Brain Functional Changes and Duloxetine Treatment Response in Fibromyalgia: A Pilot Study

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ABSTRACT

Objectives. Serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressant medications may have efficacy in relieving pain associated with fibromyalgia syndrome (FMS), even in the absence of major depressive disorder (MDD). Current practice is to use a trial-and-error treatment strategy, often requiring 8–12 weeks to determine the effectiveness of a given pharmacological intervention. The ability to predict response to antidepressant medications would facilitate clinical management of FMS. Prior work in MDD has shown that the quantitative electroencephalographic (QEEG) cordance biomarker of brain functional changes early in the course of antidepressant treatment is related to later clinical response. We hypothesized that cordance might also predict response to antidepressant medications for symptoms of FMS.

Design. Twelve adults (9 females) meeting American College of Rheumatology criteria for FMS participated in a double-blind placebo-controlled treatment trial utilizing duloxetine 60 mg. QEEG cordance changes were examined over the first week of treatment. Primary clinical outcomes included change in average pain severity on the Brief Pain Inventory (BPI) and global improvement in pain on the Patient’s Global Impressions of Improvement (PGI-I) scale at 12 weeks.

Results. Changes in left frontal QEEG cordance after the first week of duloxetine treatment significantly predicted BPI pain improvement (regression coefficient \( b = 2.9, R^2 = 0.93, P = 0.008 \)) and PGI-I global improvement (regression coefficient \( b = 0.94, R^2 = 0.81, P = 0.04 \)).

Conclusions. This pilot study suggests that QEEG biomarkers may prove useful for predicting improvement in painful symptoms during SNRI treatment in FMS. Larger studies are needed to confirm this finding.

Key Words. Fibromyalgia; Duloxetine; EEG; Cordance

Introduction

Fibromyalgia syndrome (FMS) is a debilitating condition affecting an estimated 5.0 million persons in the United States [1]. The core
symptom is chronic widespread pain of unknown etiology; diagnosis is based on subjective symp-
toms, including pain in all four muscle quadrants and axial skeletal pain, along with at least 11 of 18
tender point sites [2]. Such tender points are examples of hyperalgesia and are thought to reflect 
central sensitization of pain processing pathways [2,3]. Indeed, patients with FMS report greatly 
enhanced nociception compared with pain-free controls, suggesting differences in sensory pro-
cessing [4,5]. Consistent with subjective pain reports, brain imaging studies have provided 
evidence of physiological alterations of pain processing pathways in FMS [6,7].

A number of different pharmacologic treatments may help relieve painful symptoms in FMS [8,9]. Among the pharmacologic interventions recommended in recent evidence-based guidelines [10] are serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressants medications including tricyclics and newer reuptake inhibitors (i.e., ven-
lafaxine, duloxetine), even in patients without major depressive disorder (MDD) [11]. Given the role of serotonin (5-HT) and norepinephrine (NE) in modulating pain neurotransmission [12,13], it is not surprising that SNRIs are one modality that has been shown to benefit a number of FMS patients [9,14,15]. However, no single drug, or combination of drugs, appears to be reliably effective for a major-
ity of patients with FMS. As such, clinical manage-
ment of this syndrome calls for individualized 
selection of drugs and dosing [10].

At present, the only method for determining which patients are likely to benefit from a particu-
lar antidepressant medication is a prolonged treat-
ment trial. Current clinical practice is to start a 
medication and monitor the patient for symptom-
atic improvement for up to 8–12 weeks [16,17], a 
common length of time needed to detect consist-
tent pain relief [18]. This trial-and-error process 
can result in prolonged suffering and disability, 
and it constitutes a treatment approach that is 
frustrating and unacceptable to many patients. 
Due to the uncertainty of benefit and the problem of side effects in the early stages of treatment with an antidepressant agent, many patients may pre-
aturally discontinue a medication before they 
have had the opportunity to experience benefit.

The challenge of predicting antidepressant treatment outcome in FMS is similar to a central 
challenge in MDD. In both FMS and MDD, there is typically a long lag between the initiation of 
treatment and the symptomatic response, and it is 
unclear when, and for whom, a specific medication 
will be effective. Previous work in MDD has shown that quantitative electroencephalographic (QEEG) changes seen in electrodes overlying prefrontal, and midline-and-right-frontal (MRF), brain regions within the first week of beginning 
antidepressant treatment predict clinical outcomes at 8–12 weeks [19,20]. QEEG theta-band cordance is an especially powerful predictor of clinical outcomes in MDD that has demonstrated validity across reuptake inhibitor medications [21,22], and across research sites and institutions [20,23]. 
QEEG cordance is an easily obtained brain func-
tional measure that utilizes electrical recordings 
from the scalp; cordance has been shown to have a 
moderately strong (0.59) correlation with cortical 
perfusion underlying each electrode, and a stron-
ger relationship to perfusion than that seen with 
classical absolute and relative power QEEG mea-
ures [24].

The present study examined the usefulness of QEEG cordance biomarkers to predict treatment response to an SNRI in FMS. Given that dulox-
etine enhances 5-HT and NE transmission via 
reuptake blockade throughout the brain and spinal 
cord, it has analgesic effects that are independ-
ent of its central antidepressant effects. Efficacy 
of duloxetine, measured as pain reduction and 
improvement on health/functioning outcome 
measures, was recently demonstrated in two trials in FMS [14,15]. Because duloxetine appears to be effective for a subset of persons with FMS, and because QEEG cordance biomarkers have been 
useful in predicting reuptake inhibitor treatment 
outcomes in the context of MDD, we hypothe-
sized that QEEG cordance biomarkers after 1 
week would predict pain relief after 12 weeks of 
duloxetine treatment in FMS.

Methods

Study Design

This pilot study was ancillary to a large multisite 
double-blind placebo-controlled clinical trial 
examining the efficacy of duloxetine for pain in 
primary FMS [25], utilizing only the subjects 
enrolled at the University of California, Los 
Angeles (UCLA) site. The overall trial lasted 1 
year, with the primary end point at 6 months 
and doses of duloxetine as high as 120 mg. For this 
addendum, the primary clinical outcomes were
assessed after 12 weeks at which time point all medication subjects received the same dose (60 mg). The goal of this addendum study was to determine whether changes in QEEG cordance in the first week of randomized treatment with duloxetine or placebo would be related to improvement in pain symptoms in FMS at 12 weeks.

**Participants**

Data were gathered from 12 adults with FMS, including 9 females and 3 males with an average age of 50.1 years (standard deviation [SD] = 8.2) and an average BPI rating of 6.67 (SD = 1.9). Subjects were recruited from the community and UCLA clinics through fliers, public service announcements, and physician referral. Enrolled subjects met criteria for FMS, as defined by the American College of Rheumatology: widespread aching pain in all four quadrants of the body and axial skeletal locations for >3 months duration, and pain in ≥11 of 18 tender points under digital palpitation examination with an approximate force of 4 kg/cm² [2]. In addition, subjects met the screening criterion of a score of ≥4 on the average pain item of the Brief Pain Inventory (BPI). Subjects were permitted into the study if they met criteria for a diagnosis of MDD as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) [26]; three of six medication subjects and three of six placebo subjects in this addendum study met criteria for MDD. Exclusion criteria included: any current primary Axis I diagnosis other than MDD; primary DSM-IV Axis I diagnosis of anxiety disorder within the past year; and previous DSM-IV Axis I diagnosis of psychosis, bipolar disorder, or schizoaffective disorder. Concomitant medications with primary central nervous system activity were generally not allowed, and categorically excluded were medications including anticonvulsants, antidepressants, mood stabilizers and antipsychotic agents, triptan migraine medications, anti-Parkinsonian medications, opiate medications, monoamine oxidase inhibitors, muscle relaxants, topical anesthetics and analgesics, antispasmodics, dextromethorphan, reserpine, barbiturates, and oral or injected steroids. Benzodiazepines were allowed only for subjects who had been using a stable dose for 3 months prior to enrollment. Stable aspirin use was allowed at up to 325 mg/day for cardiac prophylaxis. Acetaminophen was the only analgesic agent allowed to address FMS pain; subjects who required narcotic analgesics for FMS pain control were not enrolled in the study.

Subjects who met entry criteria were assigned randomly to duloxetine (N = 6) or placebo (N = 6). Duloxetine was administered at a starting dose of 30 mg/day for 1 week followed by 12 weeks of duloxetine 60 mg/day. To preserve blinding, placebo dosing matched duloxetine dosing throughout the trial. Clinical assessments were obtained at weeks 1, 2, 4, 6, 8, and 12 of randomized treatment. EEGs were obtained immediately before, and 1 week after, initiating double-blinded treatment.

**Clinical Outcome Assessments**

Outcome assessments consisted of patient-rated measures of pain symptoms. Item number 3 of the BPI [27] captured “average pain severity” over the past 24 hours on a scale ranging from 0 (no pain) to 10 (pain as bad as you can imagine). Overall reduction in pain since beginning the study medication was assessed using the Patient’s Global Impressions of Improvement (PGI-I) scale [14] ranging from 1 (very much better) to 7 (very much worse). The co-primary outcome measures consisted of changes on the BPI and PGI-I from baseline to week 12 of randomized treatment.

**QEEG Procedures**

EEG recordings were performed at pretreatment baseline, and again at 1 week after beginning randomized treatment, using methods described previously [19,28]. Thirty-five recording electrodes were positioned with an electrode cap (ElectroCap, Eaton, OH) using an extended International 10–20 System (Figure 1). Recordings were obtained while subjects rested in the eyes-closed, maximally alert state in a sound-attenuated room with subdued lighting using the NuAmps system (Compumedics Ltd., Charlotte, NC) with a Pz reference montage. Eye movements were monitored using right infraorbital and left outer canthus electrodes. Data were digitized online at 250 samples/channel/s (passband 0.3–70 Hz) and were reformatted by amplitude subtraction to construct a bipolar electrode pair montage. An EEG technologist blinded to subject identity and treatment condition selected for processing the first 20–32 seconds of artifact-free data. An independent blinded technologist confirmed the selection prior to processing. A fast Fourier transform was used to calculate absolute power (the intensity of energy in a frequency band in microvolts squared) in each of four frequency bands (0.5–4 Hz, 4–8 Hz, 8–12 Hz, and 12–20 Hz).
Cordance Calculations and Topographic Maps

Cordance values were calculated from conventional QEEG absolute and relative power measures in each of the four frequency bands for each electrode site. This three-step procedure is described elsewhere in greater detail [19, 24]. First, EEG power values were computed using a re-attributional electrode montage because this montage affords a higher correlation between EEG and positron emission tomography (PET) measures of cerebral perfusion than other montages [29]. Second, the absolute and relative power values were z-transformed to measure deviation from the mean values for each electrode site (i) in each frequency band (f) for that recording, yielding \( A_{\text{norm}(i,f)} \) and \( R_{\text{norm}(i,f)} \), respectively. Third, these z-scores were summed to yield a cordance “intensity” value, \( Z_{(i,f)} = A_{\text{norm}(i,f)} + R_{\text{norm}(i,f)} \). Analyses were performed on cordance measures from the theta frequency band (4–8 Hz) because previous work from this and other laboratories has indicated that energy in the theta band is associated most strongly with the effects of antidepressant medication [19, 21, 30]. Theta cordance has been shown to have a stronger association with cerebral perfusion than either absolute or relative power measures [24].

Change in theta cordance was calculated by subtracting the cordance measure at baseline from the cordance measure at the end of week 1 for each electrode. For purposes of illustration, “cordance change” values at 1 week were displayed on brain topographic maps showing mean changes at each electrode for responder vs non-responder groups.

Statistical analyses were performed focusing on four regions of interest (ROIs). Prior work in MDD has found associations between changes in frontal and/or prefrontal EEG surface regions and later response to antidepressant medication. This is consistent with a literature in MDD pointing to frontal brain function as centrally related to changes in MDD symptoms. In FMS, we reasoned that pain symptoms might be related to regional changes in brain function as measured by electrodes overlying frontal and/or somatosensory cortex. Because this was a first attempt to identify early QEEG changes as potential predictors of response to antidepressant medication for pain in FMS, we used an exploratory approach and examined cordance changes in four brain regions designated by the following electrodes: left frontal (LF: Fpz, Fp1, Af1, F7), right frontal (Fpz, Fp2, Af2, F8), left somatosensory (Cz, Fc1, Fc5, C3, T3, Cp1, Cp5), and right somatosensory (Cz, Fc2, Fc6, C4, T4, Cp2, Cp6) (see Figure 1).

Data Analysis

We used linear regression analyses to examine change in EEG cordance at 1 week in each of the four ROIs as predictors of change in pain at 12 weeks. Separate regression analyses were conducted to examine each ROI for each of the two co-primary outcome measures. For each outcome measure (BPI and PGI-I), we applied a Bonferroni-corrected criterion of \( P < 0.0125 \) to control for the four tests (i.e., \( P < 0.05/4 \)). For analyses of dichotomous clinical outcomes, we classified subjects as BPI responders (\( \geq 50\% \) reduction) vs BPI non-responders (\(< 50\% \) reduction), and as PGI-I responders (1 = very much better or 2 = much better) vs PGI-I non-responders (3 = a little better to 7 = very much worse).

Results

Clinical Results

In total, five of six medication subjects, and two of six placebo subjects completed the protocol through the 12-week assessment point. The one medication non-completer dropped out of the study at week 4. Among the four placebo non-completers, one subject dropped out at week 1, one at week 2, one at week 3, and one at week 4. At the 12-week assessment, two of five (40%) medication subjects met BPI and PGI-I response criteria. Neither placebo completer met BPI or PGI-I
response criteria. There was no significant difference among medication responders (M-Rs), medication non-responders (M-NRs), and placebo non-responders (P-NRs) on any baseline clinical/demographic variable except for age (F[2,4] = 56.2, P = 0.001), where P-NRs were found to be younger than M-NRs (P = 0.001) and medication responders (P = 0.005) (Table 1). Subjects with MDD did not differ significantly from non-MDD subjects with respect to baseline characteristics; however, there was a strong trend in the expected direction toward higher baseline scores on the 17-item Hamilton Depression Rating Scale [31] in MDD subjects (Table 2).

**EEG Results**

The model employing only LF cordance was a significant predictor of BPI outcome in duloxetine subjects (regression coefficient = 2.9, R² = 0.93, P = 0.008) (Figure 2). None of the models employing other ROIs was significant. With regard to PGI-I outcome, the LF cordance model resulted in a regression coefficient = 0.94 with an R² = 0.81, and P = 0.04, a significance value that did not meet the corrected threshold of P < 0.0125. Other ROIs did not significantly predict PGI-I. Figure 3 shows topographic maps of 1-week cordance changes for groups of medication subjects classified as pain responders vs non-responders at 12 weeks.

Because some subjects were diagnosed with MDD in addition to FMS, we examined the LF cordance marker as a predictor of pain and global improvement outcomes while controlling for MDD. In separate models examining BPI and PGI-I outcomes, we entered dichotomous MDD status in the first block and change in LF cordance in the second block. Regarding change in BPI average pain, LF cordance remained a significant predictor while controlling for MDD (regression coefficient = 3.04, P = 0.04). MDD was not a significant predictor in either the model including both LF cordance and MDD (regression coefficient = 0.74, P = 0.78) or in the model with MDD as the only predictor (regression coefficient = −2.2, P = 0.53). Similarly for the PGI-I outcome, LF cordance remained a significant predictor while controlling for MDD (coefficient = 1.13, P = 0.045). MDD again was not a significant predictor either in the two-predictor model (regression coefficient = 0.75, P = 0.26) or in the single-predictor model (regression coefficient = −0.33, P = 0.79).

In order to test whether LF cordance worked differently to predict response in the presence vs absence of MDD, we assessed interactions between illness status and the LF cordance biomarker. Regression models were evaluated, thus offering three independent variables: illness status (dichotomous; MDD vs non-MDD), LF cordance (i.e., continuous 1-week change in LF cordance), and an illness status × LF cordance interaction term, as predictors of 12-week change in average pain, or global improvement, respectively. The interaction term was not significant in the model predicting BPI outcome (regression coeffi-

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**Table 1** Subject characteristics by response group at 12 weeks

<table>
<thead>
<tr>
<th></th>
<th>M-R (N = 2)</th>
<th>M-NR (N = 3)</th>
<th>P-R (N = 0)</th>
<th>P-NR (N = 2)</th>
<th>All 12-Week Completers (N = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.5 (SD = 2.1)</td>
<td>58.7 (SD = 2.9)</td>
<td>N/A</td>
<td>36.0 (SD = 1.4)</td>
<td>51.0 (SD = 10.6)</td>
</tr>
<tr>
<td>Females : males</td>
<td>2:0</td>
<td>2:1</td>
<td>N/A</td>
<td>2:0</td>
<td>6:1</td>
</tr>
<tr>
<td>Baseline HamD17</td>
<td>11.5 (SD = 9.2)</td>
<td>16.0 (SD = 3.0)</td>
<td>N/A</td>
<td>13.5 (SD = 10.6)</td>
<td>14.0 (SD = 6.3)</td>
</tr>
<tr>
<td>Baseline BPI</td>
<td>8.5 (SD = 2.1)</td>
<td>7.3 (SD = 0.6)</td>
<td>N/A</td>
<td>4.5 (SD = 0.7)</td>
<td>6.9 (SD = 2.0)</td>
</tr>
<tr>
<td>MDD : non-MDD</td>
<td>1:1</td>
<td>1:2</td>
<td>N/A</td>
<td>1:1</td>
<td>3:4</td>
</tr>
</tbody>
</table>

Responders met response criteria both for item number 3 of the BPI and the Patient’s Global Impressions of Improvement.

**Table 2** Characteristics of MDD vs non-MDD subjects

<table>
<thead>
<tr>
<th></th>
<th>MDD (N = 3)</th>
<th>Non-MDD (N = 4)</th>
<th>Statistic</th>
<th>Two-Tailed P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.3 (SD = 12.4)</td>
<td>52.3 (SD = 10.8)</td>
<td>t(5) = 0.33</td>
<td>P = 0.75 (two-tailed)</td>
</tr>
<tr>
<td>Females : males</td>
<td>3:0</td>
<td>3:1</td>
<td>Chi-square = 0.88</td>
<td>P = 1.0 (Fisher’s exact test; two-tailed)</td>
</tr>
<tr>
<td>Baseline HamD17</td>
<td>18.3 (SD = 2.5)</td>
<td>10.8 (SD = 6.6)</td>
<td>t(5) = −1.87</td>
<td>P = 0.06 (one-tailed)</td>
</tr>
<tr>
<td>Baseline BPI</td>
<td>7.0 (SD = 3.0)</td>
<td>6.8 (SD = 1.3)</td>
<td>t(5) = −0.15</td>
<td>P = 0.88 (two-tailed)</td>
</tr>
</tbody>
</table>

There was no statistically significant difference between groups for any of the clinical/demographic variables. However, there was a strong trend in the expected direction toward higher baseline HamD17 score in MDD subjects.

**BPI** = Brief Pain Inventory; HamD17 = 17-item Hamilton Depression Rating Scale; MDD = major depressive disorder; SD = standard deviation.
cient = -1.35, P = 0.42) or predicting PGI-I outcome (regression coefficient = -0.32, P = 0.71).

Assessment of cordance models in predicting response to placebo was not possible because only two placebo subjects completed through week 12. Of note, the two placebo non-responders exhibited changes in LF cordance of 1.33 and -1.98; respectively, these values represented the largest increase and largest decrease in LF cordance observed in this study. These observations in placebo-treated subjects were not consistent with the pattern of association between LF cordance and clinical improvement seen in duloxetine-treated subjects.

**Post Hoc Analyses**

**LF Cordance and Early Clinical Improvement**

Week 12 clinical outcome was the primary endpoint of our study as prior work has suggested that significant pain improvement with antidepressant medication might take as long as 8–12 weeks to achieve. Nonetheless, having identified a marker (LF cordance) that appeared to be associated with 12-week outcome, it was of interest to explore what association this marker might have to clinical response at an earlier time point. In this pursuit, we found that change in LF cordance at 1 week was a significant predictor of week 4 change in BPI average pain (regression coefficient = 3.37, $R^2 = 0.81$, $P = 0.015$) and week 4 PGI-I global improvement (regression coefficient = 0.73, $R^2 = 0.84$, $P = 0.03$). Figure 4 shows the linear association between week 4 change on the BPI and the week 1 LF cordance measure.

**ROIs in MDD**

QEEG cordance changes in the prefrontal region (electrodes FP1, FPz, FP2) and the MRF region (electrodes AF2, F4, F8, FP2, FPz, Fz) during the

**Figure 2** Relationship between change in left frontal (LF) cordance after the first week of duloxetine treatment and change in average pain severity (Brief Pain Inventory [BPI] item number 3) at 12 weeks. Solid dots indicate subjects with major depressive disorder (MDD); open circles indicate non-MDD subjects. R Squared Linear = the square of Pearson’s $r$.

**Figure 3** Changes in cordance after 1 week of randomized treatment for those subjects later classified as responders vs non-responders (Response defined as $\geq 50\%$ improvement on Brief Pain Inventory average pain severity at 12 weeks). Topographic maps are shown for duloxetine responders (left), duloxetine non-responders (middle), and placebo non-responders (right). None of the placebo subjects responded. Cordance maps indicate the head viewed from above with each black dot representing an electrode site. Maps represent cordance change from baseline values at 1 week, with increases shown in red and decreases in blue, as indicated on the color bars.
The first week of antidepressant treatment has been associated with improvement in depressive symptoms at 8 weeks in MDD [19–23]. These prior observations raise the question as to whether the same brain regional markers that have been shown to predict antidepressant medication response in MDD might also predict antidepressant medication response in FMS. This question is pertinent to FMS subjects with or without comorbid MDD.

To address this issue, we examined prefrontal and MRF regional cordance markers in separate analyses as predictors of average pain and global improvement in all duloxetine subjects, and in only those duloxetine subjects with MDD (eight analyses in total). None of the models was significant using a criterion of $P < 0.05$ uncorrected for multiple comparisons (data not presented).

**Discussion**

The present study found regional changes in QEEG cordance after 1 week of duloxetine treatment and change in average pain (Brief Pain Inventory item number 3) at 4 weeks. Solid dots indicate subjects with major depressive disorder (MDD); open circles indicate non-MDD subjects. $R^2$ Linear = the square of Pearson’s $r$.

The topographic region that predicted FMS response in duloxetine-treated subjects was defined by surface electrodes overlying the LF cortex. In MDD, studies using QEEG cordance have reported bilateral prefrontal decreases, and MRF decreases as predictors of response/remission of depressive symptoms at 8 weeks in subjects treated with selective serotonin reuptake inhibitor (SSRI) or SNRI antidepressant medications [19–22]. In the one report on duloxetine-treated MDD subjects, cordance decreases in the MRF region were associated with remission of symptoms of depression [32]. Therefore, it is possible that pain response in FMS is predicted by early cordance decreases in the LF region, distinct from the MRF that predicts response in MDD. Consistent with this possibility, post hoc analyses in the present FMS cohort did not find a significant relationship between MRF cordance and improvement in pain. If changes in LF cordance captured a neurophysiologic feature that was generally associated with decreased pain or pain sensitization, then we might have expected to see changes in LF cordance in association with pain reduction in FMS subjects treated with altogether different medications such as pregabalin or gabapentin. Future studies should examine the specificity of this measure for pain relief in FMS and for pain relief with distinct medication classes.

In the present sample, two of five (40%) of duloxetine-treated subjects showed significant improvement at 12 weeks. Neither of the two placebo subjects (0%) who completed through week 12 responded. Our sample size of placebo completers is clearly too small to infer placebo response rate. As a basis for comparison, a report of the parent study ($N = 520$) found a 12-week placebo response rate of 23.7% [25]. Given the small number of placebo completers, we were unable to assess any relationship between QEEG biomarkers and placebo response. The specificity of the relationship between changes in LF cordance and pain relief associated with medication, as opposed to placebo, should be examined in future studies.

Findings of this initial exploratory study of QEEG cordance biomarkers of treatment response in FMS are encouraging but should be interpreted within the limits of the study. First, this hypothesis-generating study examined only a small number of subjects, and it is possible that the outcomes in these subjects may not be representative of FMS patients overall. There are a number of sources of clinical and neurophysiologic heterogeneity in patients with FMS, perhaps most notably the presence or absence of MDD. Although there was no difference in cordance values between the subjects with and without MDD in this study, there were not a sufficient
number of subjects studied to draw any definitive conclusions. Second, there were an insufficient number of subjects who completed the protocol in the placebo group to assess any predictive relationship that might exist between QEEG cordance ROIs and placebo response in FMS. Third, the study also utilized single-item outcome measures; more comprehensive outcome measures may be useful in addressing acute pain thresholds, multiple clinical aspects of FMS (i.e., associated sleep, emotional, or cognitive symptoms), and functional status. Fourth, this study examined the response to only one specific SNRI, duloxetine, and only at a fixed dose. It would be useful to know whether cordance could be used to predict improvement with duloxetine at other doses, and, if cordance could predict response to other pharmacologic treatments for FMS. Finally, future studies with larger sample sizes should also control for potential effects of baseline pain severity and gender. This study could not control for gender as there was only one male completer; however, prior work has shown a different relationship between depression severity and FMS severity in females as compared with males [33].

Conclusion

Findings of this pilot study suggest that the QEEG cordance biomarker may predict SNRI antidepressant medication treatment response of painful symptoms in FMS. Further development of QEEG biomarkers along these lines could lead to improved clinical management of FMS. Larger and more comprehensive studies are needed to replicate present findings and determine biomarker specificity.

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Note also that the use of the cordance method for management of fibromyalgia is the subject of a provisional patent application by the regents of the University of California.

References