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Final dissertation

Title: Neurofeedback and its clinical application in the treatment of fibromyalgia

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Homo sum; humani nil a me
alienum puto:
I am a human being;
I consider nothing human alien to me

Terence

To my Grandmother, to my Parents,
To my Sisters.

CONTENTS

INTRODUCTION

Fibromyalgia Syndrome (FMS) has come a long way since its symptoms were first described and published in the medical literature. As it was in the past, also today, this widespread, poly symptomatic disease, is a difficult subject to understand, and even more difficult to treat properly. Different pharmacological and behavioral treatments have been tested and used in an attempt to improve the conditions of those who live with the symptoms of FMS. Science makes progress on a mission to maintain its great purpose, and to find answers to treat different medical conditions. An example of an answer to treat FMS symptoms is Neurofeedback, a specific application of Biofeedback. Biofeedback is a technique that allows people to learn to control physiological functions that are usually out of voluntary control (e.g., functions controlled by the Autonomic Nervous System) with particular emphasis on how the body influences the mind and vice versa. New frontiers in research have occupied themselves with the studies on the effectiveness of Neurofeedback and Biofeedback in alleviating symptoms of FMS, as an alternative to traditional pharmacological therapy. This application is aiming at making the individual self-aware, and teach them how to listen and check themselves in body-mind-brain integration. Present work will explore more in detail what Fibromyalgia Syndrome is, how the diagnosis was developed, what is and how Bio/Neurofeedback works, how it can be used, and what outcomes it has in the treatment of Fibromyalgia symptoms.

CHAPTER 1

FIBROMYALGIA

In this chapter, Fibromyalgia Syndrome will be discussed. It is important to present the description of the condition, the development of the diagnosis, and where it stands now. What is it characterized with from both mental and physical points of view, what is the symptomatology related to this syndrome, and how it affects the life of the patient suffering from it.

1.1.WHAT IS FIBROMYALGIA?

Fibromyalgia is a life-long but not deadly chronic pain illness, with pain as its main and distinguishing feature. It is an acquired systemic disorder of uncertain etiology characterized by complex poly symptomatology that comprises a wide range of symptoms, including fatigue, exhaustion, sleep difficulties, cognitive implications such as reduced attention processing and semantic memory ability, depressive episodes, and functional symptoms (that is, medical symptoms not explained by structural or pathologically defined causes; Bennett et al., 2007;Park et al., 2001;Sarzi-Puttini et al., 2020).

Clinical overlap and connection between fibromyalgia and other comparable illnesses and symptoms such as irritable bowel syndrome (IBS), primary dysmenorrhea syndrome (PDS), primary fibromyalgia syndrome (PFS) and tension-type headache (THS) is quite common. There were also statistical correlations between them and their occurrence in the same patient. Muscle spasm was hypothesized as the common pathophysiologic link between them (Yunus, 1984; see Figure 1.1).

Although patients may only encounter one of these pain syndromes in their lives, according to different studies of patients suffering from fibromyalgia symptoms and their family members, they are more likely to be affected by several of these interrelated illnesses (Arnold et al., 2004; Hudson et al., 2004).

As reported in research by Bondy et al. (1999), females made up the majority of fibromyalgia patients (84.5%). The duration of the fibromyalgia symptoms ranged from 1 to 27 years, while the age of onset ranged from 18 to 74 years with a mean of 45,3 and a standard deviation (SD) of 11,8 (Bondy et al., 1999).

Due to a low understanding of symptoms, and limitations in medical and technological evaluations, leading to non appropriate diagnostic criteria and policies for fibromyalgia and other idiopathic pain syndromes were all on shaky scientific basis until about a decade ago. However, breakthroughs in experimental pain testing, functional imaging, and genetics have led to great advances in the knowledge of these disorders, including fibromyalgia, IBS, and TMD, in a relatively short period of time (Clauw, 2009).

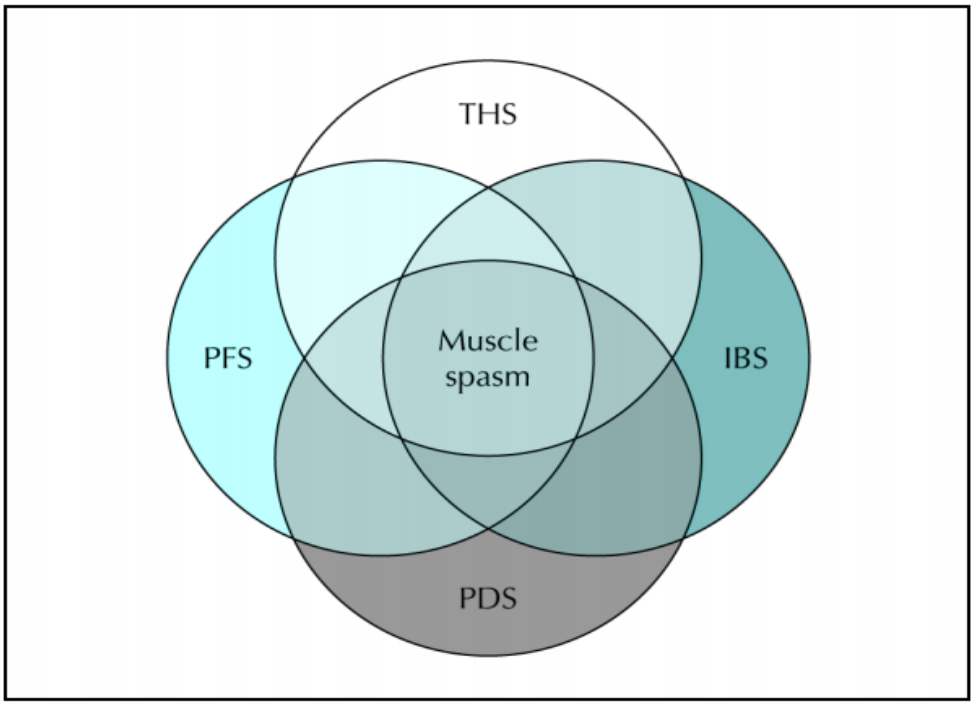

Figure 1.1 The graph displays clinical overlaps and connection between fibromyalgia and other comparable illnesses. There were also statistical correlations between them and their occurrence in the same patient. Muscle spasm was hypothesized as the common pathophysiological link between them. IBS = irritable bowel syndrome; PDS = primary dysmenorrhea syndrome; PFS = primary fibromyalgia syndrome; and THS = tension-type headache (Yunus, 1984).

1.2 HISTORICAL PERSPECTIVE OF FIBROMYALGIA

Despite the fact that the name "fibromyalgia" is new, this ailment has been documented in medical literature for decades, as a matter of fact, in 1904, Sir William Gowers invented the name "fibrositis" (Clauw, 2009). During the next half-century, fibrositis was seen to be a common cause of muscular pain by some, a sign of "tension" or "psychogenic rheumatism" by others, and a nonentity by the rheumatology community at large. Smythe and Moldofsky created the modern

notion of fibromyalgia in the mid-1970s, with the new word "fibromyalgia" reflecting greater evidence that this ailment is a pain condition ("-algia") rather than connective tissue inflammation ("-itis"; Clauw, 2009).

In 1990 the American College of Rheumatology (ACR) brought the official criteria for recognition of fibromyalgia (see figure 1.2; Wolfe et al., 1990). Before this happened, the condition was disregarded and ignored by both the National Institutes of Health (NIH), and also by physicians, and organized medicine in general (Wolfe & Häuser, 2011).

In the years that followed ACR's criteria validation, fibromyalgia received a code within the International Classification of Disease (ICD), an international acknowledgment as a source of disability and academic recognition (Wolfe & Häuser, 2011). Acceptance of the ACR criteria went a long way toward legitimizing the condition, then, patient groups formed all over the place and multiplied, and political pressure on behalf of persons affected by fibromyalgia constantly grew (Wolfe & Häuser, 2011). Since then, the number of scientific investigations into the causes of fibromyalgia has increased, and the pharmaceutical business provided large dissemination of information to the general public, as well as funding for pro-fibromyalgia educational and political initiatives, with the approval of medications for the treatment of fibromyalgia (Wolfe & Häuser, 2011). All these phenomena led to the situation in which fibromyalgia has grown from a few clinical observations to become one of the most recognized pain and rheumatic disorders in 25 years (Wolfe & Häuser, 2011).

1. History of widespread pain.

   Definition. Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved side. "Low back" pain is considered lower segment pain.

2. Pain in 11 of 18 tender point sites on digital palpation.

   Definition. Pain, on digital palpation, must be present in at least 11 of the following 18 tender point sites:
   Occiput: bilateral, at the suboccipital muscle insertions.
   Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5–C7.
   Trapezius: bilateral, at the midpoint of the upper border.
   Supraspinatus: bilateral, at origins, above the scapula spine near the medial border.
   Second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces.
   Lateral epicondyle: bilateral, 2 cm distal to the epicondyles.
   Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle.
   Greater trochanter: bilateral, posterior to the trochanteric prominence.
   Knee: bilateral, at the medial fat pad proximal to the joint line.

   Digital palpation should be performed with an approximate force of 4 kg.
   For a tender point to be considered "positive" the subject must state that the palpation was painful. "Tender" is not to be considered "painful."

* For classification purposes, patients will be said to have fibromyalgia if both criteria are satisfied. Widespread pain must have been present for at least 3 months. The presence of a second clinical disorder does not exclude the diagnosis of fibromyalgia.

Figure 1.2 The 1990 American College of Rheumatology criteria for the classification of fibromyalgia (Wolfe et al., 1990).

The ACR classification criteria were designed on one hand to standardize fibromyalgia definition for research purposes, and they have proven to be extremely useful in this regard (Clauw, 2009). The criteria for diagnosing fibromyalgia in 1990 were based mostly on a physical examination of tender points. Specifically, tender points were classified as pre-specified locations on the body that were particularly sensitive to pressure in people with fibromyalgia. These criteria also required the presence of widespread pain for a period longer than three months, as well as disrupted sleep with morning fatigue and stiffness.

The tender points examination raised a number of practical difficulties. First, in the 20 years since the 1990 criteria were published, it became obvious that the tender points assessment was frequently conducted wrongly or not at all by generalists. Without considerable expertise, it was particularly difficult to assess the cervical spine's painful spots accurately. Second, not only was 4 kg of force rarely observed during the ACR criteria study but measuring force exerted in clinical practice was nearly impossible. Overall, the tender points examination proved unreliable. Efforts to improve tender points standardization were made, but they were only acceptable in research situations (Wolfe & Häuser, 2011).

Having all this in mind, it was clear that there was a need for revised diagnostic criteria, which finally happened.

In 2010 ACR published a new revised preliminary diagnostic criteria for fibromyalgia that relied solely on two scales: the Widespread Pain Index (WPI) and the Symptom Severity (SS) Scale. (Galvez-Sanchez & Reyes Del Paso, 2020). The WPI is made up of 19 different painful locations (score range: 0–19; see Figure 1.3). Patients are asked if each spot hurts them. The SS is divided into two sections: the level of weariness, waking unrefreshed, and cognitive problems are assessed in Part SS2a (on a 4-point Likert scale; 0 to 3). Part SS2b is a 41-symptoms checklist (irritable bowel syndrome, fatigue/tiredness, muscle weakness, Raynaud's syndrome, ringing in the ears, etc). Patients must indicate whether or not they are experiencing these symptoms. Patients are assigned to one of four score ranges based on the number of symptoms they report: 0 symptoms (score 0), 1 to 10 symptoms (score 1), 11 to 24 symptoms (scoring 2), and 25 or more symptoms (score of 3). The sum of the outcomes of components SS2a (score range: 0 to 9) and SS2b (score range: 0–3) yields the total score SS (score range: 0–12). One of these two conditions must be met to diagnose FMS: a WPI of 7 and SS of 5, or a WPI of 3 to 4 and SS of 9. Symptoms must be

present for at least three months, just like in the 1990 criterion. A physician's assessment is always required by the 2010 criteria, and patient self-report should never be used in place of it.

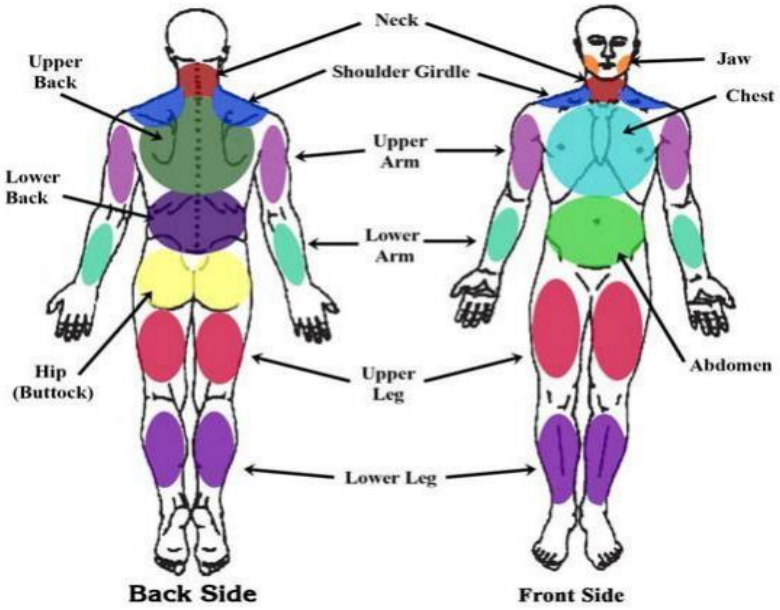

Figure 1.3 Body areas included in the Widespread Pain Index (WPI) scale of 2010 FMS ACR diagnostic criteria (Wolfe et al., 2010).

Despite the fact that there have been more revisions, such as:

- 2011 revision and modification of 2010 diagnostic criteria (Wolfe et al., 2011) that included the Polysymptomatic Distress Scale (PDS) (Wolfe et al., 2011)
- 2016 systematic review of 2010 and 2011 criteria (Wolfe et al., 2016), only the 1990 and 2010 criteria have been officially recognized by ACR (Galvez-Sanchez & Reyes Del Paso, 2020).

1.3 ETIOLOGY OF FIBROMYALGIA

1.3.1 Genetic factors

In research from Arnold et al. (2004) it was reported that fibromyalgia has a strong familial component, with first-degree relatives of fibromyalgia patients having an 8-fold higher risk of developing the condition compared to the general population (Clauw, 2009). According to recent

studies it was identified that there is an alteration in metabolism of neurotransmitters that are likely to play a role in an individual's pain and sensory processing. To be more specific, polymorphisms in genes encoding serotonin and dopamine receptors have been observed at elevated frequencies in individuals with fibromyalgia.

1.3.2 Environmental factors

It is well known that for most health problems, if there is a genetic factor for the disease onset, environmental factors play a great role in triggering the actual illness. In fibromyalgia, a physical trauma (particularly involving the trunk), certain infections, and emotional stress can all be related to the development of fibromyalgia (Clauw, 2009). Even though these stressors lead to chronic pain or fibromyalgia in approximately 5% to 10% of individuals that are affected, a great majority of individuals regain their baseline of health after these experiences. Some “stressors” capable of triggering fibromyalgia and related conditions are peripheral pain syndromes, infections (e.g., parvovirus, epstein-Barr virus, Lyme disease, Q fever), physical trauma (e.g., automobile accidents), psychological stress/distress, hormonal alterations (e.g., hypothyroidism), drugs, vaccines, certain catastrophic events (war, but not natural disasters).

Being exposed to a variety of stressors at the same time or over a period of time may increase the likelihood of eventual somatic symptoms and/or psychological consequences. According to animal research (Chrousos, 1992), reaction to stress depends on the type of the stress and the setting in which it happens following that the biggest physiologic responses are generated by experiences that are accompanied by a lack of control or support and are viewed as inescapable or unavoidable.

1.4 TREATMENT AND PROGNOSIS: generalities

The FMS literature has significant flaws, with many therapy trials being hampered by short duration and a lack of masking. The US Food and Drug Administration has not expressly approved any medical therapy for the treatment of FMS. Despite this, evidence suggests that low-dose tricyclic antidepressants, cardiovascular exercise, cognitive behavioral therapy, and patient education are all effective. Other regularly used FMS treatments, such as trigger point injections, have not been thoroughly studied (Goldenberg et al., 2005). Treatments can be seen in Table 1.1 and Table 1.2. Active fibromyalgia treatments aim to retrain the brain and nervous system to

become less responsive (Bair & Krebs, 2000). Medications are frequently used to help with symptom relief. In conclusion, to address various symptoms of fibromyalgia, most people require a combination of treatments.

Table 1.1 ***Ranking of Pharmacologic Therapies for Fibromyalgia Management***

Strong evidence of benefit	***Modest Evidence of benefit***	***Weak evidence of benefit***	***Not shown to be effective***
Dual reuptake inhibitors (venlafaxine, duloxetine, milnacipran)	Tramadol	Growth hormone	Opioids
Tricyclics (amitriptyline, cyclobenzaprine)	Selective serotonin reuptake inhibits	5-Hydroxytryptamine	Nonsteroidal Anti-inflammatory drugs
Pregabalin, gabapentin	Dopamin agonists	Tropisetron	Corticosteroids
	Hydroxybutyrate	S-adenosyl-L-methionine	Benzodiazepine and nonbenzodiazepine hypnotics
			Melatonin
			Guaifenesin
			Dehydroepiandrosterone

Adapted from JAMA (Goldenberg et al., 2005).

Table 1.2 ***Ranking of Nonpharmacologic Therapies for Fibromyalgia Management***

Strong evidence of benefits	***Modest evidence of benefit***	***Weak evidence of benefit***	***No evidence of benefit***
Cardiovascular exercise	Strength training	Acupuncture	Tender (trigger) point injections
Cognitive behavioral therapy	Hypnotherapy	Chiropractic, manual, and massage therapy	Flexibility exercise
Patient education	Biofeedback	Electrotherapy	
Multidisciplinary therapy	Balneotherapy	Ultrasound	

Adapted from JAMA (Goldenberg et al., 2005).

The prognosis of fibromyalgia can be multiple, and it depends on where the individual falls on a continuum. Some individuals with chronic pain who can be seen in primary care might respond to a single treatment, and are more capable to attain remission, while on the other end of the spectrum are patients in tertiary care settings who do not seem to improve (Littlejohn, 1995). The reasons might be that they are still experiencing high levels of distress, little social report, lack of control over the illness, etc.

Fibromyalgia is a chronic illness that can be treated but not cured (Bair & Krebs, 2000). The general goal of fibromyalgia treatment should be to maintain or improve function, improve quality of life, and manage symptoms. The best way to do this is for the doctor and the patient to work together actively. Patients can get the confidence and optimism they need to manage their disease over time by encouraging them to remain physically active and recognizing their efforts toward achieving their treatment goals.

CHAPTER 2
BIOFEEDBACK AND NEUROFEEDBACK

Before proceeding with more specific discussion related to the application of biofeedback, this chapter will be focused on presenting general ideas concerning biofeedback, such as „What is Biofeedback?“, its brief history and development, as well as what it consists of. Most importantly, Neurofeedback as a so-called „subtype“ of biofeedback will be presented, since it represents a crucial idea important for the further discussion of this work.

2.1 WHAT IS BIOFEEDBACK?

Biofeedback is a self-regulating technique which allows individuals to deliberately control bodily functions that were previously assumed to be involuntarily. With the aim of enhancing one's well-being, health and performance, biofeedback is assisting individuals in becoming more aware of and adapting their physiological functioning. A skilled biofeedback practitioner is needed to oversee the therapy as well as specialized equipment to translate physiological signals into relevant visual and aural cues (Khazan, 2013). Patients receive feedback from a screen, such as a computer monitor, that aids in their development of physiological control. Biofeedback allows patients to see inside their bodies and alter positions, expressions. A practitioner acts as a guide, instructing the patients on how to use the feedback to regulate their physiology in a healthy way. There are three objectives for biofeedback:

- *Awareness*: a better understanding of physiological, cognitive and emotional processes is essential for bringing about change (Khazan, 2013).
- *Change:* ability to make beneficial adjustments is a prerequisite for change-related self-regulation.
- *Generalization*: only when the abilities acquired in the therapist's office are transferred to the real world can long lasting progress be achieved.

2.2 BRIEF HISTORY OF BIOFEEDBACK: overview

The idea of biofeedback has deep roots in psychiatry and medicine. Yoga and transcendental meditation were traditional practices utilized by Yogis in Indian medicine (Blumenthal, 1985). The notion of feedback was formalized by cybernetics during World War II, and the name

"biofeedback," which as an analogy can be thought of as "a real-time physiological mirror" was first used in 1969. The creation of biofeedback devices represents an endeavor to integrate contemporary electronic technology with the disciplines of psychology and psychiatry (Sattar & Valdiya, 1999).

As tools, subjects of scientific inquiry, and clinical interventions, biofeedback and applied psychophysiology have advanced from speculative experiments to data-based research, from clinical trial intervention to efficacy studies and accountability (Amar, 1993).

Biofeedback is a type of intervention that aims to help patients to better control their own physiological functions. In biofeedback, a physiological function or process is systematically monitored by electronic devices and communicated back to the individual in order to teach him/her how to change it. Typically, this feedback takes the form of an audio or visual signal. One of the main discoveries of twentieth-century psychology was the finding that people can learn to control their internal responses, such as heart rate, body temperature, blood pressure, skin temperature, muscle tension, and electrical activity of the brain (Masters et al., 1987). This finding has significant therapeutic implications.

The development of biofeedback can be linked to attempts to apply learning theories to gain a better understanding of how the sympathetic and parasympathetic nervous systems, which make up the autonomic nervous system (ANS), operate. It was long believed that modifications to physiological function could only emerge from automatic or reflexive processes known as classical conditioning. In a series of animal experiments, Neil Miller challenged this notion by proving that it was possible to establish operant conditioning of a variety of ANS functions (Blumenthal, 1985). Thus, rather than starting out as a useful tool for treating clinical issues, biofeedback was first developed as a response to a theoretical debate. The best theoretical framework—operant conditioning, information processing, or skill learning—is still up for debate. Following initial excitement, it faded into obscurity for several years with the advent of pharmacological treatment. However, lately the increased use of biofeedback techniques in medical practice is a result of the broad realization of the dependence potential of benzodiazepines and the possibility of persistent withdrawal syndrome in some patients. As a result, biofeedback is once again becoming a popular form of intervention. Comparative outcome studies have revealed that benzodiazepines are less successful than non-pharmacological therapy at treating mental disorders (Higgit & Fonagy, 1992).

2.3 BIOFEEDBACK METHODS

Patients are carefully selected for biofeedback interventions. The physiological function that needs to be put under conscious control is identified, and the proper biofeedback apparatus is chosen (Sattar & Valdiya, 1999). Although there are now a number of biofeedback devices with varied degrees of sophistication available for usage, the fundamentals are still the same. The sensors detect the physiological activity (electrical, mechanical or other forms of activity), which is amplified and transmitted to a device that emits a binary or analogue signal depending on the application. The process and underlying logic of biofeedback therapy are communicated to the patient. The patient is taught to recognize the various digital, visual, and auditory forms of feedback and is given instructions to actively control the desired function, which will manifest as a change in the feedback (in example, from red to green in the color of the light, a switch from an unpleasant to pleasant sound, and an increase or decrease in the digital value). The patient needs some (about 15) sessions to reach the desired outcome, and then he is urged to keep practicing. If the patients are taught relaxation strategies before beginning biofeedback therapy, the operation will take place more smoothly.

Following are two important biofeedback methods used in medical practice:

(a) Electromyographic (EMG) biofeedback: during this technique, electrical changes in the muscle groups are recorded (EMG signals) and shown to the patient in the form of a feedback. Most EMG biofeedback procedures place three rather large surface electrodes symmetrically across the frontalis muscle about an inch above the eyebrow to measure the activity of the occipitofrontalis muscle (Flor & Birbaumer, 1993).

(b) Thermal biofeedback: is a frequently used technique for treating patients to modulate blood flow. The peripheral vasodilation/constriction that is controlled by smooth muscles that are innervated by the sympathetic nervous system determines how much blood flows through the capillaries in the fingers of the hands (Otis et al., 1995). Since the sympathetic nervous system specifically innervates the peripheral vasculature, vasoconstriction occurs in conjunction with sympathetic arousal, which lowers skin temperature. Therefore, the finger's temperature can be an index of the level of stress. The voluntary regulation of fingers' temperature reflects the voluntary control of the sympathetic nervous system. The patients experience feedback regarding variations in skin temperature, which supports their

ability to voluntarily warm their hands (Grimsley, 1994). This method has been used to treat a number of conditions, most notably hypertension, vascular headaches, and peripheral vascular diseases like Raynaud's disease.

2.4 NEUROFEEDBACK

Electroencephalographic (EEG) biofeedback (BF) is a kind of BF modality that records EEG waves. It is a technique based on operant conditioning that supports the person's capacity to alter the amplitude, frequency, or coherence of the brain's neurophysiologic dynamics (Egner & Gruzelier, 2004). Neurofeedback (NFB) is a term used to refer to the therapeutic use of EEG biofeedback (Vernon et al., 2003; Vernon 2005; Lubar 1997). Neurofeedback has been the focus of extensive research for many years. With the use of neurofeedback, patients can intentionally manage their brain waves. Electroencephalography (EEG) is actually recorded then, it is analyzed and specific components of interest of the EEG are presented to subjects via an online feedback loop as audio, video, or a combination of both presentations. Electrical pulses are generated by neurons when they are active. The electrical activity of the brain, also referred to as EEG, can be recorded by applying electrodes to the scalp (Marzbani et al., 2016). Pyramidal neurons, a particular form of synchronous neuron, are responsible for producing EEG, and their electrical output is subsequently reflected in the parts of the skin below where the electrodes are positioned. The amplitudes and frequencies of various electrical activity patterns, referred to as brain waves, could be used to identify them. The number of waves per second (Hz), which is used to measure frequency, indicates how quickly the waves oscillate. The microvolt (V), which is used to measure amplitude, indicates the strength of the waves. In neurofeedback various electrophysiological components can be feedbacked to the patients.

As a feedback, a changing bar graph can be used as an example to demonstrate the power of a certain frequency band. According to Dempster (2012) and Vernon (2005), alpha/theta ratios, beta/theta ratios, and other combinations of these are the major focus of neurofeedback treatment protocols in different clinical settings.

During this whole procedure, subjects become aware of the changes that occur during training and are able to assess their progress in order to achieve optimal performance.

Numerous research on the neurofeedback therapy's efficacy in the management of numerous disorders have been undertaken to date. There are some methodological and clinical uncertainties,

nevertheless. When it comes to alpha treatment protocols (i.e., increase alpha power in a specific area), for instance, there are some concerns to address, such as the number of sessions required before participants can learn to exert control, the number of sessions required before such training procedures produce the expected effect on the optimal performance, and the duration of the desired effects last without feedback (long-term effects).

Like other therapies, neurofeedback has advantages and disadvantages. It is a safe and non-invasive procedure that has shown improvement in the treatment of many issues and disorders, including: ADHD (Wang & Sourina, 2013); anxiety (Demos, 2005); depression (Hurt, Arnold, & Lofthouse, 2014); epilepsy (Walker, 2010); autism spectrum disorder (ASD) (Coben, Linden, & Myers, 2010); insomnia (Hammer, Colbert, Brown, & Ilioi, 2011); drug addiction (Horrell et al., 2010); schizophrenia (Surmeli, Ertem, Eralp, & Kos, 2012); learning disabilities, dyslexia, and dyscalculia (Wang & Sourina, 2013). However, NFB has some limitations, for example its validity in terms of conclusive scientific evidence of its effectiveness has been questioned, few insurance companies pay, and it can take a while before the expected benefits materialize (Mauro & Cermak, 2006).

CHAPTER 3
EFFECTS OF NEUROFEEDBACK ON FIBROMYALGIA SYNDROME

Previously, in the first chapter it was described how challenging fibromyalgia condition is. Since it is characterized with a variety of symptoms, it is quite a challenge to find an appropriate treatment. Different procedures have been suggested and applied to treat fibromyalgia and they had quite different, both successful and unsuccessful outcomes. However, taking into consideration previously mentioned (second chapter) effects of clinical application of bio and neurofeedback, it was assumed that neurofeedback treatment might be an effective intervention for fibromyalgia symptoms. It was hypothesized that sensory motor rhythm (SMR) and alpha wave neurofeedback training would improve sleep quality and cognitive function, which would in turn reduce pain and symptom severity in patients with fibromyalgia (Sterman, 1996). SMR (12-15Hz) appears to boost thalamic inhibitory processes. Enhancing SMR activity, on the other hand, has cognitive implications such as reduced impulsiveness/hyperactivity, improving attention processing, and semantic memory ability (Sterman, 1996). Sensorimotor rhythm (SMR) training is a common NFB treatment (Egner et al., 2004). Different authors decided to use this specific band in treating FMS because SMR is generally associated with a calm body and an active mind, and it is hypothesized to be formed by thalamocortical interactions during burst firing activity in ventrobasal thalamic relay nuclei involved with somatosensory afferent gating suppression (Howe and Sterman, 1972). Patients with FMS commonly complain of memory and focus problems. Poor working memory and long term memory, as well as language deficiencies and slower information processing speed, have been indicated by neuropsychological tests in FMS patients (Grace et al., 1999; Park et al., 2001). Perceptual amplification of pain and neurosensitization have been seen in FMS, and both may be related to disinhibitory mechanisms (Howe and Sterman, 1972). P300 amplitudes were found to be lowered in patients with FMS (Ozgocmen et al., 2002; Ozgocmen et al., 2003; Alanoglu et al., 2005). These findings are significant since P300 has been hypothesized to represent the activation of inhibitory mechanisms. The amplitude of P300 represents inhibition of the central nervous system (CNS); the greater the amplitude, the greater the inhibition (Tomberg and Desmedt, 1998). SMR training enhances P300 amplitudes, supporting the observation that SMR training promotes thalamocortical inhibitory processes (Egner and Gruzelier, 2001). When taking into consideration this background knowledge, it might be assumeed that NFB treatment may play an inhibitory role on CNS, and this inhibition may alter central augmentation in FMS.

In this way, it was hypothesized that NFB treatment might be effective in alleviating the symptoms and signs of FMS. In order to display this, some of interesting research will be presented.

3.1 NEUROFEEDBACK TREATMENT FOR FIBROMYALGIA: research outcomes overview

In research from Kayıran et al. (2010), the efficacy of NFB in patients with fibromyalgia syndrome (FMS) was assessed. Eighteen patients were treated with twenty sessions of NFB to increase sensory motor rhythm (SMR) over the course of 4 weeks (NFB group), while 18 patients were treated with 10 mg of escitalopram (selective serotonin reuptake inhibitor, SSRI) daily for 8 weeks (control group). At baseline and the second, fourth, eighth, sixteenth, and twenty-fourth weeks, the Hamilton and Beck Depression and Anxiety Inventory Scales, the Fibromyalgia Impact Questionnaire (FIQ), and the Short Form 36 were administered as outcome measures. Theta/SMR ratio and mean EEG rhythm amplitudes (delta, theta, alpha, SMR, beta1 and beta2) were also examined in the NFB group. In both groups, there were substantial improvements in every post-treatment measurement but it has to be noted that NFB group showed greater benefits than controls. Specifically, in the NFB group, the decrease in FIQ levels reached maximum in the 4th week. For the control group maximum reduction was found at the 8th week (Figure 1). The therapeutic effectiveness of NFB in general was discovered to start at the second week and reach a maximal effect at the fourth week. On the other hand, the benefits of SSRI therapy were also noted to start at the second week and to reach their peak effect by the eighth week, but regarding the mean amplitudes of EEG rhythms, no statistically significant alterations were found in this group. Important to note, theta/SMR ratio in the NFB group, however, exhibited a significant decrease at the fourth week compared to baseline (Figure 2). These findings confirm the effectiveness of NFB as a treatment for fibromyalgia-related pain, psychosocial problems, and decreased quality of life. The small number of patients included in the study, which could tamper with the statistical analysis' findings, is one of its main limitations (Kayıran et al., 2010). To clarify this restriction, further research involving a larger patient population and various measures with a variety of subscales over multiple time periods is required. Lack of any procedure that can explain the mechanism of NFB intervention for FMS is another gap in this study. However, this study suggests

that NFB applications may help FMS patients with pain, fatigue, sadness, anxiety, and poor quality of life. These findings imply that the NFB application may be a cutting-edge therapy approach for FMS. Quantitative EEG, ERP, or functional MRI studies are still required to fully understand the impact of NFB on brain plasticity and to pinpoint the precise processes.

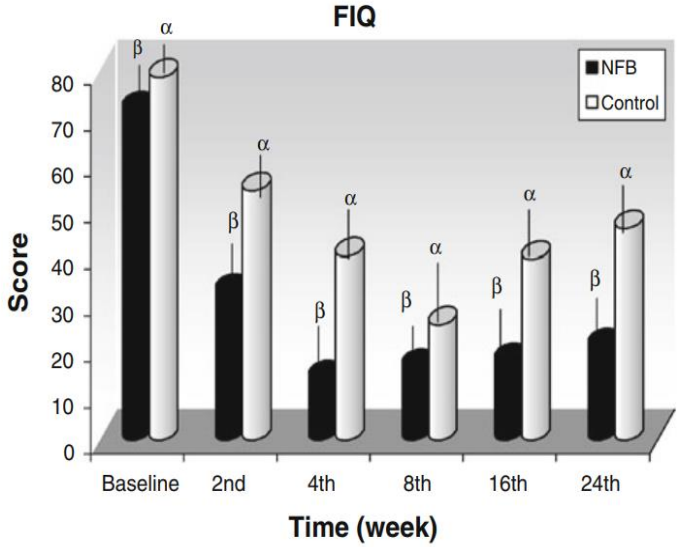

Figure 1. FIQ scores in the NFB and control groups (Kayıran et al., 2010)

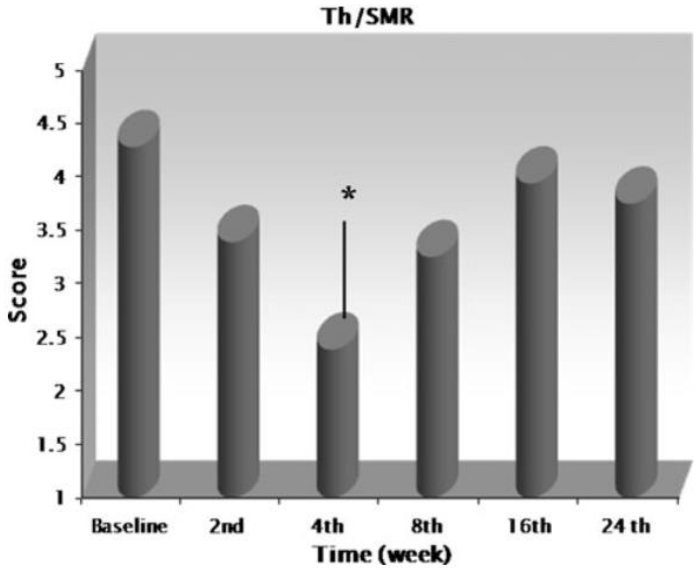

Figure 2. Theta/SMR rations in the NFB group (Kayıran et al., 2010).

In 2011, Caro and Winter conducted a pilot study. They studied fifteen FMS patients who underwent at least 40 NFB sessions. They had attention issues as shown by visual and auditory continuous performance testing (CPT). During training, a "SMR protocol" that enhanced 12–15

Hz brainwaves (sensory motor rhythm; SMR) and simultaneously inhibited theta and 22–30 Hz (high beta) brainwaves were used. Additionally, serial assessments of discomfort, exhaustion, emotional distress, morning stiffness, and tenderness were taken. As controls, 63 FMS patients received regular medical treatment but were not given NFB. Visual attention, but not auditory attention, considerably enhanced. Subjects who received NFB intervention also experienced less tenderness, pain, and fatigue. In controls, somatic symptoms did not significantly change. With an NFB SMR procedure, visual attention metrics and some somatic FMS characteristics seem to be enhanced.

It is interesting to note that the existence of attention abnormalities in FMS was demonstrated, but also that in an unblinded manner, these, along with some physical abnormalities in FMS, are improved by NFB (Caro & Winter, 2011).

Another research, A Randomized Controlled Trial from Wu et al., (2021) tried to determine the effects of NFB on pain intensity, symptom severity, sleep quality, and cognitive function in patients with FBS. Eighty participants were randomly assigned to one of two groups: a telephone support group (N = 20) or a NFB group (N = 60) that received SMR and alpha rhythm feedback for eight weeks. They concluded that patients with fibromyalgia who underwent an 8-week NFB training program of SMR and alpha brain waves reported dramatically reduced pain intensity and interference, fibromyalgia symptom severity, sleep latency, and sustained attention (Wu et al., 2021).

Despite the fact that some studies found positive effects of NFB to improve SMR activity in FMS, one meta-analysis from Glombiewski et al.(2013) suggests that EMG biofeedback might be more effective than NFB. The authors aimed to integrate and critically evaluate the evidence regarding the efficacy of biofeedback for FMS. Specifically, seven research on NFB and EMG-biofeedback (321 patients) were included in the meta-analysis. From the results, only EMG-BFB, not NFB, significantly decreased pain intensity when compared to control groups, according to subgroup analysis (g = 0.86; 95 percent CI: 0.11-1.62). This might be due to the fact that 4 studies have been carried out on the effectiveness of EMG-biofeedback, and only 3 studies on the effectiveness of NFB. Therefore, future studies should try to evaluate the real effectiveness of NFB of SMR in improving FMS symptoms.

CONCLUSION

In conclusion, this work aimed to present the possible effectiveness of NFB-based treatments for Fibromyalgia Syndrome. Some studies showed that such a procedure elicited significant remarks in alleviating symptoms of FMS. The reason why NFB with SMR is the most used application of NFB in FMS is because enhancing SMR activity, has cognitive implications such as reduced impulsiveness/hyperactivity, improving attention processing, and semantic memory ability which is in turn hypothesized to reduce pain and symptom severity in patients with fibromyalgia. (Sterman 1996). This offers hope and new prospects for future-oriented research, with the intention to find alternative ways to the pharmacological treatment of FMS, in order to avoid significant drug side effects. Published studies should not be considered the answer, but instead remain open, and means to reach clearer and more concrete answers. Neurofeedback is a possible noninvasive intervention to reduce the pain and symptoms of fibromyalgia. The findings of these studies can help fibromyalgia patients and clinicians. More research is needed to confirm the benefit of neurofeedback and the best dosage for symptom relief in the fibromyalgia population.

In conclusion, these trials show that neurofeedback is effective for decreasing pain, overall symptom severity, and maintaining attention in fibromyalgia patients. However, these results remain provisional, just as this research remains a field open to future research and studies that can confirm and expand the results so far obtained.

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