized)	Pain, catastrophizing, depression, anxiety, somatization	Decreased pain $p < .001$, however not sustained across sessions	n/a
Hassett, Radvanski, Vaschillo, et al. (2007)	HRVB	J&JJ-330 unit on computer screen and Cardiosignalizer CS-03 handheld device	N = 12; 12 F	Pilot (not randomized)	Functional status, depression, pain, sleep	Decreased pain $p = .455$ after 10 sessions, $p = .006$ after 3 months; increased functional status $p = .069$ after 10 sessions, $p = .0022$ after 3 months	n/a
Soer, Vos, Hofstra, & Reneman. (2014)	HRVB and mindfulness exercises added to Back School	Freeze-frame by Heart Math, visual biofeedback on a computer screen	N = 170; 71 F; 99 M	A retrospective cohort study comparing the intervention to Back School alone	Pain, pain disability, self-reported health status, HRV	Increased HRV $p < .01$; decreased pain $p = .15$; increased function $p = .02$	8
Berry, Chapple, Ginsberg, Gleichauf, Meyer, & Nagpal. (2014)	HRVB plus standard care	*Quick Coherence*, controlled breathing and self-induction of positive or neutral emotional state	N = 14; 1 F; 13 M	Randomized Pilot comparing the intervention to standard care	Pain, HRV, physical activity limitations	Increased HRV 191% $p = .04$; decreased pain 36% $p < .001$; decreased physical limitations 42% $p < .001$	9
Hallman, Olsson, von Scheele, Melin, Lyskov. (2011)	HRVB	*J&JJ-330-2* visual handheld device	N = 24; 21 F	Randomized Pilot comparing intervention to standard care	Pain, HRV, physical function, depression, vitality, social function	Increased resting HRV, increased LF HRV $p = .016$ interaction effect, no significant HF HRV interaction effect; decreased pain $p = .049$; decreased physical function $p = .27$; decreased depression $p = .78$; increased vitality $p = .005$; increased social function $p = .047$	10
Weeks, Tindall, Carter.(2015)	Faded HRVB	Freeze-frame by Heart Math, visual biofeedback on a computer screen	N = 20; 5 F; 6 M	Randomized Pilot comparing the intervention to full HRVB	HRV, use of BF skills, pain, functional status, kinesophobia	HRV no significant difference between groups; decreased pain $p = .291$ (no difference from the control group), improved functional status $p = .464$ (no difference compared to control group), decreased kinesophobia compared to control group $p = .102$, improved HRVB used $p = .132$ compared to control group	10

BF = biofeedback; F = female; HRV = heart rate variability; HRVB = heart rate variability biofeedback; M = male; T = transgender.

Perceived Self-Efficacy-Enhancing Interventions

Observation

The participants in all studies were instructed and coached by HRVB-trained clinicians or researchers on how to correctly use the respective HRVB device (Hallman et al., 2011; Hassett et al., 2007; Soer et al., 2014; Weeks et al., 2015; Wilson, 2017). The authors did not indicate how these instructions affected the study outcomes.

Frequency

The participants practiced HRVB in weekly sessions that ranged from 10 weeks (n = 2) to 6, 5, and 3 weeks (Berry et al., 2014;

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Table 2
Theory of Symptom Self-Management Concepts Included in Studies

Self-Management Concepts	Wilson (2017)	Hassett et al. (2007)	Soer et al. (2014)	Berry et al. (2014)	Hallman et al. (2011)	Weeks et al. (2015)
Patient characteristics						
Age	18-78	18-60	Mean 44	Adult	Mean 42	Mean 58
Gender	56 F; 15 M; 1T	12 F	71F; 99 M	1M; 13F	21 F	5 F; 6M
Mental health status	NR	NR	NR	NR	NR	NR
Sleep quality	NR	NR	NR	NR	NR	NR
Marital status	28 Married; 2 significant other; 23 single; 16 divorced; 2 separated;	NR	NR	NR	NR	NR
Employment status	28 Employed; 30 disabled; 7 unemployed; 7 retired	NR	NR	NR	NR	6 Employed; 5 unemployed
PSE interventions						
Observation	X	X	X	X	X	X
Frequency	More than 3 clinic sessions	10 Weekly clinic sessions; home practice 20 min. twice a day	6 Weekly clinic sessions	4 In clinic session	10 In clinic session; home practice 15 minutes daily, 5 days/week	3 Times a week for 3 weeks in clinic sessions
Verbal or social persuasion	Verbal	Verbal	NR	NR	NR	NR
Self-interpretation of HRVB skills	Light display	Light display	Light display	Light display	Light display	Light display
Symptoms						
Pain severity	X	X	X	X	X	X
Fatigue	NR	▲	NR	NR	NR	NR
Depression	NR	NR	▲	▲	X	NR
Low HRV	NR	X	X	X	X	X
Symptom self-management						
Correct use of HRVB	NR	NR	NR	NR	NR	X
Consistent use of HRVB	NR	NR	NR	NR	NR	X
Performance outcomes						
Functional status	NR	▲	NR	NR	NR	NR
Quality of life	NR	▲	X	NR	X	NR

X reported
▲indirectly reported
NR not reported

F = female; HRV = heart rate variability; HRVB = heart rate variability biofeedback; M = male; NR = not reported; T = transgender.

Hallman et al., 2011; Hassett et al., 2007; Soer et al., 2014; Weeks et al., 2015; Wilson, 2017). Sessions lengths varied, ranging from 10 minutes (n = 2) to 20 minutes (n = 1) to 45-60 minutes (n = 1) to a full hour (n = 1). Berry et al. (2014) did not provide the length of time per session. Hassett et al. (2007) and Hallman et al. (2011) added recommendations for daily home practice, 20 minutes twice daily and 15 minutes 5 times a week, respectively.

Verbal or Social Persuasion

Hassett et al. (2007) and Wilson (2017) reported additional verbal coaching to improve respiration rates and prevent participant hyperventilation. None of the study participants had the opportunity to observe their peers using HRVB.

Self-Interpretation of HRVB Skills

PSE can be enhanced when individuals are able to self-interpret skill mastery. All the HRVB devices reviewed provided visual feedback that allowed the participants to track HRV coherence while they breathed at the prescribed rate and depth. The *Relaxing Rhythms* training program displayed an image of a staircase on a screen when HRV was coherent and disappeared when incoherent; as the participant advanced in skill level and continued with optimal HRV, the staircase evolved into a bridge (Wilson, 2017). Blinking lights advanced from red (no synchronization) to blue (advancing synchronization) to green (optimal synchronization) on the *emWave* desktop HRVB program (Heart Math, 2004). The J&J I-330 HRVB device projected a light display onto a computer screen that moved up as the target respiratory frequency was achieved, and down as the target was lost (J&J Engineering). Only Soer et al. (2014) reported that the participants were required to demonstrate basic HRVB skill before they were able to use HRVB during stress-inducing events. The participants in the Hassett et al. (2007) study reported that the HRVB device was easy to use, and that they benefited from the biofeedback training and would recommend the treatment to others. None of the other studies provided anecdotal reports or qualitative data about the participants' self-reported experiences with HRVB.

Patient Characteristics

The ratio of women to men in the studies reviewed was almost 2:1 (62:36), and only 1 transgender individual was included. Soer et al., (2014) linear regression analysis did not report any significant relationship between a change in HRV coherence score and gender. The remaining studies did not report a relationship between gender and measured outcomes.

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Depression, anxiety, and negative moods were outcomes measured in most of the studies (Berry et al., 2014; Hallman et al., 2011; Hassett et al., 2007; Soer et al., 2014; Wilson, 2017). However, none of the studies reported how mental health status might have affected pain. Only Hassett et al. (2007) reported sleep quality. They administered the Pittsburg Sleep Quality Index, a 19-item self-rated questionnaire, and reported improved sleep quality ($p = .0148$) that was not sustained at the 3-month postintervention follow up.

Wilson (2017) was the only researcher to report marital status: 28 married, 2 with significant others, 23 single, 16 divorced, and 2 legally separated participants. There was no reported association between marital status and HRV outcomes.

Employment status was only reported in two studies (Weeks et al., 2015; Wilson, 2017). Most individuals were either employed (n = 34) or disabled (n = 30); the remaining participants were unemployed (n = 12) and retired (n = 7). Neither author reported how employment status might have affected the outcomes.

Symptoms

The symptoms of fibromyalgia covered in this review are pain, fatigue, depression, and HRV. Methods of pain measurement varied greatly between each study and are detailed in Table 1. Most studies reported a statistically significant reduction in pain with HRVB (Berry et al., 2014; Hallman et al., 2011; Soer et al., 2014; Weeks et al., 2015; Wilson, 2017). However, there was no statistically significant difference in pain reduction between the treatment and control groups ($p = .049$, $p = .15$) in the two RCTs (Hallman et al., 2011; Soer et al., 2014). Hassett et al., (2007) reported that although pain reduction was not statistically significant ($p = .0455$), it was sustained at the 3-month follow-up ($p = .006$).

Only one study measured fatigue as an outcome. Hassett et al. (2007) administered the Fibromyalgia Impact Questionnaire (FIQ), a 19-item self-reported questionnaire designed to measure fatigue among other physical impairments, and reported an improved FIQ score ($p = .0686$) at the end of session 10 compared to session 1, which was sustained at the 3-month follow-up ($p = .0022$).

Overall depression scores were decreased after HRVB (see Table 1; Berry et al., 2014; Hallman et al., 2011; Hassett et al., 2007; Soer et al., 2014). Soer et al. (2014) reported improved self-rated mental health scores in the HRVB group ($p = .38$), but they were not statistically different from those of the control group ($p = .39$).

HRV changes were reported in all but one of the studies. Overall, there was a statistically significant improvement ($p < .01$-$p = .023$) in HRV coherence (see Table 1).

Symptom Self-Management

Weeks et al. (2015) reported that participants in the faded HRVB group demonstrated improved use of unassisted biofeedback after three weeks of practice of faded visual feedback compared to full visual HRVB training. The researchers concluded that faded HRVB improved biofeedback skills because the participants were able to optimize their HRV without the use of HRVB at the end of the study.

Performance Outcomes

Functional status and quality of life were measured by Hassett et al. (2007) with the FIQ. In their study, FM patients reported improved scores ($p = .0686$) on the FIQ after HRVB training, which were significantly sustained ($p = .0022$) 3 months postintervention (Hassett et al., 2007). Hallman et al. (2011) and Soer et al. (2014) administered the SF-36, a 36-item questionnaire designed to assess health-related quality of life. They reported improved physical functioning, improved vitality, and improved social functioning after HRVB training.

HRVB Technology

The HRVB technology across all studies used visual biofeedback projected onto a screen. Freeze Frame, manufactured by HeartMath, was used in two studies (Soer et al., 2014; Weeks et al., 2015). The J&JJ-330 unit, a visual handheld device, was used by Hassett et al. (2007) and Hallman et al. (2011). Wilson (2017) used *Relaxing Rhythms* from Unyte Health, Inc. None of the authors provided reliability or validity data to support the results. None of the authors reported any contraindications to using HRVB. However, some did report participant use of beta blockers and a diagnosis of coronary artery disease as an exclusion criterion (Berry et al., 2014; Hallman et al., 2011; Soer et al., 2014).

Discussion

The purpose of this review was to examine the relationship between HRVB and FM-related pain through the lens of the TSSM and to identify the HRVB technology used to treat FM pain. However, as discussed earlier, we included studies of chronic musculoskeletal pain. When pain management was evaluated against the central tenet of TSSM, that functional and cognitive patient outcomes are improved by enhancing self-directed and self-management behaviors, significant gaps were identified.

PSE-Enhancing Interventions

Interventions that include self-management skills support self-efficacy and improve self-care (Fu et al., 2004). Lehrer et al. (2013) developed a protocol and manual for HRVB training and recommended five in-office sessions for participant instruction and home practice 20 minutes twice daily for 3 months, followed by 20-minute practice sessions every 2-3 days to maintain benefits. The frequency and duration of HRVB practice reported in this review were inconsistent, making it difficult to determine how much practice is ideal for skill mastery and optimal outcomes. The researchers and clinicians taught the participants how to use HRVB; however, we do not know how this affected the outcomes or if the participants truly understood the instructions.

Patient Characteristics

Physiological, psychological, and contextual patient characteristics significantly influence performance outcomes such as quality of life and functional status (Hoffman, 2013; Iversen, 2003). Although FM patients are more likely to suffer from depression and sleep disturbances than those with other chronic pain disorders (Cohen, 2017), the studies reviewed did not include these variables. The studies reviewed did include sex as a variable but did not report how this may have affected the outcomes. The female-to-male ratio of FM sufferers in the general population is 2:1; however, the female-to-male ratio was almost 1:1 in the studies reviewed. This review thus may not be an accurate representation of FM patient outcomes. Psychosocial issues like marital status and employment status may contribute to FM symptoms (Cohen, 2017) and are associated with increased divorce rates (Wolfe et al., 1995); nevertheless, these factors were underrepresented and their significance was not discussed in the studies reviewed.

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Symptoms

Overall, there was a statistically significant reduction in pain after HRVB compared to control groups in all but one study, supporting the current recommendations for patient-centered nonpharmaceutical pain treatment (Babu, Mathew, Danda, & Prakash, 2007; Cohen, 2017; Gevirtz, 2013) and self-management enhancing interventions (Fu et al., 2004; Hoffman, 2013). However, sustained pain reduction was evaluated in only two of the six studies and seen in only one 3-month follow-up study. Four of the studies demonstrated a statistically significant increase in HRV, but this did not translate into decreased pain, increased resilience, improved emotional state, or improved stress resistance. None of the studies discussed pharmacological treatment or its effects on pain. Sleep disturbance and fatigue are known triggers for FM pain (Clauw, 2014; Wolfe et al., 2010) and should be included as outcomes in future studies. Overall, mood improved with HRVB. Depression scores decreased (Hallman et al., 2011; Hassett et al., 2007), negative mood improved (Berry et al., 2014), and self-rated mental health scores increased, indicating improved mental health (Soer et al., 2014).

Symptom Self-Management

HRVB is designed to provide patients with a self-directed active behavior to self-manage pain. Once the patient has demonstrated adequate HRVB skills in the clinic setting, he or she may receive a prescription from the clinician for home use. The patient can then self-determine the correct use of HRVB by following the prompts from the device. Consistent and correct use of the HRVB training device can allow the patient to self-manage his or her pain. Clinicians can verify consistent and correct use outside of the clinic setting by reviewing the reports generated by the software of the HRVB device. However, only one study, Weeks et al. (2015) reported that participants who used HRVB at the prescribed frequency reported decreased pain postintervention.

Performance Outcomes

Functional status and quality of life are the performance outcomes evaluated in this review. Again, Hassett et al. (2007), the only study involving FM patients, measured outcomes with the FIQ. The FIQ is a reliable instrument used to measure quality of life and functional status (Iversen, 2003). Although the researchers reported improved scores, the improvement was not statistically significant. However, Soer et al. (2014) and Hallman et al. (2011) administered the SF-36, a questionnaire that measures quality of life by evaluating self-report of physical function, vitality, and social function. Both studies reported an increase in these measures post-HRVB intervention. These instruments would be appropriate for future studies.

HRVB Technology

This review demonstrated that there are several biofeedback devices available on the market for HRV modulation**.** The authors did not provide reliability or validity data about the HRVB devices, making it challenging to support their use in future studies. The monetary cost of the devices was not given, and there was no discussion of software or device problems reported during the study. Although there was no discussion of any contraindication to HRVB, it can be assumed that participants with coronary artery disease could face risks from HRVB.

Strengths and Limitations

There were several limitations in this review. First, the pilot studies were small and not guided by power analyses; second, the larger studies were retrospective non-randomized controlled trials. None of the studies compared HRVB to sham or other biofeedback. Second, only one of the studies was on FM exclusively, so other chronic pain studies were included, although it has been established in the literature that the pain caused by FM is different from that of other disorders (Clauw, 2014; Wolfe et al., 2010). None of the studies evaluated stress resistance, a marker of optimal HRV and a functional ANS (Cho et al., 2011; Kang et al., 2012; Meeus et al., 2013; Mostoufi et al., 2012). Additionally, no qualitative or mixed-method studies were identified. Such studies could enhance our knowledge of the effects HRVB may have on chronic pain, quality of life, and functional status. Lastly, we did not search the literature for different biofeedback devices; this may have yielded additional studies.

Conclusion

FM is a debilitating, painful condition affecting 2% of the population (Wolfe et al., 1995) with relatively few effective treatments available (Macfarlane et al., 2017). Current recommendations for FM treatment by the European League Against Rheumatism and the Canadian Pain Society include non-pharmacological therapies such as biofeedback (Clauw, 2014; Macfarlane et al., 2017). Although HRVB is a promising treatment modality for chronic pain, only one study was found that evaluated the relationship between HRVB and FM pain (Hassett et al., 2007). Future research is needed to thoroughly evaluate the relationship between FM and HRVB.

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Supplementary Data

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Manuscript 2

Feasibility and Acceptability of Heart Rate Variability Biofeedback in a Group of Veterans with Fibromyalgia

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Feasibility and Acceptability of Heart Rate Variability Biofeedback in a Group of Veterans with Fibromyalgia

Abstract

BACKGROUND: Fibromyalgia (FM) is characterized by diffuse pain, fatigue, sleep disturbance, and depression leading to decreased functional status and poor quality of life (QOL). Research suggests that autonomic dysfunction and diminished heart rate variability (HRV) may explain some symptoms of FM. The purpose of this study was to determine feasibility and acceptability of heart rate variability biofeedback (HRVB) to treat FM.

METHODS: We enrolled 10 Veterans for 8 weeks of HRVB training to determine the feasibility to adhere to a recommended HRVB protocol and to examine acceptability and satisfaction with the intervention. They were taught how to use the *emWave2* biofeedback device and asked to practice with the device at home twice daily for 20 minutes. We collected data from the device to evaluate their ability to adhere to the treatment protocol. Data collected at sessions 2-8 provided a signal of efficacy from HRVB for pain control, heart rate coherence, functional status, and QOL.

FINDINGS: Most Veterans believed HRVB is a viable treatment for FM that will reduce pain by 50-80%. Data suggest a twice-daily HRVB practice protocol is not feasible. However, once daily 20-minute HRVB home sessions were feasible and acceptable to study participants. HRVB contributed to an improvement in functional status and QOL within our sample.

CONCLUSION: It appears that although a twice-a-day HRVB practice protocol is not feasible, when Veterans did practice once daily, 20-minute HRVB sessions were acceptable. HRVB may be an effective strategy to improve functional status and QOL for Veterans with FM.

Introduction

Fibromyalgia (FM) is a complex, painful condition with predominant symptoms of pain, fatigue, depression, and sleep deprivation that lead to a significant decrease in functional status and diminished quality of life (1). Individuals with FM often report symptoms that are variable and unpredictable, leading to frustration and often feeling as if family members, friends, and health care providers do not believe them (2, 3).

The fatigue, memory problems, cognitive impairment, and functional limitations associated with FM (4, 5) contribute to 1-2% loss of national U.S. productivity (6, 7), and $12-14 billion per year in national health care costs (6). The Department of Veterans Health Administration (VA) and Department of Defense (DoD) recognize FM as an illness potentially linked to injuries and exposures sustained during the Persian Gulf War (8).

The DoD and VA have linked FM to the physical and emotional trauma sustained by service members who deployed during wars in the Persian Gulf and in Afghanistan, as well as to the various natural and artificial environmental exposures in that region (9). Individuals diagnosed with FM have a higher prevalence of traumatic events such as those experienced in combat and in physical and sexual abuse (10, 11). Repetitive muscular injuries are attributed to service members carrying over 80 pounds of equipment daily for 6-12 months during multiple deployments, which has resulted in more than 50% of service members/Veterans returning from these conflicts reporting chronic pain not related to direct injuries such as shrapnel, gunshots, or blasts (9, 12, 13). The FM cost to the military health care system in 2006 was $105.6 million, with an average individual cost of $12,472; this is five times higher than the utilization costs on non-fibromyalgia diagnosed military beneficiaries (14). The incidence of FM diagnosis and FM-related disability in the VA system is rising at an alarming rate (14).

The American College of Rheumatology has set the FM diagnostic criteria (5). FM diagnosis is satisfied with one of the following 3 conditions: 1) the Widespread Pain Index (WPI) ≥ 7, the Symptom Severity Score (SS) ≥ 5, or the WPI = 36 and the SS ≥ 9; 2); symptoms are present and at a similar level for at least 3 months; or 3) the patient lacked a disorder that would otherwise explain the pain (5).

Pathophysiology of FM

Research utilizing functional magnetic resonance imaging (fMRI) demonstrates that among individuals with FM, there is a disruption of the pain network connectivity (15). Strengthened connectivity of the brain regions involved in processing and reducing connectivity of the regions involved in pain inhibitory modulation may explain this widespread chronic pain (15). The default mode network (DMN), a constellation of brain regions engaged in self-referential thinking, is disrupted in FM during tasks like visual attention and cognitive attention, which may explain symptoms of memory problems and cognitive impairment (16, 17). An abnormally increased level of connectivity between the DMN and the insular cortex may also explain higher reported pain levels (17). Additionally, a dysfunction of the cardiac autonomic nervous system (ANS), characterized by higher sympathetic and lower parasympathetic cardiac autonomic modulation, is associated with diminished heart rate variability (HRV) and is related to the impact of FM on quality of life (18, 19).

Heart Rate Variability

Heart rate variability (HRV) is the time measurement of the oscillations of the R-to-R intervals (20-22) and reflects heart-brain interaction and the ANS (21, 23). HRV reflects the activity of the sympathetic and parasympathetic nervous systems providing information on how

the systems interact and function as a whole (24). Thus, analyzing HRV provides quantitative information about the state of the ANS (19).

HRV is measured on spectra analysis via high frequency (HF) (0.15-0.40 Hz) and low frequency (LF) (0.04-0.15) bands. The LF is influenced by sympathetic activities like significant psychological and physiological activities, and parasympathetic conditions of slow breathing (6 breaths per minute) (25). Optimal HRV, cardiac coherence, is an ordered, harmonic cardiac pattern reflecting positive emotions and a general sense of well-being (23). Low HRV, cardiac incoherence, reflects decreased resistance to stress, anxiety, and decreased emotional adaptability (19, 21, 23, 26), factors known to exacerbate chronic pain. Self-regulation techniques that increase HRV coherence can reduce pain, improve physical activity, and improve cognitive function (23).

Treatment Recommendations

The ANS dysfunction and diminished HRV associated with FM are generally not demonstrated in chronic musculoskeletal pain; thus, comparing treatment between these pain syndromes is challenging (5, 19). The most commonly used guidelines for FM treatment are from the European League Against Rheumatism (EULAR) 2008, revised in 2016, American Pain Society (APS) 2005, German Association of the Scientific Medical Societies (AWMF) 2013, Israeli Pain Society (IPS) and Canadian Pain Society (CPS) (1, 27). There is a consensus among the EULAR, APS, AWMF, IPS, and CPS guidelines that effective treatment must include a multidisciplinary approach that prioritizes nonpharmacological treatments, offers judicious pharmacological treatments (1, 27), and reflects the biopsychosocial model (1) which integrates biological, psychological and social factors into the treatment plan (28). The most recent VA/DoD Clinical Practice Guidelines for the treatment of chronic pain, which includes pain

related to fibromyalgia, are to utilize cognitive behavioral therapy, biofeedback, exercise, multidisciplinary psychosocial rehabilitation (4, 29), physical therapy, occupational therapy, acupuncture, spinal manipulation, and/or complementary and alternative medicine (1, 12). Unlike chronic musculoskeletal pain, FM treatment must improve autonomic function, optimize HRV, and improve pain network connectivity through the DMN (17, 30).

Heart Rate Variability Biofeedback

Heart rate variability biofeedback (HRVB) enables self-regulation by using technology to guide deep breathing at an average rate of 6 breaths per minute. This deep breathing is an autonomic maneuver that may intensify the interaction between autonomic and nociceptive pathways (18). HRVB induces HRV coherence (HRC) and ANS regulation through the activation of baroreceptors in the vagus nerve (18, 23, 31-34). Repeated sessions of HRVB can sustain improved HRC and, with sufficient practice, can be used by individuals before, during, or after times of increased stress or adversity, thus optimizing stress resistance and emotional adaptability to decrease pain and increase overall well-being (23, 31, 32).

The purpose of this study was to determine the feasibility and adherence to a recommended HRVB protocol using a handheld training device (*emWave2)* that objectively monitors HRV and displays the physiological level of HRC among Veterans with FM. Additionally, we examined the feasibility of recruitment and retention of Veterans diagnosed with FM, along with acceptability and satisfaction with HRVB. Finally, we collected data related to HRC, qualities of pain, and FM symptoms, including overall function and QOL, as an initial signal of the efficacy of HRVB.

Theoretical Foundation

The theory of symptom self-management (TSSM) was used to guide this study. TSSM is effective in assisting individuals in reducing, relieving, or decrease the frequency and duration of pain, through the use of self-management enhancing interventions like biofeedback (35, 36). The central tenet of TSSM is that when self-directed, self-managed, perceived self-efficacy-enhancing interventions (PSI) such as HRVB are optimized, cognitive performance outcomes, such as quality of life and functional status, are improved (36, 37). Additionally, cognitive behavioral strategies, like HRVB, improve self-efficacy and shift the individual's perception of helplessness to a sense of ability to self-improve (38).

Methods

Investigator HRVB Training

The Principal Investigator (PI) completed the HeartMath® Interventions Certification Program for Health Professionals (39), designed for physicians, advanced practice nurses, and other health professionals who want to add HRVB techniques to their practice prior to study implementation. The program consists of six 90-minute live and recorded webinars, home study, and video presentations.

Participants/Recruitment

This feasibility study was not designed to test a hypothesis, and there was no plan to report inferential statistics. We based the sample size on the pragmatics of recruiting from the VA, patient flow, and budget constraints around the purchase of the *emWave2* HRVB devices (40). Additionally, there are no concrete recommendations for sample size in a feasibility study; however, we may achieve the aims of the study with a sample of 10 participants (41) (Table 1).

This study was approved by the Medical University of South Carolina Institutional Review Board (IRB) and the Ralph H. Johnson VA Medical Center Research and Development Board. We placed IRB-approved recruitment flyers in the lobbies and exam rooms of primary care and mental health clinics of a southeastern United States VA health center. We also gave flyers to the primary care providers, mental health providers, and nurses in these clinics. Additionally, we attended the monthly meeting for clinic staff and provided information and time for questions and answers about the planned study. The health care providers and medical staff were not involved in the study and did not receive any finders' fees.

Inclusion criteria included male and female Veterans ages 18 and older with a documented diagnosis of fibromyalgia. Veterans of all races and ethnicities were eligible to participate. Exclusion criteria were any major cardiovascular disease, current use of medications that regulate heart rate, major pulmonary disease, a major psychosis diagnosis, self-reported pregnancy, or prior experience with HRVB. Study participants received a $5 gift card during each visit.

Design

We used a multi-method design to inform the following questions: 1) Is it feasible to recruit and retain Veterans from a VA on the southeast coast of the United States in a study implementing HRVB to treat FM-related chronic pain? 2) Is it feasible for Veterans to adhere to the recommended HRVB protocol? and, 3) Will Veterans find this intervention acceptable?

Procedures

Consistent with prior studies and recommendations from the developers of the *emWave2* (32, 42-44), we conducted an initial feasibility trial of HRVB practice 8 once-weekly one-hour

individual sessions with each participant. After participants provided informed written consent, we proceeded with the initial study visit.

Initial Visit

During the initial visit, the participants provided demographic data, completed the Credibility/Expectancy Questionnaire (CEQ), Revised Fibromyalgia Impact Questionnaire (FIQR), and Short form McGill Pain Questionnaire (SFMQ). Each participant received an *emWave2* handheld device, USB connector, ear sensor, quick start guide, and practice plan to use in the clinic and to take home for practice. We demonstrated the proper use and care of the device, including how to clip the enclosed photoplethysmograph (PPG) sensor on the participant's ear. Participants were shown features on the device, such as a blinking blue light that indicated the reading of the participant's pulse. The study team assisted with the configuration of initial settings to default level 1 (low) using the Quick Start Guide included in the box. The participant was provided time to practice HRVB during the initial visit, which included being able to see a rising and falling light in the Heart Action Strip with each breath, indicating heart rhythm and HRC. The participant was instructed to take slow rhythmic breaths. The goal was to increase HRC and change the coherence level indicator from red (low coherence/baseline) to blue (medium coherence/ improving), to green (high coherence/optimal), and to remain in the green zone as long as possible during the 20-minute practice session. Additionally, based on the protocols used by Lehrer et al. (45), participants were instructed to practice with the device at home for 20 minutes twice daily. We provided the participants with a phone number to call if they had any difficulty with the device in between study visits.

Visits 2-8

During visits 2-8, participants completed the SFMQ and the FIQR. We downloaded and stored the physiological data from the participant's *emWave2* and discussed the results with each participant. We discussed any problems with the device or barriers to practicing as recommended. We discussed strategies to overcome practice barriers and to troubleshoot any technical difficulties. Participants practiced on their *emWave2* devices for 20 minutes during each visit and received additional breathing technique coaching as needed.

Variables and Their Measures

We collected standard demographic data during the initial visit: age, gender, race, ethnicity, education level, employment status, mental health history, and marital status. We also asked about the frequency of aerobic physical activity, strength training, and stretching per week. See Table 1 for demographic data.

We measured treatment outcomes expectancy and credibility with the CEQ at the initial visit to assess HRVB as a perceived method of FM symptom management (46). Four CEQ questions ask if individuals expect treatment to improve their symptoms (expectancy), and two questions ask about treatment believability and logic (credibility) (46, 47). The CEQ has 2 rating scales, 1 to 9 (not at all to very much) and 0% to 100 % (not at all to very much). Percentage ratings are transformed linearly to a scale of 1 to 9 (minimum to maximum), allowing for a sum score ranging from 3 to 27 (minimal to maximum credibility and expectancy) (47). In previous studies, treatment expectancy has correlated higher with treatment outcomes than treatment credibility (46, 47). There is a high internal consistency of the expectancy factor (Cronbach's α between 0.79 and 0.90), the credibility factor (Cronbach's α 0.81 and 0.86), and a standardized α of 0.84 to 0.85 for the whole scale (both factors) (46).

We assessed the sensory and affective quality of pain with the Short-form McGill Pain Questionnaire (SFMQ). The SFMQ consists of 11 sensory and 4 affective descriptors of pain (48). Each word is scored on a 4-point ordinal scale and totaled for a Pain Rating Index of 0 to 45 (no pain to severe pain) (48). When the SFMQ was used with FM patients, Cronbach's alpha was estimated at $\alpha = 0.73\text{-}0.89$, and test-retest reliability ranged from 0.45-0.73 for one- and three-month intervals (49). The SFMQ moderately correlated with the Western and Ontario and McMaster Universities Osteoarthritis Index and the Short Form 36 Health Survey bodily pain scales ($r=0.36$ and -0.36 respectively; $p < 0.01$) in 200 patients with hip and knee osteoarthritis (50).

Participants also were asked to complete the FIQR at the start of each visit. The FIQR consists of 21 questions that are divided into 3 domains: function, global impact, and FM-related symptoms in the past 7 days (51). Questions are rated on a 0 to 10 numeric scale, with a better quality of life being a lower total FIQR score (51). The Cronbach's alpha coefficient measures in the 3 domains were 0.90 for function, 0.81 for overall impact, and 0.89 for the severity of symptoms (52). The FIQR was closely correlated with the Fibromyalgia Impact Questionnaire ($r=0.69$ to 0.88, $p< 0.01$) (51). The 3 domains in the FIQR also closely correlated with the 36-Item Short Form Health Survey: function ($r= -0.26$ - -0.80), global impact ($r= -0.30$ - -0.64), and symptoms of FM ($r= -0.43$ - -0.66) (51).

Computer software calculated HRC as the ratio between low frequency (LF) HRV divided by the sum of the high frequency (HF) and LF (53). The resulting average weighted score ranged from 0 to 200 (low coherence to high coherence) (53). We collected and recorded the HRC scores, session duration, session frequency, and heart rate from the *emWave2* at each

study visit. Data, including practice frequency and time spent using the *emWave2* device, were downloaded into the HeartMath software and reviewed with the participant at each study visit.

Results

Participant Characteristics

We enrolled 7 women between the ages of 33 and 68 years (mean=52) and 3 men between the age 33 and 54 years (mean =47). Participants were white (n=5), African American (n=4) or Hispanic (n=1). All had at least some higher education (Table1). Only 3 participants were employed. All participants had a mental health diagnosis, including depression (n=6), anxiety (n=2), and/or post-traumatic stress disorder (PTSD) (n=4). Most were married. Fifty to 60% of the Veterans self-reported that they never exercise (Table 2).

Table 1. Participant demographics and baseline history

	Number	Percent
Gender		
Female	7	70
Male	3	30
Race/ethnicity		
White	5	50
African American	4	40
Hispanic	1	10
Education		
High school/GED	10	100
Partial college	3	30
College degree	4	40
Graduate level	3	30
Employment		
Unemployed	2	20
Fulltime	2	20
Medically disabled		
Working	1	10
Unable to work	2	20
Retired	3	30
Mental health		
Depression	6	60

Anxiety PTSD	2 4	20 40
Marital status Never married Married Divorced	 2 7 1	 20 70 10

Key:
GED: General educational diploma
College: Bachelor's degree
Graduate: Post-Bachelor's degree
PTSD: post-traumatic stress disorder

Table 2. Self-reported weekly exercise frequency

	Never n / %	1-2 x/week n / %	3-4 x/week n / %	5-6 x/week n / %	7 x/week n / %
Aerobic	5 / 50	1 / 10	3 / 30	1 / 10	0
Strength	6 /60	3 / 30	0	1 / 10	0
Stretching	5 /50	1 / 10	1 / 10	3 / 30	0

HRVB Practice

Frequency. Participants were instructed to practice HRVB for 20 minutes during their weekly study visits and 20 minutes at home twice daily. All practice sessions were recorded by the *emWave2* software. The mean daily practice frequency rate was 0.80, suggesting there were days when the participants did not practice at all. One participant practiced twice daily during the first week of the study but not for the prescribed 20 minutes; after that, he only practiced 1-1.3 times per day but for longer periods (25.3 – 39.3 minutes). One participant only practiced during the first week (mean frequency 0.1), did not practice during week 2, then stopped attending, and did not return the *emWave2,* which would have allowed us to collect any additional data. Women practiced 21.46% more frequently than men (Table 3). All participants had a mental health diagnosis (Table 1); those with depression practiced 24.4% more frequently than those with anxiety and 27.16% more frequently than those with PTSD. Not employed Veterans practiced 40.54% more frequently as those who were employed (Table 3).

Time (minutes). Participants were instructed to practice 20 minutes each session. The mean practice duration in minutes was 19.36 and ranged from 0 to 58.1 (Table 3), suggesting that when participants practiced, they did so for the prescribed time. Women practiced 17.57% longer than men (Table 3). Veterans with a PTSD diagnosis practiced 22.21% longer than those with a diagnosis of anxiety, and 11.85% longer than those with a diagnosis of depression (Table 3). Those who were not employed practiced only 0.41% longer than those who were employed (Table 3).

Table 3. HRVB practice frequency and time (minutes)

	n =	Mean daily Frequency/(SD)	Mean time (min)/(SD)	Time (min) Range
	10	0.80 (0.51)	19.36 (11.36)	0 - 58.1
Female	7	0.86 (0.49)	21.12 (10.35)	0 - 58.1
Male	3	0.61 (0.60)	14.01 (16.63)	0 - 39.3
Depression	6	0.92 (0.52)	19.68 (9.6)	0 - 39.3
Anxiety	2	0.72 (0.40)	17.73 (5.71)	0 – 22.8
PTSD	5	0.70 (0.53)	22.16 (13.83)	0 – 58.1
Employed	3	0.59 (0.36)	19.31 (9.07)	0 – 37.2
Not employed	7	0.89 (0.57)	19.39 (12.4)	0 – 58.1

CEQ

We assessed CEQ at the baseline visit. Nine of the participants believed HRVB is a logical treatment and anticipated it would successfully reduce their pain (n=7). Most expected 50% or greater improvement in their pain (n=8). When asked about how the participants really feel, half of the participants (n=5) felt that HRVB would reduce their pain, and most (n=7) felt HRVB would reduce their pain by 50-80%. Prior to trialing the intervention, nine of the participants did not feel confident enough to recommend this treatment to a friend with similar symptoms.

FIQR

FIQR scores were measured at baseline and during weekly study visits thereafter; scores for each of the three domains and the total FIQR score range from low to high (Table 4). A lower score represents a better quality of life (51). Functional domain and global impact domain scores improved post-intervention, suggesting a slight improvement in functional status after HRVB (Table 4). The mean scores from symptoms of FM were essentially unchanged (63.9 - 64.9), indicating HRVB did not affect symptoms of FM. The weekly mean total FIQR scores post-intervention (128.5) were lower than at baseline (146.6), indicating HRVB improved overall quality of life.

SFMQ

Pain scores were measured using the SFMQ at baseline and at each weekly visit. Pain scores did not vary greatly pre- and post-intervention (Table 4). The mean total pain rating index score was 25.4 at baseline and 25.9 at weekly visits, suggesting there was no improvement or worsening of pain pre- and post-intervention.

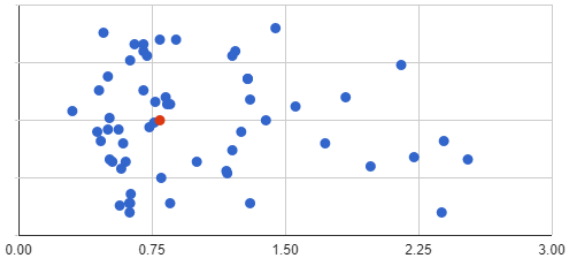
HRC

HRC was measured each time the participant practiced HRVB (Table 4). The mean HRC recorded at baseline was 1.0, with a range of 0.3 to 1.72. Post-intervention the mean score was unchanged (1.05); however, we saw a broader range (0.46 to 2.38), suggesting a 29.94% increase in HRC scores for post-intervention. The highest scores (1.83-2.52) were reached by the two participants who had the highest rates of HRVB practice frequency (1.1 and 1.9). When we examined the frequency (n=57) of mean scores, we noted 7 out of 57 practice sessions resulted in a greater HRC maximum base score of 1.72, indicating most practice sessions (n=50) did not result in improved HRC week to week (Figure 1).

Table 4. Outcomes measurements

	Baseline			Post-Intervention		
	Mean	Range	SD	Mean	Range	SD
FIQR						
Function	64.8	36-90	16.8	51.8	5-90	25.7
Global	13.9	5-20	5.9	12.4	0-20	6.1
Symptoms	63.9	51-77	9.7	64.9	16-100	25.2
Total	143.6	104-181	23.9	128.5	30-210	53.3
SFMQ						
Sensory	19.1	11-27	6.4	19.9	3-33	8.5
Affective	6.6	2-12	3.3	5.9	0-12	3.8
Total	25.4	13-39	9.7	25.9	4-45	11.9
HRC	1.0	0.3-1.72	0.51	1.05	0.46-2.38	0.59

Figure 1. Scatter plot of HRC total means



Discussion

A purpose of this study was to evaluate the feasibility of Veterans adhering to a recommended HRVB protocol of twice daily twenty-minute sessions (45) using the *emWave2* training device that objectively measures HRV and displays the physiological level of HRC. The data suggest that twice daily HRVB practice sessions were not feasible for most study participants. Only one in 10 Veterans, a male, practiced twice daily and then only for one week. However, overall women practiced more frequently and for longer periods than the men. Three of the ten participants were employed, which may have impacted their ability to practice twice daily. Three participants reported frustration with operating the device. Two of them had difficulty getting a pulse reading from the PPG sensor clipped on their ear, which caused the device to shut off automatically after a few minutes. One was not able to operate it during the

last two weeks of the study, and he did not call for assistance or come for his weekly clinic visits. One participant reported chest wall discomfort if she practiced for more than 10 minutes, so she avoided trying to practice twice daily. Veterans diagnosed with depression practiced more frequently than those with PTSD and anxiety. However, Veterans diagnosed with PTSD practiced for longer periods that those diagnosed with anxiety or depression. This group of Veterans demonstrated that when they did practice HRVB, they were able to complete a single 20-minute session and some participants tried to make up for the missed sessions with longer sessions.

The poor adherence to the practice protocol was surprising because most of the participants reported on the CEQ they believed the treatment was logical and would reduce their pain by 50-80%. In previous studies, treatment expectancy correlates with treatment outcomes (46, 47). Additionally, we expected greater adherence given weekly in person sessions with the PI. We reviewed adherence rates and discussed any barriers to protocol adherence, such as difficulties with the device and scheduling practice times, at each in person session. The participants' poor adherence is more consistent with previous reports that FM patients are skeptical of treatments (2). We have found no prior HRVB protocol feasibility studies with which to compare our results. One prior study of HRVB for FM-related chronic pain prescribed twice daily practice (32); however, the researchers did not report treatment protocol adherence rates. Other prior HRVB studies for chronic pain did not follow the treatment protocol recommendations set by Lehrer et al. (45); the studies only provided HRVB training during clinic visits (31, 43, 54, 55).

The *emWave2* software calculates the HRC scores. A lower score indicates a less coherent HRV, reflecting a dysfunctional ANS, increased pain perception, decreased physical

function, and poor quality of life (QOL) (19, 21, 56). In our study, the mean HRC scores did not change substantially from week to week, suggesting there was no improvement in HRV post-intervention. This finding is inconsistent with earlier studies, where HRC scores increased with HRVB (31, 32, 43, 54). Hassett et al. (32) conducted a pilot study of the efficacy of HRVB in patients with FM and demonstrated a statistically significant ($p=0.002$) improvement in HRC after 10 weekly sessions of HRVB training. Soer et al. (43) and Berry et al. (31) conducted pilot studies of the efficacy of HRVB on chronic pain and also demonstrated a statistically significant ($p < 0.01$ and $p = 0.01$) improvement in HRC after 6 and 4 (respectively) sessions of HRVB training.

The goal of HRVB is to improve QOL and functional status by decreasing FM-related symptoms. Data from the SFMQ and the FIQR suggest there was no improvement in pain symptoms following HRVB. However, despite the persistent pain scores, data from the FIQR suggests an improvement in the functional status, and an overall improvement in QOL post-intervention. Similar findings were reported in the HRVB study for FM patients by Hassett et al. (32) where they reported a statistically significant ($p = 0.0002$) improvement in FIQR scores 3 months post intervention, indicating an improvement in QOL. Improved QOL indicators support treatment that addresses the dysfunctional ANS present in FM (18, 19).

Conclusions

Major limitations of this study were its small size and the lack of a control group. It was not possible to make inferences about changes in pain, HRV, QOL, or functional status post-intervention. Future studies should enroll an adequate number of participants to detect true changes in outcomes pre-and post-intervention. The participants all self-selected to trial HRVB and reported a high treatment outcome expectancy of 50-80% improvement in pain. Comparing

HRVB to sham biofeedback may minimize this self-selection bias. Future studies should also investigate the protocol adherence correlations between mental health diagnoses.

In summary, it appears a protocol of twice-a-day HRVB practice is not a feasible treatment option for these Veterans with FM. Yet, the Veterans in this study demonstrated that once-daily 20-minute practice sessions are acceptable. Findings suggest HRVB was effective in improving functional status and QOL among our study participants with FM-related symptoms. Thus, additional larger controlled trials are needed to evaluate this promising self-management strategy.

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Manuscript 3

Veterans' Insights on Heart Rate Variability Biofeedback to Treat Fibromyalgia-Related Chronic Pain

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Veterans' Insights on Heart Rate
Variability Biofeedback to Treat Fibromyalgia-Related Chronic Pain

Abstract

Introduction: The repetitive musculoskeletal stress of wearing heavy gear and exposure to natural and artificial environmental hazards in the Persian Gulf region has increased the prevalence of fibromyalgia (FM) among service members. Heart rate variability biofeedback (HRVB) is a self-management strategy that guides individuals to breathe at a designated resonance frequency of the cardiovascular system. Resonant breathing may reduce FM-related symptoms as well as improve physical functioning and quality of life. Although prior research recommends HRVB for chronic pain, we found no studies testing the feasibility for individuals with FM regarding protocol adherence or acceptability of the treatment.

Methods: We enrolled 10 Veterans in a HRVB study using a recommended protocol to treat FM. Veterans were given a HRVB device, *emWave2,* and instructed to practice at home twice daily for 20 minutes per session. Following a 7-week intervention period, we conducted an end of study focus group. We used content analysis to develop themes to determine the feasibility of engaging in HRVB and adhering to the intervention protocol, as well as insights of Veterans about the intervention.

Findings: Three common themes emerged: intervention implementation, protocol adherence, and self-awareness.

Conclusions: Results of this study suggest difficulties operating the *emWave2* and scheduling challenges that interfered with HRVB implementation. However, Veterans reported self-

awareness of the benefits of HRVB to treat FM-related symptoms. Future studies require a larger sample size to provide a deeper insight.

Key Words: Fibromyalgia, Veterans, heart rate variability biofeedback, heart rate variability, focus group

Introduction

Fibromyalgia (FM) is a complex condition characterized by chronic generalized myalgia, anxiety, depression, sleep disturbance, and fatigue (1). Individual reports of symptoms are variable with time of day, mood, external stressors, ambient temperature, or the amount of sleep, leading to dissatisfaction of overall health status (2). Individuals with FM are often frustrated by the lack of clarity of diagnosis (3) and very little information about treatment options from health care providers (4).

The Veterans Health Administration (VA) and Department of Defense (DoD) acknowledge that the repetitive musculoskeletal stress of wearing heavy gear every day during multiple 6 -12-month deployments during the Gulf War and Afghanistan War increased the prevalence of FM among service members (5). Additionally, the DoD recognizes that exposure to natural and artificial environmental hazards in the Persian Gulf region may also contribute to the symptoms of FM (5). The American College of Rheumatology have set the diagnostic criteria of FM (6). The diagnosis is based upon the individual's self-evaluation of pain location and symptom severity over the past weeks, the symptoms must occur at a similar level for at least 3 months or lack a disorder that would otherwise explain the pain (6). Because the VA and DoD have recognized FM as a service-connected condition (5), Veterans have been seeking FM-related symptom management at a growing rate (7).

Pathophysiology

In individuals with FM, functional magnetic resonance imaging has demonstrated disruptions in the regions of the brain that modulate pain inhibition and engage in self-referential thinking, possibly explaining the symptoms of widespread pain, memory problems, and cognitive impairment (8, 9). Additionally, the cardiac autonomic nervous system is disrupted, resulting in an incoherent heart rate variability (HRV) and impacting quality of life (10, 11).

Heart Rate Variability

HRV provides information on the sympathetic and parasympathetic interactions between cardiac autonomic nervous system (ANS) and ANS, as well as how they function as a whole (12). HRV is non-invasively analyzed from a plethysmographic (PPG) optical sensor placed at the fingertip or earlobe (12). HRV coherence, an ordered and harmonic sine-waveform (13), reflects a healthy functioning ANS associated with minimal pain (14), stress resistance, emotional adaptability (15), and self-regulation (13). HRV incoherence, an erratic or chaotic waveform pattern (13), reflects a dysfunctional ANS associated with the chronic pain, decreased physical functioning, and poor quality of life seen with FM (10, 14, 16).

Treatment

FM treatment is complex, and treatment recommendations vary. However, there is a consensus in the major guidelines that effective treatment should prioritize non-pharmacological options that reflect the biopsychosocial model (1, 17). The most recent 2014 VA/DoD Clinical Practice Guidelines (18) recommend a step treatment for chronic pain that prioritizes multi-disciplinary non-pharmacological modalities, which includes strategies like cognitive behavior therapy, exercise, psychosocial rehabilitation, physical and occupational therapy, acupuncture, spinal manipulation, complementary and alternative medicine, and biofeedback (1, 19).

Heart Rate Variability Biofeedback

Heart rate variability biofeedback (HRVB) is a self-management strategy using visual biofeedback to guide the individual to breathe at a designated resonance frequency of the cardiovascular system (4-6 breaths per minute) (20). This breathing frequency causes the heart rate to increase with inhalation and decrease with exhalation, inducing heart rate variability coherence (HRC), as well as ANS regulation (11, 13, 21-24), which may intensify the interaction between autonomic and nociceptive pathways (11). By improving HRC and ANS regulation, HRVB can effectively assist individuals in reducing or preventing FM-related symptoms such as chronic pain, fatigue, anxiety, and memory problems (25, 26). HRVB also has the potential to improve emotion regulation, stress resistance, physical functioning (23, 24, 27), and QOL (13, 21, 24) in those with FM.

Optimal resonance breathing differs for each person, so it is difficult for individuals to achieve and sustain an optimal breathing rate to reach HRC by simply breathing slower than usual (20, 28). HRVB training must occur gradually to adjust to a such a slow rate (28). Biofeedback devices, such as the *emWave2* (29)*,* use a light display to guide the individual to breathe at his or her optimal resonant frequency, which will adapt with practice as respiratory and baroreflex function improve (28). Lehrer et al. (20) recommend 5 clinic visits for HRVB training with an HRVB-trained health care professional, along with twice-daily 20-minute at-home HRVB practice sessions (20, 28). The developers of *emWave2* recommend 4-6 training sessions with a trained health care provider (41), and previous studies assessed the efficacy of HRVB with 4 to 10 training sessions with a health care provider's guidance (33, 35, 39). However, we found no studies assessing the feasibility of individuals adhering to the

recommended HRVB protocol or the acceptability of the intervention to treat symptoms associated with FM.

Theoretical Framework

The Principal Investigator (PI) used the theory of symptom self-management (TSSM) to guide this study. The central tenant of TSSM is that when patients optimize self-directed and self-managed interventions they experience better cognitive performance outcomes for quality of life and functional status (26, 30). Additionally, perceived self-efficacy-enhancing interventions (PSI) like biofeedback can reduce, relieve, or decrease the frequency and duration of pain (25, 26). Lastly, improving patient self-efficacy with cognitive behavioral strategies like HRVB can shift the patient's perception of helplessness to confidence regarding the ability to self-improve (31).

Methods

Design

Aim one of this multi-method study was to explore the feasibility and acceptability of HRVB as a treatment for Veterans with FM-related chronic pain. Before participant recruitment, the Institutional Review Board (IRB) at the Medical University of South Carolina and the Research and Development Review Board (R&D) at the Ralph H. Johnson Veterans Health Administration (RJVA) in Charleston, South Carolina, approved the study protocol.

Recruitment & Sample

We aimed to recruit 10 participants for this study based upon recommendations for adequate sample size in a feasibility study (32, 33), as well as constraints to the purchase of HRVB devices.

The PI placed IRB and RJVA R&D-approved recruitment flyers in the lobbies and exam rooms of the primary care and mental health clinics of the RJVA Medical Center. Additionally, the PI gave flyers to the primary care providers, mental health providers, and nurses in the clinics and provided them with information about the planned study. The health care staff was not involved in the study and did not receive a finders' fees for referrals.

Inclusion criteria were as follows: Veterans of all races, ethnicities, and genders; aged 18 or older; with a documented diagnosis of fibromyalgia. Exclusion criteria were as follows: a history of a major cardiovascular or pulmonary disease, current use of heart rate regulating medications; major psychosis; self-reported pregnancy; or prior HRVB experience.

To promote participation and retention, participants received a $5 gift card following completion of each visit. The PI also reminded participants of the date and time of their next visit and called them the day before the visit to remind them again.

Intervention

After eligible participants consented, they were enrolled and started the study. Based upon practice protocols recommended by Lehrer et al. (20) and earlier studies of HRVB to treat chronic pain (23, 24, 27, 34, 35), the PI conducted 8 once-weekly one-hour individual sessions and asked each participant to participate in a 60-minute focus group session after all participants had had access to the HRVB device for 7 weeks.

During the initial study visit, the PI gathered demographic data, asked about exercise habits, and gave each participant an *emWave2* HRVB device, which included the PPG and charger. The PI provided verbal and written instructions for HRVB use, and a practice plan for home implementation. Each participant practiced HRVB for 20 minutes with the device during the initial visit and each subsequent study visit. Additionally, based on the protocol use by

Lehrer et al. (20), participants were instructed to practice HRVB using the *emWave2* at home twice-daily for 20 minutes. The participants were given a phone number to call if they had any difficulty with the device or the practice schedule, or if they experienced other urgent concerns.

During each visit the PI coached the participant to breath in a resonant pattern that increased HRC and changed the coherence level indicator on the *emWave2* from red (low coherence), to blue (medium coherence/improving), to green (high coherence/optimal). Participants were coached to breathe at the green light level as long as possible during each 20-minute practice session. Each visit, the PI downloaded data from the *emWave2* and reviewed the practice frequency, length of practice sessions, and HRC levels with each participant. The PI discussed any problems with device and tried to resolve any difficulties the participant encountered. The PI also discussed strategies to adhere to the practice protocol and encouraged the participants to continue to practice.

Focus Group Conduct

To address aims 2 and 3, the PI conducted a 60-minute post-intervention focus group session after participants had access to the *emWave2* device for 7 weeks. Before the initiation of the focus group, the PI consulted researchers with experience in focus group mediation and chronic pain management. The focus group, moderated by the PI, took place at the VA primary care clinic, where all study visits were also conducted. All study participants (n=10) were invited to participate; seven participants attended the discussion. Two of the seven participants arrived 20 minutes after the start of the session.

All focus groups participants consented to participation before attending the session. The focus group started with a short introduction, as well as reminders of participant confidentiality, such as not sharing what was said outside of the meeting and not using names during the

meeting. We informed the participants that the meeting was being audio recorded and would be transcribed verbatim for data analysis. A predetermined set of open-ended questions guided the meeting; the questions were designed to elicit qualitative information about the participants' ability to adhere to the HRVB protocol, as well as the acceptability of the intervention as a treatment for FM-related symptoms. We also asked open-ended questions about changes in pain severity and FM-related symptoms to explore the initial signal of efficacy of HRVB. We explored the hypothesis that self-directed, self-managed PSI such as HRVB would improve cognitive performance outcomes for QOL and functional status (26, 30).

Data Analysis

We assessed the feasibility of recruitment of Veterans with FM by tabulating the responses to the study advertisement and study enrollment figures. Additionally, we evaluated the frequency of respondents which met exclusion criteria. We assessed individual attendance rates as well as the number of participants which attended the focus group session to evaluate retention.

The author organized the data for content analysis using manifest and latent analysis (36) for the identification of themes regarding feasibility and acceptability. To increase data validity, a highly experienced qualitative researcher performed an independent analysis and discussed the results with the PI to obtain a consensus (36). We labeled the data with codes and categorized them into themes (36, 37).

Feasibility was defined as participants' ability to operate the *emWave2* as well as implement follow the prescribed intervention protocol. With regard to the theoretical framework, when individuals can implement the practice of HRVB, they are able to attain the established goals of following the protocol and the desired outcomes of decreasing the symptoms of FM

(26). We defined acceptability as the participants' self-reported willingness to follow the practice protocol and self-reported physiological and psychological responses to the intervention. Individuals who interpret their own strengths and weaknesses to achieve a goal are more successful with PSE enhancing interventions like HRVB (26).

Results

Recruitment/Retention

After three weeks of advertising, 13 individuals from the VA primary care and mental health clinics expressed interest. One respondent was not a Veteran; he was given the flyer by a Veteran who saw it in the lobby. One respondent could not commit to the weekly visits because of her full-time work schedule, and another respondent did not meet the eligibility requirements because he was being treated with a cardiac regulating medication. The remaining respondents, n=10, met eligibility requirements, provided informed consent, and were enrolled in the study.

Eight of the ten participants attended 75-100% of the study visits (Table 1), and seven of ten attended the end of study focus group session. Veteran 6 (Table 1) did not return to the clinic after week 3. The PI called Veteran 6 each week to remind him of his appointment, and each time he stated he would come to the following visit. The PI asked Veteran 6 why he missed the previous visit, and he reported he became distracted and forgot, had unexpected family obligations, and the last two visits he reported either he, his wife, or his children were ill with upper respiratory symptoms. Veteran 6 lives 1.5 hours away from the clinic, which may have also been a contributing factor. Veteran 5 (Table 1) attended the first two visits and the 7th visit. The PI called her the day before each scheduled visit to remind her; however, she never answered the phone, and the PI was not able to leave a message for her. During her visits, the PI asked about barriers to participating and her response was, "I was not feeling well." The PI

continued to encourage her to practice her resonant breathing between visits. The participant dropped off her device at the front desk of the clinic at the end of the study, and she did not attend visit 8 or the focus group. Data from her device indicated she practiced 27 of the 49 days (55.1%) of the study.

Table 1. Weekly attendance rate

Weeks											
	1	2	3	4	5	6	7	8	Freq	%	FG
Veteran											
1	A		A	A	A	A	A	A	7	87.5	A
2	A	A	A	A	A	A	A	A	8	100	
3	A	A	A	A		A	A		6	75	A
4	A			A	A	A	A	A	6	75	A
5	A	A					A		3	37.5	
6	A		A						2	25	
7	A		A	A			A	A	5	62.5	A
8	A		A	A	A	A	A	A	7	87.5	A
9	A	A	A	A	A	A	A		7	87.5	A
10	A	A	A		A	A	A	A	7	87.5	A

Key: A = attendance
FG = focus group

Participant Characteristics

We enrolled 7 women between the age of 33 and 68 years (mean=52) and 3 men between the ages of 33 and 54 years (mean =47). The participants were white (n=5) or African American (n=4). One participant self-selected Hispanic ethnicity yet declined to self-select race. All had at least some higher education (Table 2). Only 3 participants were employed. All participants had a mental health diagnosis of depression (n=6), anxiety (n=2), and/or post-traumatic stress disorder (PTSD) (n=4). Most (70%) were married. Four of the seven women reported exercising aerobically, with strength training and/or stretching (Table 3). One of the three men reported aerobic exercising and stretching (Table 3).

Table 2. Participant demographics and baseline history

	Frequency	Percent
Gender		
Female	7	70
Male	3	30
Race/ethnicity		
White	5	50
African American	4	40
Hispanic	1	10
Education		
HS/GED	10	100
Partial college	3	30
College degree	4	40
Graduate level	3	30
Employment		
Unemployed	2	20
Fulltime	2	20
Medically disabled		
Working	1	10
Unable to work	2	20
Retired	3	30
Mental health		
Depression	6	60
Anxiety	2	20
PTSD	4	40
Marital status		
Never married	2	20
Married	7	70
Divorced	1	10

Table 3. Self-reported weekly exercise frequency

	Overall (n=10)	Female (n=7)	Male (n=3)
Aerobic			
Never	50% (5/10)	42.8% (3/7)	66.7% (2/3)
1-2x/week	10% (1/10)	14.3% (1/7)	0
3-4x/week	30% (3/10)	28.6% (2/7)	33.3% (1/3)
5-6x/week	10% (1/10)	14.3% (1/7)	0
7x/week	0	0	0
Strength			
Never	60% (6/10)	42.8% (3/7)	100% (3/3)
1-2x/week	30% (3/10)	42.8% (3/7)	0
3-4x/week	0	0	0
5-6x/week	10% (1/10)	14.3% (1/7)	0
7x/week	0	0	0
Stretching			
Never	50% (5/10)	42.8% (3/7)	66.7% (2/3)
1-2x/week	10% (1/10)	0	33.3% (1/3)
3-4x/week	10% (1/10)	14.3% (1/7)	0
5-6x/week	30% (3/10)	42.8% (3/7)	0
7x/week	0	0	0

Feasibility of Prescribed HRVB Protocol

To address the feasibility of the HRVB protocol, the facilitator asked participants if they had difficulty following the home practice schedule of 20 minutes twice daily, and if so, what the difficulties were. The resulting data were coded as implementation and adherence.

Implementation

A common barrier to implementation of the protocol was difficulty finding time to practice. Three participants work full time jobs; one participant cares for her husband who is receiving chemotherapy and she drives him to his appointments. Another participant is a caregiver to her disabled husband and actively helps care for her young grandchildren. These barriers were also identified and addressed during the weekly individual visits. The PI addressed

these barriers and helped the participant identify strategies to overcome these barriers. Some strategies were setting aside 20 minutes before the children got up in the morning, or before they came home from school, using lunch break to sit in a quiet area of the building or in the car to practice. In the case of the participant's spouse was receiving chemotherapy, the PI suggested practicing in a quiet place while she was waiting for him to complete his treatment. Three participants were strictly adhering to a stressful schedule and preferred to practice when it was convenient. The following are salient responses:

> Veteran 7 stated, "I stressed out over it, because my work schedule's weird, so trying to get it on a consistent schedule was difficult and then, I would get frustrated with myself, because I didn't do it like I was supposed to."
>
> Veteran 1 reported, "I found it a lot easier for me to just use it anytime it was convenient for me, as I was driving, I was going for appointment, I was waiting, or whatever the case may be, I just made it work with my schedule, because if I tried to just do it twice a day at a given time, it just didn't really work for me."
>
> Veteran 3 summed it up by stating, "We are all too busy, everybody's always too busy."

Another identified barrier to protocol implementation was difficulty operating the device. The most common problem reported was with the PPG. Participants had difficulty getting a pulse when they clipped the PPG to their earlobe.

> Veteran 3 reported, "It wouldn't work on my finger. Periodically, it worked on different places on my ears."

A key feature of the *emWave2* is that the device shuts off automatically if there is no pulse reading. Some of the participants reported frustration about the device shutting off during the individual study sessions. These frustrations were reiterated during the focus group session.

> Veteran 4 stated, "It would kill my ears, I had to use my finger, and it wouldn't read the pulse all of the time."
>
> Veteran 6 reported, "Mine would completely stop working. I thought it had died, it turns off."

The PI addressed these difficulties during the study sessions. The researcher assisted the affected participants by trying different areas of the ear, and by attaching the PPG to the fingertips.

Two participants reported it would have been helpful to have a resource video to refer to for technical difficulties. One participant was able to find a freely available video online for the *emWave2* and was able to alleviate the problem of finding a pulse with the PPG.

We identified implementation facilitators during the focus group session and during individual visits with the PI. Veteran 7 and Veteran 2 implemented the practice protocol because they believe biofeedback is an acceptable treatment alternative to medications and other more invasive treatment options they have tried in the past. Veteran 9 reported he had heard of the psychological and physiological benefits of HRVB in the media and was anxious to start the prescribed protocol.

Veteran 5 reported she was able to implement the intervention if she did not try to follow a schedule. She stated it was easier for her to practice at her convenience, like when she was driving on her way to appointment or waiting in an office or waiting room. The PI advised the Veteran not to practice HRVB while driving because the practice of HRVB may detract her from driving safely. She verbalized understanding and assured the PI she would refrain from such behavior in the future.

Adherence

Four of the participants reported they tried to make up for missed practice sessions by practicing for longer than the prescribed 20-minute sessions or practicing extra sessions when they had time.

> Veteran 10 reported, “I missed some days, too, but when I do remember, I always do like three times because I actually need to bring my heart rate down back to where I need it to.”

Veteran 3 stated, “If once a day then for an hour, twice a day most times.”

One participant reported he followed the practice protocol because he had watched a video about the physiological changes that occurs when one engages with HRVB. Some participants reported the visual feedback system of the *emWave2*, the HRC indicator light changing from red (low HRC) to blue (moderate HRC) and to green (optimal HRC) (38), was a beneficial factor in their protocol adherence.

> Veteran 1 reported, “I thought the lights were helpful, when you were in bed breathing you can see a difference. You didn’t want it to stay red. It would gradually go to blue and then green. If you stayed in the green you would hear pop pop pop and I know I am doing it right.”

The study team identified some barriers to adherence. Participants reported inconveniences of carrying the *emWave2* with them. They reported they may have been more compliant with the protocol if they could have practiced on their cell phones, which they carry everywhere. Veteran 10 reported, “I don’t see it, I don’t remember.” One participant was bothered by the beeping sounds emitted from the device and curtailed the practice time to avoid the sounds. The “beeping” problem was resolved during the next clinic visit after receiving guidance about how to control the audio features.

Lastly, one Veteran reported “chest pain” if she practiced for the prescribed 20 minutes, resulting in less time spent during each practice session as well as fewer practice sessions during the week. Her reported chest pain was evaluated by the PI during the individual clinic visit and determined to be chest wall pain and not cardiac pain. Participants were instructed to seek emergency medical care for any urgent cardiac-related symptoms. Her symptoms gradually improved from week to week, and by the end of the 8-week study, she was able to practice for 20-minutes with minimal chest wall discomfort.

Acceptability of the intervention

The facilitator asked participants if the intervention helped with pain or other FM-related symptoms like sleep, depression, anxiety, or memory. One of the foundations of PSE-enhancing interventions is individual interpretation of inferences from physiological and psychological responses that indicate personal strengths and vulnerabilities to reach goals of the intervention (26). The discussion data were coded as self-efficacy of HRVB. Results related to self-efficacy of pain symptoms were mixed: 2 of 7 reported some relief in pain, 2 of 7 reported they were unsure if they experienced pain relief, and 1 of 7 reported no pain relief.

> Veteran 10 reported, “So, I had to use it to calm me down too, because I realized with it, it also by calming me down and getting my breathing under control, it would help with the pain too, because last time, I'd been in pain all the time, so it kind of helped.”
>
> Veteran 4 stated, “It's hard to tell because I still get injections in my back. I get infusions once a month because I've got multiple things going on, so it's really hard to tell. It was relaxing.”
>
> Veteran 4 added, “Yeah, and so yeah it helped with the muscle spasms and all that, but as far as the pain, I live with it.”

Participants reported changes in other FM-related symptoms, such as breathing, relaxation, cognition, and sleep. Participants recognized that when they engaged in the resonant breathing, they experienced relaxation and decreased anxiety, which directly impacted pain tolerance.

> Veteran 1 shared, “The other thing I found was you hear a lot about how your body naturally heals itself, but with this machine, you also realize how the body impacts you as a person and what you do to help your body heal itself can make a difference, because when I used the machine, I notice a lot of things about my own body, how my body reacts to how I breathe, how I feel, after the machine and even before the machine, because it made a difference in how I was feeling."
>
> Veteran 1 added, “It made a difference in my pain level too with my breathing, and I've always practiced breathing, but I've never practiced it on a machine where I could actually just see how it affected me, calmness, anxiety, different things that

> were happening at different times and that's when I realized too, use the machine at night and then, in the morning. Sometimes, at night, during the day, depending on what I'm doing and when I'm having real, I just want to slap somebody ... and noticed a difference in how I was feeling and what I was doing when I stopped and used the machine."
>
> Veteran 9 stated, "Especially when I did it in the evening, it also helped the sleeping tremendously. Because you were getting into a relaxed state, which does help you sleep."

They were aware that mental distraction increased a sense of calmness and self-corrected when the indicator lights turned red.

> Veteran 8 reported, "So, just in terms of the thought distraction helps overall calmness feeling and then, but when it did go red, it made me more aware of what I was feeling at the time physically and mentally, and it was kind of an, 'Oh,' it helped me make those connections."

We also evaluated intervention acceptability by asking the participants if they would recommend HRVB to other Veterans with FM. The responses were a unanimous yes. They felt HRVB was a good alternative to medication and an option when all else has failed.

> Veteran 9 reported, "I think there's a lot to be said with biofeedback, especially when you've tried everything else."
>
> Veteran 3 stated, "It's a good alternative to medications and other extensive medical practices."

Discussion

HRVB is a promising self-treatment option to improve the FM-related symptoms like pain, mental fog, anxiety, and sleep disturbance, as well as functional status and QOL (13, 21, 24). Lehrer et al. (20) determined individuals cannot simply achieve HRC by slowing their breathing rate and thus developed an HRVB training protocol to optimize resonant breathing to reach optimal HRC. However, we failed to find any research to support the feasibility or acceptability of the prescribed protocol for individuals with FM.

Core elements of self-management skills include decision making, resource utilization, and problem solving (26). When participants were instructed to practice HRVB twice daily for 20 minutes, they had to choose to make time to practice and to avail themselves of the resources provided, e.g., by calling the PI for any difficulties and/or discussing barriers to the practice protocol, and with the PI's guidance, problem solving any difficulties with the device.

Individual perceived self-efficacy (PSE) beliefs are not only developed through performing an activity (26). PSE is also developed by observing others successfully understanding an activity, and by social or verbal persuasion that one can be successful (26), received either from peers or healthcare providers. Our study participants did not have an opportunity to observe others practice HRVB, and they only received encouragement from the PI during the in-person session. In future trials, to help improve participant self-efficacy, we recommend providing participants with a calendar, negotiating an acceptable schedule during the initial study visit, and reviewing the schedule for adjustments as the individual encounters implementation obstacles. We also suggest conducting multiple focus groups during the study to provide opportunities for participants to discuss implementation barriers with other participants as well as observe helpful techniques.

Additional core elements of self-management skills include decision making, resource utilization, and problem solving (26). When the Veterans encountered difficulties with the PPG, they became frustrated and practiced less frequently. Participants were given a phone number to contact the PI and instructed to call at any time between the hours of 0700 and 2100. No participants called the PI for assistance. In future studies we may include an instructional video for individual reference. Future study protocols also may include instructions on how to access online help from the manufacturer of the HRVB device. HeartMath®, the makers of the

emWave2, have an online forum for technological problems (39). Some Veterans reported the device itself was inconvenient because it was another object to carry with them. HeartMath® has software for mobile phones that operates similarly to the *emWave2* device (40). Future trials may consider utilizing HRVB software that can be downloaded onto a mobile phone.

FM-related symptoms can vary from day to day, depending upon elements such as sleep, stress, or ambient temperature, potentially leading to frustration and feelings of lack of control over symptom self-management (2); those factors may contribute to skepticism of treatment recommendations (4). Gaining control with activities like HRVB may maximize symptom management (26). Although Veterans did not report complete pain relief, there was some improvement in pain and there was a consensus of overall improvement in other FM-related symptoms such as sleep, cognition, and relaxation. Ease of relaxed breathing, improvements in sleep, increased calmness, and improved cognition were all interrelated and have been demonstrated in other studies to improve QOL in individuals with FM (1, 6, 41). In their HRVB study for FM, Hassett et al. (24) reported similar results to ours: an improvement in functional status, relief of FM-related symptoms, and improvement in QOL.

In our study there was an isolated case of chest wall pain associated with the resonant breathing of HRVB. We did not discover any complaints of chest wall pain in earlier studies of HRVB to treat FM-related pain or chronic musculoskeletal pain (23, 24, 27, 35, 42, 43). However, this should be addressed and reported if discovered in future trials. Researchers should also stress the importance safely practicing HRVB, like while driving or conducting activities that requires their full attention.

Conclusion

HRVB is a promising treatment option for FM-related symptoms. Limitations of this study include the small sample size. Additionally, the PI led a single focus group session. The participants were asked to recall events and experiences over an eight-week period.

Our findings indicate that there were difficulties operating the device and scheduling challenges that interfered with implementation of the intervention. Future trials may be able to prevent some of the equipment difficulties with clearer instructions and participant access to the developer's website. Although our qualitative analysis suggests HRVB is an acceptable treatment for Veterans with FM, more detailed interviews from a larger sample are needed. Adding individual interviews at several points throughout the study may provide deeper insight into the acceptability of this novel treatment option.

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Summary

As the incidence rates of fibromyalgia (FM) rise in U.S. Veterans, (1) health care providers are challenged to find safe, effective, and acceptable treatment options. FM-related symptoms are complex (2-4), and treatment must be multi-focal (5). Heart rate variability biofeedback (HRVB) is a self-management strategy (6) that has the potential to improve emotion regulation, stress resistance (7-9), and quality of life (9, 10) for individuals with FM. Repeated sessions of HRVB can optimize stress resistance, decrease pain, and increase overall well-being (6). The overarching question of whether HRVB is a feasible and acceptable treatment for Veterans with FM-related chronic pain is covered in three manuscripts. The first manuscript is an integrative literature review examining the relationship between HRVB and FM-related chronic pain. The second and third manuscripts report the quantitative and qualitative findings of the feasibility and acceptability study we conducted of HRVB to treat FM-related chronic pain.

In the first manuscript, we examined the relationship between HRVB and FM-related pain through the lens of the TSSM. We reviewed five studies that reported the results of HRVB as a treatment for chronic musculoskeletal pain (7, 8, 11-13) and one study investigating HRVB to treat FM-related chronic pain (9). All six authors reported an overall improvement in chronic pain (7-9, 11-13); however, only Hassett et al. (9), Hallman et al. (8) and Soer et al. (11) reported changes in functional status and quality of life. Hassett et al. (9) reported improved functional status and quality of life after HRVB from results of the Fibromyalgia Impact Questionnaire (FIQ). Soer et al. (11) and Hallman et al. (8) reported improvements in vitality as well as functional and social status

after HRVB from the Short Form Health Survey (SF-36). However, these were pilot studies that were not designed to test a hypothesis (14). HRVB practice protocols reported in manuscript 1 were inconsistent, so it was difficult to determine if the researchers implemented Lehrer's (15) protocols.

Additionally, we were not able to determine if outcomes of functional status and quality of life were related to the intervention. We did not identify any studies that addressed individual adherence to the practice protocols of HRVB as an intervention to treat FM-related chronic pain. Finally, we did not locate any qualitative studies that examined participant acceptability of HRVB as a treatment for FM-related pain.

Manuscript two reported the feasibility and adherence to a recommended HRVB protocol. We enrolled 10 Veterans to evaluate feasibility and adherence to a twice a day, twenty-minute HRVB practice protocol on the *emWave2* device for eight weeks. The Veterans in our study did not adhere to the recommended twice-daily practice protocol. Veterans cited scheduling difficulties related to jobs, family care obligations, and otherwise busy schedules as barriers to the practice schedule. However, the Veterans practiced for the recommended 20 minutes whenever they made the time for practice. We examined earlier studies but did not locate any studies that allowed participants to take the HRVB device for home practice.

In manuscript two we also reported data from the FIQ and noted that overall participants did not reports any significant change in FM-related symptoms like pain, fatigue, depression or memory problems. However, consistent with findings reported by Hassett et al. (9) the participants did report a slight improvement in functional status, like

being able to complete some household chores, walking for 20 minutes or climbing one flight of stairs, and an overall improvement in the quality of life post-intervention.

As stated earlier, we did not identify any qualitative studies of HRVB to treat FM-related symptoms. To address this gap in the literature, we conducted a focus group post-intervention seeking Veterans' insights into the twice-daily 20-minute HRVB protocol and reported the results in manuscript 3. While we were able to determine the Veterans did not practice twice daily as instructed, it was valuable to discover why they did not practice. The Veterans reported family obligations, work schedules, and difficulties adhering to a new habit as barriers to practice. The participants also reported some difficulties managing the settings on the HRVB device that interfered with the practice schedule. Although not reflected in the answers reported on the FIQ, during the focus group sessions, the Veterans reported the realization of a connection between HRVB and improved FM-related symptoms like sleep and anxiety. Additionally, the participants in the focus group reported decreased pain levels; however, this was not reflected on the quantitative pain scales they completed at each individual visit. The Veterans also viewed the visual feedback of the *emWave2* as helpful in maintaining the positive effects of HRVB. This insight will be helpful when we develop future HRVB study protocols.

There were several limitations to this dissertation. This study was small (n=10) and did not have a control group. Confounding variables such as other pain treatment modalities may have influenced the outcomes of this study. Although all participants met inclusion criteria, 50% (n=5) of the study participants were known to the PI through prior care in the Veterans Administration (VA) pain clinic; thus, there was a risk of selection

bias. A larger randomized controlled trial of participants recruited from multiple clinics may minimize these limitations.

This PI had limited experience in conducting a focus group. After review of the focus group transcript and discussions with a seasoned qualitative researcher, we identified several limitations. Although the PI kept to the pre-determined focus group script, she did not recognize several opportunities to obtain deeper insight into the Veterans' experiences with the intervention. If the PI had ventured from the script and asked for further clarifications to comments by the participants, she may have gained richer valuable data about the barriers to the practice protocol as well as insights about participant self-efficacy of the benefits of HRVB. Additionally, the PI only conducted one focus group at the end of the study. When the PI was developing the study protocol, she believed one post-intervention session would be enough to gain insight into the Veterans' experiences with HRVB. However, the participants were asked to recall insights into interventions over eight weeks, and the PI now recognizes that participant recall may have been improved with additional meetings at various points throughout the study.

None of the HRVB studies we identified in our integrative literature review (manuscript 1) applied a theoretical or conceptual framework. Future research about biofeedback to treat FM-related symptoms should use a theoretical framework that addresses self-management and self-efficacy to increase treatment adherence and optimize performance outcomes such as functional status and quality of life. This dissertation study was guided by the central tenant of TSSM, that implementation of self-management interventions improves performance outcomes like quality of life and

functional status. An important construct of TSSM to consider is that activities such as social and verbal persuasions from peers and observing others perform the activity successfully can assist individuals to identify their strengths and vulnerabilities to achieve their goal (16). Peer mentorship or group visits may be useful in future studies.

I want to continue my investigation of HRVB as a treatment option for Veterans with FM. The VA is committed to developing and integrating non-pharmacological modalities into individual pain care plans. My goal is to conduct a pilot study of HRVB for the treatment of chronic pain in Veterans with FM. I will update my integrative literature review with any new studies conducted to treat FM with HRVB. I will review the findings of this study to develop a study protocol that may minimize some of the limitations identified. HRVB is being used within the VA to treat post-traumatic stress disorder, so I will communicate with the champions of HRVB, and discuss strategies for obtaining the HRVB devices, planning a study protocol, and recruitment strategies. I plan to apply for the VA Nursing Research Initiative grant and work closely with pain team members and seasoned researchers.

Implications

The results of this dissertation have several implications for health care provider education, clinical practice, and future research for FM-related chronic pain treatment. This dissertation introduces medical providers to an alternative to pharmacological treatment for FM-related chronic pain that is safe and accepted by individuals with FM. The information provided in the integrative literature review (manuscript 1) will inform health care providers of the gap in the literature concerning the feasibility of following the recommended HRVB protocol and lack of studies of HRVB as a treatment option for

FM-related pain. The quantitative study (manuscript 2) informs health care practitioners who plan to implement HRVB into their pain treatment plan that a twice-daily 20-minute practice protocol is not feasible for individuals with FM and may require adjustment. Although this quantitative study (manuscript 2) was not designed to provide inferential statistics, we did recognize a suggestion of individual improvement in functional status and quality of life post-intervention. Results of the qualitative study (manuscript 3) will inform practitioners that individuals reported difficulties following the treatment protocol because of scheduling and family obligations. Health care providers can use this information to anticipate barriers to the prescribed protocol and help patients identify pre-determined scheduling conflicts and develop an individual schedule that is easy to maintain. Health care providers will learn that although the participants were unable to follow the recommended protocol, they acknowledged the positive physiological and psychological effects.

The implementation of HRVB for FM-related chronic pain follows current treatment guidelines that prioritize nonpharmacological treatments based on the biopsychosocial model (5, 17). The *emWave2* device is affordable and readily available on the general market (18). With this novel approach, health care providers may empower individuals to self-manage their FM-related chronic pain. Additionally, FM patients are often skeptical of pharmacological treatments for their symptoms (19) and are more receptive to holistic providers (20) that offer treatments like HRVB.

Future research

The integrative literature review (manuscript 1) demonstrates the need for additional research investigating the use of HRVB as an acceptable treatment option to

manage the chronic pain associated with FM. Additionally, we were unable to locate prior studies that address the feasibility of individuals with FM to adhere to the recommended HRVB protocol. Although our quantitative study (manuscript 2) results suggested an improvement in functional status and quality of life in individuals with FM, randomized controlled trials that are adequately powered to determine HRVB outcomes are needed. The integrative literature review (manuscript 1) also supports the need for qualitative studies that will investigate individual insight into this novel approach, so that health care providers can provide an acceptable and safe treatment alternative.

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Appendices

Appendix A

IRB approval letter for study reported in manuscripts 2 & 3

Institutional Review Board for Human Research (IRB)
Office of Research Integrity (ORI)
Medical University of South Carolina

Harborview Office Tower
19 Hagood Ave., Suite 601, MSC857
Charleston, SC 29425-8570
Federal Wide Assurance # 1888

APPROVAL:
This is to certify that the research proposal **Pro00079144** entitled:
Feasibility and Acceptability of Heart Rate Variability Biofeedback to Treat Fibromyalgia-Related Chronic Pain

submitted by: **Robert Friedman**
Department: **ANESTHESIA AND PERIOPERATIVE MED - MUSC**
Sponsor: **Stewart Dissertation Award**

for consideration has been reviewed by **IRB-II - Medical University of South Carolina** and approved with respect to the study of human subjects as adequately protecting the rights and welfare of the individuals involved, employing adequate methods of securing informed consent from these individuals and not involving undue risk in the light of potential benefits to be derived therefrom. No IRB member who has a conflicting interest was involved in the review or approval of this study, except to provide information as requested by the IRB.

WHILE YOUR STUDY HAS BEEN APPROVED BY THE MUSC IRB, YOU MAY NOT BEGIN WORK ON YOUR RESEARCH STUDY AT THE VAMC UNTIL YOU HAVE RECEIVED VAMC R&D COMMITTEE APPROVAL.

Original Approval Date: **10/16/2018**
Approval Expiration: **10/15/2019**

Type: **Full IRB Review**

Chair, **IRB-II - Medical University of South Carolina**
Susan Sonne*

Statement of Principal Investigator:

As previously signed and certified, I understand that approval of this research involving human subjects is contingent upon my agreement:

1. To report to the Institutional Review Board for Human Research (IRB) any adverse events or research related injuries which might occur in relation to the human research. I have read and will comply with IRB reporting requirements for adverse events.
2. To submit in writing for prior IRB approval any alterations to the plan of human research.

3. To submit timely continuing review reports of this research as requested by the IRB.
4. To maintain copies of all pertinent information related to the research activities in this project, including copies of informed consent agreements obtained from all participants.
5. To notify the IRB immediately upon the termination of this project, and/or the departure of the principal investigator from this Institution and the project.

∗***Electronic Signature****: This document has been electronically signed by the IRB Chairman through the HSSC eIRB Submission System authorizing IRB approval for this study as described in this letter.*

Appendix B
IRB approval letter for amendment to study reported in manuscripts 2 & 3

Institutional Review Board for Human Research (IRB)
Office of Research Integrity (ORI)
Medical University of South Carolina

Harborview Office Tower
19 Hagood Ave., Suite 601, MSC857
Charleston, SC 29425-8570
Federal Wide Assurance # 1888

APPROVAL: **Protocol: MS1_Pro00079144**
MUSC Amendment #: Ame1_Pro00079144
Amendment Title: Amendment 1 for IRB Study #Pro00079144

This is to certify that the amendment to the research proposal entitled:
Feasibility and Acceptability of Heart Rate Variability Biofeedback to Treat Fibromyalgia-Related Chronic Pain

and submitted by: **Robert Friedman**
Department: **ANESTHESIA AND PERIOPERATIVE MED - MUSC**
Sponsor: **Stewart Dissertation Award**

for consideration has been reviewed by **IRB-II - Medical University of South Carolina** and approved with respect to the study of human subjects as adequately protecting the rights and welfare of individuals involved, employing adequate methods of securing informed consent from these individuals and not involving undue risk in the light of potential benefits to be derived therefrom. No IRB member who has a conflicting interest was involved in the review or approval of this amendment, except to provide information as requested by the IRB. If this amendment required a change in the currently approved Informed Consent, then all previous Informed Consent documents should be marked obsolete.

Approval Date: **12/11/2018**

Amendment Type: **Expedited**

Chair IRB II,
Susan Sonne, Pharm D

* ***Electronic Signature****: This document has been electronically signed by the IRB Chairman through the HSSC eIRB Submission System authorizing IRB approval for this study as described in this letter*

Appendix C

R&DC approval letter for the study reported in manuscript 2 & 3

Department of Veterans Affairs MEMORANDUM

R&DC Approval Date: December 6, 2018

From: ACOS for Research & Development (151)

Subject: Research & Development Committee Approval of Research Proposal

To: Robert Friedman, M.D.

1. Your research proposal entitled *"Feasibility and Acceptability of Heart Rate Variability Biofeedback to Treat Fibromyalgia-Related Chronic Pain"* has been reviewed by the Research & Development Committee and found to be satisfactory. We acknowledge that it has IRB approval. Your study is now activated at the Ralph H. Johnson Medical Center. **You must submit an expenditure report to the Research Office on a yearly basis. You must also inform the R&D office when this study ends, and forward the subcommittee termination paperwork to the R&D Program Manager.** If for any reason the status of this project or your role in the project changes, please notify the VA Research Office immediately in writing. Should you have any questions, please contact Rudell Ryant, R&D Program Manager, at 789-6711.

2. You, the Principal Investigator, are responsible for notifying your Service Chief, Impacted Services/Clinics and Pharmacy Service (if applicable) of IRB and R&D approval. You, the Principal Investigator, are also responsible for notifying your Service Chief, Impacted Services/Clinics and Pharmacy Service (if applicable) when a study has been terminated.

3. Please take the time to read the attached VHA Handbook 1200.19, dated July 10, 2014. It describes VA policy regarding acknowledgment of Department of Veterans Affairs affiliation and research support in presentations and publications. In publications, the proper terminology is: This work is supported by the Office of Research and Development, Medical Research Service, Department of Veterans Affairs.

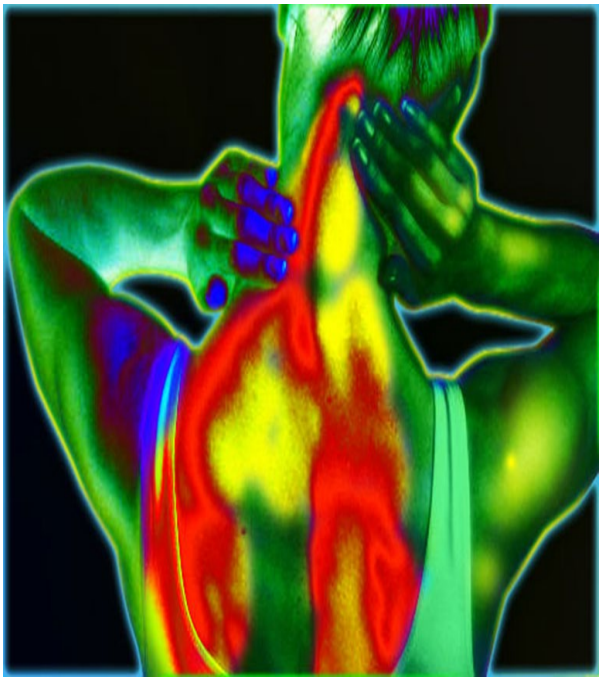
4. **All research staff that are not VA employees must be registered as WOC employees and their credentials confirmed.**

R. Amanda C. LaRue, Ph.D.

Attachment: VHA Handbook 1200.19

Appendix D

Recruitment flyer for study reported in manuscript 2 & 3



FIBROMYALGIA PAIN?

Research Study

Researchers at the R. Johnson VA and Medical University of South Carolina are looking for volunteers with Fibromyalgia to participate in a research study to investigate the effect of a non-drug treatment on pain and quality of life.

Who is eligible?

Veterans over 18 Diagnosed with Fibromyalgia

What is involved?

Interviews and questionnaires

Non-medication pain management technique

Duration

12 weeks

Compensation is available

CO-INVESTIGATOR

Marcelaine Haire

843-367-9220

Marcelaine.haire@va.gov

R. Johnson Department of Veterans Affairs

Goose Creek Clinic

Appendix E

Focus group questions for study reported in manuscript 3

Focus Group Questions

Set 1 Questions

1. How often did you use the device?
2. Did you look forward to using it?
3. Do you think if helped your pain?
4. Did it help anything else besides pain?
5. Was there a downside to using it?
6. Do you think there could be a better way of teaching this to people?

Set 2 Questions

7. Did you have any technical difficulties? If so, what were they? How did they get resolved? Did the problem(s) change your practice schedule?
8. Were you frustrated with the device?
9. Did you have any difficulty following the home practice schedule? If so, what were they? What kind of changes did you make to the home practice schedule?
10. If you could talk to other Veterans with FM, what would you tell him/her about your experience with HRVB?

Appendix F

Demographics questionnaire for study reported in manuscripts 2 & 3

GENERAL BACKGROUND INFORMATION

1. Today's date: __/__/___ (month/day/year)

2. Age: ____

3. Gender: (check one)
   1. __Female
   2. __ Male

4. Race (check all that apply)
   1. __White
   2. __ Black or African American
   3. __ American Indian or Alaskan Native
   4. __ Asian
   5. __ Native Hawaiian or Other Pacific Islander

5. Ethnicity
   1. __ Hispanic or Latino

6. Highest level of school completed (check one)
   1. __ High School graduate (includes GED)
   2. __ Partial college or vocational training
   3. __ College or university graduate
   4. __ Graduate professional training

7. Employment status
   1. __ Unemployed
   2. __ Seeking employment
   3. __ Medically disabled, unable to work
   4. __ Medically disabled, working
   5. __ Part-time employed
   6. __ Full-time employed
   4. __ Retired

8. Mental health history (check all that apply)
   1. __ Depression
   2. __ Anxiety disorder
   3. __ PTSD
   4. __ Panic disorder
   5. __ Other, please specify (_____)

9. Marital status (check all that apply)

1. __ Never married
2. __ Married
3. __ Separated
4. __ Divorced
5. __ Widowed

10. How many days per week do you walk, use elliptical machine, bike, swim, dance or perform other movement activities for at least 30 minutes? (check one)
    1. __ Never
    2. __ 1-2 times a week
    3. __ 3-4 times a week
    4. __ 5-6 times a week
    5. __ 7 times a week

11. How many days per week do you use any weights to strengthen your muscles for at least 15 minutes? (check one)
    1. __ Never
    2. __ 1-2 times a week
    3. __ 3-4 times a week
    4. __ 5-6 times a week
    5. __ 7 times a week

12. How many days per week do you stretch your muscles for at least 15 minutes? (check one)
    1. __ Never
    2. __ 1-2 times a week
    3. __ 3-4 times a week
    4. __ 5-6 times a week
    5. __ 7 times a week

Appendix G

Credibility/Expectancy questionnaire for study reported in manuscript 2

Credibility/Expectancy Questionnaire

We would like you to indicate below how much you believe, *right now*, that the treatment you are receiving will help reduce your pain. Belief usually has two aspects to it: 1) what one *thinks* will happy and 2) what one *feels* will happen. Sometimes these are similar; sometimes they are different. Please answer the questions below. In the first set, answer in terms of what you *think.* In the second set answer in terms of what you really and truly *feel*.

Set I

1. At this point, how logical does the biofeedback treatment offered to you seem?

1	2	3	4	5	6	7	8	9
not at all logical				somewhat logical				very logical

2. At this point, how successfully do you think this biofeedback treatment will be in reducing your pain?

1	2	3	4	5	6	7	8	9
not at all useful				somewhat useful				very useful

3. How confident would you be in recommending this biofeedback treatment to a friend who experiences similar problems?

1	2	3	4	5	6	7	8	9
not at all confident				somewhat confident				very confident

4. By the end of the biofeedback treatment period, how much improvement in your pain do you think will occur?

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%

Set II

For this set, close your eyes for a few moments, and try to identify what you really *feel* about the treatment and its likely success. Then answer the following questions.

1. At this point, how much do you really *feel* that the biofeedback treatment will help you to reduce your pain?

1	2	3	4	5	6	7	8	9
not at all			somewhat			very much		

2. By the end of the biofeedback treatment period, how much improvement in your pain do you really *feel* will occur?

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%

Appendix H

Fibromyalgia impact questionnaire for study reported in manuscript 2

REVISED FIBROMYALGIA IMPACT QUESTIONNAIRE (FIQR)

Unique Identifier:
Age:
Duration of FM symptoms (years) : **Time since FM was first diagnosed (years):**

Directions: For each of the following 9 questions check the box that best indicates how much your fibromyalgia made it difficult to perform each of the following activities during the past 7 days. If you did not perform a particular activity in the last 7 days, rate the difficulty for the last time you performed the activity. If you can't perform an activity, check the last box.

Brush or comb your hair	**No difficulty**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very difficult**
Walk continuously for 20 minutes	**No difficulty**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very difficult**
Prepare a homemade meal	**No difficulty**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very difficult**
Vacuum, scrub or sweep floors	**No difficulty**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very difficult**
Lift and carry a bag full of groceries	**No difficulty**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very difficult**
Climb one flight of stairs	**No difficulty**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very difficult**
Change bed sheets	**No difficulty**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very difficult**
Sit in a chair for 45 minutes	**No difficulty**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very difficult**
Go shopping for groceries	**No difficulty**	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very difficult**

Sub-total ***(for internal use only)*** ☐

Directions: For each of the following 2 questions, check the box that best describes the overall impact of your fibromyalgia over the last 7 days:

Fibromyalgia prevented me from accomplishing goals for the week	**Never** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Always**
I was completely overwhelmed by my fibromyalgia symptoms	**Never** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Always**

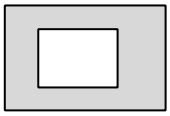
Sub-total *(for internal use only)* ☐

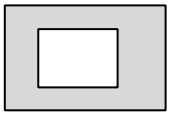
FIQR – USA/English – Original version
FIQR_AU1.0_eng-USori

Directions: For each of the following 10 questions, select the box that best indicates your intensity of these common fibromyalgia symptoms over the past 7 days

Please rate your level of pain	**No pain** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Unbearable pain**
Please rate your level of energy	**Lots of energy** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **No energy**
Please rate your level of stiffness	**No stiffness** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Severe stiffness**
Please rate the quality of your sleep	**Awoke well rested** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Awoke very tired**
Please rate your level of depression	**No depression** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very depressed**
Please rate your level of memory problems	**Good memory** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very poor memory**
Please rate your level of anxiety	**Not anxious** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very anxious**
Please rate your level of tenderness to touch	**No tenderness** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Very tender**
Please rate your level of balance problems	**No imbalance** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Severe imbalance**
Please rate your level of sensitivity	

to loud noises, bright lights, odors and cold	**No sensitivity** ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ **Extreme sensitivity**	

Sub-total ***(for internal use only)*** 

FIQR TOTAL ***(for internal use only)*** 

FIQR – USA/English – Original version
FIQR_AU1.0_eng-USori

Appendix I

Short-form McGill pain questionnaire for study reported in manuscript 2

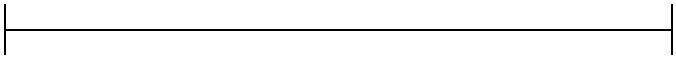
I. Short-Form McGill Pain Questionnaire

A. PLEASE DESCRIBE YOUR PAIN DURING THE LAST WEEK. *(Check off one box per line.)*

	None	Mild	Moderate	Severe
1. Throbbing	0 ☐	1 ☐	2 ☐	3 ☐
2. Shooting	0 ☐	1 ☐	2 ☐	3 ☐
3. Stabbing	0 ☐	1 ☐	2 ☐	3 ☐
4. Sharp	0 ☐	1 ☐	2 ☐	3 ☐
5. Cramping	0 ☐	1 ☐	2 ☐	3 ☐
6. Gnawing	0 ☐	1 ☐	2 ☐	3 ☐
7. Hot-burning	0 ☐	1 ☐	2 ☐	3 ☐
8. Aching	0 ☐	1 ☐	2 ☐	3 ☐
9. Heavy (like a weight)	0 ☐	1 ☐	2 ☐	3 ☐
10. Tender	0 ☐	1 ☐	2 ☐	3 ☐
11. Splitting	0 ☐	1 ☐	2 ☐	3 ☐
12. Tiring-Exhausting	0 ☐	1 ☐	2 ☐	3 ☐
13. Sickening	0 ☐	1 ☐	2 ☐	3 ☐
14. Fear-causing	0 ☐	1 ☐	2 ☐	3 ☐
15. Punishing-Cruel	0 ☐	1 ☐	2 ☐	3 ☐

II. B. PLEASE RATE YOUR PAIN DURING THE LAST WEEK.

The following line represents pain of increasing intensity from “no pain” to “worst possible pain”. Place a vertical mark (|) across the line in the position that best describes your pain **during the last week.**



No Pain — **Worst Possible Pain**

Score in mm *(Investigator’s use only)*

III. C. CURRENT PAIN INTENSITY

0 ☐ No pain
1 ☐ Mild
2 ☐ Discomforting
3 ☐ Distressing
4 ☐ Horrible
5 ☐ Excruciating

Questionnaire Developed by: Ronald Melzack