# Neurofeedback for Fibromyalgia

Adam A. Kristevski

A Dissertation Submitted to the Faculty of

The Chicago School of Professional Psychology

In Partial Fulfillment of the Requirements

For the Degree Doctor of Psychology

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Abstract

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This study examined the effects of neurofeedback on individuals diagnosed with fibromyalgia syndrome (FMS). Neurofeedback is a non-invase form of brainwave biofeedback in which participants receive real-time visual and auditory feedback of their brainwave activity. Upon receiving this feedback, participants are reinforced via visual and auditory means for producing particular brainwave patterns which have been associated with mental concentration and bodily relaxation. The existing literature on neurofeedback for fibromyalgia syndrome suggests that individuals experience lasting benefits in symptom reduction post-treatment. It was expected that participants would experience substantial improvements in their symptoms over the course of this study.

Therapeutic improvement was measured with a variety of self-report measures and neurophysiological metrics. Particpants were randomly placed into either an active treatment group or a wait-list control. The wait-list control group received active treatment after a speficied control period, during which self-report and EEG data were collected. Active treatment involved approximately 30-minute neurofeedback sessions once or twice per week, depending on participant availability. Brief pre- and post-session measuress were obtained to track within-session improvements. In addition, a psychometric battery was administered at baseline, and weeks 2, 4, 6, and 8 to track therapeutic improvement and outcome. Participants received eight to 16 sessions of neurofeedback.

All participants showed improvements in subjective ratings of pain and fatigue throughout the course of treatment. Participants also decreased their Fibromyalgia Impact Questionnaire-Revised Edition (FIQR) scores, exhibited changes on EEG indices, and reported being satisfied with the treatment. The majority of participants experienced improvements on symptom frequency and intensity on the ME/CFS Fatigue Types Questionnaire (MFTQ), had significant pre-post session decreases in fatigue (assessed via a paired samples t-test), and had pre-post session changes on one or more EEG indices (also assessed with a paired samples t-test). Visual Analog Scale (VAS) pain and fatigue scores and EEG indices appeared to change when participants completed their wait-list control condition and entered active treatment, which offers evidence that neurofeedback had an additional therapeutic impact when compared to other concurrent treatments. These positive findings are consistent with the results of existing studies of neurofeedback for fibromyalgia, and offers additional support for utilizing neurofeedback in the treatment of individuals with fibromyalgia; thus further studies of neurofeedback as a treatment for fibromyalgia are warranted.

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# Chapter 1: Nature of the Study

## Professional Relevance

Advancements in neuroscience have had an undeniable impact on the practice of clinical psychology and the field of mental health in general, both in terms of assessment (Cantor, 1999) and intervention (Jensen, Sherlin, Hakimian, & Fregni, 2009). This development is the result of innovations in several fields, including neuroimaging (Malhi & Dewan, 2001), pharmacology (Rose, 2004) and psychophysiology (Andreassi, 2001). These advancements are driven by developments in technology, which allow for faster and more precise analysis of anatomical images and physiological signals, as well as progress in biological sciences such as genetics and molecular biology.

It can be argued that these advancements, in turn, have steered the future course of professional psychology toward empirical methods of diagnosis, intervention, and assessing outcome. Evidence of this development can be seen in the current emphasis on evidence-based practice, as well as objective methods of assessing psychiatric disorders (such as quantitative electroencephalography [QEEG], SPECT and PET imaging, fMRI, and so forth). With regard to the current dissertation, it should be recognized that psychologists (both in research and in clinical practice) have been involved in assessing and intervening on behalf of the brain's electrophysiological activity (see Jensen et al., 2009). Due to the aforementioned "push" toward

empiricism in psychology, it should be expected that this movement will continue to gain prominence in the various mental health disciplines.

These neuroscience-based approaches (often collectively labeled as "clinical neuroscience") are gaining prominence in the assessment and treatment of pain-related conditions. Such approaches are supported by both imaging research (such as QEEG and fMRI), which are uncovering the neural correlates of pain at both cortical and subcortical levels of processing (Moseley & Flor, 2012), as well as neuromodulatory interventions (that is, neurofeedback and brain stimulation techniques such as transcranial magnetic stimulation or TMS) which have been shown to modify neural processing on both cortical and subcortical levels (Jensen et al., 2009; Ros et al., 2013). These approaches offer non-pharmacological and non-invasive means for assessment and intervention of the neural correlates of pain, which fits the current scientific paradigm and offers pain patients a form a therapy that differs from both traditional psychotherapeutic approaches (such as therapy and hypnosis) and pharmacological methods of pain reduction.

**Socioeconomic Relevance**

Several studies have shed light on the psychosocial and economic burdens experienced by those who have fibromyalgia syndrome, or FMS (see Schaefer et al., 2011; Palacio et al., 2010; Turkyilmaz, Kurt, Karkucak, & Capkin, 2012). Turkyilmaz, Kurt, Karkucak, and Capkin (2012) found that individuals with FMS have a lowered functional capacity and quality of life when compared with controls. This study suggests that these two variables are highly correlated with FMS symptoms such as fatigue, sleep disturbance, and anxiety. Schaefer et al. (2011) found

that 50% of their sample of FMS patients experienced employment disruption and productivity loss despite treatment. It should be noted that one of the early studies to examine the effects of neurofeedback on FMS found that 37% of their sample improved in terms of employment status (Mueller, Donaldson, Nelson, & Layman, 2001). Palacio et al. (2010) found that FMS patients had significantly higher healthcare utilization costs when compared with controls. These costs were largely comprised of office visits, tests, medical procedures, and use of pain-related medications, which was twice as high as use by controls. Thus, FMS has been shown to affect not only the well-being and productivity of those who have received the diagnosis, but it also contributes to increased healthcare utilization and costs.

**Personal Relevance**

The author's initial interest in biofeedback was sparked when his father returned home from a Prescribing Psychologists Register (PPR) conference and described meeting a psychologist (Bernard Brucker) who could rehabilitate patients with severe spinal cord and brain injuries. There were claims that individuals could even be rehabilitated to the level of motor function that they possessed before the injury. Basically, Dr. Brucker could induce an almost miraculous "cure" so that patients with a supposed "severed" spinal cord (this is a common misconception in spinal cord injury) could walk again.

As an undergraduate psychology student, the author of the current study examined the evidence, which consisted of several days-worth of presentations by Brucker, as well his published scientific papers (see Brucker & Bulaeva, 1996). The author came to the conclusion that Brucker could indeed dramatically improve his patients' motor function through a high-level

version of electromyographic (EMG) biofeedback that measured and displayed faint neuromuscular signals which represented the functioning of intact spinal cord tracts unaffected by injury. Through this form of operant conditioning, patients were able to regain motor function by becoming aware (through visual and auditory modalities of feedback) of intact spinal cord tracts and nerve cells which were not destroyed by the injury. By being brought into awareness through visual and auditory feedback, these intact pathways grew in complexity, strength, and eventually resulted in unexpected levels of motor rehabilitation. The author found this treatment to be absolutely fascinating and began to explore biofeedback in-depth.

Soon after discovering the Brucker biofeedback method, this author learned of brain-based forms of biofeedback in which one could learn to regulate neuronal functioning through visual, auditory, and even tactile feedback (that is, EEG biofeedback, neurotherapy, or simply neurofeedback). This form of biofeedback seemed more closely related to traditional psychology than Brucker's approach, which seemed to be more associated with physical rehabilitation medicine as it pertained to strictly physical injuries. Neurofeedback, on the other hand, is an approach which can treat psychiatric disorders (such as ADHD, PTSD, Depression, and so forth), since many (if not all) of these disorders are mediated by some degree of abnormal EEG activity. Furthermore, unlike most psychological approaches to assessment and intervention, neurofeedback offers a method of systematically assessing and manipulating a biomarker (such as EEG activity) which is closely tied to the functioning of the brain as a whole (that is, in terms of overall arousal, interhemispheric connectivity, and so forth). As such, it offers the clinician and researcher a physiological means of assessment and intervention, in addition to traditional psychometric and psychotherapeutic methods.

The author chose to focus the current dissertation on neurofeedback for fibromyalgia for several reasons. First, his current therapy practicum site (Northshore Integrative Healthcare, NIH) receives the majority of its referrals from pain and rheumatology clinics, and he was curious about the research supporting biofeedback and neurofeedback as viable options in the treatment and management of pain-related conditions. Second, the author became more interested in the prospect of doing a dissertation on neurofeedback since the pain literature seemed to emphasize that the experience of pain is a neurophysiological phenomenon, and as such, may require a neuroscience-based clinical approach (such as cranial electrotherapy, TMS, and/or neurofeedback) which specifically treats aberrant brain activity, rather than a traditional biofeedback approach that treats bodily (that is, non-brain) physiological functions. Third, upon performing a literature review of studies which examined the effects of neurofeedback on pain-related conditions, the author discovered that the majority of studies focused on fibromyalgia. Thus, it made sense to construct a dissertation study based on the largest body of preexisting research (in addition to having access to this population of patients). Lastly, neurofeedback seems to be one of the fastest-growing modalities of biofeedback (along with heart rate variability biofeedback or HRV), and it will be advantageous to stay on the cutting edge of developments in research and clinical practice.

# Chapter 2: Review of the Psychophysiological Literature

## Overview of Biofeedback

Biofeedback can be defined as the process of measuring and feeding-back information regarding a subject's (human or animal) physiologic activity so that this subject may alter this activity through mechanisms such as increased awareness (on both conscious and unconscious levels) and operant conditioning (Moss, 1999). This process of measurement and feedback is achieved through the use of sensors (or electrodes) placed either on the surface of the skin (through measuring muscle tension via surface electromyography or SEMG) or intra-vaginally/intra-anally (in the treatment of vaginal pain and fecal incontinence). These sensors measure a variety of physiologic processes such as skin temperature, sweat gland activity (that is, electrodermal response or galvanic skin response), heart rate or heart rate variability, respiration, brain waves (that is, electroencephalographic activity used in neurofeedback), and so forth. Once these physiological signals are measured by sensors, they are then processed and amplified through a specialized instrument known as a differential amplifier and displayed to the subject through visual (such as moving images on a computer monitor), auditory (such as a tone increases as skin temperature increases and vice versa), and in some cases, tactile means (such as a teddy bear that vibrates when children are producing a correct physiological response). Through the use of feedback, a subject gains greater awareness of and control over his or her physiological processes (Moss, 1999).

The discipline of biofeedback emerged during the 1960s, which was an era in which researchers and clinicians from diverse fields such as neurophysiology, cybernetics, behaviorism, and computer science, began to correspond and realize their potential for mutual growth in both research and clinical practice (Peper & Shaffer, 2010). The term "biofeedback" was coined in 1969 at the first Biofeedback Research Society meeting in Santa Monica CA, which offered a name for this novel convergence of diverse disciplines (Moss, 1999). However, it's important to note that this meeting was preceded by several other conferences (which both took place in 1969) that also helped launch the discipline, including a Veteran's Administration conference in Denver, and a Conference on Altered States of Consciousness.

These conferences included presentations on many of the same biofeedback modalities being used today (such as EMG, EEG, and so forth) and helped popularize psychophysiological concepts such as self-regulation (that is, learning to regulate one's physiologic responses through increased awareness), auto-regulation, and feedback (that is, the concept of feedback loops, which was borrowed from cybernetic theory). These conferences not only aided the progression of biofeedback as both a research methodology and therapeutic technique, but also helped disseminate biofeedback to the worlds of "hard-nose" empirical science, as well as Eastern spiritual traditions, the Western Humanism movement, and the general public.

Although biofeedback techniques often had their origin in relatively "pure" physiological research methodologies, they frequently became applied to the treatment of clinical disorders and/or the optimization of human functioning. For example, the early EEG research of Joe Kamiya was geared toward investigating the subjective conscious states which accompany specific brainwave patterns (such as the alpha rhythm). Kamiya initially sought to determine

whether subjects could be taught to distinguish when they were producing alpha waves or other brainwave frequencies (Moss, 1999). Not only did he gather evidence suggesting that subjects could reliably discern when they were producing alpha, he also discovered that the alpha rhythm is associated with a relaxed and open meditative state of mind, which led to the hypothesis that training one to enter this state could have therapeutic benefit (Moss, 1999).

Kamiya's hypothesis has been tested in a number of studies investigating the enhancement of cognitive processing, pain reduction, and reducing symptoms associated with co-morbid substance abuse and PTSD (see Moss, 1999 for a review). Thus, learning to alter a specific physiologic signal can have numerous therapeutic benefits in the treatment of clinical disorders (both purely "medical" and psychological) and the optimization of functioning (such as peak performance training for athletes). This exporting of basic physiologic research science into real-world clinical settings has been achieved by clinicians utilizing various biofeedback modalities (for example, SEMG, EEG, HRV, and so forth).

## Overview of Electroencephalographic (EEG) Brain Wave Activity

Brain wave or electroencephalographic activity (EEG) is commonly recorded through the use of surface EEG electrodes placed on the scalp, but can also be recorded intracranially (with the electrodes being placed on exposed brain tissue). The electroencephalogram is a graphic representation of EEG activity and results from the summed electrical activity of millions or even billons of neurons (Cantor, 1999). The summated electrical activity of these neurons (those under the active electrode recording site) can be represented by one oscillating signal or wavelike pattern that is comparable to other physiological signals such as the electrocardiogram (Peper &

Shaffer, 2010). These raw and unprocessed EEG signals can be divided into specific frequency ranges (measured in Hertz or Hz, meaning cycles per second) that are associated with specific states of consciousness, attention, and neurocognitive processes. It is important to note that researchers and clinicians often disagree as to where one range starts and another begins (in terms of Hz values). Hence, the following outline of the various frequency ranges and their neurocognitive attributes is derived from several reputable EEG researchers and clinicians.

The slowest frequency is the Delta range (0 – 4 Hz). Delta waves are long and smooth in appearance and are most prominent in newborn infants (40% of their total EEG is in the Delta range), and individuals with traumatic brain injury and learning disabilities (Demos, 2005). Delta is uncommon in the brain of an awake adult (but common in states of deep sleep), and accounts for only 5% of the EEG at any given time. However, this frequency has been found to appear in college students engaged in problem solving tasks (2005).

Theta is the frequency that ranges from 4 to 8 Hz and is commonly associated with undesirable attentional states such as drowsiness and sleepiness (Peper & Shafer, 2010), and symptoms common in ADHD, such as inattention, distractibility, and poor impulse control (Demos, 2005); however, it is also associated with hypnotic states (such as eyes-closed visualization and daydreaming) and creativity. Theta becomes prominent when one is in an internally-oriented state, which can be contrasted with externally-oriented states in which one is focusing on external stimuli (wherein Beta activity is more prominent). Like Delta, Theta is more prominent in children and is involved in important memory functions such as consolidation and retrieval (Peper & Shafer, 2010). Excessive Theta activity is associated with numerous chronic

pain conditions (such as complex regional pain syndrome or migraine) and is hence often inhibited or down-trained in neurofeedback treatment protocols (Jensen et al., 2009).

Alpha is the frequency that ranges from 8 to 12 Hz and is more prominent in the parietal and occipital regions of the brain. If Alpha is excessive in more anterior regions (such as the frontal lobes), then symptoms of inattention and depression may result. This is because Alpha is an inhibitory or "slow wave" frequency (like Delta and Theta) and is associated with the slowing of neurocognitive functioning (Demos, 2005); however, normal levels of Alpha are associated with a calm mental state, the perception of dimensionality, and meditation practices. Alpha is associated with visual inactivity and is thus more prevalent when one's eyes are closed. Alpha training (that is, rewarding increased Alpha in posterior regions) is often utilized in the treatment of PTSD and substance abuse, as well as in relaxation training (Demos, 2005).

The Beta frequency range is often cited as being between 12 Hz (low end) and 32 to 36 Hz (high end). In contrast with the aforementioned inhibitory frequencies (Delta, Theta, and Alpha), Beta is a largely an excitatory frequency which represents increased arousal; however, Beta may also have some specific inhibitory properties, which are described below (Sterman & Egner, 2006). Due to its broad frequency range, Beta is frequently divided into discrete sub-ranges which are thought to possess unique electrophysiological and neurocognitive properties (Demos, 2005; Peper & Shafer, 2010; Lubar, 2003).

The low Beta range (12 – 15 Hz) is often referred to as Sensory Motor Rhythm (SMR), which is a frequency range relatively localized to the somato-motor cortex (involving both the sensory and motor cortical areas). SMR activity produces a neurocognitive state in which one's body is still and relaxed (that is, motor inhibition) while one's mental activity is actively focused

on incoming environmental stimuli (Demos, 2005). This frequency is associated with numerous therapeutic benefits such as the reduction of seizure activity (Sterman & Egner, 2006), an increased ability to attend to and concentrate upon incoming external stimuli (Lubar, 2003), improved functioning of the immune system (Peper & Shafer, 2010), and a decrease in chronic pain and fatigue symptoms (Kayiran, Dursun, Ermutlu, Dursun, & Karamürsel, 2007; Kayiran, Dursun, Dursun, Ermutlu, & Karamürsel, 2010; Jensen et al., 2009). Due to its positive therapeutic effects on individuals with chronic pain (such as FMS and migraine), SMR is the frequency range that will be reinforced in the current dissertation study.

Beta activity in the 16 to 20 Hz frequency range is commonly referred to as Beta 2 and is associated with motor activity and conscious analytic problem solving (Demos, 2005); however, once this problem solving method is learned and mastered, Beta activity in this range decreases during the particular problem solving task (Peper & Shafer, 2010). Excessive activity in this range is associated with hyperactivity, OCD, anxiety, and muscular tension, which can be conceptualized as symptoms of overarousal (Demos, 2005). Similarly, Beta activity in the 19 to 22 Hz range is associated with emotional intensity and excessive effort (Peper & Shafer, 2010). High Beta is thought to be between 20 Hz and 36 Hz and is associated with excessive cognitive processing, rumination, and a family history of substance addiction (Peper & Shafer, 2010). The presence of excessive high Beta could be an indication of analogous excessive Theta activity; thus, production of high Beta may be the brain's attempt to establish a homeostatic balance despite dysfunction (Demos, 2005). Excessive activity in the high Beta range is rarely (if ever) reinforced in neurofeedback protocols, since it is associated with overarousal.

Gamma is a frequency range (38 – 42 Hz) associated with global brain activity (rather than being restricted to a specific localized region like SMR) and is thus thought to represent an organizational or binding function in the brain (Demos, 2005). Thus, Gamma is thought to be crucial in integrating disparate neural information (that is, occurring in different regions of the brain) into unified conscious percepts (Hughes, 2008). Hameroff (2010) proposed that Gamma synchrony (that is, the occurrence of Gamma in close spatiotemporal proximity) is the process by which consciousness originates from brain activity: when Gamma synchrony occurs, conscious awareness comes online. Similarly, Gamma is measured during states of selective attention, alertness, problem solving, and following states of sensory stimulation (Hughes, 2008); however, when the nervous system is not engaged in conscious problem solving, Gamma becomes inactive (Demos, 2005).

**Overview of Neurofeedback**

Neurofeedback, first and foremost, is the measurement and near real-time display of one's electroencephalographic (EEG) activity, which one can learn to regulate (perhaps on an unconscious level) via operant conditioning (Sherlin et al., 2011). However, in the case of the Low Energy Neurofeedback System (LENS) and its predecessors (such as electroencephalographic-driven stimulation [EDS] and Flexyx® neurofeedback), operant conditioning principles do not apply (Ochs, 2007). Thus, neurofeedback has its historical roots in the development of the electroencephalogram, which is attributed to the pioneering work of Hans Berger, who in 1929 measured oscillating electrical activity on the human scalp (Cantor, 1999). It wasn't until the late 1960s that researchers began investigating the extent to which EEG

activity could be subjectively perceived and self-regulated. This early research is often attributed to two researchers who, working independently and without knowledge of the other, examined the therapeutic effects of neurofeedback.

During the 1960s, Joe Kamiya, who was then a researcher at the University of Chicago, discovered that the presence of Alpha waves could be accurately and reliably discerned by his research subjects (through reporting whether or not they were in a psychophysiological state in which Alpha was appearing in posterior regions), and could be trained through operant conditioning procedures (Myers & Young, 2012). Kamiya was interested in studying the EEG correlates of various states of consciousness, especially those associated with creativity, openness to experience, and meditative states (Moss, 1999). This work quickly became associated with the counter-culture movement of the 1960s, most notably in relation to altered states of consciousness via substances, spiritually-awakened states of mind, and Eastern religions. Kamiya's work was eventually utilized therapeutically as a treatment for substance abuse, PTSD, depression, as well as in relaxation training (Peniston & Kukolsi, 1991). Alpha neurofeedback training continues to be a valuable research methodology and clinical tool to this day and its therapeutic effects on brain function are being measured through fMRI and other neuroimaging modalities (Ros et al., 2013).

Also in the 1960s, another researcher working independently of Kamiya, Barry Sterman, discovered an EEG frequency range over the somato-sensory cortices of cats (termed sensory-motor rhythm or SMR) which was associated with the suppression of motor excitability and concurrent mental alertness (Sterman, LoPresti, & Fairchild, 2010). This work took place in the context of the Cold War and the Space Race. The United States was experimenting with high-

thrust rocket propellant fuel, which resulted in numerous technicians and crew members developing convulsive symptoms. With the aid of an Air Force grant, Sterman began studying the toxicity and effects of Monomethyl Hydrazine (MMH) exposure on cats, as well as an intervention (that is, operant conditioning of the SMR above the somato-sensory cortices) which was shown to raise the cats' seizure threshold and tolerance for MMH (2010). Sterman's work was soon applied to controlling medication-resistant seizure activity in humans (Sterman & Egner, 2006) in the treatment of ADHD (Moss, 1999) and in pain-related conditions such as fibromyalgia syndrome (Kayiran et al., 2007, 2010).

# Chapter 3: Review of the Fibromyalgia Pathophysiology and Treatment Literature

## Overview of Fibromyalgia Syndrome

Fibromyalgia syndrome (FMS) is a chronic condition characterized by musculoskeletal discomfort (pain, stiffness, and tenderness in muscles, tendons, and joints), genitourinary complaints (such as irritable bowel syndrome), sleep and fatigue difficulties (such as insomnia and chronic fatigue), and other psychological symptoms such as anxiety and depression (Jahan, Nanjo, Qidwai, & Qasim, 2012). Research on FMS dates back to the work of British neurologist Sir William Gowers, who in 1904 coined the term "Fibrositis" ("Fibro" denoting fibrous muscle tissue and "-itis" denoting inflammation) to describe individuals who presented with symptoms of modern-day FMS (Schwartz, 1995). This assumption of an inflammatory process involved in FMS would later be proven false (Waddell, 1996). In 1979, Hugh Smythe, a rheumatologist, published an important paper on fibrositis in which he described the symptomatology and proposed that individuals with such symptoms did not fit existing diagnostic categories of musculoskeletal disorders (1996). The term "fibromyalgia syndrome" (myalgia denoting muscle pain) emerged in 1986 during a series of medical meetings held in San Francisco, and replaced the term "fibrositis" due to its unfounded original meaning (that is, the lack of evidence of an inflammatory process).

The etiology of FMS is currently unknown and appears to vary widely. Epidemiological studies estimate that fibromyalgia Syndrome (FMS) affects 2% to 5% of the general population,

with 80% of those affected being women (Jensen et al., 2012; McCarberg, 2012). The factors contributing to this gender disparity are unknown, but it is known that non-inflammatory musculoskeletal diseases are more common in women (Bartels et al., 2009). It can manifest with a gradual and/or nonspecific onset, or with a sudden onset as the result of a physical trauma or injury (Riberto, Pato, & Battistell, 2006). It has been associated with both psychological and physical trauma. For example, Oliveri, Solitar, and Dubois found childhood sexual and physical abuse to be risk factors for developing FMS (2012), while Hauser et al. found that 45.3% of their sample of FMS participants also met diagnostic criteria for posttraumatic stress disorder (PTSD; Hauster et al., 2013). Al-Allaf et al., found that 39% of their participant sample (n=152) had experienced a physical trauma within the 6 months preceding the onset of their FMS (2002). Thus, psychological and physical factors should carefully be taken into account in both research and clinical settings.

Although biochemical, metabolic, and immunoregulary abnormalities have been the topic of recent and ongoing FMS research (Jahan et al., 2012), it can be argued that the current FMS research paradigm emphasizes the importance of understanding abnormalities associated with the autonomic and central nervous systems, and the mechanisms by which these abnormalities lead to the symptomatology often seen in FMS (Holman, 2007). Holman proposed that individuals with benign hypermobility syndrome (BHS) are particularly prone to developing FMS due to their excessive range of motion in joints, increased risk of spinal and other injuries, and an elevated sympathetic tone (compared to individuals without BHS; 2007). This increased sympathetic tone (that is, increased heart rate, respiration, electrodermal response, and startle response) is the result of genetic factors contributing the brainstem's baseline autonomic

functioning. Sendur, Gurer, and Bozbas (2007) found a higher rate of hypermobility in individuals diagnosed with FMS compared to controls ($p<.05$). In addition, Ting el al. (2012) found that 48% of their sample of 141 individuals with juvenile FMS had BHS, as well as greater pain sensitivity, lower tender point pain thresholds, and more tender points than juvenile FMS participants without BHS. Individuals with BHS make up approximately 25% of the US population, and have a higher rate of dysautonomias, gastrointestinal symptoms, and chronic fatigue (Clark, Khattah, Carr, Palmer, & Scheper, 2014).

In addition to high rates of BHS, up to 90% of individuals with FMS report significant sleep difficulties, characterized by light, non-restful sleep, as well as problems with sleep onset and maintenance (Moldofsky, 2008). Research pioneered by Moldofsky in the early 1990s found distinctive sleep abnormalities in the EEGs of individuals with FMS (Schwartz, 1996). For example, it was discovered that an Alpha abnormality (that is, disruptive Alpha waves) caused arousal disturbances during states 2, 3, and 4 of non-REM sleep. Experimental studies of sleep disturbance in healthy individuals demonstrated that symptoms of widespread pain, tenderness, and fatigue resulted from the disruption of stage 4 sleep via an auditory stimulus. Thus, Moldofsky proposed that much of the symptomatology of FMS is attributable to sleep abnormalities rather than psychiatric factors. Holman postulated that these sleep abnormalities may be due to an exaggerated startle response or similar dysautonomic symptoms, which are common in individuals with increased sympathetic tone (such as individuals with BHS). In addition, these sleep abnormalities may be due to the increased pain and discomfort associated with BHS (Holman, 2007).

In addition to BHP and autonomic dysfunction which results in poor sleep, Holman (2008) and Wood (2010) proposed that positional cervical spinal cord compression (PC3) may account for many of the symptoms experienced by individuals with FMS. PC3 involves pain and/or spinal cord compression upon neck extension and flexion. In individuals with PC3 the spinal cord may become compressed by discs and cerebral spinal fluid may become blocked, resulting in irritation of the cervical spinal cord (Holman, 2007). Spinal cord irritation and PC3 may result in many of the symptoms of FMS, including autonomic dysfunction, pain, fatigue, cognitive dysfunction, and so forth. Research has demonstrated that touching an anesthetized rat's spinal cord results in the stimulation of the sympathetic nervous system, and sleep deprivation in rats with spinal cord lesions will result in pain behavior (2007). Holman's 2008 study found that 65% of a sample of patients presenting with rheumatologic conditions showed MRI evidence of PC3. Of the patients diagnosed with FMS, 71% showed evidence of PC3, and of the patients with widespread unexplained pain not meeting diagnostic criteria for FMS, 85% showed evidenced of PC3 (Holman, 2008). Holman noted that these participants' MRI findings were normal if imaged in the neutral condition; however, if imaged in flexion and extension views (that is, looking down and up), these same participants often showed evidence of PC3 (2008).

In addition to conducting numerous neuroimaging studies of FMS, Wood's review of the research on this topic offers convincing evidence of abnormal brain activity in FMS (2010). Gracely, Petzke, Wolf, and Clauw (2002) conducted an fMRI study in which pressure was applied to the thumbs of healthy controls and participants with FMS. The fMRI results demonstrated significant group differences in cortical and subcortical regions involved in pain

processing. The FMS group showed evidence of augmented pain processing (Gracely, Petzke, Wolf, & Clauw, 2002). Cook et al. (2004) conducted a similar study in which non-painful and painful heat were applied to participants with FMS and healthy controls. Significant group differences were seen with both painful and non-painful stimuli. Participants with FMS responded to non-painful stimuli with activation of their prefrontal cortex, supplemental motor cortex, insula, and anterior cingulate cortex, which are regions known to be involved with attention, affective processing, and pain processing (Cook et al., 2004). Thus, it could be argued that individuals with FMS perceive non-painful stimuli as painful at a neuronal level. This study also found increased insula activation in the FMS group upon receiving painful stimuli (Cook et al., 2004).

Emad et al. (2008) utilized magnetic resonance spectroscopy (MRS), a technique for imaging the chemical composition of the brain, to assess hippocampal function in FMS participants and healthy controls. This study found significant group differences, with FMS participants showing less n-acetylaspartate in both hippocampi compared to controls (Emad et al., 2008). The study authors interpreted this finding as indicative of metabolic dysfunction which can affect cognition, sleep, and pain perception (all functions of the hippocampus; Emad et al., 2008). These findings were replicated by Wood, Ledbetter, Glabus, Broadwell, and Patterson, who proposed that these results do not necessarily entail brain atrophy, but may be evidence of a smaller brain size at birth (2010).

These findings may shed light on several studies involving FMS and FMS EEG profiles (Hargrove et al., 2010; Johnstone, Gunkelman, & Lunt, 2005). Hargrove et al. (2010) compared the averaged QEEGs of 85 individuals diagnosed with FMS to age- and gender-matched

controls. It was found that individuals with FMS had profound deficiency in their levels of frontal Delta, Theta, and Alpha activity compared to the control group (Hargrove et al., 2010). Thus, participants with FMS exhibited a deficiency in frontal slow wave EEG activity. Hargrove et al. discovered three distinct QEEG abnormalities in individuals with FMS (deficient frontal slow wave activity, excessive fronto-central beta activity, and excessive frontal hypocoherence), and found that 100% of his sample had at least one abnormality, 94.1% had two abnormalities, and 64.7% had all three abnormalities (2010). While Hargrove et al. theorized that these results may stem from systemic organ dysfunction (2010), Johnstone, Gunkelman, and Lunt proposed that such an EEG profile (that is, a low voltage EEG) may indicate a metabolic disorder (2005); however, these authors noted that low EEG power may impede quantitative analysis and result in distorted results (Johnstone et al., 2005).

Another neuroimaging study which investigated neurochemical abnormalities in FMS was conducted by Harris et al. in 2007. This study utilized positron emission tomography (PET) to image the functioning of the mu-opioid receptor in FMS participants and healthy controls (Harris et al., 2007). The mu-opioid receptor is involved with endorphin activity (implicated in opioid medications) and the modulation of pain. These receptors functioned abnormally in the FMS group and exhibited reduced binding potential in the nucleus accumbens, amygdala, dorsal and anterior cingulate, and other regions involved in pain and affective processing (Harris et al., 2007). Study authors theorized that these findings may explain why opioid medications are often not effective in managing the symptoms of FMS (Harris et al., 2007).

Like Holman (2007, 2008), Wood also proposed that PC3 may account for many of the symptoms experienced by individuals with FMS, and cited cases in which FMS ceased following

PC3 surgery (2010). The cognitive dysfunction experienced by individuals with FMS (often referred to as fibro fog or attributed to ADHD) is highly correlated the degree of PC3. On the basis of this evidence, Wood proposed that there is likely numerous and distinct subgroups of FMS, each with a unique etiology, pathophysiology, and treatment (that is, individuals with and without PC3; 2010). Thus, Holman and Wood both stressed the importance of treating the cause of fibromyalgia based upon a thorough assessment, rather than merely treating symptoms via medication and lifestyle management.

## Psychosocial Treatments and Medication Management of FMS

There are currently no uniform guidelines for the treatment of FMS (McCarberg, 2012). Some authors, such as Jahan, Nanjo, Qidwai, and Qasim (2012), have stressed a more psychosocial approach to treatment, since existing medications for FMS have a limited scope in the management of chronic symptoms. Such approaches emphasize stress management, treating co-morbid depression, addressing pain coping skills, and improving general lifestyle habits. Other authors, such as McCarberg (2012), have advocated a more pharmacological-based approach in which an evidence-based medication should be the first-line treatment for moderate to severe FMS, and evidence-based psychosocial approaches (such as exercise, CBT, and education) should then be considered based on patient preference and needs. Since there is currently no known cure for FMS, treatment tends to be multimodal and often includes pharmacotherapy, psychotherapy, biofeedback (EMG and thermal modalities are common), exercise, and complementary and alternative modalities (Jahan et al., 2012).

Numerous studies have investigated the efficacy of psychosocial approaches for FMS and have generally found positive results (Scheidt et al., 2012; Thieme & Turk, 2012; Woolfolk, Allen, & Apter, 2012; Kashikar-Zuch et al., 2012). Individual and group cognitive behavioral

therapy (CBT) and psychodynamic psychotherapy have been used in clinical trial research, with CBT-based approaches receiving the most empirical support (Woolfolk et al., 2012). Furthermore, the neurobiological benefits of CBT have been studied using fMRI as an outcome measure (Jensen et al., 2012). A 2012 study conducted by Jensen, Sherlin, Hakimian, and Fregni found that CBT improved functioning in frontal regions of the brain which were correlated with therapeutic improvements.

McCarberg (2012) reviewed numerous evidence-based medications for FMS, which included: amitriptyline (strong evidence); SSRIs / SNRIs, anti-epileptic medications, and tramadol (all moderate to strong evidence); and Pregabalin, Duloxetine, and Milnacipran (currently the only three FDA-approved medications for treating FMS). Duloxetine and Milnacipran are SNRI agents which increase the amount of serotonin and norepinephrine in the synapse, while Pregabalin is thought to aid the modulation of neuronal excitability (McCarberg, 2012). Medications including opioids, corticosteroids, and non-steroidal anti-inflammatory drugs (NSAIDs) have a weaker evidence base in treating FMS symptoms. Jahan et al. (2012) listed antidepressants (tricyclics, SSRIs, and SNRIs) as being mild to moderately effective in treating FMS and other chronic pain conditions. These authors also cited the use of muscle relaxants, dopamine agonists, growth hormone, and sodium oxybate (with the latter three being newer agents in the treatment of FMS).

Despite the ongoing development of numerous psychosocial and pharmacological approaches to treating FMS, new and effective therapies are needed. For example, although pharmacological approaches have proven to be a partially effective means of symptom reduction, approximately 50% of FMS patients do not take their medication as directed by their physician

(McCarberg, 2012). In addition, medications have their own risks and side effects, and many patients prefer a non-pharmacological approach to treatment (Jahan, 2012). Psychosocial approaches have been shown to improve functioning and reduce some of the symptoms of FMS, but numerous researchers are beginning to advocate a more brain-based approach to the treatment of FMS due to recent neuroimaging studies, as well as a general paradigm shift in both research and clinical practice. The shift from traditional psychological treatments of FMS (that is, therapy and hypnosis) to neurophysiological interventions (that is, neurofeedback and brain stimulation) is reflected in this dissertation.

## Review of the Published Studies on Neurofeedback for Fibromyalgia

The following section includes a review of the six studies which have assessed the therapeutic effects of neurofeedback on patients diagnosed with fibromyalgia syndrome (FMS). Each study will be described in terms of the treatment approach, outcome measures, and results. The pros and cons of each study, as well as limitations of study design and methodological flaws, will also be assessed. By doing a relatively in-depth analysis of these six existing studies, this principal investigator (PI) hopes to utilize what is useful, while avoiding the flaws of prior studies in the design of the current dissertation.

The first study which examined the effects of neurofeedback on patients with fibromyalgia syndrome (FMS) took place in 2001 (Mueller et al., 2001). This was a prospective and exploratory study conducted with 30 patients who were treated at a private practice. The study was uncontrolled and did not utilize randomization; however, it can justifiably be termed ecologically valid in that it did not utilize stringent inclusion /exclusion criteria, and treated FMS

patients with a wide array of co-morbid medical and psychiatric disorders (Mueller et al., 2001). Neurofeedback treatment involved a unique form of brainwave training called electroencephalograph-driven stimulation (EDS), which involves "entraining" (that is, systematically matching or phase-locking) the patient's electroencephalographic (EEG) activity with a particular stimulus (the current study utilized frequency-driven light stimulation via LED goggles). Once the patient's EEG is entrained (that is, matched or phase-locked) with the frequency-driven light stimulus, then the stimulus can be systematically altered (such as by manually increasing or decreasing the frequency of flashing light) in order to modify the patient's EEG (increasing or decreasing its dominant frequency at a specific scalp site). This process involves conditioning brainwaves according to classical conditioning principals (Cantor, 1999), which makes it unique in relation to most neurofeedback protocols, which utilize operant conditioning. EDS is unlike other forms of neurofeedback in that it does not involve one's active participation in trying to alter the feedback stimulus.

EDS treatment consisted of 1-hour sessions which were initially conducted three to five times per week (Mueller et al., 2001). The aim of these sessions was to decrease slow wave activity (that is, in delta, theta, and low alpha ranges). EDS sessions continued until three criteria were met: (1) EEG activity began to exhibit less slow wave activity, and more activity above the 10 Hz range; (2) patients reported increased cognitive clarity, improved sleep, increased mental and physical energy, and less affective disturbance; and (3) patients began to become aware of localized rather than diffuse pain (Mueller et al., 2001). Study authors did not indicate if they had a standardized method of determining whether these criteria had been met. Once it was deemed that these three criteria had been met, EDS sessions were reduced to one to two sessions per

week, and weekly massage therapy, physical therapy, and surface electromyography (sEMG) were added to their treatment. These treatments were added to treat the onset of localized pain, as well as patients' balance, posture, and myofascial tension (Mueller et al., 2001).

Study authors reported that the cognitive improvements induced by EDS allowed patients to engage in these treatments for the first time (Mueller et al., 2001). Multiple outcome measures assessed therapeutic efficacy, which included: the Modified Fibromyalgia Impact Questionnaire (MFIQ); Symptom Checklist 90-Revised (SCL-90-R); Visual Analog Scales (VAS); physical examination (including tender point count, which is a diagnostic procedure in which pressure is applied to localized body regions as a means of assessing the presence or absence of tenderness and pain at those regions); drawing of pain distribution on a human figure; and EDS EEG assessment. Significant improvements were noted on the SCL-90-R, VAS symptom scales (greatest improvements noted for sleep quality, cognitive clouding, and pain intensity), EEG assessment (delta and theta decreased at the $p < 0.0001$ level; alpha decreased at the $p < 0.01$ level; no significant change in frequencies above alpha), tender point count, and pain distribution drawings (Mueller et al., 2001). Study authors reported that patients generally did not meet the American College of Rheumatology (ACR) criteria for FMS at the conclusion of this study, since many had 11 or fewer tender points (Mueller et al., 2001). In addition, patients greatly reduced their medication use. On average, patients indicated that they improved 62.2% at the conclusion of the study (on an unidentified self-report scale ranging from 0 to 100%; Mueller et al., 2001).

Study authors hypothesized that EDS treatment played the significant role in therapeutic outcome, while the other therapies played a more ancillary role; however, these additional

therapies were found to significantly decrease patients' pain intensity (Mueller et al., 2001). The patients' VAS scores were also thought to reflect the primary role of EDS in the treatment of FMS. Nonetheless, this study was uncontrolled and randomization did not occur. Study authors concluded the study by affirming the importance of testing EDS under more randomized, double-blind, placebo-controlled designs (Mueller et al., 2001).

It took 5 years before the next study of neurofeedback for FMS would be published, and like the study conducted by Mueller et al. (2001), this one was also in the tradition of EDS neurofeedback. Kravitz, Esty, Katz, and Fawcett (2006) conducted a randomized, double-blind, placebo-controlled trial of low-intensity neurofeedback with 64 patients diagnosed with FMS. This form of neurofeedback involved exposing participants to low levels of photic stimulation that were not consciously perceptible (that is, below the threshold for conscious perception or awareness; Kravitz, Esty, Katz, & Fawcett, 2006). During low-intensity neurofeedback, participants sat with their eyes closed and weren't engaged in any specific cognitive or behavioral activity. Feedback consisted of photic stimulation (that is, pulses of light which flash on and off and are similar to a strobe light) delivered via specialized goggles which were attached to the neurofeedback system. Photic stimulation was guided by the use of an EEG assessment procedure unique to the Flexyx ® neurofeedback system (Kravitz et al., 2006). Thus, the frequency of the photic stimulation (the number of times the lights flashed per second in terms of Hz) was produced from the frequency of each participant's EEG (that is, the rate of neuronal firing per second in terms of Hz). Low-intensity neurofeedback is thought to modify the EEG by exposing the brain to an external stimulus that is time-locked to its own Hz rate of activity. Photic stimulation was administered from 1 to 3 seconds each session, and a maximum

of three EEG sites were trained per session (Kravitz et al., 2006). This is a very different approach than a typical session of neurofeedback, which often lasts from 30 minutes to an hour.

Patients participated in 22 sessions over an 11-week time span (two sessions per week). Primary and secondary outcome measures were thought to reflect the heterogeneous symptom presentation of FMS (Kravitz et al., 2006). The primary outcome measures consisted of the Clinical Global Impressions Scale (CGI-I) and the Participant Global Impressions Scale (PGI-I). These were chosen as the primary outcome measures, since an earlier study proposed that the most sensitive indicator of change in clinical trials for FMS was the physician's global assessment (White & Harth, 1996). The secondary outcome measures consisted of a dolorimetry-based tender point count (that is, an instrument used to apply 4 kg of pressure to a specific body region during a tender point count), seven Likert FMS symptom scales, Symptom Checklist-90-R, Fibromyalgia Impact Questionnaire (FIQ), CNS Dysfunction Questionnaire, and evoked EEG amplitudes of delta, alpha, and total EEG activity (these amplitudes were evoked or triggered as a result of the light stimulus, and subsequently measured; Kravitz et al., 2006).

The results of this study demonstrated a significant difference between the sham and active-treatment groups, as measured on the CGI-I (Kravitz et al., 2006). This difference in the active-treatment group was noted at session 22 ($p < 0.05$), but decreased to a non-significant trend one week post treatment ($p > 0.07$). Remaining primary and secondary outcome measures did not detect significant differences between sham and active-treatment groups (Kravitz et al., 2006). Study participants who judged themselves to be remitted of FMS symptoms rated the neurofeedback treatment as being more efficacious than prior medical treatments at session 22 (this was reported to be more effective by 100%); however, this was not true of participants who

did not rate themselves as remitted. These patients rated the treatment as being only 29% more effective than prior treatments at session 22 (Kravitz et al., 2006).

Based on these results, the study authors concluded that low-intensity neurofeedback should not be used as a stand-alone therapy in the treatment of FMS (Kravitz et al., 2006); however, Ochs (2006) argued that the entire study was essentially invalid due to a subsequently discovered hardware flaw that impeded the therapeutic effect of the photic stimulation. This occurred because the newer amplification system used in the study (that is, the hardware device which amplifies faint raw EEG signals into useful digital information) had stronger electromagnetic characteristics than prior amplification systems due to an additional built-in processing unit (which wasn't included in the older systems) that contained a crystal clock. This processing unit was determined by the Lawrence Livermore National Laboratory (a federally funded institution which conducts scientific research for national security purposes) as the source of the additional electromagnetic field strength. Furthermore, the wires and electrodes used in both active-experimental and control conditions conducted this additional electromagnetic field and overpowered the effects of photic stimulation. Thus, any therapeutic effects of the photic stimulation were minimal due to electromagnetic noise in the immediate environment (Ochs, 2006).

The next study of neurofeedback for fibromyalgia was a short case series published one year later (Kayiran, Dursun, Ermutlu, & Karamürsel, 2007). This study was the first to utilize a protocol which was not in the tradition of EDS and low-intensity neurofeedback. This study examined the effects of sensory-motor rhythm (SMR) neurofeedback on three individuals diagnosed with FMS (Kayiran et al., 2007). Study authors reported that the symptoms of these

FMS patients were greatly reduced as a result of ten sessions of SMR neurofeedback (Kayiran et al., 2007). These patients were taking only simple analgesics during the study and no other medications. Treatment efficacy was assessed in terms of multiple outcome measures including: the Visual Analog Scales for pain and fatigue (VAS); Short Form-36 (SF-36); the Hamilton Scales for depression (HDS) and anxiety (HAS); and the Beck Depression and Anxiety Inventories (BDI and BAI). These measures were taken at pre-treatment (baseline) and post-treatment (Kayiran et al., 2007). EEG was assessed during each session at the C4 site (see below under "procedures" for more description of the International 10-20 system of electrode placement), with patient-individualized artifact-rejection to correct EEG fluctuations resulting from eye and body movements (that is, artifacts or EEG fluctuations that originate from sources other than the brain, such as muscle tension, the heartbeat, or telecommunications systems; Kayiran et al., 2007).

Participants received three sessions of SMR neurofeedback per week (using one active electrode at C4, a standardized site of recording located on the right side of the scalp above the somatosensory cortex), with each session being 30 minutes long (Kayiran et al., 2007). Participants were reinforced whenever they increased SMR and inhibited theta at the C4 site relative to pre-feedback baseline EEG. Visual and auditory feedback was utilized (through a graphic point tally and auditory beeps). These researchers reported that most of the symptoms of their participants were decreased after ten sessions, and found that their outcome measures showed "certain progressions" (that is, clinically significant improvements; Kayiran et al., 2007).

In what is arguably the most promising study on neurofeedback for FMS to date, Kayiran et al. (2010) designed a follow-up to their 2007 study which tested the efficacy of SMR

neurofeedback on 18 patients diagnosed with FMS. These patients received 20 sessions of neurofeedback during a 4-week time span (five sessions per week, 30 minutes per session; Kayiran et al., 2010). The experimental group was compared to a control group comprised of 18 FMS patients who received only pharmacotherapy (10 mg of Escitalopram per day over 8 weeks). This study's inclusion criteria stated that patients must be 16 to 49 years of age, meet ACR criteria for FMS, and not be receiving medications or treatments for FMS or other diseases. Exclusion criteria stated that participants couldn't have another major medical problem or laboratory test abnormality (Kayiran et al., 2010).

Treatment efficacy was assessed in terms of multiple outcome measures, including several utilized in their first study (VAS, SF-36, HDS, HAS, BDI, BAI), as well as additional measures such as the Fibromyalgia Impact Questionnaire (FIQ) and the Structured Clinical Interview for DSM-IIR Personality Disorders (SCID-I; Kayiran et al., 2010). These measures were taken at baseline and weeks 2, 4, 8, 16, and 24. Thus, much of this assessment was post-treatment (since treatment ended at week 4), and attempted to ascertain the long-term effects of neurofeedback in FMS (Kayiran et al., 2010). In addition, eyes-open EEG was assessed every session. These assessments involved ten consecutive feedback-free recording periods, with each recording being one minute long (Kayiran et al., 2010).

Similar to the 2007 study, neurofeedback protocol consisted of enhancing SMR and inhibiting theta at the C4 site (Kayiran et al., 2010). Treatment sessions were 30 minutes total and were subdivided into ten training periods (3 minutes each). Neurofeedback training involved the use of a computer game in which participants were instructed to widen a virtual river (Kayiran et al., 2010). Participants were told to relax and concentrate and no other instructions

were given. Participants were then reinforced via a visual graphic of a widening river, an accumulating point-tally, and auditory beeps each time they increased SMR and inhibited theta relative to pre-neurofeedback baseline EEG (Kayiran et al., 2010).

The results of this study showed that both the experimental and control groups had significant improvements on all outcome measures at the $p < 0.05$ significance level (Kayiran et al., 2010). However, the neurofeedback group obtained greater outcomes than the medication control group on all measures. The therapeutic efficacy of neurofeedback was found to begin at week 2 (during sessions 6 through 11) and peaked at week 4 (during sessions 16 through 21), whereas the therapeutic efficacy of the Escitalopam control group began at week 2 and peaked at week 8 (Kayiran et al., 2010). Thus, the therapeutic effects of neurofeedback appeared to be "faster acting" than the effects of Escitalopam for patients with FMS. In addition, the neurofeedback group's EEG demonstrated a significant decrease in its theta/SMR ratio, which offers electrophysiological evidence of the therapeutic efficacy of neurofeedback (Kayiran et al., 2010). However, this study contains potentially problematic between-group differences which may have skewed the outcomes. It was noted that the control group had significantly higher scores on measures of depression and anxiety at baseline (the control group, on average, had an additional 5.78 raw score points on measures of depression and anxiety; Kayiran et al., 2010). This disparity may partially account for significant between-group differences in outcome.

Kayiran et al. hypothesized that neurofeedback proved more efficacious than medication through utilizing processes such as neuroplasticity (that is, beneficial structural changes in the morphology of the brain due to operant conditioning of the EEG) and the normalization of central nervous system disinhibition (that is, increasing inhibitory processes via reinforcing SMR

and inhibiting theta) which has been implicated in FMS through fMRI-based neuroimaging studies (2010, also see Jensen et al., 2012). For example, the 2012 fMRI study on FMS conducted by Jensen et al. demonstrated abnormal functioning in the rostral anterior cingulate cortex (rACC) and the thalamus, which are two regions involved in pain inhibition. This research suggests that the pain experienced by individuals with FMS is partially due to the less than optimal functioning of these inhibitory regions. Kayiran et al. (2010) suggested that since the thalamus may be normalized via neurofeedback training, inhibitory networks may be brought online to inhibit, and thus decrease, pain.

In addition, prior research has established that individuals with FMS have a reduced P300 response (Ozgocmen et al., 2003), which may contribute to an augmentation in their perception of pain. P300 is an EEG response to novel stimuli (typically evoked in laboratory conditions via visual and/or auditory stimulation), which is thought to represent an inhibitory function as it requires an "update" or accommodation of pre-existing memory so that novel stimuli may be processed and stored (Kaufmann et al., 2012). SMR neurofeedback has been shown to increase the amplitude and elongate the latency of the P300 response (Egner & Gruzelier, 2001; 2004), which offers further empirical and theoretical support in its use as an intervention for individuals with FMS.

The same year that Kayiran et al. published their follow up study (2010), Nelson et al. published a study in the EDS/low-intensity neurofeedback tradition. This study, which can be considered a follow up to the Kravitz et al. (2006) study, tested the effects of the Low Energy Neurofeedback System® (LENS) on 34 patients diagnosed with FMS (Nelson et al., 2010). Unlike the low-intensity neurofeedback utilized in the Kravitz el al. (2006) study, LENS delivers

minute pulses of electromagnetic feedback onto the patient's scalp (via electrodes), which is thought to correct dysfunctional EEG patterns. These pulses of feedback are individualized to each patient's momentary peak brainwave frequency (the dominant frequency), which is determined through a specialized LENS EEG assessment similar to the one utilized in the Kravitz el al. (2006) study. Goggles and photic stimulation were not used in the study by Nelson et al. (2010). Participants received a total of 22 sessions. The study authors did not specify the number of treatment sessions per week. LENS treatment consisted of short durations of stimulation (from 1 to 3 seconds) to a maximum of three electrode sites per session (Nelson et al., 2010). Stimulation involved adding 20 Hz of electromagnetic stimulation to each participant's dominant EEG frequency and then delivering this stimulation to the participant's scalp via electrodes. Participants did not report adverse side effects (Nelson et al., 2010).

Like Kravitz el al. (2006), Nelson et al. utilized a randomized, double-blind, placebo-controlled design (2010). Participants were assigned to active-LENS or sham neurofeedback based on randomization. Therapeutic outcome was assessed through a variety of outcome measures, including: physical examination (including dolorimetry-based tender point assessment); Quantitative Sensory Testing (QST); Fibromyalgia Impact Questionnaire (FIQ); Profile of Mood States Bi-Polar Form Clearhead-Confused Scale (POMS-BI-CC); Brief Fatigue Inventory (BFI); Medical Outcomes Sleep Study Scale (MOS-Sleep); Brief Symptom Inventory Global Distress Index (BSI-GSI); Patient Health Questionnaire-9 (PHQ-9); and Numerical Rating Scales of symptoms (Nelson et al., 2010).

Both sham and active treatment groups improved on the study's primary outcome measure (the FIQ), and there was no statistical difference between groups at post treatment

(Nelson et al., 2010). Both groups also improved on the tender point examination, POMS-BI-CC, BFI, and BSI-GSI. It was observed that the sham group was taking a greater number of classes of pain related medications post treatment (not in terms of dosage, but in terms of variety of classes), which may have nullified between-group differences (Nelson et al., 2010). Study authors also noted a potential methodological flaw in the equipment which may have further muted between-group differences. The wires for the reference and group cables were not severed in either condition, which may have resulted in the sham group receiving electromagnetic stimulation (Nelson et al., 2010). Thus, the sham group may have been receiving some degree of active-LENS treatment; however, there was a significant between-group difference in session-by-session measures of symptom severity and overall activity level of the last 24 hours. These significant findings only appeared in the active LENS treatment group; however, these positive effects waned shortly after the study ended (Nelson et al., 2010).

The most recent publication on neurofeedback for FMS was published in 2011 by authors Caro and Winter. These authors reasoned that since cognitive and attention difficulties are often co-morbid with FMS, and since neurofeedback has been used in the treatment of cognitive and attention problems such as ADHD, neurofeedback could be used to treat the attention and cognitive problems associated with FMS (Caro & Winter, 2011). These authors also reasoned that their neurofeedback protocol (SMR training over site CZ at the top and middle of the scalp) may also improve their participants' somatic symptoms, since SMR neurofeedback has been associated with improvements in central nervous system functioning (Caro & Winter, 2011).

This was a pilot/exploratory study, and did not utilize control or randomization. One-hundred twelve FMS patients were recruited, but only 15 were included in the final analysis

(Caro & Winter, 2011). This small sample may be due, in part, to the study's protocol, which required 40 or more sessions of SMR training at the CZ site. SMR neurofeedback involved reinforcing 12 to 15 Hz (SMR) at CZ, while inhibiting theta (4-7 Hz) and high beta (22-30) frequencies (Caro & Winter, 2011). The clinician manually modified reward and inhibition criteria in order to appropriately challenge each patient. These 15 patients (14 female and one male; age range 37 to 84 years) had attention problems, and the study authors hypothesized that SMR neurofeedback could improve both attention and somatic problems as they had observed that these domains are often positively correlated in terms of treatment improvement or decline (Caro & Winter, 2011).

Therapeutic outcome was assessed via: the CPT (Continuous Performance Test) Test of Variables of Attention (TOVA); physician assessment of tenderness (PAT); Global Pain Scale (0 – 10); Fatigue Scale (0 – 10); Psychological Distress Scale (0 – 10); Stiffness Scale (0 – 360 minutes; Caro & Winter, 2011). These latter four scales were simple verbal reports which preceded each neurofeedback session. The TOVA was the primary outcome measure, and was administered at pre-treatment baseline and every ten neurofeedback sessions (Caro & Winter, 2011). At the conclusion of treatment, four out of six CPT subtests showed significant improvements: ADHD ($p < 0.003$ - indicating the presence of ADHD); commission errors ($p < 0.0005$ – related to impulsivity); response time variability ($p < 0.008$ – related to consistency of attention); and d prime ($p < 0.002$ – related to performance degradation). Patients did not display significant improvement in the auditory CPT (Caro & Winter, 2011). In addition, PAT, Global Pain, and fatigue scores all improved significantly, and although psychological distress and

morning stiffness did not significantly improve, they did show a trend toward improvement (Caro & Winter, 2011).

In addition to a lack of patient randomization, the study authors noted that the patients who experienced the greatest improvements required 40 or more sessions of neurofeedback, which represents a small subset of their total sample and an even smaller subset of the FMS population in general (Caro & Winter, 2011). Thus, selection bias is a potential confounding variable. The authors also mentioned the possibility of a placebo effect as well (Caro & Winter, 2011). Nonetheless, this study suggests that SMR neurofeedback can improve attention at a highly significant level, as well as somatic symptoms in FMS patients.

The research literature on neurofeedback for FMS is still in its infancy. As such, it is still an experimental approach that is not widely accepted as an evidence-based approach. Although it shows promise in alleviating some of the symptoms of FMS, placebo-controlled trials of SMR-based neurofeedback are lacking. The most stringent research designs came out of the EDS/low-intensity/LENS tradition. These studies did not produce particularly promising results and included hardware difficulties which may have invalidated their findings. On the other hand, the tradition of SMR neurofeedback shows promising results and good long-term follow up (Kayiran et al., 2010). The next step in testing the efficacy of SMR neurofeedback for FMS requires the use of a wait-list control to assess the additional therapeutic effects of neurofeedback above and beyond standard treatment; such a design has not been utilized in the literature.

Lastly, it should be noted that SMR neurofeedback dates back to the late 1960s (see Sterman & Egner, 2006), although it has undergone some degree of modernization through improvements in EEG amplification systems, computer hardware and software, and treatment

protocols. More modern forms of neurofeedback have remained largely unutilized in research on FMS and other forms of chronic pain. These forms of neurofeedback include (but are not limited to): alpha-theta training, difference training, infraslow fluctuation training, coherence training, slow cortical potential training, homeoencephalography, real-time fMRI neurofeedback, multichannel surface z-score training, and 19-channel LORETA z-score training (see Larsen, 2012 for a review of these modalities). Thus, there are many distinct neurofeedback modalities which train the brain in a variety of ways. These forms of training are not comparable to SMR training or LENS neurofeedback, which have been the dominant neurofeedback methodologies used in FMS research to date. This gap necessitates further research studies on the therapeutic effects of each form of neurofeedback on FMS. The current dissertation is merely assessing one form of neurofeedback amongst many. Thus, the results of this dissertation are not generalizable to research or clinical contexts which involve the use of a different neurofeedback protocol.

# Chapter 4: Methods

## Participants

Twelve individuals diagnosed with fibromyalgia syndrome (FMS) were recruited through the pain management services of several Northshore Integrative Healthcare (NIH) operating facilities. Five participants completed the study, four dropped out of the study after completing one or several sessions, and three never scheduled a meeting with the principle investigator after signing the consent form. Inclusion criteria included: (1) a diagnosis of FMS, and (2) participants had to be at least 18 years of age. These participants were diagnosed, referred, and/or treated by the referring rheumatologist. Exclusion criteria included: (1) any prior neurofeedback treatment. Individuals were not excluded for possessing other comorbid psychiatric or medical conditions as comorbidities such as irritable bowel syndrome, rheumatoid arthritis, depression, or PTSD, which are common in individuals with FMS (Mease, 2009). Individuals who consented to participate did not receive financial compensation, but received up to sixteen free neurofeedback sessions.

Participants were randomly divided into two groups: a wait-list control and an active neurofeedback treatment group. Group randomization was performed by an online random number generator (http://www.random.org/), which is computed from atmospheric noise. To ensure random assignment, the principle investigator did not perform randomization with the generator; rather, randomization was performed by a colleague at NIH or the office manager

(based on the availability of each). Participants were also given a code (ranging from 1 to 1,000) produced by the random number generator; again, randomization was performed by a colleague or the office manager at NIH. This code was used to identify each participant's psychometric and EEG data. The only form that includes the participant's full name is the consent form.

The wait-list control group was given baseline measures and session-by-session measures (two wait-list assessments per week) for up to 4 weeks. At the conclusion of their wait-list control period, participants received active neurofeedback treatment which allowed them to serve as their own control. This method was utilized to increase the likelihood of detecting treatment effects. In addition, there was an active neurofeedback treatment group which did not undergo a wait-list control condition. Thus, two groups began the study simultaneously. The active neurofeedback group received eight to 16 sessions (approximately 30 minutes per session), totaling a minimum of 4 weeks of treatment and a maximum of 8 weeks. If, at the conclusion of session 8, FMS symptoms were reduced by 50% (as measured by the Revised Fibromyalgia Impact Questionnaire) then this individual was deemed to have completed their active neurofeedback treatment and their participation in the study then ended. This flexible strategy was instituted with the goal of obtaining as large a sample size as possible. An adequate sample for this study would be approximately three to ten participants, which is a common sample size in biofeedback and neurofeedback studies (Shindo et al., 2011; Koberda, Koberda, Bienkiewicz, Moses, & Koberda, 2013; Kayiran et al., 2007).

**Neurofeedback Protocol**

A NeXus 10 Mark-II amplifier was used to measure and amplify the EEG signal, and BioTrace+® software was utilized for signal processing and display of the EEG signal for the purpose of neurofeedback training (MindMedia, BV, The Netherlands). Neurofeedback sessions utilized a protocol co-developed by John S. Anderson, MA, LADC, BCB, BCN, QEEGD, of the Minnesota Neuro-Training Institute and this principle investigator. This protocol, although termed "sensory motor rhythm" or SMR training (that is, reinforcing 12-16 Hz activity above the sensory-motor cortices), also included a theta and high beta inhibit (see blue screen below). Thus, this protocol is termed "SMR training" due to convention, but may be more accurately described as SMR enhancement, theta inhibition, and high beta inhibition training.

Reinforcement was obtained when these three frequencies were all within proper parameters, which consisted of raising SMR amplitude beyond threshold while keeping theta and high beta amplitudes below threshold levels. Threshold levels (see percentages directly below the three frequency columns on the right side of the blue screen below) were based on the most recent 60 seconds of EEG activity in each frequency bandwidth (SMR, theta, and high beta) and the percentage of that activity that was above threshold (for SMR reinforcement) or below threshold (for theta and high beta inhibition). The principle investigator tracked these percentages with the goal of manually adjusting reinforcement and inhibition thresholds anywhere between 65 and 75% (70% is the ideal). Thus, participants were rewarded (via visual and auditory rewards) whenever 70% of their most current 60 seconds of EEG bandwidth activity was above or below manually set thresholds.

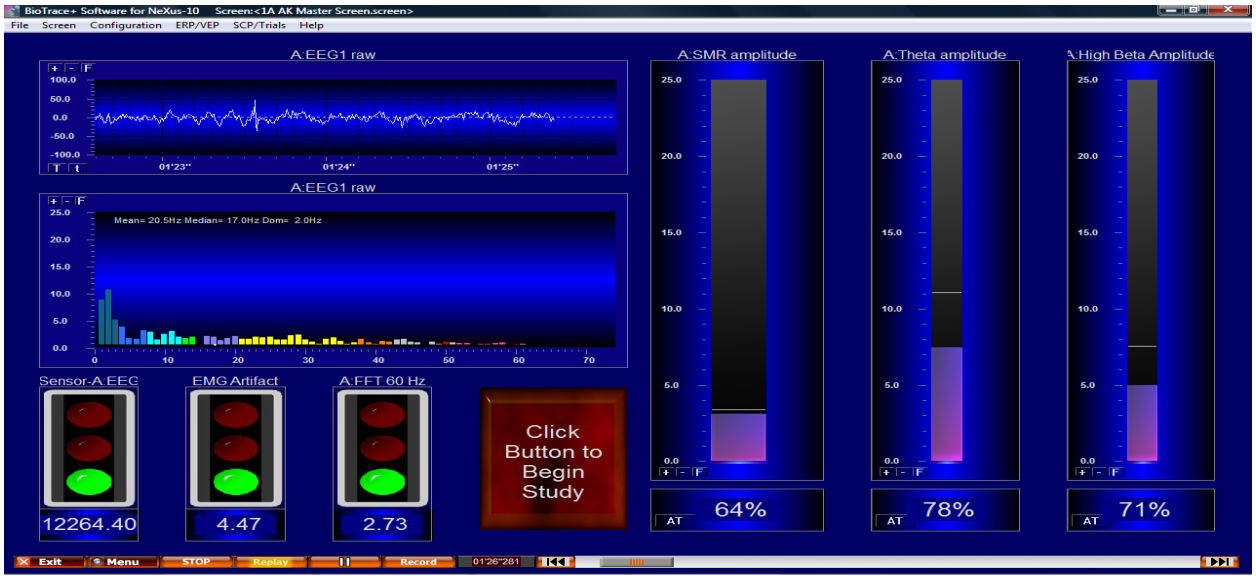



*Figure 1. An Image of the Principal Investigator's Screen*

Two monitors were utilized in this neurofeedback protocol. One monitor was tracked and manipulated by the principle investigator (see image above) during each session, and the other monitor (see image below) was situated at a comfortable distance from participants who were seated. The principle investigator used his screen to observe the raw EEG (top-left), real-time spectral array (middle-left), and the EMG artifact "traffic light" for any indications of excessive muscle tension, movement artifact, or blinking that would have impeded the EEG signal and interfered with an optimal training experience. If artifacts were present in these displays, the principle investigator would ask the participant to calm their body through suggestions for relaxation (for example, "Try to relax your eyebrows and feel your jaw becoming looser and limper."), which often eliminated artifacts and allowed participants improved feedback of their EEG activity. Behavioral observations were also used to note the source of artifacts (such as excessive eye blinking, furrowing the brow, and so forth). The sensor contact and 60 Hz artifact

"traffic lights" were used to assess adequate electrode contact and EEG signal, as well as artifact originating from electromagnetic sources (such as electronic equipment, cell phones, and so forth).

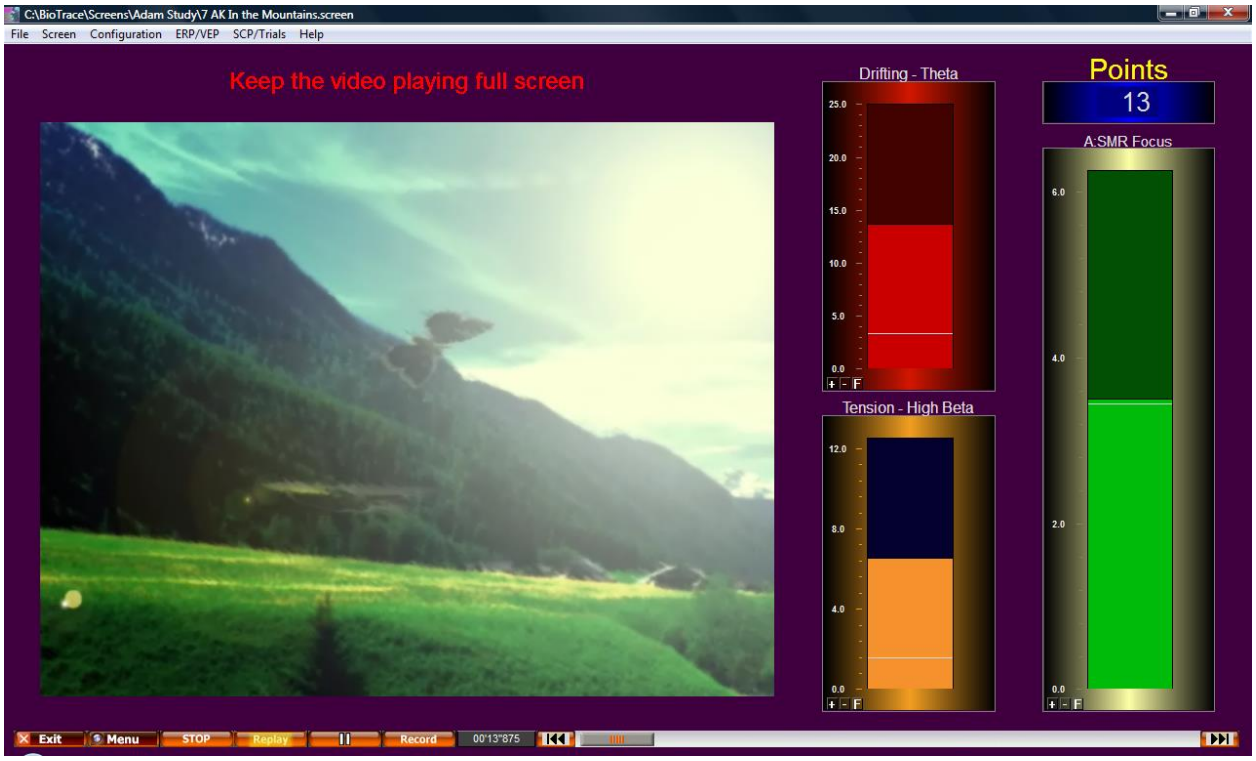



*Figure 2. An Image of One of the Training Screens Viewed By Participants*

Figure 2 above presents an example of one of the training screens viewed by participants. Participants could view the nature scene, as well as their amplitudes of theta, high beta, and SMR. Participants could observe their EEG amplitudes increasing and decreasing in real-time in relation to the set threshold (the white line on the red and orange bars). Thus, they could observe whether they were above or below threshold parameters. The nature screen would expand if participants' EEG amplitudes were approaching threshold parameters, but would shrink if EEG

amplitudes were moving away from these parameters (that is, “proportional feedback”). The nature screen would remain fully expanded and the participant would hear a bell sound if EEG amplitudes stayed within parameters for .25 seconds (that is, “discrete feedback”).

Participants received feedback via nine training screens that consisted of various nature scenes, including a beach, a waterfall, a flower in front of a Milky Way background, and so forth. These scenes were chosen on the basis of their relaxing quality and variety. Each scene was a short motion picture (such as the butterflies flying in the meadow above). Participants also viewed a screen of a woman in a meditative posture (such as seated in a lotus position on a beach) instructing them to relax with their eyes open during their pre-session EEG assessment, in between each training period (for a 15-second break between training periods), and during their post-session EEG assessment.

**Study Design and Data Analysis**

Data was collected and evaluated in the context of a case-series design in which each participant’s data was analyzed separately. A case-series design was the most suitable option given the relatively small sample size of this study (five participants completed treatment, three stopped treatment after several sessions, and three never began treatment). Data was analyzed via quantitative statistical analysis (paired samples t-tests), qualitative visual inspection of reported symptoms (such as pain and fatigue) throughout the course of treatment, qualitative visual inspection of EEG indices throughout the course of treatment, and noting the improvements (or lack thereof) on several outcome measures (such as the FIQR and MFTQ). Participants were also debriefed at the conclusion of treatment to inquire about their experience of neurofeedback and

whether they found it helpful. Thus, this dissertation utilized mixed-methods (that is, quantitative statistical tests, visual inspection, and debriefing).

## Outcome Measures

**Fibromyalgia Impact Questionnaire Revised (FIQR).** The FIQ was developed to assess both common difficulties experienced by FMS patients, as well as treatment efficacy. It consists of 20 items. In terms of psychometric properties, it has credible construct validity, reliable test-retest characteristics (0.56 on pain and 0.95 for physical functioning), and is a sensitive measure of therapeutic change (Burkhardt, Clark, & Bennett, 1991; Williams & Arnold, 2011). In addition to tracking variables such as pain and physical functioning, it also tracks psychological variables (such as depression and anxiety). The measure was utilized in four of the six studies on neurofeedback for FMS, and evidenced positive findings on two of these studies.

The FIQR is a revised version of the FIQ that was developed with the goal of correcting the ethnocultural bias and complicated scoring procedures of the FIQ (Bennett et al., 2009). It is a free tool and permission is not required for its use. It was included in this study's baseline/post-treatment battery, and was also administered at the conclusion of weeks 2, 4, 6 and 8 to track treatment improvements.

**Visual Analog Scales (VAS).** The Visual Analog Scales (VAS) comprise two of the three domains measured on the FIQR (such as symptoms); thus, they are included in the FIQR. These scales have proven useful as pre-post session measures which track therapeutic improvements within and between sessions (see Kayiran et al., 2007, 2010), and were used for

this purpose in the present dissertation. These scales are essentially graphic lines (10 cm long) wherein the participant indicates symptom severity by marking a point on the line (0 = no symptoms and 10 = severe symptoms). Following the work by Kayiran et al. (2007, 2010), two of the seven scales (measuring pain and fatigue) were given to participants at the beginning and end of every session to track within-session improvements.

**EEG.** EEG assessment was performed with the NeXus Mark-II amplifier (the same system used for neurofeedback) and analyzed through the use of Biotrace+ ® software. Artifact rejection (artifacting) was performed to clean the data of eye-blink and muscle tension or movement artifact prior to data analysis. Artifacting involved excluding EEG activity from data analysis if it exceeded 10 microvolts in the delta bandwidth (which is typical of EEG artifacts resulting from blinking) or 10 microvolts in the EMG bandwidth (which is typical of muscle movement artifact); however, an upper limit of 20 microvolts was allowed for some participants if their EEG activity appeared particularly prone to artifact. The EEG was analyzed in terms of the amplitudes of SMR, theta, and high beta, as these were the target frequencies for operant conditioning. In addition, the theta-beta ratio was assessed, as Kayiran et al. (2010) reported significant changes in the SMR-theta ratio after neurofeedback training, and cited this as evidence of a physiological marker of therapeutic improvement. EEG was recorded from site C4 (following the work of Kayiran et al., 2007, 2010) for 2 minutes pre-session and 2 minutes post-session to track EEG changes immediately after the session.

**ME/CFS Fatigue Types Questionnaire (MFTQ).** This 22-item scale was developed in 2009 for the purpose of assessing fatigue in individuals diagnosed with Chronic Fatigue Syndrome (CFS), especially in terms of symptom specificity and sensitivity (Jason et al., 2011). Jason et al. (2011) found that most measures of fatigue have significant problems with both specificity and sensitivity. These researchers found that the MFTQ was the most psychometrically sound instrument for measuring fatigue symptoms. The MFTQ's post-exertional subscale (that is, excessive exhaustion following physical activity) is cited by these researchers as the most promising and sensitive scale in the MFTQ. The principle researcher used the MFTQ to measure physical and occupational functioning, symptom severity and symptom frequency during the course of treatment.

## Procedure

This study investigated the effects of SMR neurofeedback on individuals diagnosed with FMS in the context of a case-series design. Participants were recruited in several ways. In some cases, the PI contacted FMS patients (via patient databases located at NIH operating facilities) who had given consent to be contacted for research and clinical purposes. In other cases, potential participants contacted the PI upon seeing a flyer outlining the study, potential benefits, inclusion/exclusion criteria, and PI contact information. Flyers were posted at clinics and hospitals that have a good relationship with NIH; however, flyers were only posted when approved by staff. Participants who were not referred by their physicians or contacted through databases (that is, self-referral participants) were asked to bring proof of their FMS diagnosis (via an electronic medical record printout). Other ways participants were recruited were by

sending advertisements of the study to FMS support groups in the Chicago-land area (via web forums and by directly contacting leaders in these groups). Finally, some participants were referred to Northshore Integrative Healthcare (NIH) by their physicians and given the PI's contact information.

Potential participants were given a recruitment form outlining the study, potential benefits, and inclusion/exclusion criteria. Written consent forms were given to potential participants, and if they were eligible and chose to sign the consent, they were then randomly assigned to either the wait-list control or active treatment group. After random assignment participants began assessments and/or neurofeedback (depending on which group they were randomly assigned to), often on the same day. The initial wait-list control session involved EEG assessment (approximately 2 minutes), administering symptom questionnaires, and was followed by neurofeedback (for the active-treatment group). EEG was recorded from the C4 site (international 10-20 system; see figure below), which was the site utilized in the studies by Kayiran et al. in 2007 and 2010.

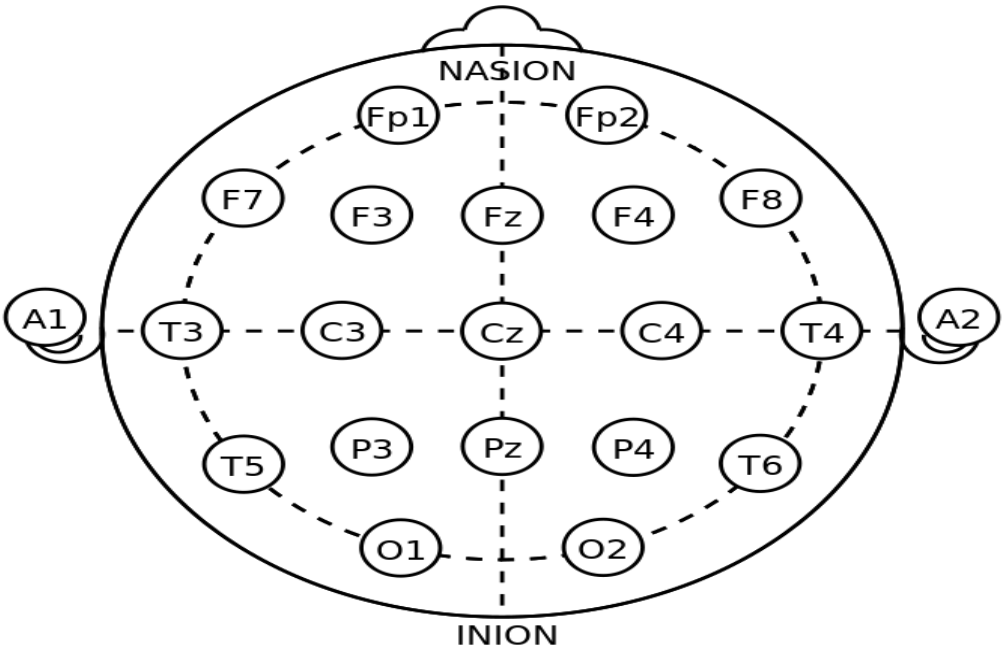



*Figure 3. A Graphic Representation of the International 10-20 System of Electrode Placement*

The *nasion* refers to the frontal region, the *inion* to the posterior region, and A1 and 2 to each ear. Letters denote each of the four lobes, with the addition of C for the central region (F is frontal, T is temporal, P is parietal, and O is occipital). Odd numbers represent regions on the left hemisphere and even numbers represent regions on the right hemisphere.

Once the neurofeedback training was complete, the session concluded with another 2 minutes of post-treatment EEG assessment. Participants then completed two post-session VAS scales for pain and fatigue. Neurofeedback consisted of approximately 27 minutes and 15 seconds of SMR neurofeedback (with theta and high beta inhibition as well). Participants sat comfortably in front of a table with a mounted computer monitor that displayed visual and auditory feedback representing their EEG activity. Each neurofeedback session was 31 minutes and 15 seconds in duration (comprised of two 2-minute assessments and 27 minutes and 15 seconds of training) and consisted of ten discrete training periods (approximately 2.7 minutes per

period), which allowed approximately 15 seconds of rest between each period. This approach was modeled after the protocol utilized by Kayiran et al. (2007, 2010).

Neurofeedback training involved reinforcing SMR (12 – 15 Hz) while inhibiting theta (4 – 7 Hz) and high beta (22-30 Hz) at the C4 site. Reinforcement occurred via task success on a given neurofeedback game. For example, one game involved the participant concentrating on a computer-animated video of a jet aircraft in flight. When the participant was successfully producing SMR while inhibiting theta and high beta, the jet smoothly flew through a mountainous environment, but when the participant failed to meet these EEG thresholds, the video then stopped playing. This acts as a cue that reorients the participant to the task, which aids in the production of the neurophysiological function sufficient to gain reinforcement. Participants received numerous guidelines on how to obtain reinforcement, such as how to relax one's body (emphasizing calmness, stillness, and being loose and limp), while concentrating on the computer game (Kayiran et al., 2010). Participants were also given a script before the start of neurofeedback which described the training process and strategies for obtaining reinforcement (for example, being open and receptive to the feedback, while not attempting to "force" the process through trial and error cognitive or behavioral strategies). This script was written by the principle investigator and molded after suggestions by Birbaumer (2011). This protocol was used in three of the six studies covered in the literature review (Kayiran et al., 2007, 2010; Caro & Winter, 2001).

**Ethical Issues**

The principal investigator (PI) has obtained appropriate education and training in neurofeedback through formal graduate-level coursework, attending workshops, and participating in regular neurofeedback sessions as a client and therapist under the supervision of experienced practitioners, as well as reading the latest literature and continually consulting with numerous experts in the field. Participants were informed of their right to discontinue their participation in the study at any time. Participants were asked about their prior experience and/or knowledge of neurofeedback, and were further educated to correct any misconceptions as well as to better inform each participant. The PI continually solicited feedback from participants throughout the study in an effort to promote collaboration and rapport.

The risks of adverse side effects resulting from neurofeedback are minimal and have not received adequate systematic study in the research literature. This is likely due to the widespread agreement of neurofeedback's safety and low level of risk. SMR neurofeedback essentially amounts to a relaxation technique, in which participants learn to calm their body while staying mentally alert and focused on a task. The PI was only able to identify one article on possible side effects of neurofeedback (Hammond & Kirk, 2008). This article mainly consists of anecdotal case reports which were taken from Internet list groups of unidentified neurofeedback practitioners. The professional credentials and training of these individuals remained anonymous. It is important to note that many individuals currently practicing neurofeedback are not licensed health care providers, which may account for some of these anecdotal reports of side effects.

Hammond and Kirk's 2008 article mentions three studies, dating from the 1970s and '80s, which investigated side effects resulting from inappropriate training protocols, as well as

A-B-A reversal and A-B-A crossover designs. For example, Hammond and Kirk mentioned one study in which theta was inhibited and SMR was reinforced in the treatment of ADHD, which resulted in symptom improvement (that is, reduction of ADHD symptoms); however, when theta was reinforced, symptoms worsened (2008). These authors mentioned another study in which theta was inhibited and SMR was reinforced in the treatment of epileptiform activity, which resulted in an 18% decrease in epileptiform activity; however, when theta was reinforced and SMR inhibited, epileptiform activity then rose by 29 percent. Upon reversing the protocol (inhibiting theta and reinforcing SMR), epileptiform activity again decreased by 60% (Hammond & Kirk, 2008).

Thus, it can be argued that the systematic study of the adverse effects of neurofeedback is, paradoxically, a testament to its safety and effectiveness in stabilizing potentially dangerous medical conditions. Furthermore, none of the three SMR neurofeedback studies on FMS covered in this literature review indicated negative side effects. Nonetheless, based on Hammond and Kirk's recommendation, study participants were informed (during informed consent) that side effects can occasionally occur. The PI inquired about side effects at the start of every session and was ready to inform his supervisor (a licensed psychologist) of any negative side effects. Although some participants experienced occasional unpleasant side effects, such as headache, increased pain, and increased fatigue, such reactions appeared to be tolerable and transitory. In addition, study participants did not have to discontinue any medical or pharmacological treatment during this study and had their usual care. Thus, neurofeedback offered participants an additional level of attention, care, and treatment.

In general, the authors of the existing studies on neurofeedback for FMS stress the importance of designing studies that are methodologically rigorous and seek to assess the "specific effects" of neurofeedback, rather than the nonspecific effects associated with experimenter-participant rapport, giving the participant prolonged attention and encouragement, and placebo effects; however, therapeutic rapport and adequate coaching throughout treatment may be inherent to neurofeedback itself. For example, Cannon (2012) reported that the presence or absence of a clinician had a notable impact on learning curves during neurofeedback training of the anterior cingulate. Thus, the current study was designed and carried out with the goal of being as ecologically valid and clinically relevant as possible, despite its numerous limitations (such as relatively small sample size, lack of a placebo-control, and so forth). This dissertation involved carrying out the first case-series study of SMR neurofeedback for FMS that included a wait-list control group, as well as outcome measures which haven't been used in prior studies of neurofeedback for FMS (specifically, FIQR and MFTQ).

# Chapter 5: Results

## Description of Enrolled Participants

The data from the five participants who completed their course of neurofeedback treatment (that is, 8 to 16 sessions) were used in this analysis. The results of the four participants who did not complete their course of neurofeedback treatment will not be reviewed in this analysis; however, it should be noted that two participants dropped out after the first session for unknown reasons, and the remaining two participants dropped out after the fourth and fifth sessions (one for unknown reasons and the other reported that the treatment was unhelpful). The remaining three participants who consented chose not to participant in the study for unknown reasons. With regard to age, marital status, and employment, the majority of the participants were in their 20s (mean age = 36, mode = 25, std deviation = 14.7, minimum = 25, maximum = 54), married (three married and two single), employed either full or part time (two full time, two part time, and one unemployed), had been experiencing symptoms of FMS for an average of 15 years (std. deviation = 13, minimum = 1.75, maximum = 34), and reported comorbid conditions (three with other diagnoses and two without).

| | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|
| FIQR | 42.67 | 85.30 | 61.3620 | 16.77514 |
| VAS_P | 3.60 | 7.80 | 5.2600 | 1.67272 |
| VAS_F | 5.50 | 8.30 | 6.9400 | 1.15888 |
| Phys_and_Occ | 2.00 | 6.00 | 4.0000 | 1.58114 |
| Sx_freq | 1.20 | 3.30 | 2.1400 | .95289 |
| Sx_sev | 40.90 | 87.40 | 59.9960 | 19.84006 |

*Figure 4. Summary of Participants' Pre-Treatment Assessment Scores*

On average, participants' FIQR scores indicated severe FMS symptoms. VAS pain and fatigue scores were calculated by averaging the first three pre-session scores. Note the higher levels VAS levels of fatigue compared to pain.

**Description of Data Analysis Procedures**

Paired-samples t-tests were utilized to assess the immediate post-session effects of neurofeedback on subjective reports of pain and fatigue, as well as immediate post-session EEG changes. Linegraphs plotting pre- and post-session pain and fatigue scores were visually assessed to track symptom improvement during the course of treatment. EEG indices were also plotted on linegraphs and visually assessed to track relevant EEG changes that occurred during the course of treatment. If a participant was randomized to the wait-list control condition, then their VAS pain and fatigue scores, as well as their EEG indices, were visually inspected in a side-by-side comparison. FIQ-R and MFTQ scores were assessed to track symptom improvement during the course of course of treatments. The pre- and post-treatment scores of all participants (that is, on the outcome measures) were averaged and improvements, or lack thereof, were noted. Lastly, each participant was debriefed regarding their experience of neurofeedback and whether they found it to be beneficial.

**Participant 407.** Participant 407 is a 26-year-old, single Caucasian female who was unemployed upon enrolling in the study, but gained part-time employment several weeks after beginning treatment. She reported that she has been experiencing FMS symptoms for 19 years. She believes that she may also have rheumatoid arthritis. She reported that she has not been diagnosed with chronic fatigue syndrome. She was randomized to the active treatment group, was seen twice per week (with the exception of missed sessions), and completed 16 sessions of neurofeedback.

A two-tailed paired sample t-test revealed a significant difference between pre- and post-session VAS reports of fatigue ($p < .05$), but not pain. This nonsignificant finding for pain is likely attributable to several post-session ratings in which her pain was greater after the session (sessions 4 and 5); however, visual inspection of both graphs indicates that her pain and fatigue scores decreased during the course of treatment. Graphs representing her pre- and post-session pain and fatigue scores throughout treatment can be seen below.

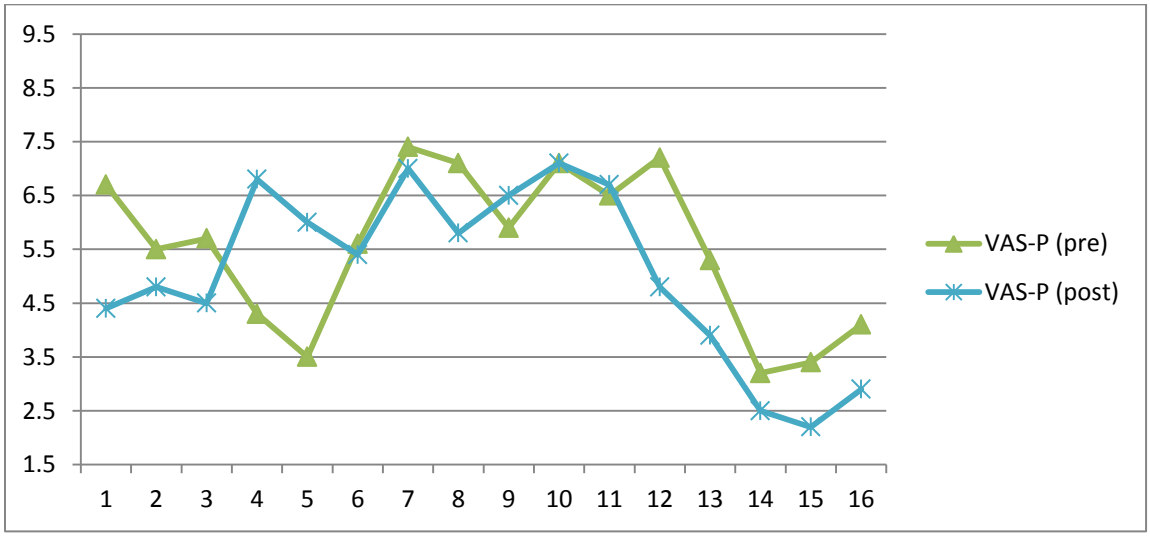



*Figure 5. Participant 407's Pre- and Post-session Reports of Pain on the VAS Scale*

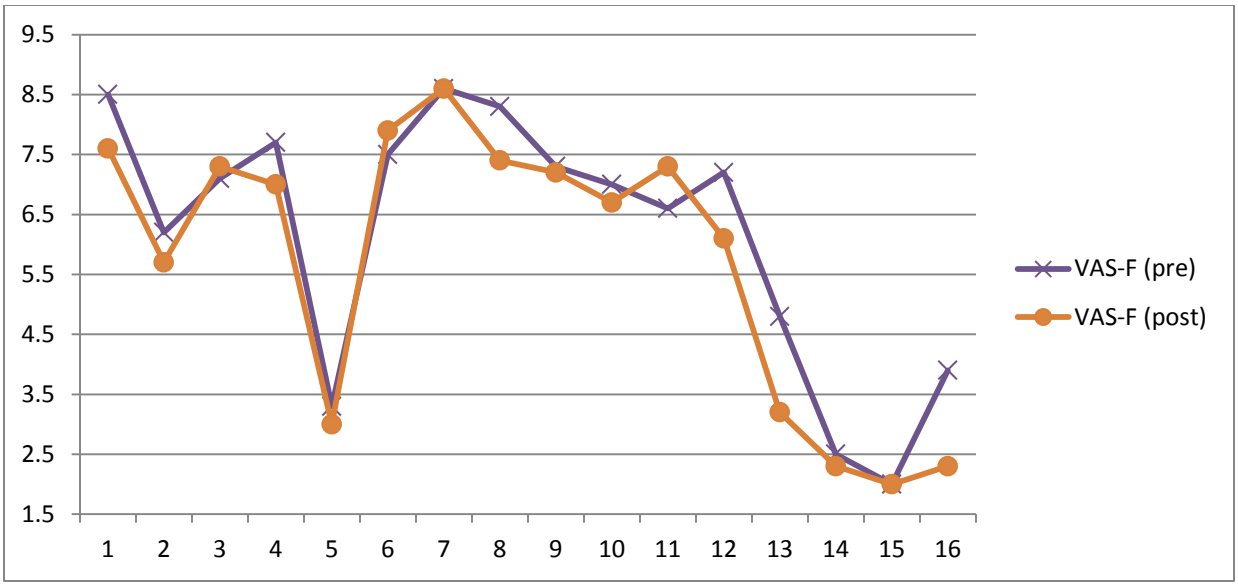



*Figure 6. Participant 407's Pre- and Post-session Reports of Fatigue on the VAS scale*

The severity of Participant 407's symptoms as measured by the FIQ-R did not improve to a moderate or mild range throughout the course of treatment, although it decreased from baseline (see Table 1).

*Table 1. Participant 407's Scores on the FIQR*

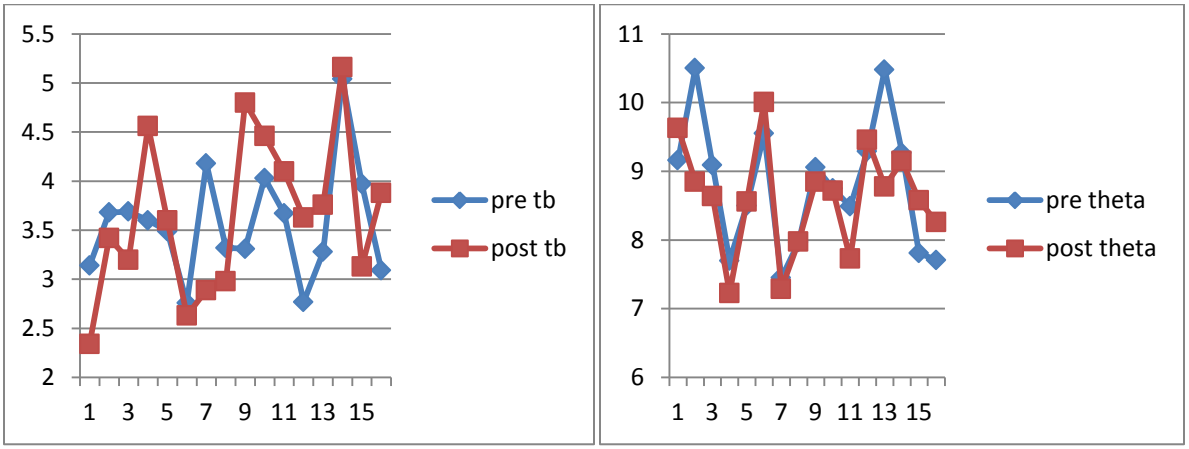
| Session | Raw Score | Quartile Range |
|---|---|---|
| 1 (baseline) | 70.17 | Severe |
| 3 | 75.67 | extreme |
| 7 | 75 | extreme |
| 11 | 72.5 | Severe |
| 16 (post-treatment) | 68.5 | Severe |

Participant 407's physical and occupational capacity, symptom frequency, and symptom severity improved throughout the course of treatment (see Table 2).

*Table 2. Participant 407's Scores on the MFTQ*

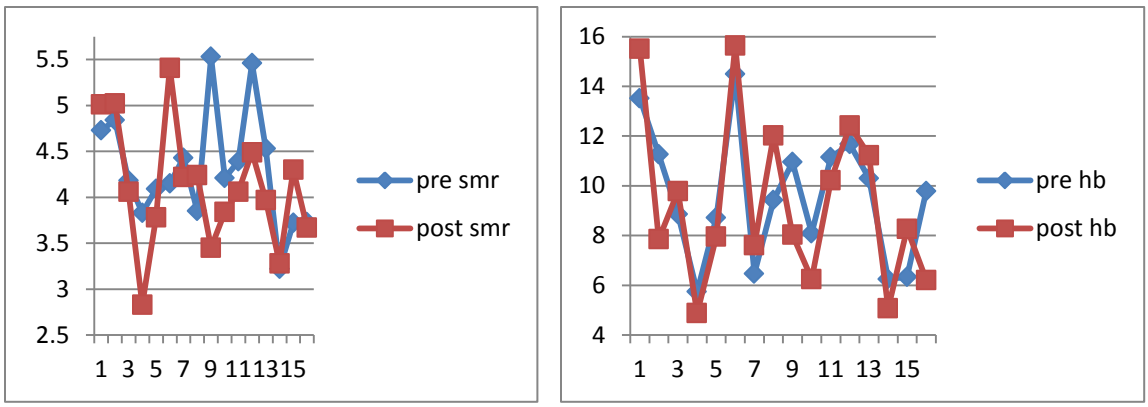
| Session | Physical and Occupational Capacity (0-7) | Symptom Frequency (average) | Symptom Severity (average) |
|---|---|---|---|
| 1 (baseline) | 2 | 3.3 | 87.4 |
| 3 | 2 | 2.9 | 76.1 |
| 7 | 4 | 2.8 | 75.5 |
| 11 | 4 | 2.8 | 73.6 |
| 16 (post-treatment) | 4 | 2.7 | 75 |

Paired samples t-tests did not reveal significant pre- to post-session EEG changes for this participant (see Figures 7 through 10).




*Figures 7 (left) and 8 (right). Sample t-test Data Examining Theta-to-Beta Ratio and Theta EEG Changes for Participant 407*

Figures 7 and 8 show an increase in the theta-to-beta ratio during the course of treatment, while theta appeared consistent.




*Figures 9 (left) and 10 (right). Sample t-test Data Examining SMR and High Beta EEG Changes for Participant 407*

Figures 9 and 10 show decreases in SMR and high beta during the course of treatment.

***Debriefing.*** When asked about her experience of neurofeedback and if she found it to be helpful in reducing symptoms of fibromyalgia, Participant 407 replied:

> I liked it. I liked learning how to relax my face and I now realize more when I tense up. I noticed a difference when I wasn't doing neurofeedback. I would recommend it to other people with fibromyalgia. After sessions I was tired but relaxed, and noticed that my sleep has slightly improved.

**Participant 561.** Participant 561 is a 26-year-old, married Caucasian female who is employed full-time. She has been experiencing symptoms of FMS for approximately 1.5 to 2 years. She reports not having any other diagnoses and has not been diagnosed with chronic fatigue syndrome. She was randomized to the wait-list control condition and subsequently completed 16 sessions of neurofeedback. Graphs displaying her wait-list control pain (WLC) and fatigue scores and EEG indices can be seen below. Her pain reports increased during the WLC period, while her fatigue appeared fairly consistent. Her levels of theta and SMR appeared to decrease during WLC, while her high beta and theta-to-beta ratio appeared fairly consistent.

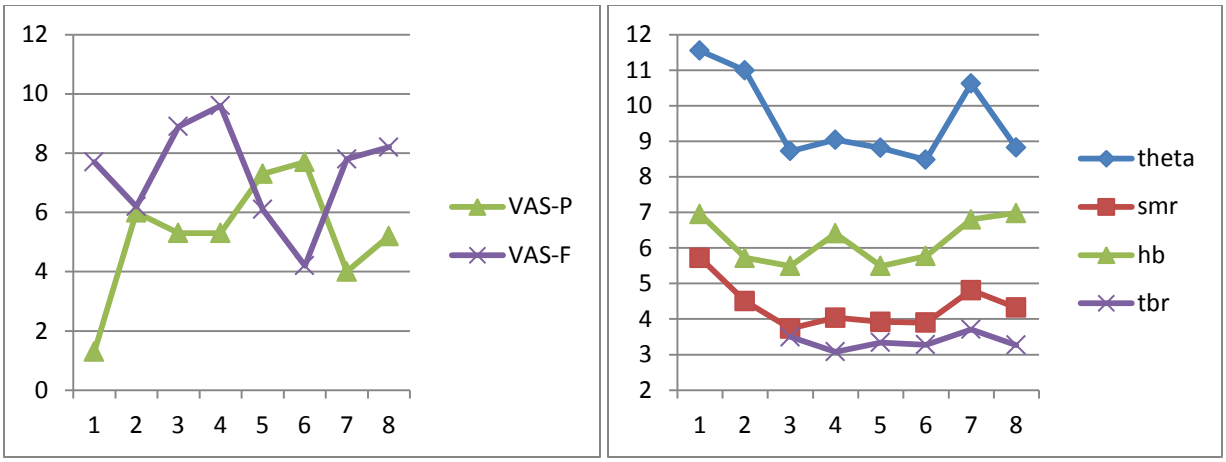



*Figure 11 (left). Participant 561's Reports of Pain and Fatigue on the VAS Scale During WLC*
*Figure 12 (right). Participant 561's WLC EEG Indices*

Figure 11 shows participant 561's reports of pain and fatigue on the VAS scale during her WLC period, and Figure 12 shows her WLC EEG indices.

A two-tailed paired sample t-test revealed a significant difference between pre- and post-session VAS reports of pain ($p < .05$) and fatigue ($p < .001$). It should be noted that Participant 561's fatigue generally increased post-session. Visual inspection of both graphs indicates that her pain and fatigue scores decreased during the course of treatment after her wait-list control period. Graphs representing her pre- and post-session pain and fatigue scores throughout treatment can be seen below.

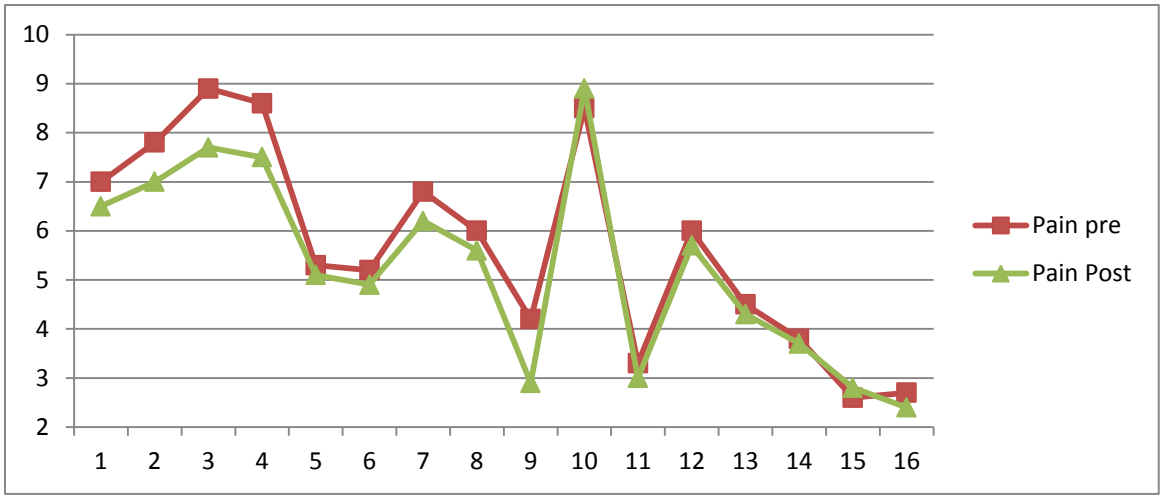



*Figure 13. Participant 561's Pre- and Post-Session Reports of Pain on the VAS scale*

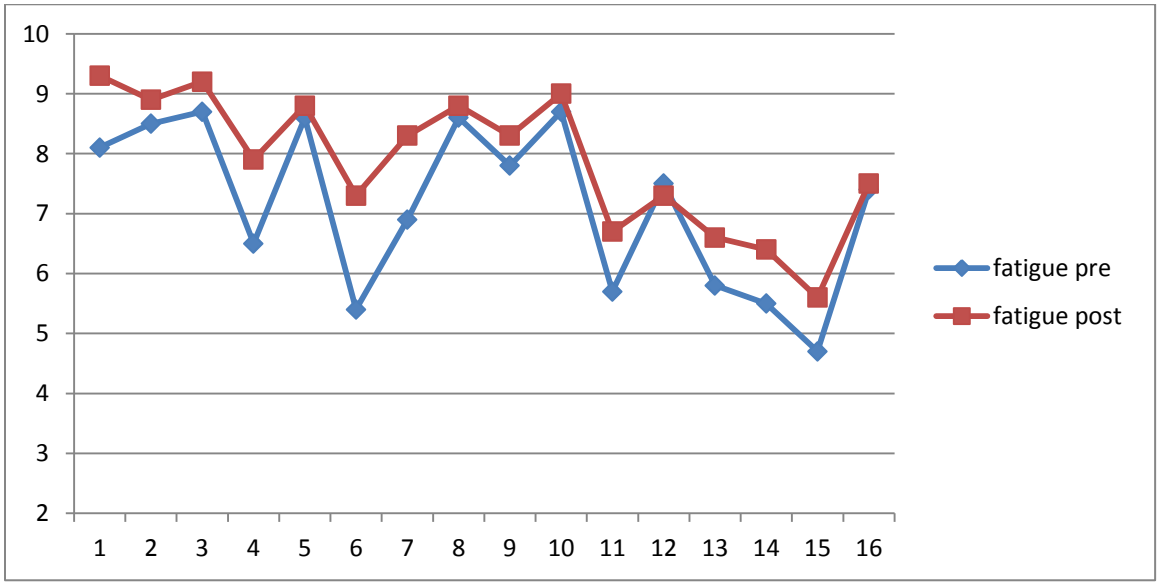



*Figure 14. Participant 561's Pre- and Post-session Reports of Fatigue on the VAS scale*

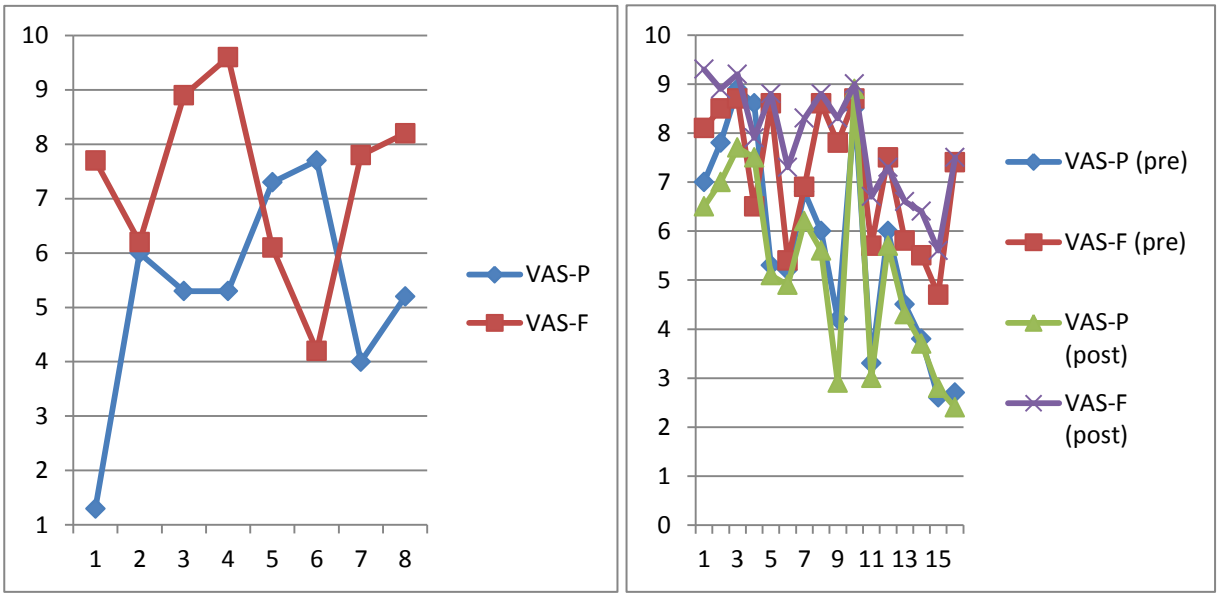



*Figure 15. Side-by-side Comparison of Participant 561's WLC VAS Scores (left) and Active-treatment Scores (right)*

The severity of Participant 561's symptoms as measured by the FIQ-R improved from a moderate to a mild range during the course of treatment (see Table 3).

*Table 3. Participant 561's Scores on the FIQR*

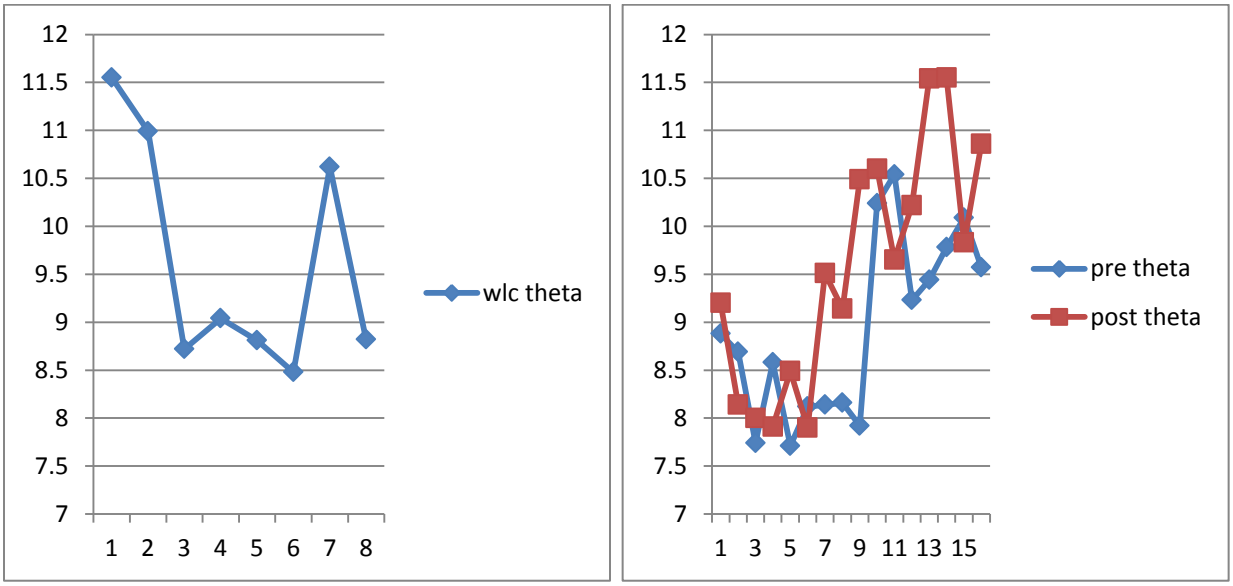
| Session | Raw Score | Quartile range |
|---|---|---|
| 1 (WLC baseline) | 58 | Moderate |
| 1 (pre-treatment baseline) | 51.33 | Moderate |
| 3 | 56 | Moderate |
| 7 | 57.5 | Moderate |
| 11 | 48.5 | Moderate |
| 16 | 41.3 | Mild FM |

Participant 561's physical and occupational functioning remained relatively stable while her symptom frequency and severity increased during the course of treatment (see Table 4).

*Table 4. Participant 561's Scores on the MFTQ*

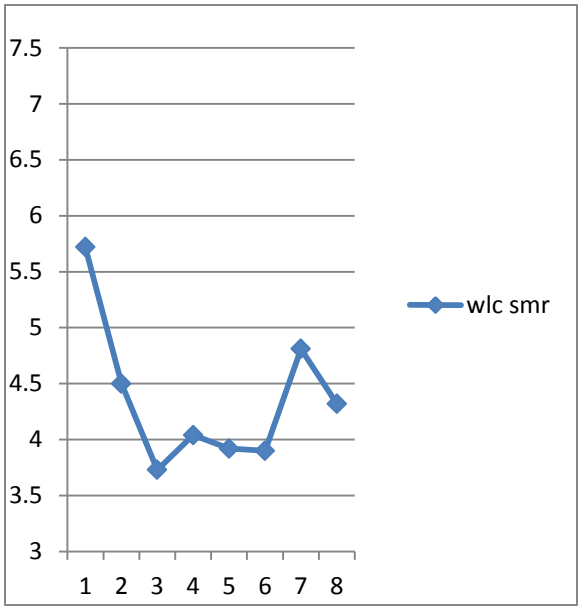
| Session | Physical and Occupational Capacity (0-7) | Symptom Frequency (average) | Symptom Severity (average) |
|---|---|---|---|
| 1 (wlc baseline) | 5 | 1.2 | 40.9 |
| 1 (pre-tx baseline) | 6 | 1.6 | 39.77 |
| 3 | 6 | 1.8 | 38.64 |
| 7 | 5 | 2 | 45.68 |
| 11 | 5 | 2 | 37.73 |
| 16 (post-treatment) | 5 | 2.2 | 55.68 |

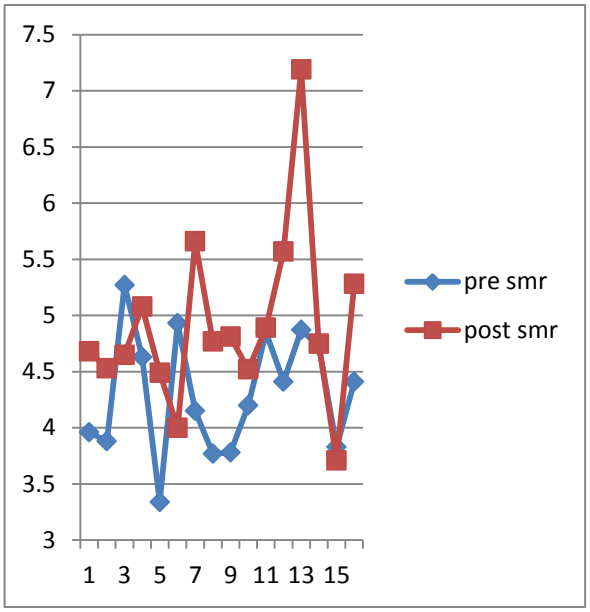
Paired samples t-test revealed a significant difference between pre- and post-session levels of SMR ($p = .01$) and theta ($p < .05$).




*Figures 16 (left) and 17 (right). Wait-list Control and Sample t-test Data Examining Theta EEG Changes for Participant 561*

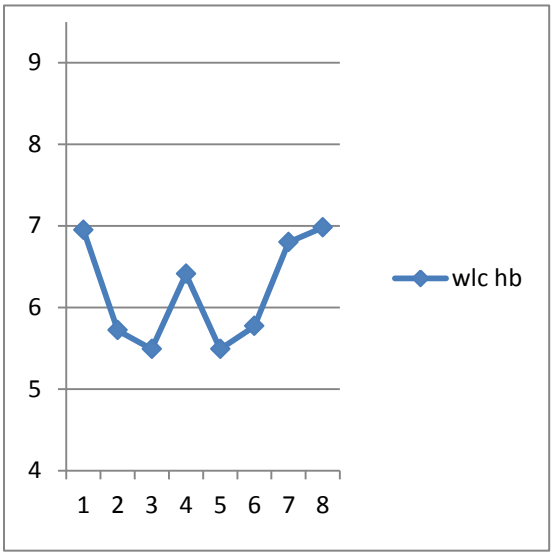
Figures 16 and 17 show a decrease of theta during the WLC condition, and an increase in theta during active treatment.

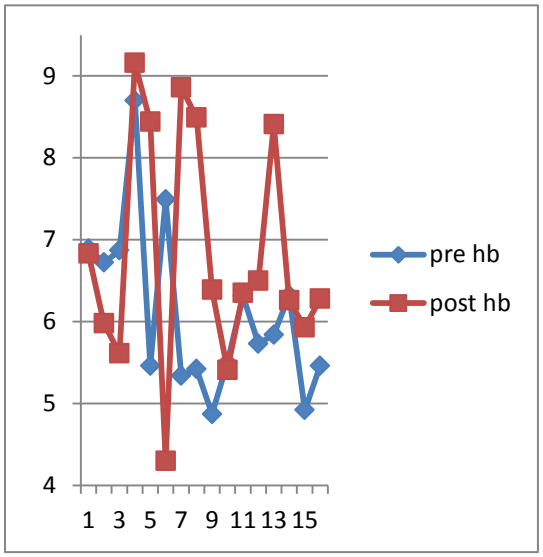



*Figures 18 (left) and 19 (right). Wait-list Control and Sample t-test Data Examining SMR EEG Changes for Participant 561*

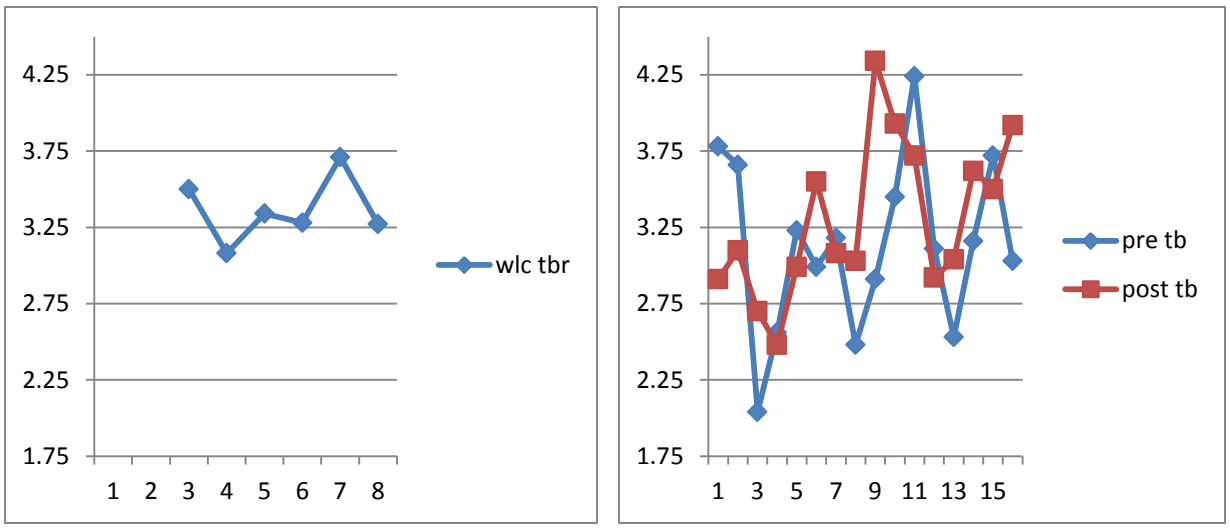
Figures 18 and 19 show a decrease in SMR during WLC, and an increase in post-session SMR during active treatment.




*Figures 20 (left) and 21 (right). Wait-list Control and Sample t-test Data Examining High Beta EEG Changes for Participant 561*

Figures 20 and 21 show a relatively stable level of high beta during the WLC condition, but a more variable post-session level of high beta.




*Figures 22 (left) and 23 (right). Wait-list Control and Sample t-test Data Examining Theta-to-Beta Ratio EEG Changes for Participant 561*

Figures 22 and 23 show a relatively stable theta-to-beta ratio during the WLC condition, but a more variable theta-to-beta ratio during active treatment.

***Debriefing.*** When asked about her experience of neurofeedback and if she found it to be helpful in reducing symptoms of fibromyalgia, Participant 561 replied:

> It helped in the moment and I felt better in the evening after training, but it didn't seem to last beyond that, although I know my pain scores have been going down. It was calming, but I don't know how to use it when I'm not doing it. I would recommend it for others who've had fibromyalgia for a while to see if it works independent of other treatments.

**Participant 499.** Participant 499 is a 25 year-old, married Caucasian female who is employed full-time. She reported that she has been experiencing FMS symptoms for 4 years. She reported that she has not been diagnosed with chronic fatigue syndrome, but believes that she suffers from the condition. She was randomized to the WLC condition, has been seen once per week (with the exception of missed sessions), and completed eight sessions of neurofeedback. Graphs showing her WLC pain and fatigue scores and EEG indices can be seen below.

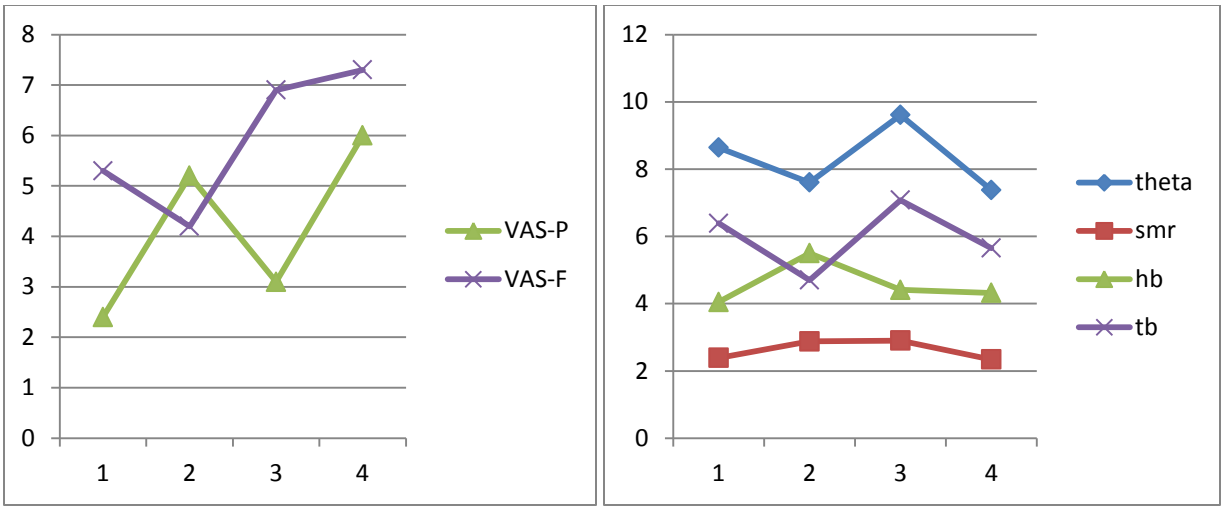



*Figure 24 (left). Participant 499's Pain and Fatigue Score during the WLC Period*
*Figure 25 (right). Participant 499's EEG Indices During the WLC Period*

Figure 24 shows participant 499's pain and fatigue scores during the WLC period, which both appeared to increase. Figure 25 shows her EEG indices during the WLC period, which appeared fairly consistent.

A two-tailed paired sample t-test revealed a significant difference between pre- and post-session VAS reports of pain ($p < .01$), but not fatigue. Graphs representing her pre- and post-session pain and fatigue scores throughout treatment can be seen below.

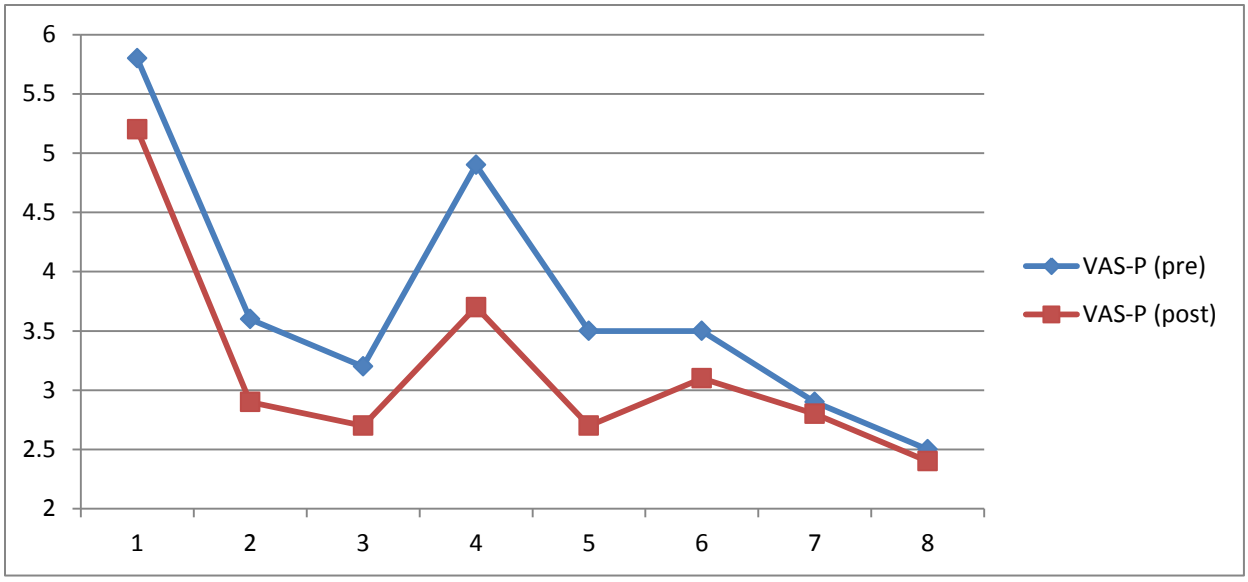



*Figure 26. Participant 499's Pre- and Post-session Reports of Pain on the VAS Scale*

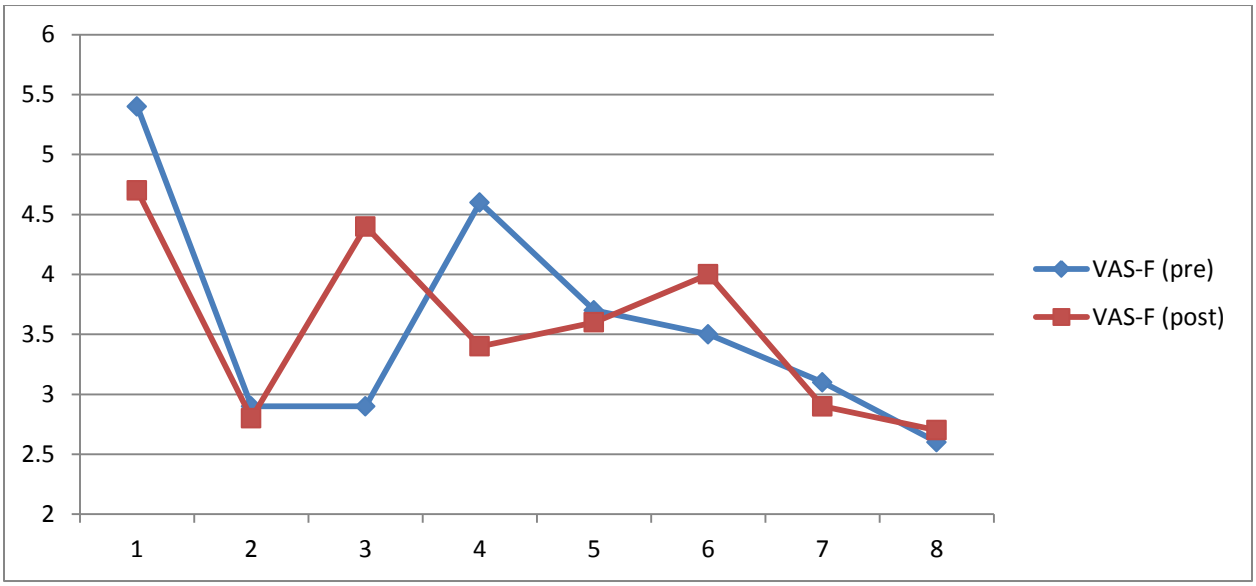



*Figure 27. Participant 499's Pre- and Post-session Reports of Fatigue on the VAS Scale*

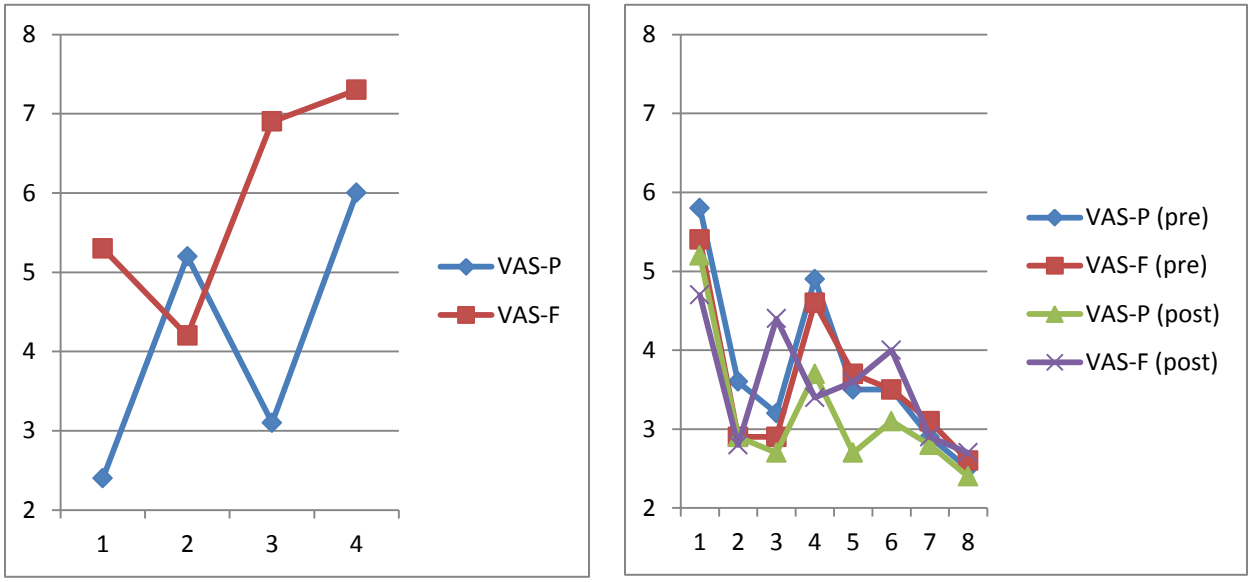



*Figure 28. Side-by-side Comparison of Participant 499's WLC VAS Scores (left) and Active-treatment Scores (right)*

As can be seen from the table above, the severity of her symptoms as measured by the FIQ-R improved from a moderate to a mild range throughout the course of treatment (see Table 5).

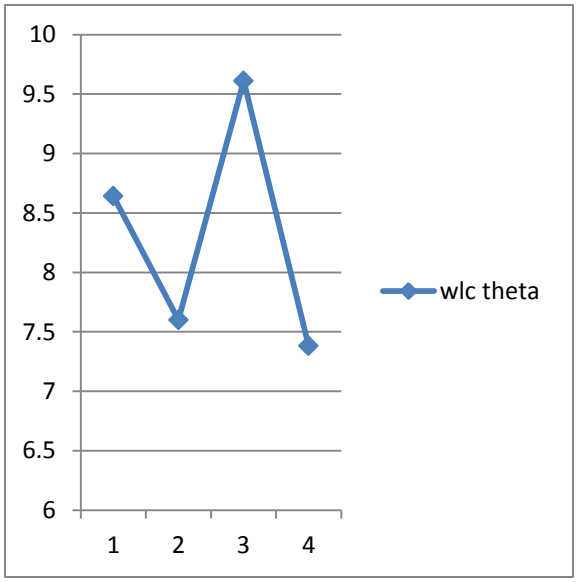
*Table 5. Participant 499's Scores on the FIQR.*

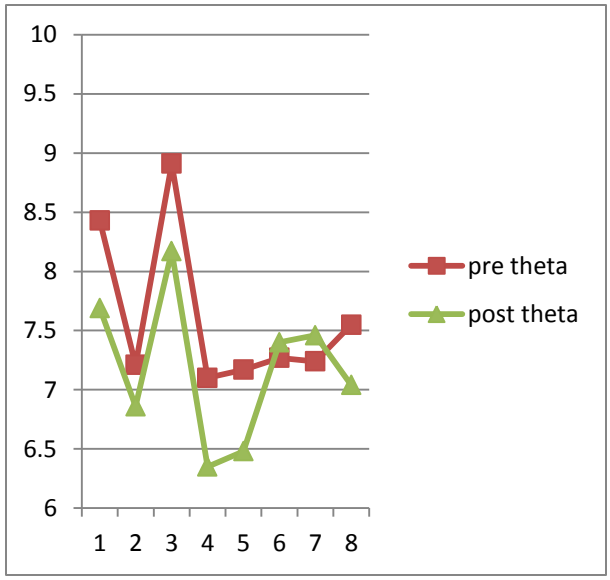
| Session | Raw Score | Quartile range |
|---|---|---|
| 1 (wlc baseline) | 50.67 | Moderate |
| 1 (pre-treatment baseline) | 48.17 | Moderate |
| 3 | 51 | Moderate |
| 7 | 23.33 | Mild |

Participant 499's physical and occupational functioning remained relatively stable while her symptom frequency and severity decreased throughout the course of treatment (see Table 6).

*Table 6. Participant 499's Scores on the MFTQ*

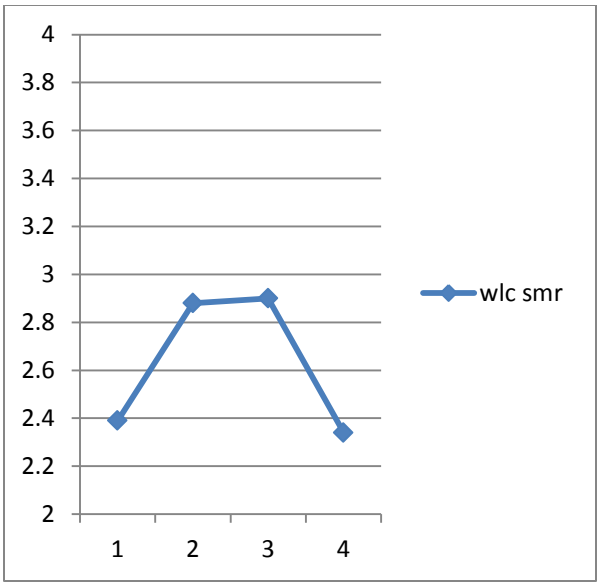
| Session | Physical and Occupational Capacity (0-7) | Symptom Frequency (average) | Symptom Severity (average) |
|---|---|---|---|
| 1 (wlc baseline) | 6 | 1.8 | 45.68 |
| 1 (pre-tx baseline) | 6 | 2 | N/A |
| 3 | 5 | 2.2 | 40 |
| 7 | 6 | 1.4 | 29.09 |

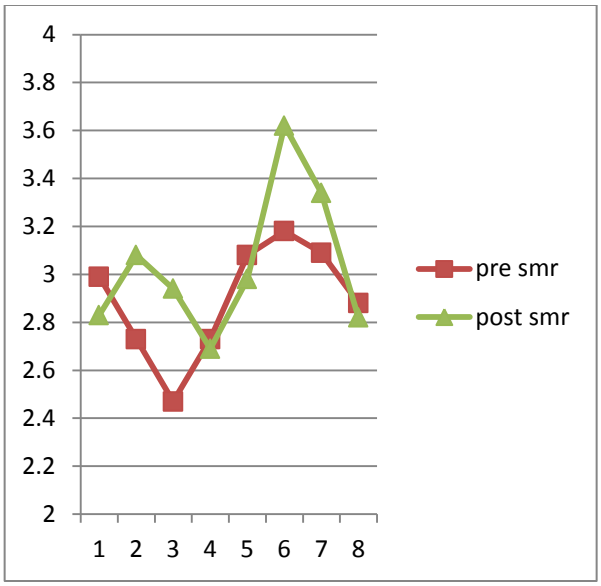



*Figures 29 (left) and 30 (right). Wait-List Control and Sample t-test Data Examining Theta EEG Changes for Participant 499*

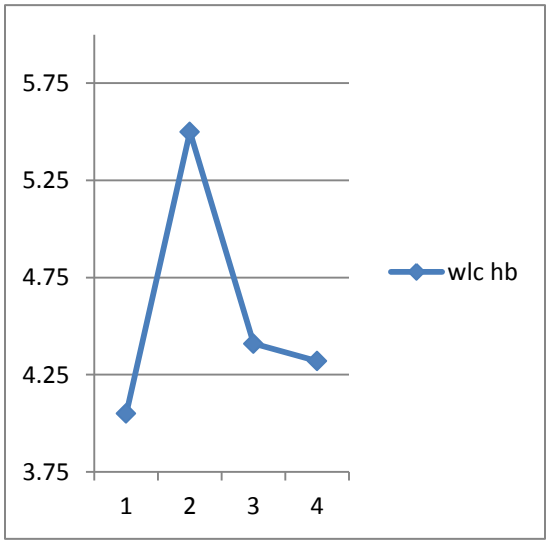
Figure 29 shows a decrease in Participant 499's levels of theta during active-treatment compared to her WLC theta levels.

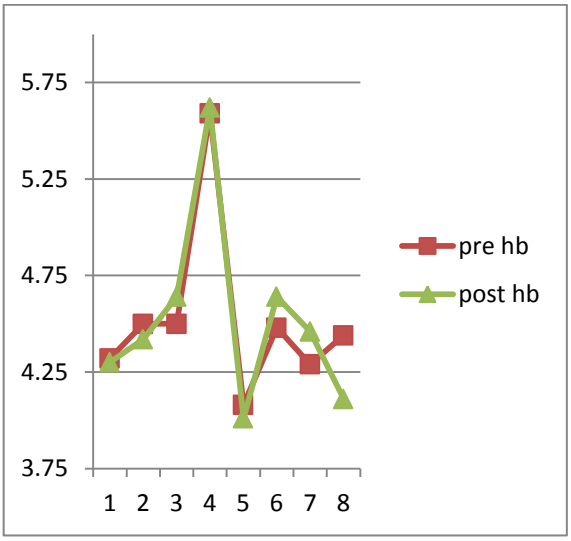



*Figures 31 (left) and 32 (right). Wait-List Control and Sample t-test Data Examining SMR EEG Changes for Participant 499*

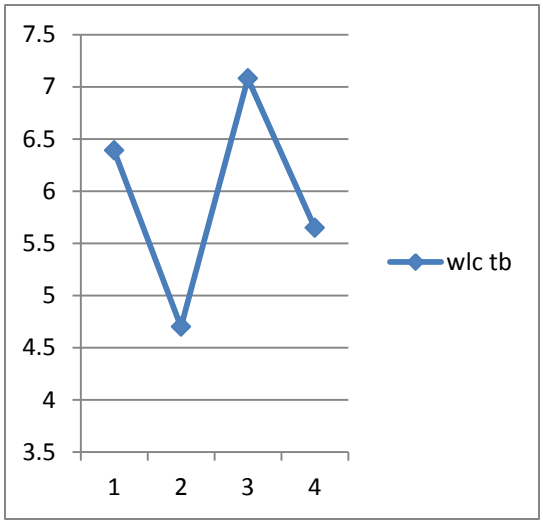
Figures 31 and 32 show an increase in Participant 499's levels of SMR during active-treatment compared to her WLC SMR levels.

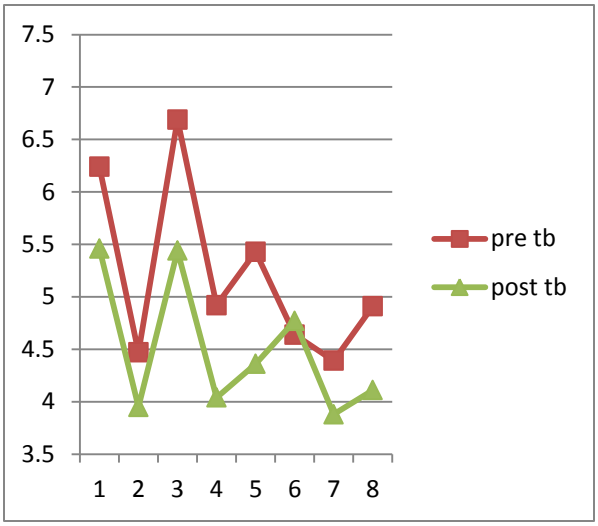



*Figures 33 (left) and 34 (right). Wait-List Control and Sample t-test Data Examining High Beta EEG Changes for Participant 499*

Figures 33 and 34 suggest that Participant 99's levels of high beta do not vary between WLC and active-treatment conditions.




*Figures 35 (left) and 36 (right). Wait-List Control and Sample t-test Data Examining Theta-to-beta Ratio EEG Changes for Participant 499*

Figures 35 and 36 show a marked decrease in her theta-to-beta ratio during active-treatment.

Paired samples t-test revealed significant pre- to post-session changes in the theta-to-beta ratio ($p < .01$) and levels of theta ($p < .05$).

***Debriefing.*** When asked about her experience of neurofeedback and if she found it to be helpful in reducing symptoms of fibromyalgia, Participant 499 replied, "I think the eight weeks of treatment were helpful."

**Participant 793.** Participant 793 is a 50-year-old, married Caucasian female who is employed part time. She reported that she has been experiencing FMS symptoms for 16 years. She reported that she has not been diagnosed with chronic fatigue syndrome. She reports a history of meningitis and encephalitis. She broke her leg during the course of treatment, but continued attending neurofeedback sessions nonetheless. She was randomized to the active

treatment group, has been seen once per week (with the exception of missed sessions), and completed 16 sessions of neurofeedback.

A two-tailed paired sample t-test revealed a significant difference between pre- and post-session VAS reports of fatigue ($p < .01$), but not pain. Graphs representing her pre- and post-session pain and fatigue scores throughout treatment can be seen below.

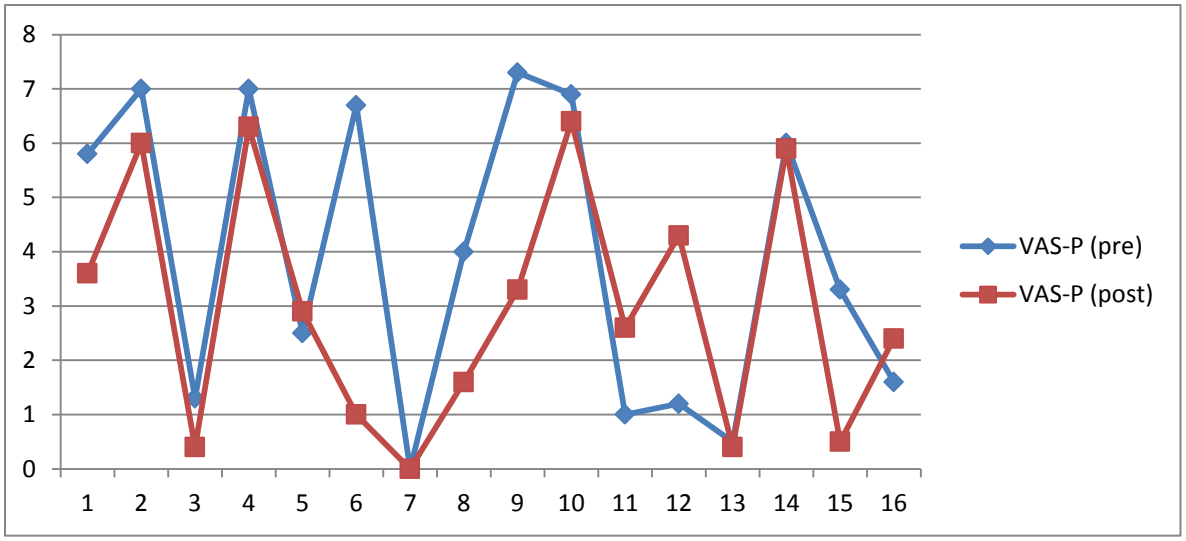



*Figure 37. Participant 793's Pre- and Post-session Reports of Pain on the VAS Scale*

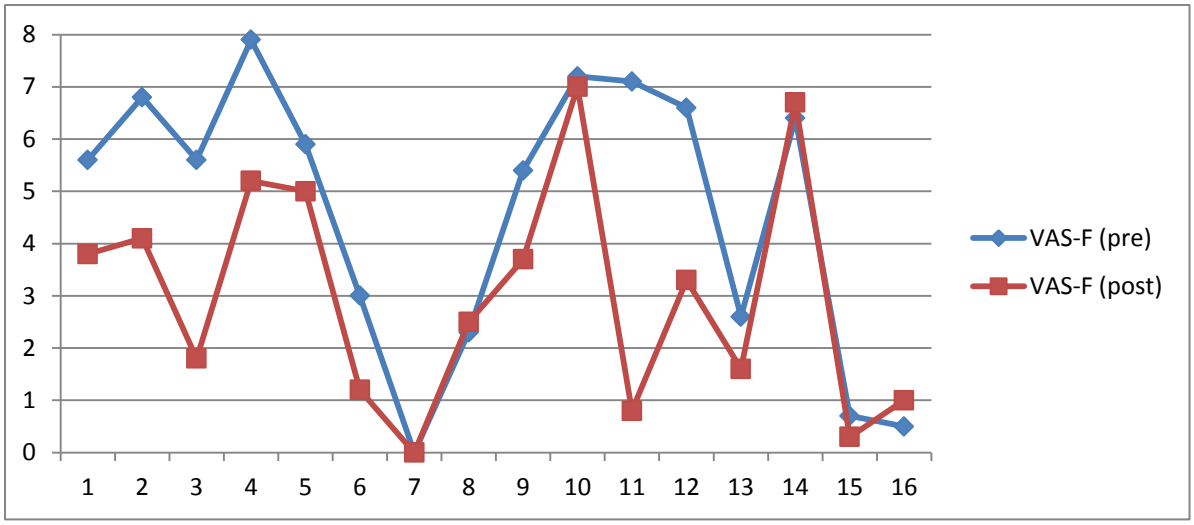



*Figure 38. Participant 793's Pre- and Post-session Reports of Fatigue on the VAS Scale*

The severity of Participant 793's symptoms as measured by the FIQ-R improved from approximately "mild to moderate" to mild throughout the course of treatment (see Table 7).

*Table 7. Participant 793's Scores on the FIQR.*

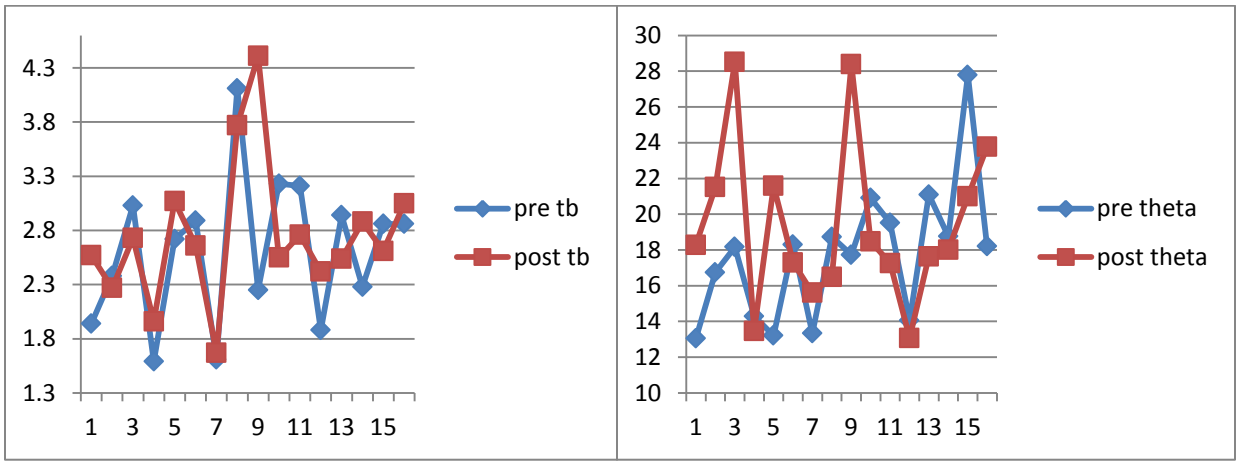
| Session | Raw Score | Quartile Range |
|---|---|---|
| 1 (baseline) | 42.67 | Mild to moderate |
| 3 | 54.17 | Moderate |
| 7 | 35 | Mild |
| 11 | Missing data | Missing data |
| 16 (post-treatment) | 22.3 | Mild |

Her physical and occupational capacity and symptom frequency appeared stable, while her symptom severity decreased throughout the course of treatment (see Table 8).

*Table 8. Participant 793's Scores on the MFTQ*

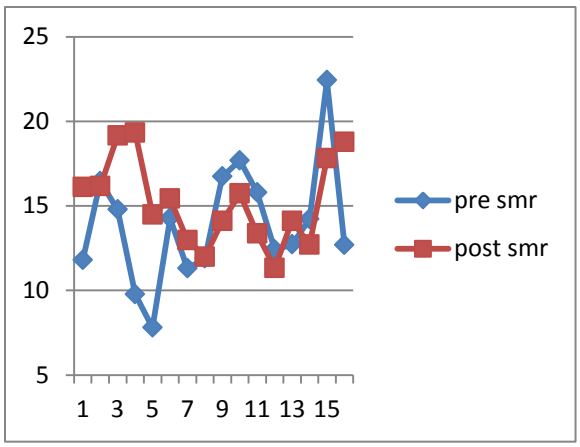
| Session | Phys and Occu Capac (0-7) | Symptom Frequency (ave) | Symptom Severity (ave) |
|---|---|---|---|
| 1 (baseline) | 4 | 1.4 | 52.14 |
| 3 | 4 | 1.4 | 23.18 |
| 7 | 3 | 2 | 30.68 |
| 11 | Missing data | Missing data | Missing data |
| 16 (post-treatment) | 4 | 1.4 | 37.5 |

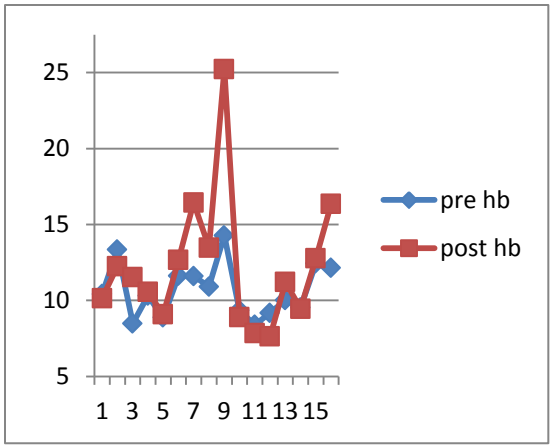
Paired samples t-test revealed no significant pre- to post-session EEG changes for this participant.




*Figures 39 (left) and 40 (right). Sample t-test Data Examining Theta-to-Beta Ratio and Theta EEG Changes for Participant 793*

Figures 39 and 40 show a fairly consistent theta-to-beta ratio, while pre-session levels of theta appeared to increase during the course of treatment.



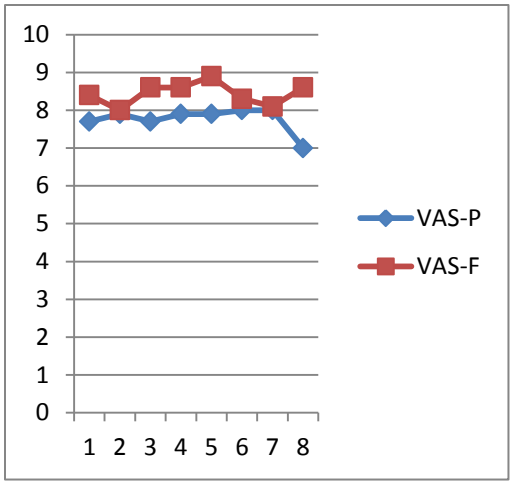



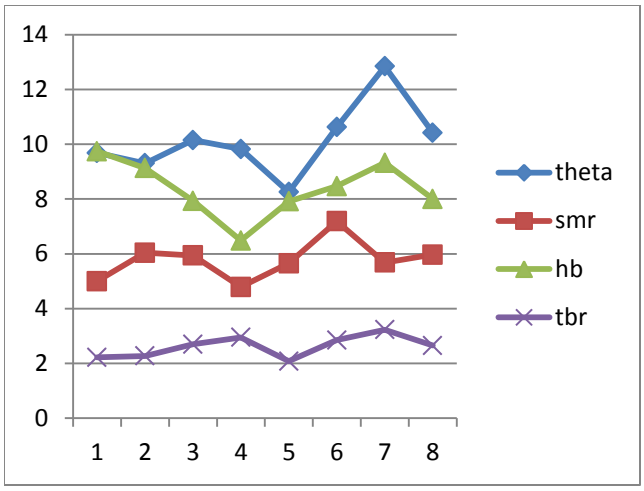

*Figures 41 (left) and 42 (right). Sample t-test Data Examining SMR and High Beta EEG Changes for Participant 793*

Figures 41 and 42 show an increase in pre-session levels of SMR, while high beta appeared fairly consistent during the course of treatment.

***Debriefing.*** When asked about her experience of neurofeedback and if she found it to be helpful in reducing symptoms of fibromyalgia, Participant 793 reported that it decreased her pain, and stated that she wouldn't have attended all the sessions had it not.

**Participant 919.** Participant 919 is a 54-year-old, unmarried Caucasian female who is unemployed. She reported that she has been experiencing FMS symptoms for 34 years. She reported that she has been diagnosed with chronic fatigue syndrome. She was randomized to the WLC condition and subsequently completed 16 sessions of neurofeedback. Graphs displaying her WLC pain and fatigue scores and EEG indices can be seen below.




*Figures 43 (left). Participant 919's Pain and Fatigue Scores During the Wait-list Control Period. Figure 44 (right). Participant 919's EEG Indices During the Wait-List Control Period.*

Figure shows fairly consistent levels of pain and fatigue during the wait-list control period. Figure 28 shows fairly consistent EEG indices with the exception of a theta increase.

A two-tailed paired sample t-test revealed a nonsignificant difference between pre- and post-session VAS reports of pain and fatigue. Graphs representing her pre- and post-session pain and fatigue scores throughout treatment can be seen below.

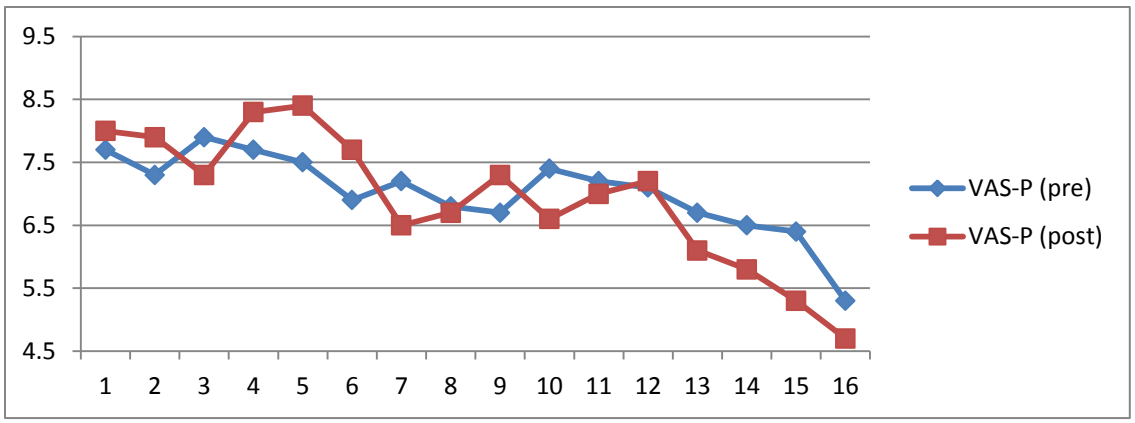



*Figure 45. Participant 919's Pre- and Post-session Reports of Pain on the VAS Scale*

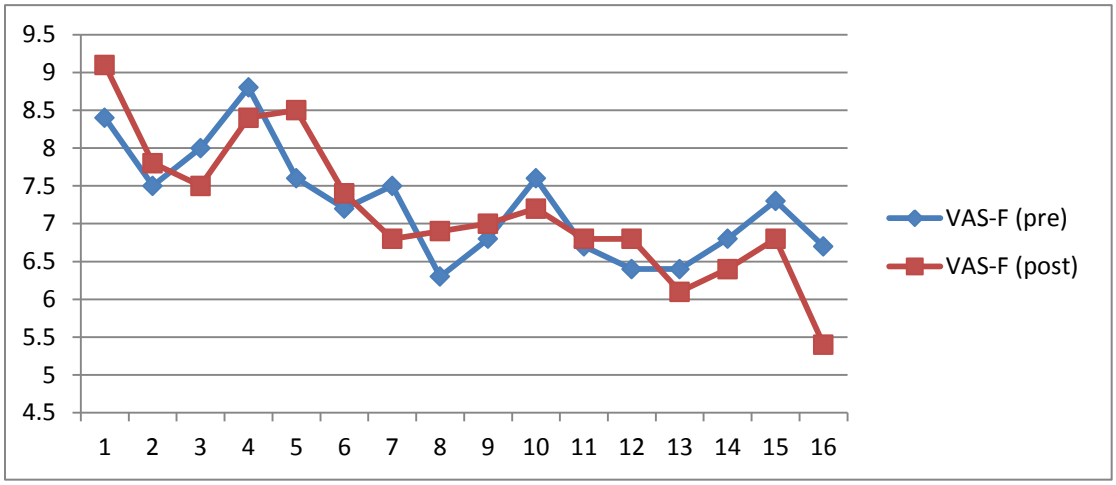



*Figure 46. Participant's 919 Pre- and Post-session Reports of Fatigue on the VAS Scale*

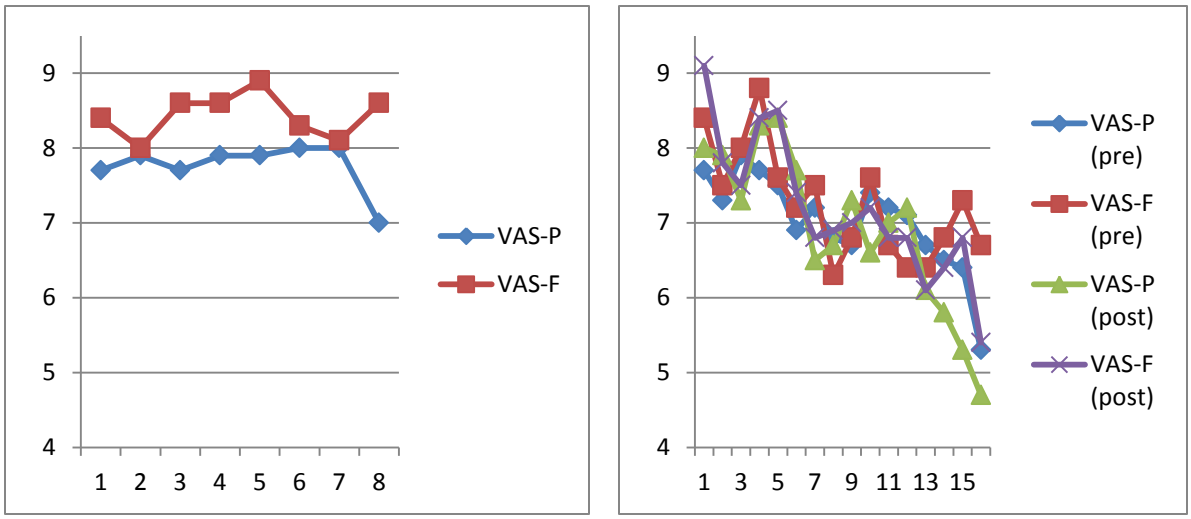



*Figure 47. Side-by-side Comparison of Participant 919's WLC VAS Scores (left) and Active-treatment Scores (right).*

The severity of Participant 919's symptoms as measured by the FIQ-R improved from extreme to severe (moderate = 43 – 59) throughout the course of treatment (see Table 9).

*Table 9. Participant 919's Scores on the FIQR*

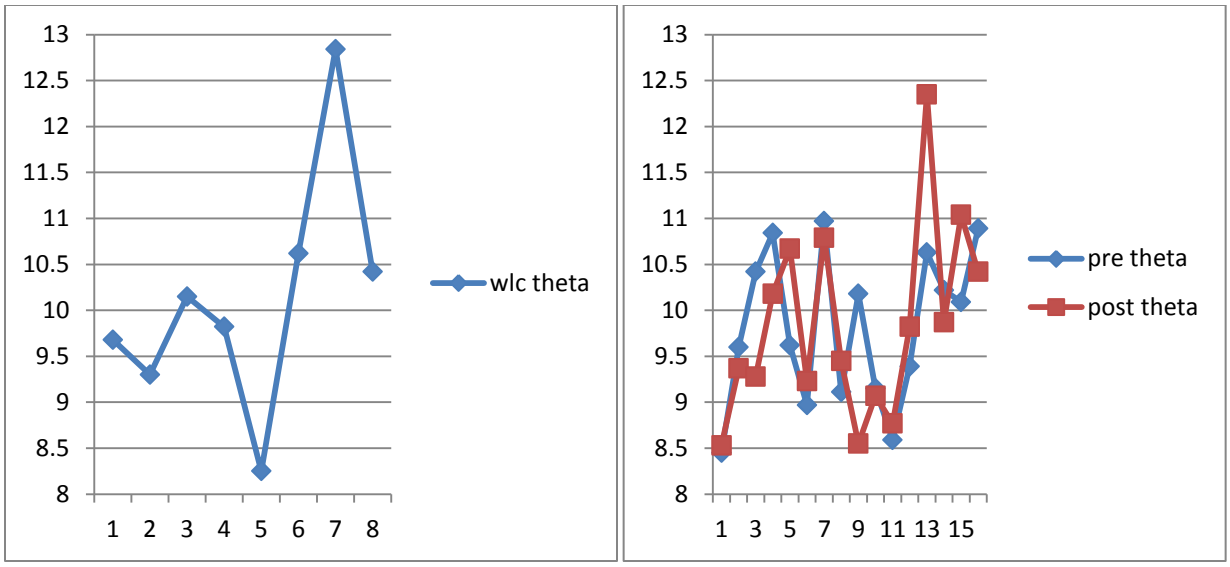
| Session | Raw Score | Quartile Range |
|---|---|---|
| 1 (baseline WLC) | 85.3 | Extreme |
| 1 (baseline tx) | 81.5 | Extreme |
| 3 | 85.5 | Extreme |
| 7 | 80.7 | Extreme |
| 11 | 73.17 | Severe |
| 16 (post-treatment) | 60.8 | Severe |

Participant 919's physical and occupational capacity and symptom frequency appeared stable, while her symptom frequency decreased throughout the course of treatment. Symptom severity could not be assessed due to missing data (see Table 10).

*Table 10. Participant 919's Scores on the MFTQ*

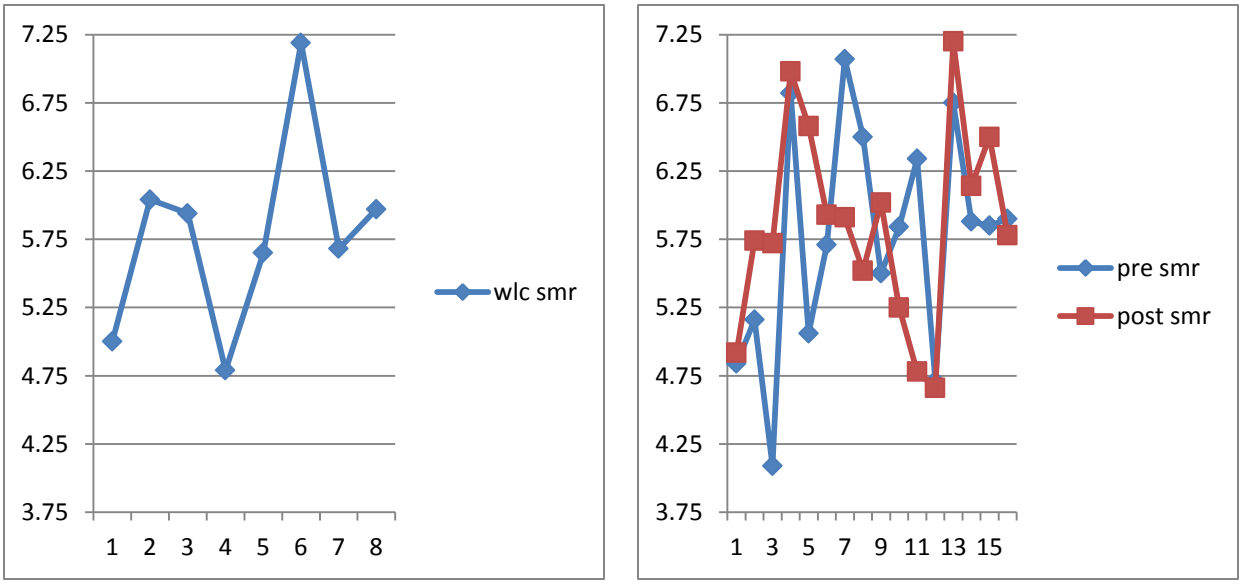
| Session | Physical and Occupational Capacity (0-7) | Symptom Frequency (average) | Symptom Severity (average) |
|---|---|---|---|
| 1 (baseline WLC) | 3 | 3 | 73.86 |
| 1 (baseline tx) | 3 | 2.7 | 57.91 |
| 3 | Missing data | 3.1 | 78.86 |
| 7 | Missing data | Missing data | Missing data |
| 11 | 3 | 2.7 | Missing data |
| 16 (post-treatment) | Missing data | 1.6 | Missing data |

Paired samples t-tests revealed significant a pre- to post-session increases in high beta ($p < .01$).



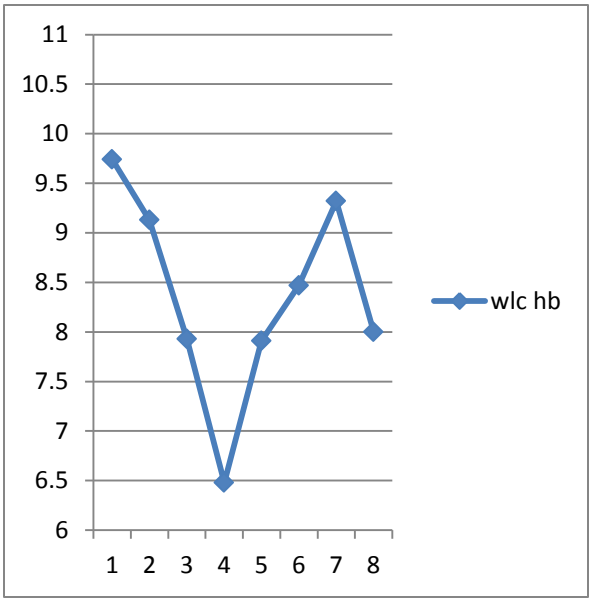

*Figures 48 (left) and 49 (right). Wait-List Control and Sample t-test Data Examining Theta EEG Changes for Participant 919*

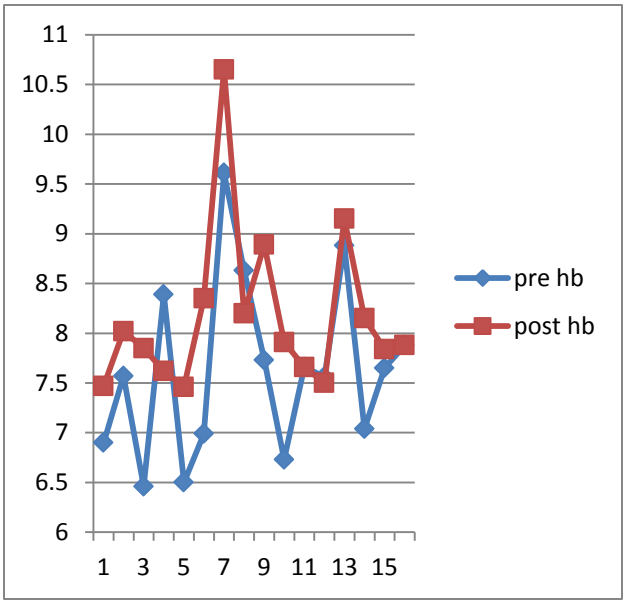
Figures 48 and 49 suggest that Participant 919's levels of theta do not vary between the wlc and active-treatment periods.




*Figures 50 (left) and 51 (right). Wait-List Control and Sample t-test Data Examining SMR EEG Changes for Participant 919*

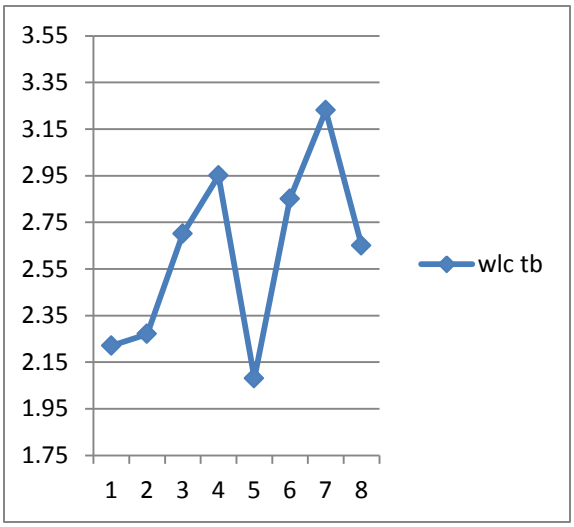
Figures 50 and 51 suggest that the Participant 919's levels of SMR do not vary between the wlc and active-treatment periods.

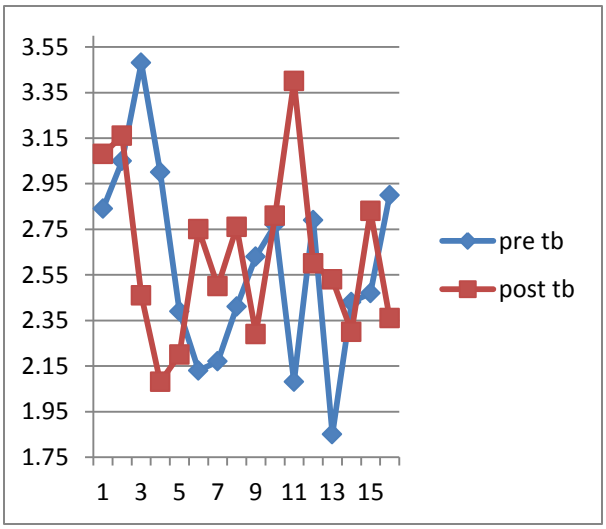



*Figures 52 (left) and 53 (right). Wait-List Control and Sample t-test Data Examining High Beta EEG Changes for Participant 919*

Figures 52 and 53 suggest that her levels of high beta do not vary between the wlc and active treatment periods.




*Figures 54 (left) and 55 (right). Wait-List Control and Sample t-test Data Examining Theta-to-Beta Ratio EEG Changes for Participant 919*

Figures 54 and 55 suggest that Participant 919's theta-to-beta ratio levels do not vary between the WLC and active-treatment periods.

***Debriefing.*** When asked about her experience of neurofeedback and if she found it to be helpful in reducing symptoms of fibromyalgia, Participant 919 replied:

> It helped more than I expected. My pain level and neck problems are now much lower. After eight sessions I saw stability; my pain was ridiculous. My chiropractic adjustments became less painful and the chiropractor was surprised how well I began holding adjustments. I've had 20 years of continuous chiropractic treatment so I could notice the difference and am positive it was due to the neurofeedback. My brain is clearer, my sight is better, and my reasoning is improved. I can now express my emotions verbally and didn't expect this to happen. I feel that two sessions per week, every other week, would've been better for me. It helped my anxiety, my sleep improved, and was shocked at how much relief I got so quickly. I don't understand why it's not used more. I didn't expect the level of effort it would require. At first it took every bit of my energy, but it became easier and I started experiencing small changes. At the end it was easy.

## Summary of Results

Two of the five participants had a significant difference in their pre- to post-VAS levels of pain on the paired samples t-test, and three participants had a significant difference in their pre- to post-VAS levels of fatigue on the paired samples t-test. All of the participants' reports of pain and fatigue on the VAS scales showed visible decreases during the course of treatment and when compared to the WLC condition. All participants improved on their FIQR scores (average point reduction from baseline = 18.12). Only one participant reported an improvement in their level of physical and occupational functioning on the MFTQ. Three participants reported a reduction in their symptom frequency on the MFTQ and one participant reported an increase in her frequency of symptoms. Three participants reported a reduction in their symptom intensity on the MFTQ, and one participant reported an increase in her symptom intensity. Three participants had a significant difference in one or more of their pre- to post-session EEG indices on the paired samples t-test; however, this finding should be interpreted with caution, as it is not

known whether these changes are beneficial because they were not compared with norms. One or more of the EEG indices of all participants showed visible EEG changes during the course of their treatment, but this finding should also be interpreted with caution.

*Table 11. Summary of Participants' averaged Pre- and Post-assessment Scores*

| | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|
| FIQR | 42.67 | 85.30 | 61.3620 | 16.77514 |
| VAS_P | 3.60 | 7.80 | 5.2600 | 1.67272 |
| VAS_F | 5.50 | 8.30 | 6.9400 | 1.15888 |
| Phys_and_Occ | 2.00 | 6.00 | 4.0000 | 1.58114 |
| Sx_freq | 1.20 | 3.30 | 2.1400 | .95289 |
| Sx_sev | 40.90 | 87.40 | 59.9960 | 19.84006 |
| | Minimum | Maximum | Mean | Std. Deviation |
| FIQR | 22.30 | 68.50 | 43.2460 | 21.12508 |
| VAS_P | 2.50 | 5.30 | 3.3000 | 1.13358 |
| VAS_F | 2.20 | 6.50 | 4.1600 | 2.03298 |
| Phys_and_Occ | 4.00 | 6.00 | 4.7500 | .95743 |
| Sx_freq | 1.40 | 2.70 | 1.8600 | .57271 |
| Sx_sev | 29.09 | 75.00 | 49.3175 | 20.40325 |

Pre-assessment scores are featured on the top level, and post-assessment scores are featured on the bottom level. VAS pain and fatigue scores were calculated by averaging the first and last three pre- and post-session scores.

*Table 12. Summary of the Results from Each Participant*

| **Partic-ipant #** | **Signif pre-post session VAS-P (t-test)** | **Signif pre-post session VAS-F (t-test)** | **VAS-P decreases pre-post tx** | **VAS-F decreases pre-post tx** | **FIQ-R Point Reduc** | **Phys and Occu Funt +** | **MFTQ Sx Freq Reduc** | **MFTQ Sx Intens Reduc** | **Signif pre-post session EEG changes (t-test)** | **Signif pre-post tx EEG changes (trends)** |
|---|---|---|---|---|---|---|---|---|---|---|
| 407 | N | Y | Y (3.5) | Y (5.1) | 1.67 | Y | 0.6 | 12.4 | N | Y |
| 561 | Y | Y | Y (1.2) | Y (1.1) | 16.7 | N | +1 | +14.8 | Y | Y |
| 499 | Y | N | Y (0.8) | Y (2.3) | 27.34 | N | 0.4 | 16.6 | Y | Y |
| 793 | N | Y | Y (1.8) | Y (3.3) | 20.37 | N | 0 | 14.6 | N | Y |
| 919 | N | N | Y (2.5) | Y (2.1) | 24.5 | N | 1.4 | N/A | Y | N |

The 1st column identifies each participant by their numerical code; the 2nd and 3rd columns show whether there were significant pre-post session pain and fatigue findings on the paired samples t-test (Y = yes, N = no); the 4th and 5th columns show whether pain and fatigue scores decreased during the course of treatment based on visual inspection of linegraphs, and the number in the parentheses indicates the difference between the last three values (averaged) and the first three (also averaged); the 6th column shows the difference between each participant's baseline and post-treatment FIQR score (that is, baseline minus post-treatment); the 7th column shows whether each participant indicated an increase in their level of physical and occupational functioning on the MFTQ; the 8th column shows the difference between each participant's baseline and post-treatment symptom frequency score on the MFTQ (that is, baseline minus post-treatment); the 9th column shows the difference between each participant's baseline and post-treatment symptom intensity score on the MFTQ (that is, baseline minus post-treatment); the 10th column shows whether there were significant pre-post session EEG findings on the paired samples t-test; the 11th column shows whether EEG indices changed during the course of treatment.

# Chapter 6: Discussion

## Implications

In addition to the three existing studies on SMR neurofeedback for fibromyalgia, the current study offers further evidence that SMR neurofeedback can be a helpful adjunctive treatment for individuals diagnosed with fibromyalgia. In the current study, all participants showed improvements in subjective ratings of pain and fatigue throughout the course of treatment, decreased their FIQR scores, exhibited changes on EEG indices, and reported being satisfied with the treatment. The majority of participants experienced improvements on symptom frequency and intensity on the MFTQ, had significant pre-post session decreases in fatigue (assessed via a paired-samples t-test), and had pre-post session changes on one or more EEG indices (also assessed with a paired-samples t-test). VAS pain and fatigue scores and EEG indices appeared to change when participants completed their wait-list control condition and entered active treatment, which offers evidence that SMR neurofeedback had an additional therapeutic impact when compared to other concurrent treatments being received by participants. These positive findings are consistent with the results of the three existing studies on SMR neurofeedback for fibromyalgia, and offers additional support for using this treatment for individuals with fibromyalgia. This warrants further studies of SMR neurofeedback as a treatment for fibromyalgia.

**Limitations**

Although these findings appear promising in several respects, this study had numerous limitations which should be taken into account when interpreting its findings. This study had a small N, which prevented the use of many statistical tests and limited its generalizability to individuals diagnosed with FMS. It lacked an adequate control group (that is, only three of the five participants completed a wait-list control condition) and did not control for the placebo-effect through the use of a sham-feedback control (that is, giving participants feedback based on another individuals EEG activity rather than their own EEG activity). Thus, the positive outcomes of this study may be due to the placebo effect, a desire to please the experimenter, or other non-specific effects such as remaining in a seated position and focusing one's attention for a sustained period of time.

It is not known if this study's positive outcomes were due to the beneficial effects of other concurrent treatments, as this variable was not measured throughout treatment. Neither is it known if the beneficial effects of SMR neurofeedback were sustained after treatment ended due to the lack of follow up. Lastly, like the existing SMR neurofeedback studies for fibromyalgia, this study did not utilize normative EEG software. Thus, it is ultimately unknown whether changes in the observed EEG indices were beneficial in "normalizing" EEG activity (that is, training EEG to be more normative relative to age and gender-matched normative databases) or was detrimental (that is, training it away from the norm).

Although this study had several limitations deserving mention and elaboration, several of these limitations can be addressed in a practical manner. Studies with relatively small sample sizes are common in the neurofeedback literature due to the complexity of the treatment (for

example, the formal training required to administer neurofeedback treatment, operate the software, adjust to software difficulties and unforeseen clinical situations, and so forth), the level of commitment required by participants (one can contrast engaging in numerous 30 to 45 minute sessions that require effort versus simply taking a medication in a drug trial), the relative lack of funding of neurofeedback research, and so forth. Furthermore, although small sample sizes limit generalizability to some degree, relatively larger sample sizes with stringent inclusion and exclusion criteria can also limit generalizability by excluding participants who are representative of individuals with fibromyalgia (such as excluding individuals with comorbid medical and psychiatric diagnoses). This may potentially lead to studies only accepting more "mild" cases of fibromyalgia (Holman, 2007).

Although a placebo-controlled protocol was not utilized in this current study, it should be noted that such research designs are being used with greater frequency, and have shown significant differences between placebo and active-treatment groups (Ros et al., 2013), but nonetheless have drawbacks. For example, participants in the placebo group receiving sham feedback may become aware that the feedback is not of their own EEG activity. In addition, the experimenter may become unblinded in double-blind neurofeedback studies if he or she notices the participant is behaving in a manner not congruent with their EEG activity. The use of a wait-list control period offered some evidence that the positive findings of this study were not due to concurrent treatments. Pain and fatigue scores appeared fairly consistent or otherwise actually increased during wait-list control periods, whereas EEG indices appeared fairly consistent overall. Once participants entered the active phase of treatment, their VAS pain and fatigue reports began to improve and their EEG indices began to change. Lastly, although it is not

known whether the positive findings of this study were sustained after the final neurofeedback session, results of the 2010 study by Kayiran et al., which demonstrated sustained improvements at a 5-month follow-up, suggest that this possibility is likely.

**Directions for Future Research**

With the inclusion of the current study, four studies on SMR neurofeedback for fibromyalgia have demonstrated positive findings, which suggests that SMR neurofeedback can significantly reduce the symptoms of Fibromyalgia either through direct (that is, by teaching individuals how to modify and improve their EEG activity through visual and auditory feedback of SMR, theta, and high beta) or indirect (that is, the placebo effect, cultivating a therapeutic relationship, learning to sit and/or sustain one's attention for a prolonged prior of time, and so forth) means. Future research may utilize a SMR protocol with a placebo-control group, which would help differentiate therapeutic effects resulting from direct and indirect sources.

Neurofeedback research may significantly benefit from the use of modern protocols based on normative databases and EEG source localization techniques (Arns & De Ridder, 2011). Rather than training the cortical amplitude fluctuations at one or several 10-20 sites, as in traditional forms of neurofeedback such as SMR and Alpha-Theta training, contemporary forms of neurofeedback, such as 19-channel LORETA z-score training, can train the deep cortical sources of EEG dysfunction (such as the anterior cingulate cortex, the insula, and so forth) by utilizing nineteen 10-20 scalp sites and comparing the individual's "global" EEG activity to age and gender-matched norms, while reinforcing normalization of the EEG (that is, being reinforced when EEG parameters are within one or two standard deviations of the norm). This form of

neurofeedback has been utilized in the pain literature and has been reported to result in significant therapeutic gains in the context of short-term (ten sessions or less) treatment (Koberda et al., 2013). Furthermore, through the use of quantitative EEG norms, modern neurofeedback approaches offer researchers greater capacities for measurement, intervention, and statistical analysis of the data. Proponents of modern neurofeedback approaches will have to conduct head-to-head studies against traditional protocols to determine if these novel and normative methods should completely replace amplitude-based training at one or several scalp sites (as is commonly used).

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