

A MIND-BODY TECHNIQUE FOR SYMPTOMS RELATED TO FIBROMYALGIA AND CHRONIC FATIGUE

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Context: A novel mind–body approach (amygdala retraining) is hypothesized to improve symptoms related to fibromyalgia and chronic fatigue.

Objective: To examine the use of a mind–body approach for improving symptoms related to fibromyalgia and chronic fatigue.

Design: This was a single-blind, randomized controlled trial.

Setting: The study was conducted in a tertiary-care fibromyalgia and chronic fatigue clinic.

Patients: Patients with fibromyalgia, chronic fatigue, or both were included.

Interventions: Patients were randomly assigned to receive amygdala retraining along with standard care or standard care alone. Standard care involved attending a 1.5-day multidisciplinary program. The amygdala retraining group received an additional 2.5-hour training course in which the key tools and techniques adapted from an existing program were taught to the patient. A home-study video course and associated text were

provided to supplement the on-site program. Both groups received telephone calls twice a month to answer questions related to technique and to provide support.

Main Outcome Measures: Validated self-report questionnaires related to general health, well-being, and symptoms, including Short Form-36, Measure Yourself Medical Outcome Profile, Multidimensional Fatigue Inventory, Epworth Sleepiness Scale, and Fibromyalgia Impact Questionnaire.

Results: Of the 44 patients randomly assigned who completed baseline assessments, 21 patients completed the study (14 in the standard care group and 7 in the study group). Median age was 48 years (range, 27–56 years), and female subjects comprised 91% of the group. Analyses demonstrated statistically significant improvements in scores for physical health, energy, pain, symptom distress, and fatigue in patients who received the amygdala retraining compared with standard care.

Key words: Fibromyalgia, mind–body techniques, randomized controlled trial

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INTRODUCTION

Fibromyalgia and chronic fatigue are debilitating disorders with significant symptom burden related to pain, fatigue, mood alteration, and sleep difficulties.¹ Despite the progress made in the past several years with both pharmacologic and nonpharmacologic therapies, few options are currently available to patients seeking modalities to self-manage symptoms. One novel mind–body technique that may be helpful for improving symptoms related to fibromyalgia and chronic fatigue is called amygdala retraining. Elements of this program are available commercially on the Internet and were used in this study.

Amygdala retraining has theoretical roots in the neurobiological theory and empirical work of LeDoux² and other neuroscientists,^{3,4} which implicates the amygdala in conditioning processes that occur during aversive and sometimes traumatic events. LeDoux's model suggests that environmental events such as painful electric shock can be thought of as conditioned

stimuli that elicit threat and emotional responses that are largely directed by the functioning of the amygdala.² The amygdala has long been a central focus of the neurobiological system, directing fear responses to threatening environmental events.³ Additional research has suggested that the amygdala-mediated, fear-conditioning mechanism is controlled by a higher-order cortical network involving not only the amygdala but also the insula, anterior cingulate, and medial prefrontal cortex, along with other areas.^{5,6} Fear conditioning mediated through the amygdala that is not sufficiently controlled by higher-order centers is thought to be involved in disorders such as posttraumatic stress disorder.^{7,8} In fact, some evidence points to insufficient suppression of amygdalar activity in some patients with posttraumatic stress disorder.^{7,9}

The basis of amygdala retraining as a method of decreasing symptoms in fibromyalgia and chronic fatigue is the theory by Gupta^{10,11} that dysregulated amygdala fear conditioning underlies some of the symptoms related to these conditions. According to Gupta, as a consequence of psychological stress and trauma, perhaps with accompanying viral infection and/or chemical or physiologic stressors, the amygdala becomes hyper-vigilant to deviations from physiologic homeostasis. Chronic oversensitization of the amygdala to internal sensations results in chronic overactivation of the amygdala-mediated fear response. This results in exhaustion of the neuroendocrine and

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immune systems and chronic physical and mental exhaustion, as well as many secondary symptoms and ongoing complications. Furthermore, a self-perpetuating cycle of amygdala oversensitivity, homeostatic dysregulation, and further amygdala overactivation is perpetuated.

The purpose of the present study was to examine the efficacy of mind-body tools and techniques adapted from an amygdala retraining program in providing relief of symptoms related to fibromyalgia and chronic fatigue. Based on Gupta's clinical audit,¹¹ we hypothesized that patients receiving this training will experience improvements in health and quality of life compared with patients receiving standard care.

METHODS

Design and Procedure

We conducted a single-blind, randomized controlled trial that comprised patients seen at the fibromyalgia and chronic fatigue clinic at our institution and recruited from November 2009 through May 2010. Follow-up continued through November 2010. Inclusion criteria were as follows a confirmed diagnosis of fibromyalgia, chronic fatigue, and/or chronic fatigue syndrome; age 18 to 59 years; and access to a DVD player. No patients were excluded on any other basis. This study was approved by our institutional review board and is registered with ClinicalTrials.gov as NCT01046370.

After providing informed consent, patients were randomly assigned to receive amygdala retraining along with standard care or standard care alone. Patients receiving standard care participated in a 1.5-day multidisciplinary program with an emphasis on cognitive-behavioral therapy and graded exercise therapy described elsewhere.¹²⁻¹⁴ In addition to receiving standard care, patients in the amygdala retraining group attended a 2.5-hour training course, in which the key tools and techniques were taught to the patient.

Amygdala retraining serves to restore a more normal state of homeostasis through deconditioning the amygdala-mediated fear response to distressing internal sensations and thoughts. This is accomplished through several mind-body techniques that promote relaxation and attempt to reorient attention away from the distressing symptoms of the viscera or catastrophizing thoughts. For instance, one technique called "soften and flow" uses methods of systematic desensitization to allow patients to become aware of internal symptoms while remaining calm and relaxed. Other techniques such as stopping negative thoughts, cultivation of awareness, meditation, and breathing exercises are incorporated to promote physiologic reconditioning.

A home-study video course and associated text were also provided to supplement the on-site program. Patients were instructed to practice the techniques daily in response to distressing internal sensations and thoughts. Both groups of patients then received telephone calls twice a month from the study staff to answer questions related to technique and to provide support. During telephone calls, any questions or concerns that patients may have had were addressed. In this article, we are reporting results of assessments at baseline (T1) and at follow-up 1-month after the training class (T2).

Measures

Short Form-36. The Short Form-36 (SF-36) is a widely used measure of health outcomes in patient samples.¹⁵ The 36 items are scored to create eight different subscales, including physical, role physical, role emotional, energy, well-being, social functioning, pain, and general health.¹⁶ The SF-36 has been shown to be reliable and valid in numerous studies.^{16,17} In the present study, the eight subscales were scored and used in analyses. Subscales were internally consistent at T1 (α , .76-.96) and T2 (α , .81-.94).

Measure Yourself Medical Outcome Profile. The Measure Yourself Medical Outcome Profile (MYMOP-2) is an assessment of the patient's perspective on his/her most salient symptom and resulting degree of distress. The assessment includes five items rated on Likert-type scales. The MYMOP-2 has been shown to be reliable and valid.¹⁸ Because of an error during baseline data collection, only items 1 through 4 are included in this scale's total score. In the present study, the MYMOP-2 was internally consistent at T1 (α = .90) and T2 (α = .89).

Multi-Dimensional Fatigue Inventory. The Multi-Dimensional Fatigue Inventory (MDFI) is a 20-item assessment that indexes several different aspects of fatigue (19). This assessment is arranged in 5 4-item subscales assessing general fatigue, physical fatigue, mental fatigue, low motivation due to fatigue, and low activity due to fatigue. Items are scored on a 5-point Likert-type scale. The MDFI has been shown to be reliable and valid.¹⁹ In the present study, all subscales of the MDFI were internally consistent at T1 (α , .58-.84) and T2 (α , .66-.92).

Epworth Sleepiness Scale. The Epworth Sleepiness Scale (ESS) is a measure of general daytime sleepiness. This is an eight-item scale, each scored on a four-point Likert-type scale. The ESS has been shown to be reliable and valid.²⁰ In the present study, the ESS was internally consistent at T1 (α = .87) and T2 (α = .86).

Fibromyalgia Impact Questionnaire. The Fibromyalgia Impact Questionnaire (FIQ) is perhaps the most widely used measure to assess intrusion of symptoms on quality of life in patients with fibromyalgia and related disorders such as chronic fatigue syndrome. The FIQ is a 20-item assessment that scores each item on Likert-type scales. In the past few decades, the FIQ has become a popular and sensitive tool for use in evaluating effective therapeutic approaches to fibromyalgia.²¹ The FIQ has a long history of psychometric support for its reliability and validity.²¹ In the present study, the FIQ was internally consistent at T1 (α = .88) and T2 (α = .91).

Demographics and Diagnosis. Data on age, sex, and diagnosis were collected from the patients in this study. Diagnosis categories included fibromyalgia, chronic fatigue, and comorbid fibromyalgia and chronic fatigue.

Analytic Plan

Data were analyzed with one-way analysis of variance (ANOVA), mixed-model repeated-measures ANOVA, and the χ^2 test. For primary analyses of health outcomes, η^2 is provided as a measure of effect size. Mixed-model repeated-measures ANOVAs are followed with simple effects tests of within-subjects parameters. All statistical tests are conducted using $\alpha < .10$. A more liberal α level was chosen because sample size was quite small and the risk of type II error is inflated with small samples.²² In an attempt to better control type II error and yet remain within reasonable bounds of type I error, we chose $\alpha < .10$ as our hypothesis testing probability level. This approach has been advocated and used in previous work when sample size cannot be feasibly increased and no other means of controlling type II error are available (eg, increasing effect size or decreasing error).²³ All data analyses were conducted using SPSS software version 19 (IBM, Somers, New York).

RESULTS

Of 183 patients invited to participate in this study, 126 declined. The 57 patients who agreed to participate were randomly assigned to 1 of the 2 groups in the study (Figure 1). Of these, only 21 patients completed all study-related procedures and measures (“completers”). Therefore, all analyses are determined on the basis of these 21 patients for whom all data points were available. Median age was 48 years (range, 27-56 years) and most ($n = 19$; 90%) were women. Patient diagnoses were fibromyalgia ($n = 15$), chronic fatigue ($n = 3$), and comorbid fibromyalgia and chronic fatigue ($n = 3$).

Attrition Analyses

Of the 57 patients randomly assigned, six in the amygdala retraining group dropped out before receiving the allocated intervention, and seven in the control group did not complete baseline assessments (Figure 1). To determine whether there were statistically significant differences in the remaining 44 patients between the 21 completers mentioned previously and the 23 patients who did not complete all measures (“noncompleters”), we examined all key outcome variables at baseline by using one-way ANOVA. Completers reported higher levels of energy ($M_{\text{completer}} = 24.76$, $M_{\text{noncompleter}} = 11.74$; $F_{1,42} = 7.56$, $P = .01$) and well-being ($M_{\text{completer}} = 66.67$, $M_{\text{noncompleter}} = 54.74$; $F_{1,42} = 3.70$, $P = .06$) but also reported greater levels of fatigue on the general ($M_{\text{completer}} = 10.14$, $M_{\text{noncompleter}} = 9.07$; $F_{1,40} = 3.66$, $P = .06$), motivation ($M_{\text{completer}} = 13.24$, $M_{\text{noncompleter}} = 10.57$; $F_{1,40} = 6.31$, $P = .02$), and activity ($M_{\text{completer}} = 10.38$, $M_{\text{noncompleter}} = 8.18$; $F_{1,39} = 3.42$, $P = .07$) subscales of the MDFI. There were no differences in sex or diagnosis by completer/noncompleter status. There was a statistically significant association between group and completion status ($\chi^2 [1, N = 44] = 11.03$, $P = .001$). Twice as many standard care patients ($n = 14$) completed the study as amygdala retraining patients ($n = 7$).

Randomization Analyses

To ensure that the randomization process worked effectively to provide two equal groups for this trial, we used one-way ANOVA to determine whether statistically significant differences existed between amygdala retraining and standard care groups on sex, age, and diagnosis. No differences were observed for any of these variables (all $P > .10$).

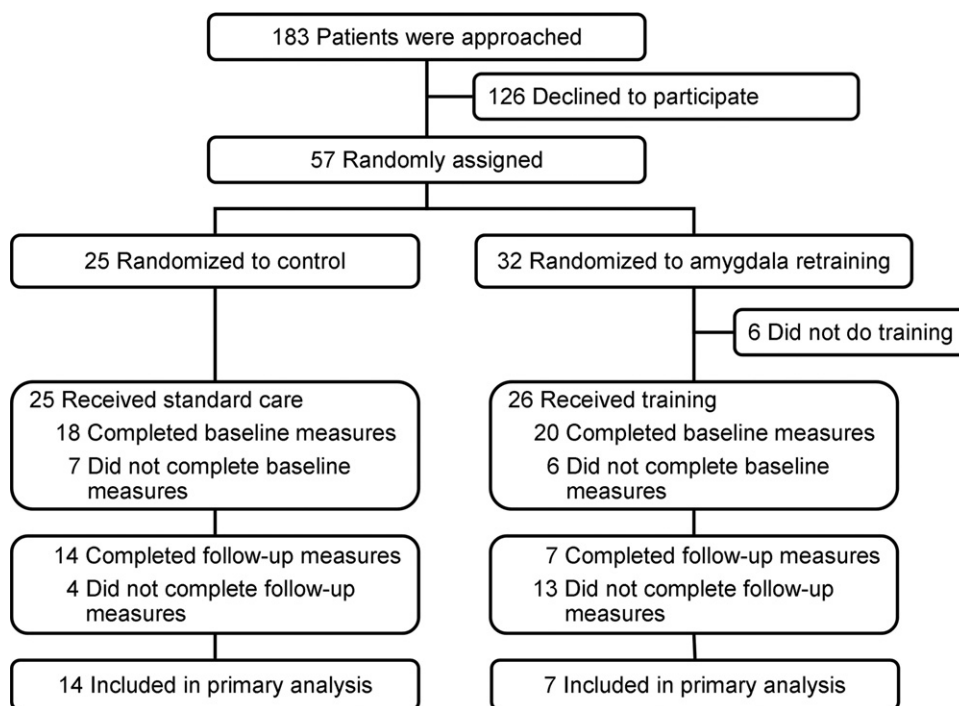


Figure 1. Flow of patients through the study.

Mixed-Model ANOVAs

To evaluate treatment efficacy of the amygdala retraining program, we examined changes from baseline to follow-up in outcome measures across both groups using mixed-model repeated-measures ANOVA. Results of these analyses showed that patients receiving

amygdala retraining showed significant improvements on several outcome measures from baseline to follow-up, whereas patients receiving standard care had unchanged outcome measures. This pattern of findings held for SF-36–physical, SF-36–energy, SF-36–pain, MYMOP-2, MDFI–motivation, MDFI–activity, and FIQ

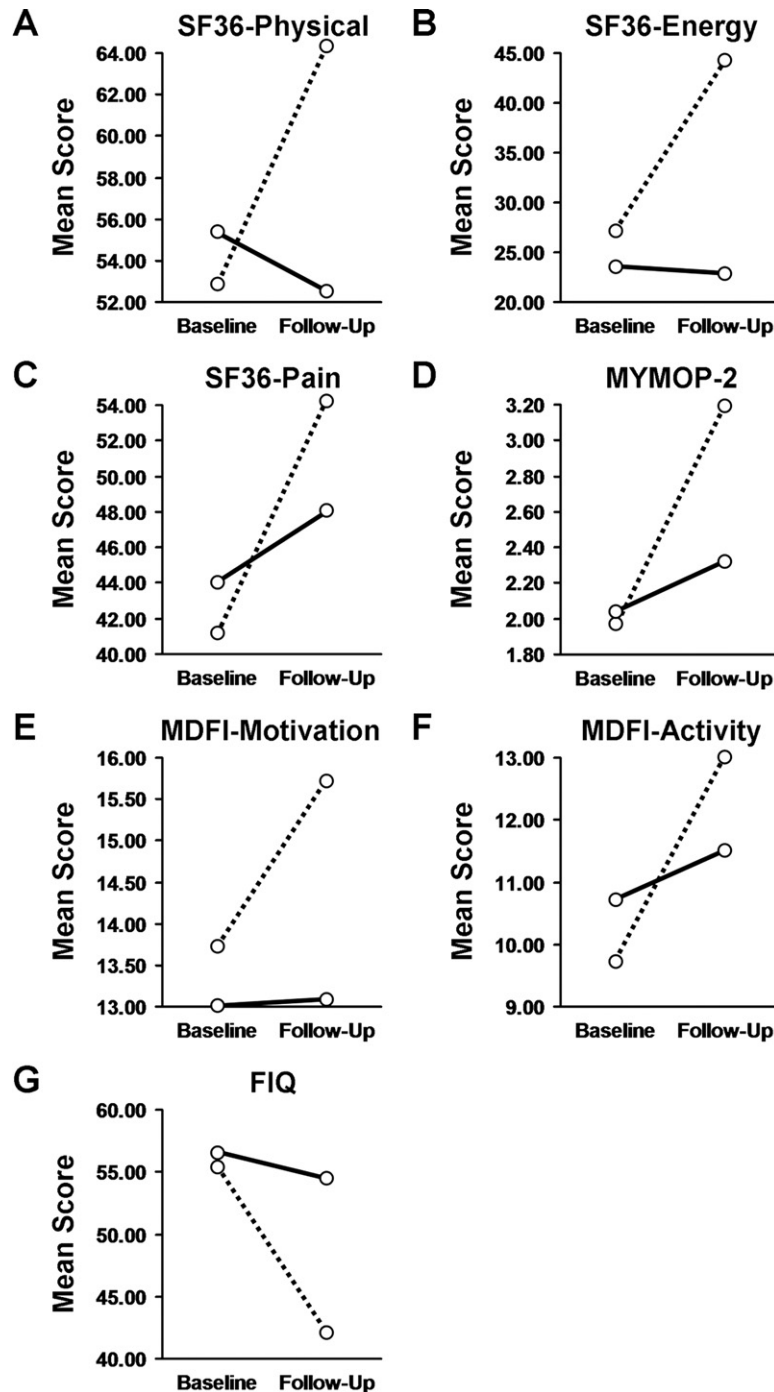


Figure 2. Change in scores from baseline to follow-up for amygdala retraining ($n = 7$, dashed lines) and standard care ($n = 14$, solid lines) groups on several measures. (A) Short Form-36 (SF-36) physical health score. (B) SF-36 energy score. (C) SF-36 pain score. (D) Measure Yourself Medical Outcome Profile (MYMOP-2) score. Score reversed. (E) Multi-Dimensional Fatigue Inventory (MDFI) –Motivation score. (F) MDFI–Activity score. (G) Fibromyalgia Impact Questionnaire (FIQ) score.

Table 1. Mixed-Model Repeated-Measures ANOVA Across Both Groups from Baseline (T1) to Follow-Up (T2)

Measure	Standard Care (n = 14) ^a		Amygdala Retraining (n = 7) ^a		F ^b	P Value	η^2
	T1	T2	T1	T2			
SF-36–Physical	55.4 (24.5)	52.5 (27.9)	52.9 (19.8)	164.3 (24.7)	5.09	.04	0.21
SF-36–Role Physical	21.4 (42.6)	33.9 (41.2)	7.1 (12.2)	7.1 (12.2)	1.14	NS	0.06
SF-36–Role Emotional	59.5 (49.2)	57.1 (42.2)	52.4 (46.6)	57.1 (46.0)	0.16	NS	0.01
SF-36–Energy	23.6 (22.4)	22.9 (23.3)	27.1 (18.9)	44.3 (16.2)	8.23	.01	0.30
SF-36–Well Being	64.3 (19.3)	66.0 (19.7)	71.4 (14.7)	78.9 (10.3)	1.13	NS	0.06
SF-36–Social Functioning	45.4 (35.2)	56.3 (38.5)	39.3 (15.2)	48.2 (11.3)	0.07	NS	0.01
SF-36–Pain	43.9 (25.5)	48.0 (26.6)	41.1 (27.0)	54.3 (29.0)	2.97	.10	0.14
SF-36–General Health	43.9 (23.3)	44.3 (25.0)	49.3 (16.9)	58.6 (29.7)	1.12	NS	0.06
MYMOP-2 ^c	2.0 (1.4)	2.3 (1.4)	2.0 (0.6)	3.2 (1.0)	6.01	.02	0.24
MDFI–General	9.9 (1.7)	9.5 (2.1)	10.7 (2.7)	11.1 (2.4)	0.45	NS	0.02
MDFI–Physical	10.0 (4.6)	9.9 (4.0)	9.4 (3.3)	11.1 (3.6)	2.23	NS	0.11
MDFI–Mental	11.3 (4.3)	11.6 (5.1)	12.9 (4.1)	12.6 (5.1)	0.26	NS	0.01
MDFI–Motivation	13.0 (3.3)	13.1 (4.2)	13.7 (4.0)	15.7 (2.0)	2.92	.10	0.13
MDFI–Activity	10.7 (4.5)	11.5 (4.9)	9.7 (3.2)	13.0 (4.3)	2.83	.11	0.13
ESS	9.6 (5.1)	8.7 (4.8)	11.0 (5.2)	9.3 (4.5)	0.53	NS	0.03
FIQ	56.4 (22.8)	54.5 (23.7)	55.4 (14.1)	42.0 (18.2)	4.76	.04	0.20

ANOVA, analysis of variance; ESS, Epworth Sleepiness Scale; FIQ, Fibromyalgia Impact Questionnaire; MDFI, Multi-Dimensional Fatigue Inventory; MYMOP-2, Measure Yourself Medical Outcome Profile; SF-36, Short Form-36.

^aValues are mean (SD).

^bDegrees of freedom for each *F* test is 1, 19.

^cScore reversed.

(Figure 2, Table 1). No statistically significant findings were observed for the ESS or for any other subscales of the MDFI or SF-36.

Simple Effects

To investigate these findings more completely, we conducted simple effects tests examining change from baseline to follow-up separately for the amygdala retraining and standard care groups. Results of these analyses are provided in Table 2. The consistent pattern that emerges from these analyses is that amygdala retraining had a large effect on each outcome whereas standard care showed generally smaller effect sizes. In most cases the

changes from baseline to follow-up were statistically significant for the amygdala retraining group but not for the standard care group. Even when this does not hold true, the effect on amygdala retraining outcomes was two to three times the magnitude of the standard care effect.

DISCUSSION

This study provides preliminary insight into the potential for a new and innovative mind–body approach for helping patients with symptoms related to fibromyalgia and chronic fatigue. As defined

Table 2. Simple Effects Tests for Changes in Outcome Measures From Baseline to Follow-Up

Measure	Patient Group					
	Standard Care (n = 14)			Amygdala Retraining (n = 7)		
	df	F	η^2	df	F	η^2
SF-36–Physical	1, 13	1.20	.09	1, 6	2.37	.28
SF-36–Energy	1, 13	.08	.01	1, 6	5.63 ^a	.48
SF-36–Pain	1, 13	3.38	.21	1, 6	4.67 ^a	.44
MYMOP-2	1, 13	4.10 ^a	.24	1, 6	6.18 ^b	.51
MDFI–Motivation	1, 13	.02	.00	1, 6	3.23	.35
MDFI–Activity	1, 13	1.08	.08	1, 6	4.96 ^a	.45
FIQ	1, 13	.60	.04	1, 6	6.04 ^b	.50

FIQ, Fibromyalgia Impact Questionnaire; MDFI, Multi-Dimensional Fatigue Inventory; MYMOP-2, Measure Yourself Medical Outcome Profile; SF-36, Short Form-36.

^a*P* < .10.

^b*P* < .05.

by the National Center for Complementary and Alternative Medicine, mind–body medicine focuses on interactions among the brain, mind, body, and behavior, with the intent to use the mind to affect physical functioning and promote health. Mind–body therapies include meditation, yoga, acupuncture, and guided imagery. This study used a combination of mind–body therapies that promote relaxation and attempt to reorient attention away from the distressing symptoms or catastrophizing thoughts.

Although the results look promising, three key limitations of this study should be noted. First, the sample size is small. Although many of the effects were large enough to overcome the underpowered nature of this study, conducting a larger clinical trial would certainly allow for a more sensitive statistical approach to detecting reliable effects.²² A larger sample also might offer better diversity in terms of diagnosis, age, and sex. Second, attrition was a significant concern in this study. Patients lost to follow-up are always a concern because their missing data may bias the statistical results.²⁴ That said, our attrition rate of approximately 40% is not unlike many other randomized controlled trials.^{25,26} Third, attrition was greater for the amygdala retraining group than for the standard care group. This is especially problematic because it may indicate that the extra effort required for the amygdala retraining program may not have been well received by the patients. Just as some pharmacotherapies contain too many adverse effects or regimens are too complicated or demanding and patients discontinue their use, mind–body approaches may require extra effort that causes patients to discontinue the program. If this were the case, future work would need to carefully identify which aspects of the program were too demanding for the patients and what could be done to reduce that patient load.

Our results are more modest than the clinical effects reported by Gupta in his clinical audit.¹¹ One possible reason for this difference may be that a clinical audit is not a standardized study procedure; therefore, it is not optimal to directly compare a clinical audit and a clinical trial. Another reason may be the difference in procedure. For example, in the clinical audit patients received lengthy weekly or fortnightly calls from specially trained amygdala retraining program staff to check whether they were complying and to encourage correct use of the technique. Compared with this, our follow-up calls were brief and mainly for answering questions, since our focus was to evaluate whether this program could be widely used without the intense individualized approach.

The findings from this pilot randomized clinical trial of amygdala retraining provide reason for guarded optimism regarding the addition of mind–body techniques in helping patients cope with symptoms of fibromyalgia and chronic fatigue. As with most pilot studies, the limitations of the present study may be overcome with more significant replication studies. These future studies should emphasize improvements in recruitment, retention, and procedure. Specifically, future studies should aim to draw on larger patient samples and encourage retention of enrolled patients. Resources afforded by grant-funded, large-scale investigations would allow research staff to focus on broader and more intensive recruitment, to develop and maintain a relationship with each patient, and to offer more individualized attention. This would be more in line with the established approach currently offered by Gupta.¹¹

These kinds of comprehensive and large-scale trials require significant funding to support the necessary research staff, assess-

ment costs, and other needs. One potentially important addition to future work would be the inclusion of some measure of autonomic function (eg, cortisol or heart rate variability). This could be useful because much of the theory and research surrounding the etiology, management, and treatment of disorders such as fibromyalgia and chronic fatigue center on dysregulation in the autonomic nervous system. Having the ability to directly index the extent to which a technique like amygdala retraining might help modulate autonomic dysregulation could offer important insights into the effectiveness of this type of mind–body technique for these types of disorders.

Our hope is that this study provides a beginning point for further investigation into mind–body interventions for fibromyalgia and chronic fatigue. Given the limited effectiveness of standard approaches to treating fibromyalgia and chronic fatigue, it seems a worthwhile venture to consider the addition of complementary and alternative options that may provide some relief in coping with the often debilitating symptoms that significantly impair quality of life.

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