

Brief Research Report

Neurotherapy of Fibromyalgia?

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Abstract

Objective. To evaluate the efficacy of a novel variant of electroencephalograph biofeedback, the Low Energy Neurofeedback System (LENS), that utilizes minute pulses of electromagnetic stimulation to change brainwave activity for the amelioration of fibromyalgia (FM) symptoms.

Design. Randomized, double-blind, placebo-controlled clinical trial.

Setting. Tertiary referral academic medical center, outpatient.

Patients. Thirty-four patients diagnosed with FM according to 1990 American College of Rheumatology classification criteria.

Interventions. Active or sham LENS, depending on randomization, for 22 treatment sessions.

Outcome Measures. Primary outcome measure was the Fibromyalgia Impact Questionnaire total score. Secondary outcome measures included number of tender points (TPs) and pressure required to elicit TPs on physical examination, quantitative sensory testing heat pain threshold, and self-reported cognitive dysfunction, fatigue, sleep problems, global psychological distress, and depression obtained at baseline, immediate post-treatment, and 3- and 6-month follow-up.

Results. Participants who received the active or sham interventions improved ($P_s < 0.05$) on the primary and a variety of secondary outcome measures, without statistically significant between group differences in evidence at post-treatment or 3- or 6-month follow-up. Individual session self-reported ratings of specific symptoms (cognitive dysfunction, fatigue, pain, and sleep, and overall activity level) over the course of the 22 intervention sessions indicated significant linear trends for improvement for the active intervention condition only ($P_s < 0.05$).

Conclusion. LENS cannot be recommended as a single modality treatment for FM. However, further study is warranted to investigate the potential of LENS to interact synergistically with other pharmacologic and nonpharmacologic therapies for improving symptoms in FM.

Key Words. Fibromyalgia; Complementary Therapies; Biofeedback

Introduction

Fibromyalgia (FM) is a common, chronic, often debilitating musculoskeletal pain syndrome involving widespread pain at specific tender points (TPs) on physical examination (PE), and often accompanied by fatigue, disordered sleep, cognitive complaints, an array of other somatic complaints, as well as psychological distress [1]. Although initial investigations of the pathophysiology of this condition focused on attempts to identify inflammation in fibrous muscle tissue as

the primary dysfunction (hence, the original term “fibrositis”), the lack of evidence for peripheral damage led to a paradigm shift with an increasing focus on central nervous system mechanisms [2,3]. Currently, there is considerable evidence for neurobiological underpinnings of FM in terms of central sensitization or other augmentation of central pain processing. This is manifested, for example, in reduced pain thresholds or other amplification of the pain experience on a widespread basis throughout the body [4].

Treatments for FM have typically been only partially effective and of modest efficacy. Many patients remain persistently dysfunctional and often disabled [5]. Given the limited effectiveness of current treatments, many patients seek complementary and alternative medicine (CAM) therapies [6]. Within CAM, recent developments in the field of electroencephalograph (EEG) biofeedback, along with the increasing convergence of evidence pointing to neurophysiological dysfunction in FM, have suggested some promise for application of EEG-based treatment to FM [7,8]. EEG biofeedback, one form of neurotherapy, involves the use of sensors placed on the scalp to detect, amplify, and record brainwave activity. This information is transformed into an external modality (e.g., auditory tone or visual display) as subjects learn physiological control via computer software-generated feedback for rewarding or inhibiting the production of certain wavebands at one or more “active” recording sites [9].

The Low Energy Neurofeedback System (LENS), however, is a novel variant of EEG biofeedback. Rather than having subjects learn voluntary control over the production/inhibition of brainwave activity, the LENS provides minute pulses of feedback on an electromagnetic (EM) carrier wave to catalyze changes in brainwave patterns. This is done by linking the feedback frequency to the momentary peak frequency detected by the system. In LENS procedures, subjects are not consciously learning to change brainwave activity; instead, the brainwave changes are the result of the brain continuously interacting with the resonant changes in the feedback pulses. In this manner, LENS is believed to disrupt the way the person’s brain may continue to meet changing sensory afferents with the same narrow unchanging range of frequency responses, to develop instead a wider range of responses to varying sensory afferents [10]. This novel form of neurotherapy has been suggested for application to FM.

Previous uncontrolled research examining a series of 30 clinic patients diagnosed with FM according to 1990 American College of Rheumatology (ACR) criteria [11] suggested significant benefit from treatment with EEG-Driven Stimulation (EDS), a precursor of the current LENS, persisting to long-term (mean 8 months) follow-up in terms of pain, fatigue, cognitive dysfunction, sleep, and mood [8]. Both EDS and LENS rely on strategic distortion of the dominant EEG frequency with EM stimulation. EDS incorporated subliminal flashing lights in goggles worn by patients, while LENS involves much smaller pulsed EM energy conducted through the EEG leads and not via goggles.

LENS differs from other forms of external brain stimulation, such as repetitive transcranial magnetic stimulation (rTMS) in that the electromagnetic fields in LENS are believed to be equivalent to less than pico-tesla in strength, whereas rTMS at the intensity of magnetic stimulation from coil may be in the multiple-tesla range. Further, the EM stimulation of LENS is delivered on a specifically regional basis emanating from a particular single set of scalp electrode sites at any given feedback exposure, while rTMS emits a larger field of stimulation even though targeted focally [12]. LENS ultimately proceeds in a manner that results in widespread stimulation but does so on a single site basis progressing through a sequence that covers the standard international 10/20 EEG recording sites. In contrast to research on rTMS that has begun to elucidate mechanisms of change due to neuromodulation of cortical excitability [13], the extent to which LENS modulates or enhances cortical excitability, corticothalamic loops, inter-regional connectivity, dysfunctional neurochemistry, and/or other central pain modulatory systems remains to be explored. Finally, and most significant, the feedback from the LENS mirrors as a feedback system the changes in frequency activity at the sites from which it measures the EEG, while the rTMS signals change in neither frequency nor intensity in relation to changes in the brain activity. In other words, rTMS is not a feedback system.

The specific aim of this study was to evaluate the efficacy of LENS for the reduction of FM symptoms in a randomized, double-blind, placebo-controlled trial comparing two groups of patients who received either the active or a sham intervention for the same number of sessions. It was hypothesized that the active (vs sham) intervention would result in significant reduction of negative global functional impact of FM, reduction in total number of TPs and greater pressure required to elicit pain at TPs on PE, increased heat pain threshold on quantitative sensory testing (an indicator of central nervous system sensitization), and improvements on specific symptom measures of cognitive dysfunction, fatigue, sleep problems, global distress, and level of depression.

Methods

All research procedures were approved by the institutional review board of the Oregon Health and Science University (OHSU).

Patients

Participants were recruited from the extensive fibromyalgia data base of the OHSU Division of Arthritis and Rheumatic Diseases and study advertisements at OHSU and in the community. Eligibility criteria were: diagnosis of primary FM on PE according to 1990 ACR criteria; duration of FM symptoms ≥ 1 year; age ≥ 18 years; admission on self-report of cognitive difficulties; no other major chronic pain condition; no neurological disorder; no history of traumatic brain injury; no chronic infection; no other unstable medical condition; no history of spinal, including neck, surgery; not psychotic, imminently suicidal, or homicidal;

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no current substance abuse; not currently taking sustained release opiates on a daily basis; willing to maintain stable FM treatments throughout the study; no history of electroconvulsive therapy (ECT); able to read and understand English; and not presently engaged in or planning litigation regarding their physical condition or applying for disability. Such stringent criteria (e.g., no history of ECT, traumatic brain injury, or neck/spinal surgery) were used to minimize potential confounds possibly due to a history of central nervous system trauma in the interpretation of the results of the intervention. Furthermore, participants did not start any new treatments before beginning the experimental procedures. Forty-two (41 female, 1 male) of a total of 82 individuals screened met criteria for inclusion.

Physical Examination

PEs were performed by a research assistant (RA) with a master's in nursing and included assessment of 18 TPs specified in the 1990 ACR criteria. Number of positive TPs and degree of pressure with a dolorimeter required to elicit pain was recorded [11].

Quantitative Sensory Testing (QST)

The temperature probe of the TSA-II NeuroSensory Analyzer (Medoc Advanced Medical Systems, Minneapolis, MN) was applied by the RA to the flat area posterior to the right medial malleolus followed by the thenar aspect of the right hand to obtain the mean heat pain threshold (QST-HPT). This QST measure, which has been used as an index of central sensitization, has demonstrated the most consistent differences between FM patients and healthy controls [14,15].

Self-Report Questionnaires

A number of self-report questionnaires comprised the primary and additional secondary outcome measures. All, discussed below, have demonstrated excellent psychometric properties. In addition, all of these measures, as well as the PE and QST procedures, were administered at baseline pre- and immediate post-treatment and 3- and 6-month follow-ups.

Fibromyalgia Impact Questionnaire (FIQ)

The FIQ is a 10-item instrument that assesses physical functioning (with 10 sub-items), work status, depression, anxiety, sleep, pain, stiffness, fatigue, and well-being. Initial good reliability and validity information has been confirmed in numerous additional studies utilizing the FIQ, including its sensitivity to change over time as a function of treatment. The total score, which measures global impact of FM, was the primary outcome measure [16].

Profile of Mood States Bi-Polar Form Clearhead-Confused Scale (POMS-BI-CC)

The 12-item POMS-BI-CC assesses over the past week the subjective perception of being attentive and cognitively

efficient vs confused, forgetful, inattentive, or dazed on a list of adjectives rated by participants. This scale was used to measure participants' perceived cognitive functioning. Test-retest reliability is adequate ($r = 0.72$). A number of validity studies support the scale's conceptual basis and sensitivity to change as a function of drug and nondrug interventions and other factors [17].

Brief Fatigue Inventory (BFI)

The 4-item BFI assesses primarily the severity dimension of fatigue and appears to have good reliability (Cronbach's alpha >0.90) and validity [18]. It was used to measure participants' subjective perceptions of fatigue.

Medical Outcomes Study Sleep Scale (MOS-Sleep)

The 9-item overall sleep problems index from the MOS was used to assess sleep disturbance. The MOS-Sleep has been used extensively in quality of life and other health studies, has reported internal consistency of 0.86, as well as content, face, concurrent, and discriminative validity [19].

Brief Symptom Inventory Global Distress Index (BSI-GSI)

The BSI is the 53-item short form of the parent Symptom Checklist-90-Revised (SCL-90-R) designed to assess psychological symptom patterns. The BSI yields various subscale scores as well as overall distress indices. Very strong internal consistency coefficients have been reported for the various subscales, as well as high test-retest reliabilities (e.g., $r = 0.90$ for the BSI-GSI). Numerous validity studies have been performed with the SCL-90-R and very high correlations exist between the symptom dimensions of the SCL-90-R and BSI (range = 0.92–0.99). The BSI-GSI was used to measure global emotional distress [20].

Patient Health Questionnaire-9 (PHQ-9)

The 9-item depression module from the PHQ-9 based on the PRIME-MD structured interview for diagnosing common mental disorders in primary care settings was used to measure severity of depressive symptoms. Respondents rate each of nine symptoms corresponding to DSM-IV diagnostic criteria for major depression over the past 2 weeks. Excellent criterion validity has been demonstrated for total scores for correspondence to experienced clinicians' independent diagnoses of major depression, generally meeting or exceeding those obtained with the full PRIME-MD interview format [21].

Numerical Rating Scales

In addition, at the beginning of each of the 22 intervention sessions, eight separate 0–10 numerical rating scales with appropriate anchors were completed by participants regarding their current/past 24 hours levels of pain (e.g., 0 = no pain, 10 = unbearable/worst imaginable

pain), cognitive clouding, fatigue, quality of sleep, anger/irritability, anxiety, and depression, as well as overall activity level. In all instances, higher ratings indicated greater dysfunction. The reliability and validity of such measures has been consistently demonstrated in pain assessment and treatment [22].

LENS Assessment and Treatment

The LENS consisted of a Pentium IV laptop computer, J & J Engineering (Poulsbo, WA) I-300 C-2 Compact 2 Channel EEG module with on-board feedback generating power, (proprietary) LENS USE-3 software, and MS Office. The C-2 EEG module samples raw EEG data at 512 samples/sec. The software links the digital EEG recording (C-2 module) device through the computer which then sets the parameters for the C-2 module to emit pulsed EM stimulation. The system returns a signal to the participant via conduction from the C-2 module, which is a function of the detectable momentary peak frequency. The system provides feedback for EEG activity based on the principle of strategic distortion in that the feedback changes at the same time the peak EEG frequency changes, but is offset from it in a manner specified by the algorithm in the treatment software.

Pulses of EM energy operate at a duty cycle of 1%, that is, of the maximum permissible on-time for each pulse, they are powered no more than 1% of the time (e.g., the maximum on-time at 1% for 1 Hz pulse is 0.01 second). Evaluation at the University of California Lawrence Livermore Laboratory of the EDS system, the precursor of LENS, demonstrated radiation conducted from the wire from the C-2 module to the glasses of 10^{-12} watts. Vendor's estimate for radiation conducted through the wire to the active lead in LENS is of three orders of magnitude lower or approximately 10^{-15} watts.

LENS Assessment

Initial recording of EEG activity was conducted with serial (not simultaneous) sampling done at each of 19 scalp electrode sites, based on the International 10/20 system, in a predetermined order: FP1, F7, T3, T5, O1, O2, T6, T4, F8, FP2, F3, C3, P3, P4, C4, F4, FZ, CZ, PZ. This did not allow for a quantitative EEG map but did produce a rank ordering of sites according to total amplitude at each site. This sequence was utilized as the order in which to target treatment sites, beginning with the site with the lowest amplitude and continuing through to the one with the highest amplitude. During both assessment and treatment, participants sat with eyes closed and engaged in no specific activity. A referential monopolar montage was used, with initial impedances kept below 5 Kohms.

LENS Treatment

Depending upon random assignment, participants received active or placebo treatment conducted by a second master's level RA. All sessions appeared identical,

but EM stimulation was administered only in the active condition. Separate coded electrode cables were used for the two conditions. The wire in one set of cables was severed and tested by a third party in another state to ensure that no current could be conveyed through the active lead. None of the other investigators, RAs, or participants knew which set of cables was capable of conducting stimulation. The program eliminated all EEG information from the computer screen. The EEG was monitored and the dominant frequency reset every 0.5 second. At a time pre-set in the software the dominant, or peak, EEG frequency had added +20 Hz of EM stimulation to it for a maximum 1-second burst of alternating on/off pulsing. For example, if the momentary dominant frequency was 10 Hz, the EM stimulation frequency for a maximum of 1 second pulsing was 30 Hz.

The first intervention session included 1 second of stimulation for one site only. The number of sites treated in each session was then increased in one-step increments to a maximum of three different sites (maximum 3 seconds of stimulation) proceeding through the sequence of sites determined by the initial assessment. If a participant reported increased bothersome symptoms or discomfort within or between sessions, the therapist had the option to reduce the level of stimulation by one site (i.e., 1 second) or hold off and reschedule the session. No stimulation was conducted through the active site electrode cable in the sham condition, although all procedures otherwise were followed in terms of incremental progression in number of sites treated in session from one to a maximum of three and modifications permissible according to any report of discomfort. Modifications were typically not required in either group. No significant adverse events attributable to the intervention were reported.

At the beginning of each session, participants completed the eight separate current symptom and overall activity 0–10 numerical rating scales. When the initial sequence of sites was exhausted, a repeat 19-site nonstimulation assessment was performed to determine the next sequence of sites through which to proceed for intervention, again beginning with the lowest amplitude site through to the site with the highest amplitude. The maximum total number of these assessments was three.

Data Analysis

Data analysis was carried out according to a pre-established analysis plan with SPSS 14.0: *t*-tests or chi-square tests of association for pre-treatment between group differences and post-treatment and follow-up between group differences on additional FM treatments obtained; repeated measures analyses of variance (ANOVAs) for each of the primary and secondary outcome measures over four assessment time points; and trend analyses on the individual session symptom and overall activity ratings using curve estimation regression procedures.

Table 1 Demographic and clinical characteristics of participants receiving active LENS and sham interventions

	Active LENS Patients (N = 17)	Sham Patients (N = 17)
Sex, no. male/no. female	0/17	1/16
Age, years	51.6 ± 8.6	52.0 ± 11.4
Education, years	15.8 ± 2.9	16.1 ± 3.1
Ethnic/racial background, no. non-Hispanic White	15	15
Employment status, no. working part- or full-time	8	7
Marital status, no. married	11	11
Months since FM diagnosis	159.1 ± 211.2	100.2 ± 63.8
Months since FM symptom onset	206.2 ± 110.1	223.5 ± 186.7
No. of classes of pain-related medications	2.9 ± 1.4	2.8 ± 1.6

Except where otherwise indicated, values are mean ± SD.
LENS = Low Energy Neurofeedback System; FM = fibromyalgia.

Results

Characteristics of Patients

Of the 42 patients assigned to the two intervention conditions (N = 21 each), 34 (N = 17 each) completed the immediate post-treatment outcome assessment and 32 (N = 16 each) completed all assessments through the 6-month follow-up. Reasons for dropping out in the active condition included three individuals who had difficulty keeping appointments due to distance, sickness, or other commitments; another who refused to complete any post-treatment measures; and one participant who did not return to complete extended follow-up without giving a reason. In the sham condition, two individuals withdrew due to time and travel difficulties, one to undergo back surgery, and another who did not provide a reason; an additional participant who completed the immediate post-treatment assessment required hospitalization for another medical condition and declined to return for follow-ups. Characteristics of participants who completed assessment at least through the immediate post-treatment are summarized in Table 1. There were no statistically significant pre-treatment between group differences on any of these demographic or clinical characteristics.

Primary and Secondary Outcome Data

The outcome data for the 32 participants who completed all follow-up assessments are presented in Table 2. With regard to the primary outcome measure, the FIQ total score, there were no significant pre- to immediate post-treatment or pre- and post-treatment to 3- and 6-month follow-up group differences. Both groups exhibited significant decreases in the FIQ from pre- to immediate post-treatment. Relative to the immediate post-treatment time point, there was a significant group difference ($P < 0.05$) at the 3-month follow-up, with the active treatment group worsening and the sham group continuing to improve. However, at the 6-month

follow-up, the active treatment group had once again improved and the difference between the two groups from pre- or immediate post-treatment to the 6-month follow-up, while still present, did not reflect a statistically significant difference.

With regard to the secondary outcome measures, the only statistically significant changes were a decrease for both groups from pre- to immediate post-treatment for number of TPs, self-reported cognitive dysfunction (POMS-BI-CC), fatigue (BFI), and global distress (BSI-GSI), as well as sustained decreases in number of TPs at 3- and 6-month follow-ups and decreased fatigue at 6-month follow-up; however, there were no statistically significant between group differences on any of these or the other secondary outcome measures at any study time point.

The information obtained from each participant at each session regarding symptom severity and overall activity level for the preceding 24 hours revealed highly significant linear trends in evidence in the *active treatment group only* for decreased pain ($\beta = -0.21$; $R^2 = 0.04$, $F[1,395] = 17.75$, $P < 0.001$), cognitive clouding ($\beta = -0.16$; $R^2 = 0.03$, $F[1,395] = 11.12$, $P = 0.001$), and fatigue ($\beta = -0.11$; $R^2 = 0.01$, $F[1,395] = 4.64$, $P = 0.03$), and increased overall activity levels ($\beta = 0.14$; $R^2 = 0.02$, $F[1,395] = 7.83$, $P = 0.005$); nonsignificant changes were in evidence for improved sleep and for decreased anxiety/nervousness, depression, and anger/irritability (all P s > 0.05). No significant linear trends were in evidence on any of these ratings for participants in the sham condition.

An analysis of self-reported patterns of utilization of other FM-related (physical, pharmacological, psychological) therapies indicated no significant between group differences at any time point except for the following. Pain-related medication usage in terms of total number of classes of pain-related (e.g., short- and long-acting opioid, antidepressant, neuropathic, NSAID, sedative-hypnotic) medications used by members of each group were signifi-

Table 2 Means ± SDs for primary and secondary outcome measures at each study time point (pre-treatment baseline, immediate post-treatment, and 3- and 6-month follow-ups) for active LENS and sham intervention groups

	Active LENS Patients (N = 16)	Sham Patients (N = 16)	Active LENS Patients (N = 16)	Sham Patients (N = 16)
FIQ				
Baseline	44.75 ± 11.46	39.25 ± 6.46		
Post-treatment	38.63 ± 14.41	33.00 ± 11.53		
Follow-up				
3-month	48.19 ± 14.72	35.19 ± 10.28		
6-month	39.56 ± 13.88	36.63 ± 11.48		
No. of TPs				
Baseline	14.38 ± 2.09	14.80 ± 2.04		
Post-treatment	12.00 ± 3.03	14.00 ± 3.16		
Follow-up				
3-month	12.13 ± 3.65	12.80 ± 3.34		
6-month	12.00 ± 3.14	12.53 ± 3.29		
Ave. TP pain threshold				
Baseline	2.72 ± 1.29	3.00 ± 1.39		
Post-treatment	2.53 ± 0.78	2.73 ± 1.05		
Follow-up				
3-month	2.87 ± 1.02	2.70 ± 0.88		
6-month	2.72 ± 0.95	2.80 ± 0.68		
QST-HPT				
Baseline	42.33 ± 3.86	42.80 ± 3.96		
Post-treatment	41.91 ± 4.00	42.82 ± 3.87		
Follow-up				
3-month	42.06 ± 3.63	43.64 ± 2.67		
6-month	41.59 ± 3.70	42.62 ± 3.27		
POMS-BI-CC				
Baseline	19.31 ± 8.96	23.13 ± 6.80		
Post-treatment	22.44 ± 8.13	25.25 ± 6.79		
Follow-up				
3-month	19.63 ± 10.49	24.31 ± 7.04		
6-month	21.31 ± 10.02	23.00 ± 8.26		
BFI				
Baseline			5.31 ± 1.66	4.38 ± 1.71
Post-treatment			4.88 ± 2.47	3.44 ± 1.86
Follow-up				
3-month			5.88 ± 2.25	3.56 ± 1.79
6-month			4.75 ± 2.41	3.31 ± 2.09
MOS-Sleep				
Baseline			50.33 ± 14.35	49.47 ± 16.67
Post-treatment			46.51 ± 14.87	45.52 ± 18.14
Follow-up				
3-month			53.22 ± 17.65	49.06 ± 16.76
6-month			44.37 ± 12.25	46.45 ± 20.37
BSI-GSI				
Baseline			61.13 ± 6.79	57.44 ± 5.81
Post-treatment			60.07 ± 6.19	55.13 ± 5.90
Follow-up				
3-month			61.87 ± 8.31	56.19 ± 6.71
6-month			59.07 ± 8.06	56.69 ± 8.29
PHQ-9				
Baseline			9.45 ± 3.47	7.14 ± 3.18
Post-treatment			8.02 ± 4.09	6.56 ± 3.35
Follow-up				
3-month			10.90 ± 6.06	7.56 ± 3.92
6-month			8.19 ± 3.80	8.00 ± 4.10

Ave TP pain threshold = average pressure required to elicit pain at TP with dolorimeter in kg/cm².

QST-HPT in °C.

Higher scores indicate worse functioning except for Ave. TP pain threshold, QST-HPT, and POMS-BI-CC, where higher scores indicate better functioning.

TP = tender point; FIQ = Fibromyalgia Impact Questionnaire total score; POMS-BI-CC = POMS Bi-Polar Clearhead-Confused scale; BFI = Brief Fatigue Inventory; MOS-Sleep = Medical Outcomes Study Sleep scale; BSI-GSI = Brief Symptom Inventory Global Severity Index; PHQ-9 = Patient Health Questionnaire-9 Depression scale; QST-HPT = Quantitative sensory testing heat pain threshold.

cantly higher for the sham participants immediately post-treatment. Similar, but not statistically significant, differences were in evidence at 3- and 6-month follow-ups.

Discussion

The results suggest that LENS cannot be relied on as a single modality treatment for FM. There were indications based on the primary outcome measure, the FIQ total score, and some of the secondary outcome measures that participants in both treatment conditions experienced some significant decrease in bothersome symptoms, but this was not sustained to the time of the follow-up assessments. One explanation is that a placebo or attention nonspecific benefit of simply coming to treatment sessions may have exerted a strong influence during the intervention (vs follow-up) phase of participants. Somewhat greater usage of classes of pain-related medications in the sham condition at post-treatment and follow-ups may have also muted detection of between-group differ-

ences. However, the trend analyses suggest that the active treatment group may actually for the duration of the intervention have experienced some potential benefit in terms of significantly decreased pain, fatigue, and cognitive clouding, and in terms of increased overall activity levels. None of these changes were observed in the sham group. Nonetheless, these effects were not enduring.

These findings do not justify concluding that LENS is of no potential benefit to persons with FM. However, they do raise significant caution regarding claims of efficacy of LENS as a single modality treatment. One hypothesis, based on the individual session trend analyses, is that LENS may have some effect on “toning” the nervous system in a favorable direction, but a multi-modal treatment approach to capitalize on these incipient changes may be required for more enduring benefit. Accordingly, the next step would be to compare LENS alone vs LENS in combination with other appropriate treatment(s) and usual customary care. Previous work with the precursor of

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LENS, EDS, demonstrated in a nonblind study the benefit of adding specifically targeted physical therapy, massage therapy, or surface electromyography (sEMG) once patients reported some incipient benefit from initial EDS. The addition of other therapies at that time resulted in a rapid positive response relative to lack of response prior to receiving EDS [8]. One potential future research design would be to compare three groups that undergo different sequences of single and/or combined interventions; for example, LENS only, LENS followed by sEMG, and sEMG followed by LENS. Also, while the cable for the active lead was incapable of conducting pulsed EM stimulation in the sham condition, the wires in the reference and ground cables for either condition were not severed; this may have resulted in an unknown amount of variable EM stimulation transmitting through these cables with uncertain effects.

The present study has some noteworthy limitations. We cannot generalize to non-White ethnic/racial groups or to men with FM. In addition, pre-treatment FIQ total scores were notably lower for our participants than those obtained for the mean scores reported in the original scale development publications. This may have resulted, at least in part, from our stringent inclusion/exclusion criteria and sources of recruitment producing a floor effect. Many of our participants had previously enrolled in other FM treatment studies, and may have already taken more steps than many patients to maximize benefits from various standard and experimental interventions. Such a select group of research participants may have made it more difficult to detect effects from LENS and may not have approximated the true nature of more typical, dysfunctional clinical populations of patients with FM.

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References

- 1 Bennett RM. Clinical manifestations and diagnosis of fibromyalgia. *Rheum Dis Clin North Am* 2009;35:214–32.
- 2 Bennett RM. Fibrositis: Misnomer for a common rheumatic disorder. *West J Med* 1981;134:405–13.
- 3 Wall PD. The mechanisms of fibromyalgia: A critical essay. In: Vaeroy H, Merskey H, eds. *Progress in Fibromyalgia and Myofascial Pain*. Amsterdam: Elsevier; 1993:53–9.
- 4 Williams DA, Clauw DJ. Understanding fibromyalgia: Lessons from the broader pain research community. *J Pain* 2009;10:777–91.
- 5 Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. *JAMA* 2004;292:2388–95.
- 6 Sarac AJ, Gur A. Complementary and alternative medical therapies in fibromyalgia. *Curr Pharm Des* 2006;12:47–57.
- 7 Staud R, Rodriguez ME. Mechanisms of disease: Pain in fibromyalgia syndrome. *Nat Clin Pract Rheumatol* 2006;2:90–8.
- 8 Mueller HH, Donaldson CCS, Nelson DV, Layman M. Treatment of fibromyalgia incorporating EEG-Driven Stimulation: A clinical outcomes study. *J Clin Psychol* 2001;57:933–52.
- 9 Jensen MP, Hakimian S, Sherlin LH, Fregni F. New insights into neuromodulatory approaches for the treatment of pain. *J Pain* 2008;9:193–9.
- 10 Ochs L. The Low Energy Neurofeedback System (LENS): Theory, background, and introduction. *J Neurotherapy* 2006;10:5–39.
- 11 Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: Report of the multicenter criteria committee. *Arthritis Rheum* 1990;33:160–72.
- 12 Fregni F, Freedman S, Pascual-Leone A. Recent advances in the treatment of chronic pain with non-invasive brain stimulation techniques. *Lancet Neurol* 2007;6:188–91.
- 13 Harris AR, Schwerdtfeger K, Luszczynski M-A, Sandvoss G, Strauss DJ. Adaptive time-scale feature extraction in electroencephalographic responses to transcranial magnetic stimulation. *Conf Proc IEEE Eng Med Biol Soc* 2007;2007:2835–8.
- 14 Hilz MJ, Stemper B, Axelrod FB, Kolodny EH, Neundorfer B. Quantitative thermal perception testing in adults. *J Clin Neurophysiol* 1999;16:138–44.
- 15 Kosek E, Ekholm J, Hansson P. Sensory dysfunction in fibromyalgia patients with implications for pathogenic mechanisms. *Pain* 1996;68:375–83.
- 16 Burckhardt CS, Clark SR, Bennett RM. The Fibromyalgia Impact Questionnaire: Development and validation. *J Rheumatol* 1991;18:728–33.
- 17 Lorr M, McNair DM. *Manual Profile of Mood States Bi-Polar Form (POMS-BI)*. San Diego, CA: Educational and Industrial Testing Service; 1984.

- 18 Cleeland CS, Wang XS. Measuring and understanding fatigue. *Oncology* 1999;13:91–7.
- 19 Hays RD, Stewart AL. Sleep measures. In: Stewart AL, Ware JE Jr, eds. *Measuring Functioning and Well-Being: The Medical Outcomes Study Approach*. Durham, NC: Duke University Press; 1992:235–59.
- 20 Derogatis LR. *Brief Symptom Inventory (BSI) Administration, Scoring, and Procedures Manual*, 3rd edition. Minneapolis, MN: National Computer Systems; 1993.
- 21 Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. Validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
- 22 Jensen MP, Karoly P. Self-report scales and procedures for assessing pain in adults. In: Turk DC, Melzack R, eds. *Handbook of Pain Assessment*, 2nd edition. New York: Guilford Press; 2001:15–34.

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