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EEG Biofeedback Treatment Improves Certain Attention and Somatic Symptoms in Fibromyalgia: A Pilot Study

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Abstract Fibromyalgia (FMS) is a chronic, painful disorder often associated with measurable deficiencies in attention. Since EEG biofeedback (EEG-BF) has been used successfully to treat attention problems, we reasoned that this modality might be helpful in the treatment of attention problems in FMS. We also speculated that improvement in central nervous system (CNS) function might be accompanied by improvement in FMS somatic symptoms. We studied fifteen FMS patients with attention problems, demonstrated by visual and auditory continuous performance testing (CPT), while completing 40 or more EEG-BF sessions. Training consisted of a "SMR protocol" that augmented 12–15 Hz brainwaves (sensory motor rhythm; SMR), while simultaneously inhibiting 4–7 Hz brainwaves (theta) and 22–30 Hz brainwaves (high beta). Serial measurements of pain, fatigue, psychological distress, morning stiffness, and tenderness were also obtained. Sixty-three FMS patients who received standard medical care, but who did not receive EEG-BF, served as controls. Visual, but not auditory, attention improved significantly ($P < 0.008$). EEG-BF treated subjects also showed improvement in tenderness, pain and fatigue. Somatic symptoms did not change significantly in controls. Visual attention parameters and certain somatic features of FMS appear to improve with an EEG-BF SMR protocol. EEG-BF training in FMS deserves further study.

Keywords Fibromyalgia · Chronic fatigue syndrome · Complementary and alternative medicine · EEG Biofeedback · Continuous performance test

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Introduction

Symptoms of the fibromyalgia syndrome (FMS) remain surprisingly stable over prolonged periods of time, even when treated by specialists having a particular interest in the disorder (Wolfe et al. 1997a, b). Besides complaints of widespread pain, fatigue, and stiffness, FMS patients often describe significant cognitive dysfunction including inadequate attention span, poor short-term memory, impaired verbal fluency and vocabulary, and impaired mental alertness (Park et al. 2001; Côté and Moldofsky 1997). Additionally, FMS patients may have significant CNS perfusion abnormalities, as measured by regional cerebral blood flow (rCBF), brain functional magnetic resonance imaging (fMRI), and brain single photon emission computed tomography (SPECT) scan (Gracely et al. 2002; Mountz et al. 1995; Mountz et al. 1998; Kwiatek et al. 2000; Johansson et al. 1995). These findings, coupled with abnormalities in the hypothalamic–pituitary–adrenal axis (Demitrak and Crofford 1998; Crofford 1998; Griep et al. 1998), suggest that cerebral dysfunction in FMS may be widespread.

Many abnormalities in brain function and CNS blood flow are known to be associated with changes in the electroencephalogram (EEG). In that regard, we have previously observed significant EEG abnormalities in FMS patients with cognitive dysfunction, as measured by the quantitative electroencephalogram (QEEG) (unpublished observations).

EEG biofeedback (EEG-BF) has been shown to ameliorate some conditions associated with brain electrical dysfunction (Evans and Abarbanel 1999). This modality ties the standard theory of biofeedback, that is, instrument-based operant conditioning, to EEG derived brain electrical activity (Lubar 1995; Monastra et al. 2005; Monastra 2008). This is a particularly attractive strategy since certain EEG frequency bands are known to reflect behavioral states, viz., the "theta band" (4–8 Hertz; Hz), normally associated with twilight sleep, the "alpha band" (8–12 Hz) normally associated with a relaxed, passive and defocused attention state, and the "beta band" (13 Hz or greater) normally associated with higher order cognition. Theoretically, any manipulation of the amplitude of such bands should be reflected by changes in behavior.

EEG-BF has been reported to improve attention in children and adults with a diagnosis of attention deficit hyperactivity disorder (ADHD) (Lubar 1995; Monastra et al. 2005; Monastra 2008). We reasoned, therefore, that FMS patients with cognitive and attention complaints might benefit from an EEG based modality aimed at mitigating CNS electrical dysfunction. We chose, therefore, to employ an EEG-BF protocol commonly used in treating ADHD patients.

In our experience many FMS symptoms correlate with one another, i.e., when one symptom worsens or improves, other symptoms tend to worsen or improve in tandem. Therefore, we speculated that if EEG-BF ameliorated cognitive complaints in FMS it might simultaneously improve somatic complaints as well. This speculation was supported by two other studies of EEG-BF that reported improved symptoms in FMS patients (Kayiran et al. 2007; Mueller et al. 2001).

We report here a review of FMS patients receiving EEG-BF for complaints of attention difficulties. We noted an improvement in their attention measurements, and also noted improvement in certain other FMS somatic complaints.

Materials and Methods

One hundred twelve consecutive FMS patients who had failed standard medical therapy for FMS were recruited for EEG-BF training. All were seen in an outpatient rheumatology office setting under the care of one of the coauthors who has a special interest in FMS and EEG-BF (XJC). Each subject had undergone a complete history, physical examination, and laboratory testing. None had any other rheumatologic or general medical condition that could explain their cognitive complaints.

The diagnosis of FMS followed criteria suggested by the American College of Rheumatology (Wolfe et al. 1990). This required the presence of widespread pain in soft tissues both above and below the waist, on both sides of the body, and in an axial skeletal distribution of longer than 3 months duration. The presence of eleven of eighteen "tender points" was also required for the diagnosis.

We chose the completion of forty sessions of EEG-BF as a cut-off point for inclusion in this study since, in the authors' experience, this number of sessions is required to assure consistently measurable changes in cognitive function in FMS. There were 32 of the original 112 FMS subjects who completed forty or more EEG-BF sessions. Of these, 15 had sufficient chart information, including periodic CPT tests (TOVA®, Universal Attention Disorders, Los Alamitos, CA) to allow for complete analysis. The other 17 FMS patients who had completed 40 or more EEG-BF sessions were not included mainly due to insufficient CPT data. This data was not acquired in every patient, usually due to insurance considerations.

Of the remaining 15 FMS subjects (14 female, 13 Caucasian, 2 Hispanic; 37–84 years old) only 3 had any other condition that might partially explain their pain (3 Rheumatoid Arthritis). Other significant medical and/or rheumatologic diagnoses in these subjects included: sicca syndrome (2 patients), irritable bowel syndrome (1 patient), regional osteoarthritis (6 patients), osteoporosis (6 patients), CREST syndrome (1 patient), and rotator cuff tear (2 patients). All subjects had previously failed standard treatment (at least one nonsteroidal medication, and one low dose tricyclic medication) for FMS. Group demographics are presented in Table 1.

Our test of attention consisted of repeated measures of four variables, using a computer based, continuous performance test (CPT), "Test of Variables of Attention" (TOVA® Co., Los Alamitos, CA). The stimulus variables were visual or auditory, with each being presented for 21.6 min without interruption or rest. During the visual CPT either of two easily discriminated visual stimuli (i.e., targets; black square or light square) were shown on a computer screen. During the auditory CPT the targets were two easily discriminated audible tones (middle G and middle C).

One target was the true stimulus, requiring the test subject to respond with a hand held button, while the other was a "false" target, requiring the test subject to suppress their response. External and situational variables were controlled, to the extent that they could be, for all participants (Corkum and Siegel 1993) by performing the CPT at the same time of day and in the same room, using the same testor (with testor leaving the room after initiating the CPT). Participants were required to have spent a restful night before each testing session, and to have abstained

Table 1 Demographic data for EEG-BF patients and controls

	EEG-BF FMS patients	Controls (1,2)
Number tested	15	63
Number female (%)	14 (93)	50 (79)
Mean age ± SD years	66.7 ± 12.3	50.5 ± 13.9
Number caucasian (%)	13 (87)	55 (88)
Mean number of EEG-BF sessions (range)	58 (40–98)	0

SD years standard deviation in years

from stimulants and depressants (e.g., caffeine, nicotine, alcohol, etc.) for at least 12 h prior to testing.

The CPT recorded four main results: (a) the number of errors of omission, i.e., the number of designated target stimuli missed (thus, a measure of inattention); (b) the number of errors of commission, i.e., the number of incorrect responses following non-designated stimuli (thus, a measure of impulsivity); (c) mean time, calculated to within one-millisecond, to respond to the designated target, i.e., the subject's response speed; and (d) response time variability, i.e., the variability in the subject's response time (thus, a measure of consistency of attention). In addition, both CPT tests computed a "d prime score" and the visual CPT computed an "ADHD score" (Attention Deficit Hyperactivity Disorder score). The d prime score is a measure of performance degradation over time (Mussgay and Hertwig 1990). The ADHD score correlates in a positive fashion with the presence of attention deficit hyperactivity disorder (Greenberg and Kindschi 1996).

EEG-BF training was accomplished using a desktop, computerized EEG-BF system (Neurocybernetics ® Software Package; EEG Spectrum International, Encino, CA). Raw EEG brain waves from non-invasive scalp electrodes were digitally filtered into desired frequency bands and displayed onto a therapist's monitor. The therapist then chose the frequency bands to be rewarded or inhibited, rewarding the subject for producing increasing amplitudes within the desired frequency bands. Simultaneously, the subject was not rewarded (i.e., inhibited) for producing high amplitudes in any undesirable band. In order to keep the EEG-BF challenging for the participant, the therapist varied the reward/inhibition criteria according to the subject's progress.

Brainwave sampling was at Cz (Jasper 1958). One earlobe served as an electrical reference, while the other served as a ground. Our EEG-BF training protocol consisted of a scored game on a separate computer monitor that rewarded augmentation of the sensorimotor rhythm frequency band (SMR, 12–15 Hz) with concurrent inhibition of the theta (4–8 Hz) and high beta (22–30 Hz) frequency bands.

Before each EEG-BF session, the patient's subjective sense of pain, fatigue, and psychological distress were verbally reported using a 0–10 scale, where 10 was maximally abnormal. Additionally, the subject's global tender point score was recorded prior to the start of the EEG-BF training program, and periodically thereafter. This assessment was conducted by one coauthor, a rheumatologist (XJC) who is skilled in this examination, and followed criteria suggested by the American College of Rheumatology (Wolfe et al. 1990) for identifying tender points. A formal tender point count was not performed at each visit, however. Instead each subject was assigned a numerical tenderness score by the examiner, from 0 (no tenderness) to 3 (maximal tenderness), based on the total number and sensitivity of tender points elicited during the examination.

Visual and auditory CPTs were administered prior to starting the EEG-BF treatment program and then re-administered after the completion of every ten EEG-BF sessions. We used these CPT results to calculate correlations between the FMS symptoms and the four measured CPT scores (Omission Errors, Commission Errors, Response Time in milliseconds, and Response Time Variability in milliseconds) along with the two calculated scores, d Prime and ADHD score. The d Prime score is a response sensitivity score reflecting the ratio of the hit rate to the false alarm rate. It is considered to be a measure of performance decrement, i.e., the rate of deterioration of performance over time (Mussgay and Hertwig 1990). The ADHD score is a comparison between the subject's CPT performance and the performance of an age matched, known-ADHD control group (Leark et al. 1999). In this way we were able to determine if any of the CPT variables, i.e., sub-test score(s), correlated with observed changes in patients' symptoms.

We compared our current EEG-BF FMS participants to a similar, nationally collected historical control group of 583 FMS patients, naïve to EEG-BF (Wolfe et al. 1997a, b). A subgroup of these subjects, consisting of 63 FMS patients, were followed by our center for 6 years. This study was approved by the Northridge Hospital Medical Center Institutional Review Board (IRB).

Results

Our FMS EEG-BF study group differed significantly from FMS controls in terms of mean age, but not in any other demographic or clinical feature of their FMS (e.g., length

Table 2 Improvement in final CPT visual sub-test scores compared to baseline after EEG-BF treatment in FMS

CPT Sub-test	CPT Norms ± SD*	Assessment		P**
		Baseline mean score ± SD	Final mean score ± SD	
ADHD	NA	0.18 ± 3.24	1.85 ± 3.71	0.003
Omission errors (%)	0.22 ± 0.31	0.60 ± 1.17	2.06 ± 5.21	NS
Commission errors (%)	2.69 ± 2.53	3.06 ± 2.38	1.09 ± 1.21	0.0005
Response time (ms)	442.75 ± 57.71	415 ± 69	416 ± 72	NS
Response time variability (ms)	81.67 ± 16.73	103 ± 18	84 ± 30	0.008
d Prime	5.76 ± 1.23	5.21 ± 1.07	6.34 ± 1.54	0.002

ms milliseconds, *NA* not applicable, *NS* non-significant

* CPT Norms for females (TOVA® Co), age 60–69 [for comparison purposes only]

** Wilcoxon signed-rank test, one-tailed

Table 3 FMS symptom score improvement at completion of EEG biofeedback

Symptom	Completion compared to baseline	
	Mean symptom score improvement	Statistical significance*
Physician assessment of tenderness (0–3)	79%	$P = 0.002$
Global pain (0–10)	39%	$P = 0.006$
Fatigue (0–10)	40%	$P = 0.006$
Psychological distress (0–10)	27%	Not significant
Stiffness (0–360 min)	32%	Not significant

* Evaluation by Wilcoxon signed-rank test, one-tailed, compared to baseline

Table 4 Correlation (*r*) between CPT Sub-score means and patient symptom means

CPT Visual sub-score	Correlation (r) of patient symptom to CPT score		
	Fibromyalgia pain	Global pain	Fatigue
ADHD Score	−0.64*	−0.16	−0.29
Commission errors standard score	−0.85*	−0.40	−0.46*
d Prime standard score	−0.69*	+0.08	−0.15

* $P < 0.05$, one-tailed

of illness, average tender point score, morning stiffness, or fatigue score) (Table 1).

The EEG-BF treated FMS group means for baseline and final CPT sub-test scores (i.e., mean sub-test scores at completion compared to baseline) are shown in Table 2. TOVA CPT normal values, established by the TOVA Co. for females within the 60–69 year old group, are also provided for purposes of comparison. Four of the six final CPT subtest parameters showed significant improvement compared to baseline: Commission Errors, Response Time Variability, d Prime, ADHD score. EEG-BF treated FMS patients did not show significant improvement in auditory CPT scores.

Table 3 shows the improvement in clinical measures for our EEG-BF treated FMS group. All subjects received a minimum of 40 EEG-BF sessions (range 40–98, mean = 58). "Physician Assessment of Tenderness (PAT)" scores were generated approximately every 10 EEG-BF sessions. PAT, Global Pain, and Fatigue had all improved significantly at the conclusion of EEG-BF treatment. Psychological Distress and Morning Stiffness scores trended toward improvement but did not reach statistical significance.

Statistical analysis of the 583 non-biofeedback treated FMS historical controls in Wolfe's (Wolfe et al. 1997a, b) study showed no significant change in pain rating, fatigue, anxiety, or depression over a median of 6.4 years. Results of further analysis of our subgroup of 63 Los Angeles participants in that study showed that they also did not change significantly during the study period. There was no attempt at a formal tender point count assessment in either Wolf's (Wolfe et al. 1997a, b) study or the current one.

To determine if the CPT visual test could be used as a monitor of EEG-BF treatment of FMS, correlations were calculated between the three most sensitive participant clinical changes and the three most statistically significant CPT visual score changes. Results are presented in Table 4.

Discussion

FMS remains an enigmatic, painful multisystem disorder whose etiology is debated. Nevertheless, a consensus exits that the era of viewing FMS as a purely "psychological disorder" is no longer tenable (Aaron et al. 1996; Yunus et al. 1991). Instead, FMS is now considered a physiologically based syndrome with measureable CNS (Lee et al. 2011) and peripheral nervous sytem (PNS) abnormalities (Caro et al. 2008; Staud 2010) whose manifestations may be colored by the affective state (Glesecke et al. 2003). We reasoned, therefore, that its successful treatment might require a multisystem approach, and engender a role for EEG-BF therapy. Therefore, we set out here, in an exploratory fashion, to examine the potential for EEG-BF in improving FMS features, as measured by changes in a CPT and certain clinical findings.

A CPT seemed appropriate in measuring a portion of the CNS lesion in FMS since it is an objective and easily reproducible test directly affected by CNS function, particularly in ADHD (Epstein et al. 2003), a disorder that occurs with striking frequency in FMS (Reyero et al. 2010). CPT results might also be helpful to investigators interested in psychometric testing in FMS since CPT scores may correlate with the affective state (Chen et al. 2004; Bedwell et al. 2009), even in the pre-clinical setting (Bove 2008).

CNS functioning is known to be sub-optimal in FMS (Glass and Park 2001; Grace et al. 1999; Dick et al. 2002). Besides attention problems, these abnormalities include difficulties with working memory (the amount of mental power available in any given situation), episodic memory (the ability to remember specific events), verbal fluency (ability to access stored knowledge about words) (Glass and Park 2001), and hypervigilance (heightened sensitivity, increased attention to external stimulation, and preoccupation with pain sensations) (McDermid et al. 1996), but not with information processing speed (Glass and Park 2001). These CNS abnormalities appear to correlate with the degree and duration of the FMS patient's pain (Glass and Park 2001). Interestingly, they do not correlate with coincident anxiety or depression unless there is evidence of major depression (Glass and Park 2001; Landro et al. 1997; Christensen et al. 1997). Our patients had long standing FMS, refractory to other treatments, but no history of major depression.

In this pilot study we administered EEG-BF to our FMS subjects to determine if it might be helpful for their attention problems, much as it is in children with ADHD (14). We also determined the effect of EEG-BF on certain physical complaints in FMS (see Tables 3 and 4).

We chose to use a continuous performance test (CPT), the TOVA®, to measure our subjects' attention abilities longitudinally despite the limitations of CPT in the research setting (Corkum and Siegel 1993). These limitations may include difficulty in discriminating between subtypes of ADHD, and even between ADHD and other psychiatric disorders (Solanto et al. 2004). The CPT is, however, reasonably good at tracking changes in brain functioning over time or after treatment interventions in ADHD subjects (Riccio et al. 2001; Grizenko et al. 2004). The test–retest reliability of this CPT has also been shown to be reasonably good, and its results cannot be improved through practice alone (Greenberg and Kindschi 1996).

Our data show that certain TOVA® sub-tests of attention, i.e. the ADHD score, Commission Errors, Response Time Variability, and d Prime (a measure of performance degradation over time), all improved significantly during EEG-BF in FMS subjects. One other measure of attention, Response Time, was slightly faster than that reported in CPT norms, but the difference was not statistically significant ($P = 0.2$) (Table 2). These findings are similar to those of Glass (Glass and Park 2001) and Grace (Grace et al. 1999), whose studies showed that information processing speed is not impaired in FMS subjects.

Our results also show that the Standard Scores of the FMS subjects' Commission Errors is potentially useful in tracking FMS subjects' pain scores (correlation coefficient = -0.85; Table 4). We are unaware of any other tracking modality that correlates as well as the Commission error score for FMS pain.

It is noteworthy that Wolfe's national cohort (Wolfe et al. 1997a, b) of FMS subjects, which included our own Los Angeles subjects, did not improve their FMS symptoms after 6.7 years of longitudinal follow-up. It is likely, therefore, that the visual CPT subtest score improvements seen in our EEG-BF treated subjects were not a coincidence.

We can not, however, readily explain why auditory CPT scores did not improve with EEG-BF while visual CPT scores did. It may be that auditory detection of CPT stimuli demands a higher level of capacity loading in FMS much as it does in other disordered CNS problems (Mussgay and Hertwig 1990). It is also possible that our pilot study was under-powered to find significant changes in certain of our clinical measures (e.g., Psychological Distress and Stiffness, Table 3) or a real difference in auditory function. Finally, it is possible that the "eyes-open" EEG-BF conditioning protocol used here precluded optimal auditory training. Perhaps another study using an "eyes-closed" EEG-BF protocol would lead to different auditory CPT results.

Our 15 FMS subjects did not differ demographically, except for their mean age (Table 1), from our 63 historical FMS controls (Wolfe et al. 1997a, b). Although we have no ready explanation for this age difference we speculate that an older aged group may be more amenable to a greater number of EEG-BF treatment sessions. The FMS subjects who most improved in our study required 40 or more EEG-BF sessions. Thus, our EEG-BF study group represented a small percentage of the original sample, a subset of the overall FMS population, making selection bias a concern here. That is, our subjects may have self-selected themselves based on issues as diverse as insurance support of EEG-BF, type or degree of cognitive complaint, time available for biofeedback purposes, or certain other unobserved confounding variables. Even a placebo effect cannot be excluded here.

This study also suggests that certain important physical signs and symptoms of FMS improve significantly with EEG-BF (see Tables 3 and 4). These symptoms may include a physician assessed tenderness score. One author in our study (XJC) used a generalized physician assessed tenderness score, rather than a formal tender point count, to assess the effect of EEG-BF on our subjects' tenderness over time. Intra-rater agreement using this approach is "very good" (Tunks et al. 1995), and probably not significantly different than scores generated by formal dolorimetry (Cott et al. 1992).

We also measured FMS subjects' verbal scores of pain, associated fatigue, and morning stiffness. The inclusion of these factors in our study outcome measures is consistent with newer attitudes toward fibromyalgia, i.e., understanding FMS to be a multifaceted, constitutional disorder, and not simply a pain problem (Wilke 2009).

When we began our study we were unsure of which, if any, FMS symptoms might improve with EEG-BF. Therefore, we decided to measure those factors that we thought might logically represent the global nature of FMS symptoms. We recognize, however, that measuring several different clinical and CPT factors increases the possibility of introducing Type 1 measurement errors. Theoretically, this possibility might be mitigated by the use of certain statistical maneuvers, such as either the Bonferroni or Holm correction protocol (Aickin and Gensler 1996). We chose not to utilize these procedures because of the exploratory nature of our study.

Though not statistically significant, there was also a trend toward improvement in psychological distress and morning stiffness. These improvements trended to become more apparent with increasing number of EEG-BF sessions, usually greater than forty (data not shown).

The improvements in physical well being seen in our EEG-BF treated FMS subjects are consistent with other reports. In a limited case-series Kayiran et al. (2007) reported improved pain, fatigue, depression and anxiety in three FMS subjects using an EEG-BF SMR protocol similar to ours. Their study was somewhat more limited than ours, however, because of the small number of participants, the absence of an "objective" test such as the CPT, and the inclusion of younger FMS subjects (age range 31–33 years).

Mueller et al. (2001) reported improved mental clarity, mood, sleep, and self-reported pain with an EEG-driven photic-entrainment protocol in thirty FMS patients. Their study, while larger than ours (thirty participants), used a variety of treatment protocols incorporating nutraceuticals (i.e., borage oil, co-enzyme Q10, DHEA, flaxseed oil, garlic powder, gingko biloba, ginsing, L-tryptophan, melatonin, NADH, peppermint oil, and "high potency mineral oil and vitamin supplements"), massage and physical therapy, surface elctromyography (sEMG) BF combined with relaxation training, and photic stimulation EEG-BF. This multimodal approach to treatment makes assessment of their results difficult at best.

The CNS is likely to play an important role in FMS pain perception (Lee et al. 2011). Nevertheless, our findings should not be taken as evidence for an isolated CNS pathogenesis in FMS since unequivocal peripheral abnormalities have been identified in this syndrome. These abnormalities include those of muscle tissue (Olsen and Park 1998; Park et al. 2000; Sprott et al. 2004), the PNS, and the autonomic nervous system (Raj et al. 2000; Cohen et al. 2001; Ulas et al. 2006; Caro et al. 2008), and the immune system (Caro 1989; Salemi et al. 2003; Caro and Winter 2005; Caro and Winter 2008; Caro et al. 2008). Nevertheless, it is known that CNS pain perception may interact somewhat with attention related cognition (Pickering et al. 2002). Perhaps this is the pathway for improvement in pain by our EEG-BF treated FMS subjects. Additionally, a psychoneuroimmunologic connection can not be excluded (Ader 2007).

We have, then, confirmed that attention abnormalities exist in FMS, and—in an unblinded manner—shown that these, and certain physical abnormalities in FMS improve with EEG-BF. Attention measuring tests, such as the computer based CPT used here, may be useful modalities for following FMS patients over time and during interventional EEG-BF studies. They also may help avoid any examiner bias in following FMS subjects' response to therapy. The role of EEG-BF in treating FMS remains to be more fully elucidated, but our findings suggest that further study of this modality is warranted.

Conflict of interest None.

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