ORIGINAL ARTICLE

# Effect of a Randomized, Controlled Trial of Exercise on Mood and Physical Function in Individuals With Fibromyalgia

S. E. GOWANS,[1] A. deHUECK,[1] S. VOSS,[1] A. SILAJ,[1] S. E. ABBEY,[2] AND W. J. REYNOLDS[3]

***Objective.*** **To evaluate the effect of exercise on mood and physical function in individuals with fibromyalgia.**
***Methods.*** **Subjects were randomly assigned to an exercise (EX) or control (CTL) group. EX subjects participated in 3 30-minute exercise classes per week for 23 weeks. Subjects were tested at entry and at 6, 12, and 23 weeks. Tests included the Beck Depression Inventory (BDI), 6-minute walk, State-Trait Anxiety Inventory (STAI), Mental Health Inventory (MHI), Fibromyalgia Impact Questionnaire (FIQ), Arthritis Self-Efficacy Scale (ASES), and a measure of tender points and knee strength.**
***Results.*** **Fifty subjects (27 EX, 23 CTL) completed the study, and 31 (15 EX, 16 CTL) met criteria for efficacy analyses. In efficacy analyses, significant improvements were seen for EX subjects in 6-minute walk distances, BDI (total, cognitive/affective), STAI, FIQ, ASES, and MHI (3 of 5 subscales) scores. These effects were reduced but remained during intent-to-treat analyses.**
***Conclusion.*** **Exercise can improve the mood and physical function of individuals with fibromyalgia.**

**KEY WORDS.** Fibromyalgia; Physical therapy; Exercise therapy; Depression; Anxiety.

## INTRODUCTION

Fibromyalgia is a condition characterized by widespread pain and pain at specific tender points (1). Although anxiety and depression are not part of the diagnostic criteria for fibromyalgia, they are also common complaints in individuals with fibromyalgia (2–4).

Treatment options for patients with fibromyalgia are limited but include exercise. Evidence regarding the efficacy of exercise for individuals with fibromyalgia has grown (5,6) since the classic study by McCain and colleagues demonstrated that exercise could improve fitness, tender point pain, and patient/physician global assessment ratings (7).

Typically, exercise studies have focused on the effect of exercise on physical outcomes such as pain (8–16), function (8–10,17,18), strength (8,10–12,14,18), or cardiovascular fitness (11,12,14,16,18). However, a large body of literature suggests that exercise can also improve participants' mood (19,20). The few studies that have evaluated the mood of individuals with fibromyalgia following exercise have had mixed results: Mood has improved in some (8,13,15,21) but not all studies (9,14,16). These discrepant results may be due, in part, to the psychometric strength of the measures chosen to evaluate mood. For example, mood improved following exercise when a robust measure of mood such as the Brief Symptom Index (13) or the Symptom Checklist-90–Revised was used (8) but not when anxiety or depression was assessed with weaker instruments such as visual analog scales (9,16). Robust measures for mood were more likely to be used when exercise is part of a multidisciplinary program (22–25), but it is difficult to determine the isolated effect of exercise on mood in these studies.

The current study was designed to examine the effect of exercise on mood and physical function. Because meta-analyses indicated that the effect of exercise on depression was larger (19) than the effect of exercise on anxiety (20), the primary outcome for mood in this study was a widely used measure of depression: the Beck Depression Inventory (BDI). We chose to measure depression with the BDI because it generates a total score and subscores for cogni-

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tive/affective and somatic items. This was an important methodologic consideration because somatic symptoms of fibromyalgia can parallel the somatic symptoms of depression. Using measures that do not separate somatic items from cognitive/affective items can erroneously identify decreases in depression, when what has, in fact, decreased are the somatic complaints of fibromyalgia. By studying the effect of 23 weeks of exercise, this study also adds to the literature on the effect of exercise on physical function. Most exercise studies have examined the effect of 6 to 12 weeks of exercise (8–11,13–15,17) on physical function. We chose to evaluate the effect of a longer exercise program, because meta–analyses indicated that the effect of exercise on mood was dependent on the length of the exercise program (19,20). We postulated that exercise would improve both the mood and physical function of individuals with fibromyalgia over the 23-week intervention period.

## SUBJECTS AND METHODS

**Subjects.** Subjects were recruited by advertisements placed in the Rheumatology Ambulatory Care area of a large, urban teaching hospital and in newsletters for local fibromyalgia support groups. To be included in the study, subjects had to meet the diagnostic criteria for fibromyalgia (1) and be willing to comply with the experimental protocol. Subjects were excluded from the study if they: 1) had been diagnosed with high blood pressure or symptomatic cardiac disease, 2) had other serious systemic diseases (e.g., systemic lupus erythematosus, cancer, diabetes), 3) intended to change medications for anxiety or depression or seek professional treatment for anxiety or depression during the study period, 4) were enrolled in or intended to begin an aerobic exercise program.

**Design.** Subjects were stratified by sex and randomly assigned to a supervised exercise (EX) group or a control (CTL) group that continued ad libitum activity. Subjects were enrolled in 4 cohorts at approximately 6-month intervals (February/March/April or September/October) to balance potential seasonal effects on mood (26). All subjects who completed testing at entry and 23 weeks were included in the intent-to-treat analyses. To be included in the efficacy analyses, EX subjects had to attend 45% or more of the exercise classes, CTL subjects could not begin an aerobic exercise program during the study period, and no subject could change a potentially mood-altering medication or seek professional treatment for mood disturbances or stress during the study period. Subjects were tested at entry, 6 weeks, 12 weeks, and 23 weeks with one exception: Subjects who failed to meet criteria for efficacy analyses were tested on schedule until they were known to have failed efficacy criteria and then were retested only at 23 weeks. Exercise classes were suspended for 1 week at each testing point to allow testing to proceed. Testing time was not counted as part of the 23-week intervention period.

**Exercise program.** EX subjects attended 3 hospital-based exercise classes per week for 23 weeks. Exercise classes were held during the day and consisted of 10 minutes of stretching (5 minutes before and 5 minutes after exercise) and 20 minutes of aerobic exercise. To facilitate compliance and minimize postexercise pain, classes for the first 6 weeks were conducted in a warm therapeutic pool. At 7 weeks, subjects progressed to 2 walking classes in a gymnasium and 1 pool class. The aerobic component of the classes was designed to generate heart rates equivalent to 60% to 75% of age-adjusted maximum heart rates (210 − age [years]). Subjects were taught to monitor their heart rates and adjust their activity during classes to maintain their heart rates at this level of intensity. Classes were designed to ensure that target heart rates were attained as subjects' conditioning improved. For example, subjects progressed from gentle arm and leg exercises against water resistance (week 1) to running in the pool (week 6) to slow, continuous walking with arm movements in a gymnasium (week 7) to intermittent jogging in the gymnasium (week 23).

**Primary outcomes.** There were 2 primary outcomes: the Beck Depression Inventory (BDI) (27) and the 6-minute walk test (28), which assessed mood and physical function, respectively. The BDI is a measure for self-reported depression that consists of 21 items (range 0–63), with a higher score indicating greater depression. The BDI generates a total score and 2 subscores (cognitive/affective, somatic). The BDI has been shown to be sensitive to exercise-induced changes in healthy adults (29) and in patients with major depression (30) and has been used to detect changes in depression in fibromyalgia patients enrolled in a 6-month multidisciplinary program (20).

The 6-minute walk test is a reliable and valid measure of physical function (31–33) that is sensitive to change in patients with fibromyalgia who are enrolled in an exercise and education (34) or multidisciplinary program (20). In our administration of the 6-minute walk, subjects were instructed to walk at a fast, comfortable pace between 2 pylons set 20 meters apart. Their distance was recorded to the nearest meter by an assessor blinded to subjects' group assignments. Subjects completed 2 walk tests, on separate days at each assessment point, to control for potential practice effects (31–33). However, average walk distances from each testing point were subsequently used in all analyses, because post hoc testing of distances for trials 1 and 2 at entry were not significantly different (walk 1, 418.4 ± 12.0 meters; walk 2, 424.6 ± 12.0 meters, all subjects [n = 50], intent-to-treat analyses). To ensure that changes in walk distance at retesting were not due to greater effort, subjects also rated their level of perceived exertion at the end of each walk test using a 15-point categorical scale (range 6–20) (35). Subjects' ratings of perceived exertion for 6-minute walks were averaged at each testing point during analyses.

**Secondary outcomes.** There were 6 secondary outcomes: 2 for mood (anxiety, general mental health), 2 for physical status (number of tender points, isokinetic max-

imal voluntary strength right knee), 1 disease-specific outcome (Fibromyalgia Impact Questionnaire [FIQ]) and 1 outcome for self-efficacy (Arthritis Self-Efficacy Scale [ASES]).

Anxiety was assessed with the State version of the State-Trait Anxiety Inventory (STAI; range 20–80) (36). The STAI is a 20-item questionnaire, with a higher score indicating greater anxiety. The STAI has been widely used to measure anxiety in psychiatric and medical samples and has been shown to be sensitive to exercise-induced changes in anxiety (37). General mental health was assessed with the Mental Health Inventory (MHI) (38). The MHI is an 18-item questionnaire with demonstrated validity (39) that is scored such that a higher score indicates better mental health. The MHI was included because one of its subscales measures "positive affect," and there has been a recent interest in the effects of exercise on positive affect (40). For completeness, we report all 5 subscales of the MHI (anxiety, depression, loss of behavioral/emotional control, positive affect, and emotional ties).

Tender points were assessed using a standard protocol (1) by an assessor who was blinded to subjects' group assignment. Tender points were recorded as the number of positive tender points (range 0–18). Isokinetic maximal voluntary strength of the right quadriceps was assessed as the average peak torque of 6 maximal, concentric contractions at 60°/second and 120°/second (from 80° knee flexion to 10° knee flexion, with an intertrial rest period of 30 seconds). Strength testing was conducted over 2 days (3 test trials at each speed/day) by an assessor blinded to subjects' group assignments.

The FIQ (range, 0–100) (41) is a disease-specific outcome measure that assesses subjects' perceptions of their physical function, well-being, pain, fatigue, stiffness, anxiety, and depression (2 subscales pertaining to work were excluded [lowering the maximum score to 80], because few subjects were employed). The FIQ has been widely used to describe the severity of fibromyalgia in study samples and to evaluate the effect of interventions and is scored such that a higher score indicates greater impairment.

The ASES (42), which has 3 subscales (pain, function, other symptoms; range 0–100), was included to determine whether subjects' self-efficacy was increased by participation in an exercise program. To be suitable for use in a fibromyalgia study, the word "arthritis" in the ASES was changed to "fibromyalgia." For example the item, "How certain are you that you can make a small to moderate reduction in your arthritis pain by using methods other than extra medication" was changed to ". . . your fibromyalgia pain. . . ." A higher score on the ASES indicates greater self-efficacy.

**Analyses.** Demographic characteristics of EX and CTL subjects were compared with chi-square tests (categorical data) or 2-tailed independent *t*-tests (continuous data). Study outcomes were analyzed on an efficacy and an intent-to-treat basis. One-tailed, independent *t*-tests (EX versus CTL) of change scores ($n^{th}$ testing point − entry) were used to probe for group differences over the study period. Changes in BDI total scores at 23 weeks were also analyzed on a categorical basis using a chi-square test. In BDI categorical analyses, depression was categorized by subject, at entry and 23 weeks, as not depressed (<12), mildly depressed (12–16), moderately depressed (17–23) or severely depressed (>24). Then depression change (23 weeks versus entry) was categorized by subject as better (depression level decreased by 1 or more category), worse (depression level increased by 1 or more category), or unchanged (remained in the same category on retesting). The BDI severity categories noted above were chosen as a compromise between the many cutoffs adopted by others in medically ill samples (43) and closely approximate the cutoff points advocated in the classic paper on the use of the BDI (44). To determine if changes in self-efficacy were related to changes in the primary outcomes, Pearson's correlations (2-tailed) were computed between 23-week change scores in self-efficacy and 23-week change scores for BDI cognitive/affective or 6-minute walk distances. To begin to explore if there was a dose-response relationship between exercise and changes in primary outcomes, Pearson's correlations (2-tailed) were computed between class attendance (%) and change scores for the primary outcomes at 23 weeks for all subjects enrolled in the study (class attendance was set to 0% for control subjects). Statistical significance for all analyses was set at $P < 0.05$. Unless otherwise stated, variability is expressed as a standard deviation.

## RESULTS

Fifty-seven subjects completed baseline testing and were randomized in 4 cohorts to EX (n = 30) or CTL (n = 27) groups. Six subjects (3 EX, 3 CTL) subsequently declined to participate in the study on the basis of their group assignments. Thus, 51 subjects (27 EX, 24 CTL) were enrolled in the study.

**Efficacy analyses.** Outcomes of 31 (15 EX, 16 CTL) subjects were analyzed. Twenty subjects were excluded from efficacy analyses, because they changed medications that could potentially affect mood (4 EX, 6 CTL), sought professional support for stress (2 EX, 1 CTL), failed to attend 45% or more of the exercise classes (6 EX, 3 of whom returned to work), or failed to return for testing at 23 weeks (1 CTL). There were no differences on primary outcomes at entry between the 31 subjects who were included in the efficacy analyses and the 19 subjects who were excluded (not shown).

Table 1 summarizes the entry characteristics of the 31 subjects in the efficacy analyses. EX subjects were similar to CTL subjects, except that EX subjects were more likely to be taking antidepressant-class medications for any cause (e.g., sleep disturbances). Mean attendance at exercise classes over the 23-week study period by the 15 EX subjects was 67% (range 46–84%). Testing results at entry and 6, 12, and 23 weeks are presented in Table 2.

**Primary outcomes.** BDI total and BDI cognitive/affective scores were decreased in EX subjects and unchanged

**Table 1. Subjects' characteristics at entry**

| | Efficacy analyses | | Intent-to-treat analyses | |
|---|---|---|---|---|
| | Control subjects (n = 16) | Exercise subjects (n = 15) | Control subjects (n = 23) | Exercise subjects (n = 27) |
| Sex | 15 women/1 man | 13 women/2 men | 20 women/3 men | 24 women/3 men |
| Mean age ± SD | 49.1 years ± 7.2 | 46.7 years ± 10.3 | 49.8 years ± 7.3 | 44.6 years ± 8.7* |
| Duration symptoms ± SD | 6.4 years ± 7.0 | 11.6 years ± 10.4 | 8.4 years ± 7.6 | 9.6 years ± 8.6 |
| Duration diagnosis ± SD | 3.2 years ± 3.3 | 3.5 years ± 3.2 | 4.2 years ± 4.4 | 2.8 years ± 2.6 |
| Marital status | | | | |
| Single | 5 | 5 | 6 | 7 |
| Married | 8 | 7 | 12 | 13 |
| Divorced/separated | 3 | 3 | 5 | 7 |
| English as first language (n) | 5 | 9 | 9 | 19* |
| Highest education (n) | | | | |
| College/university | 6 | 9 | 9 | 14 |
| High school | 5 | 4 | 8 | 9 |
| Elementary school | 5 | 2 | 6 | 4 |
| Employment status (n)† | | | | |
| Currently employed | 2 | 1 | 2 | 2 |
| Previously employed | 13 | 14 | 20 | 25 |
| Never employed | 1 | 0 | 1 | 0 |
| Duration unemployed ± SD | 3.2 years ± 3.6 | 4.2 years ± 4.9 | 3.1 years ± 3.2 | 3.6 years ± 4.0 |
| Not employed for health-related reasons (n) | 9 | 13 | 16 | 22 |
| Involved in litigation (n) | 0 | 2 | 0 | 2 |
| Comorbidities (n)‡ | | | | |
| Thyroid disease | 2 | 3 | 2 | 5 |
| Asthma | 1 | 1 | 3 | 3 |
| Osteoarthritis | 1 | 3 | 1 | 3 |
| Medication use (n)§ | | | | |
| Pain (non-narcotic) | 9 | 5 | 12 | 10 |
| Pain (narcotic) | 2 | 4 | 6 | 7 |
| Nonsteroidal antiinflammatories | 4 | 5 | 5 | 9 |
| Muscle relaxants | 4 | 1 | 6 | 5 |
| Antidepressants | 3 | 9* | 8 | 13 |
| Anxiolytics | 2 | 5 | 5 | 7 |
| Sleep | 0 | 2 | 0 | 3 |
| Drugs for fibromyalgia symptoms¶ | 15 | 15 | 21 | 25 |
| Other prescription drugs# | 6 | 9 | 10 | 15 |

* $P < 0.05$ (exercise vs. control subjects).
† Employed = full-time or part-time employment.
‡ Self-reported.
§ Medications were coded by class of drug, not by reason for use (e.g., subjects who took antidepressants for sleep were coded as taking antidepressants, not sleep medication).
¶ Use of at least one medication from the categories: pain (non-narcotic), pain (narcotic), nonsteroidal antiinflammatories, muscle relaxants, antidepressants, anxiolytics, sleep.
# Not related to fibromyalgia (e.g., cholesterol-lowering drugs, gastrointestinal drugs, thyroid drugs, hormone replacement therapy).

in CTL subjects over the study period (see Figure 1). When changes (better, worse, unchanged) in the depression level (not depressed, minimally depressed, moderately depressed, severely depressed) of EX versus CTL subjects, as indicated by BDI total scores, were analyzed on a categorical basis (see Table 3), a trend was generated ($\chi^2 = 5.74$; $P < 0.06$). There was also a trend for changes in BDI somatic scores to vary between EX and CTL subjects at 23 weeks ($P < 0.07$). As Figure 2 indicates, EX subjects increased 6-minute walk distance over the 23-week program (+75 meters), while CTL subjects decreased their 6-minute walk distance (−10 meters). *T*-tests (EX versus CTL) on change scores for the 6-minute walk test were significant at all retesting points, in the absence of change in rates of perceived exertion over the same time period.

**Secondary outcomes.** Anxiety, as measured by the STAI, decreased in EX subjects and appeared to increase in CTL subjects over the study period (see Figure 3). Independent *t*-tests (EX versus CTL) of STAI change scores were significant at 12 and 23 weeks. MHI positive affect scores increased in EX subjects and decreased in CTL subjects, relative to their respective values at entry, and these differences were significant at 23 weeks (see Figure 4). MHI depression scores improved in EX subjects over the study period, generating significant differences in

**Table 2. Mean values (SD) on outcome measures in the efficacy study**

| Scale | Subscale | Control subjects (n = 16) | | | | Exercise subjects (n = 15) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Entry | 6 weeks | 12 weeks | 23 weeks | Entry | 6 weeks | 12 weeks | 23 weeks |
| BDI | Total | 20.1 (10.4) | 19.3 (10.2) | 20.5 (10.2) | 19.4 (10.8) | 20.1 (12.9) | 16.5 (9.6) | 16.8 (11.9) | 13.6 (7.9) |
| | Cognitive/affective | 11.9 (7.0) | 11.1 (7.5) | 12.4 (8.2) | 11.4 (8.0) | 11.9 (10.1) | 9.3 (7.3) | 9.6 (9.2) | 7.1 (6.4) |
| | Somatic | 8.2 (3.8) | 8.3 (3.3) | 8.1 (2.7) | 8.0 (3.3) | 8.2 (3.3) | 7.2 (3.5) | 7.2 (3.0) | 6.5 (2.9) |
| Walk | 6-min walk distance (meters) | 419.7 (96.7) | 402.0 (103.3) | 412.4 (96.2) | 409.3 (89.7) | 414.1 (100.3) | 448.1 (102.5) | 475.9 (103.4) | 489.0 (118.0) |
| RPE | Exertion rate (during 6-min walk) | 13.0 (2.4) | 13.7 (3.8) | 14.1 (3.3) | 13.3 (3.6) | 13.1 (3.0) | 13.3 (2.6) | 13.1 (2.5) | 12.6 (2.5) |
| STAI | State anxiety | 45.9 (15.6) | 50.9 (12.4) | 52.9 (14.8) | 50.7 (12.9) | 41.7 (15.7) | 42.3 (13.0) | 39.1 (12.6) | 36.8 (10.8) |
| MHI | Anxiety | 45.3 (20.0) | 44.1 (22.0) | 45.3 (23.6) | 42.8 (24.2) | 62.7 (29.6) | 64.7 (25.4) | 68.3 (19.6) | 69.0 (20.0) |
| | Depression | 50.6 (24.5) | 46.8 (22.7) | 52.5 (22.7) | 46.3 (27.1) | 58.9 (26.1) | 67.7 (21.8) | 65.3 (18.6) | 71.7 (17.6) |
| | Behavioral/emotional control | 56.6 (24.1) | 56.6 (20.8) | 58.8 (21.4) | 56.3 (26.2) | 69.0 (26.4) | 70.3 (26.5) | 73.3 (21.6) | 76.7 (19.8) |
| | Positive affect | 40.8 (17.3) | 40.8 (18.2) | 45.0 (19.5) | 36.5 (16.9) | 47.1 (22.8) | 50.4 (27.4) | 56.7 (27.2) | 55.2 (23.1) |
| | Emotional ties | 48.8 (29.2) | 43.8 (35.9) | 48.8 (31.8) | 46.3 (32.4) | 62.7 (26.0) | 65.3 (31.6) | 58.7 (31.6) | 64.0 (33.1) |
| Tender points | Number | 14.7 (2.5) | 14.6 (2.4) | 14.2 (3.0) | 15.0 (2.2) | 15.2 (2.6) | 14.5 (2.2) | 15.1 (3.2) | 15.1 (2.3) |
| Knee strength | Extension @ 60°/s (Nm) | 59.9 (34.6) | 67.7 (33.7) | 63.1 (37.6) | 60.9 (28.1) | 66.8 (39.6) | 79.1 (43.1) | 68.9 (33.6) | 74.5 (40.4) |
| | Extension @ 120°/s (Nm) | 49.2 (29.2) | 51.5 (27.2) | 51.6 (31.7) | 45.8 (23.1) | 53.2 (32.6) | 59.3 (34.2) | 54.2 (29.8) | 56.1 (32.8) |
| FIQ | Total | 57.8 (10.4) | 56.8 (12.7) | 54.3 (11.5) | 54.4 (11.1) | 53.8 (12.4) | 51.4 (13.4) | 51.0 (12.7) | 44.1 (14.4) |
| ASES | Pain | 51.6 (24.0) | 41.3 (18.2) | 36.0 (14.0) | 39.5 (22.1) | 50.6 (25.9) | 54.9 (21.2) | 61.4 (20.9) | 62.4 (19.0) |
| | Function | 67.6 (18.9) | 57.2 (28.0) | 59.4 (28.5) | 59.1 (30.4) | 61.5 (21.8) | 67.5 (21.4) | 73.7 (16.9) | 73.8 (20.4) |
| | Symptoms | 49.7 (20.5) | 36.4 (13.3) | 43.9 (17.7) | 42.2 (22.6) | 57.9 (23.7) | 59.9 (22.4) | 65.1 (14.5) | 66.9 (16.4) |

BDI = Beck Depression Inventory; RPE = rate of perceived exertion; STAI = State-Trait Anxiety Inventory; MHI = Mental Health Inventory; FIQ = Fibromyalgia Impact Questionnaire; ASES = Arthritis Self-Efficacy Scale.

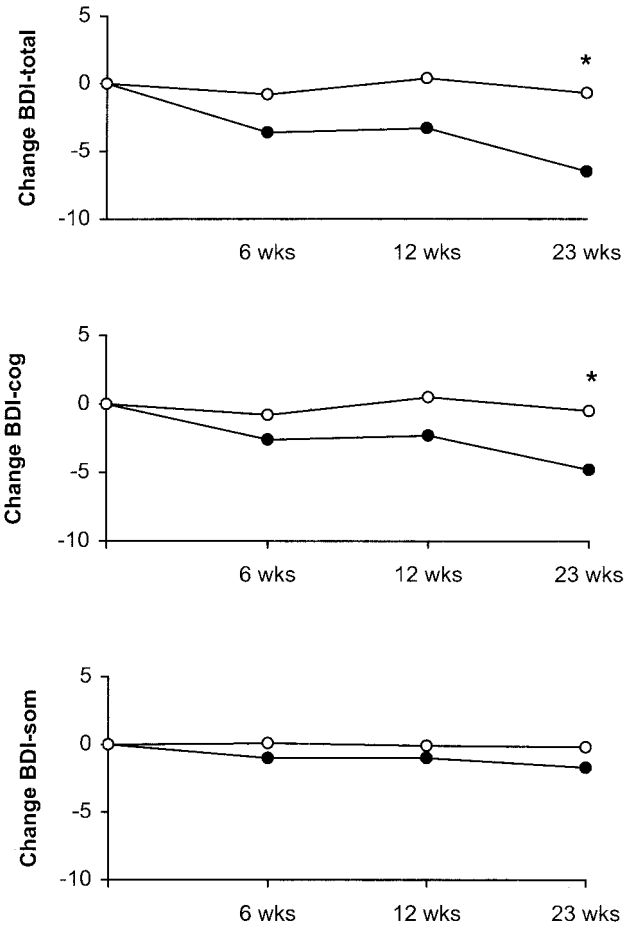


**Figure 1.** Changes (testing point–entry) in Beck Depression Inventory (BDI) scores (total, cognitive/affective, and somatic) for Exercise (●) and Control (○) subjects in the efficacy study. $*P < 0.05$, *t*-test on change scores (EX vs. CTL).

change scores between EX and CTL subjects at 6 weeks and 23 weeks. MHI behavioral/emotional control scores improved in EX subjects, and EX change scores were again significantly different from those noted in CTL subjects at 23 weeks. Changes in the MHI subscales for anxiety and emotional ties were not significantly different between EX and CTL subjects at any test point. Self-efficacy (all subscales) increased in EX subjects and decreased in CTL subjects over the study period, and these differences in change scores were significant at all retesting points (see Figure 5). FIQ total scores appeared to decrease in both EX and CTL subjects, but these decreases were larger in EX subjects, and FIQ change scores were significantly different at 23 weeks. There were no significant differences between EX and CTL subjects in changes in the number of tender points or isokinetic maximal voluntary knee strength over the study period.

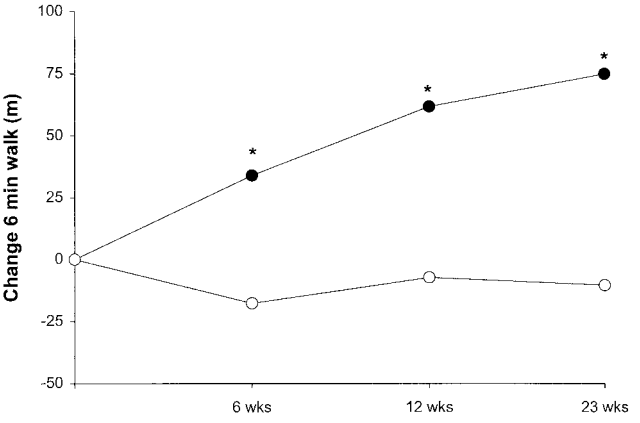


**Figure 2.** Changes (testing point–entry) in 6 min-walk distances for Exercise (●) and Control (○) subjects in the efficacy study. $*P < 0.05$, *t*-test on change scores (EX vs. CTL).

To determine if changes in self-efficacy were related to changes in primary outcomes, 23-week change scores in self-efficacy (all scales) were correlated with 23-week BDI cognitive/affective change scores or 23-week changes in 6-minute walk distances (see Table 4). Significant correlations were found between BDI cognitive/affective change scores and 2 subscales of the ASES (pain, function). A significant correlation was also found between changes in 6-minute walk distance and changes in the ASES (function) subscale.

**Intent-to-treat analyses.** Fifty (27 EX, 23 CTL) of the 51 subjects (27 EX, 24 CTL) who were enrolled in the study returned for testing at 23 weeks. EX subjects were similar to CTL subjects, except EX subjects were slightly younger

**Table 3. Categorical changes* in total Beck Depression Inventory scores at 23 weeks versus entry**

| | Efficacy analysis† | | Intent-to-treat analysis‡ | |
|---|---|---|---|---|
| | EX (n = 15) | CTL (n = 16) | EX (n = 27) | CTL (n = 23) |
| Better | 8 | 5 | 13 | 5 |
| Worse | 0 | 5 | 2 | 7 |
| Unchanged | 7 | 6 | 12 | 11 |

* Each subject's level of depression was categorized at entry and 23 weeks, using Beck Depression Inventory (total) scores, as not depressed (<12), mildly depressed (12–16), moderately depressed (17–23) or severely depressed (>24). Depression change (23 weeks vs. entry) was then categorized by subject as better (depression level decreased by 1 or more category), worse (depression level increased by 1 or more category) or unchanged (remained in the same category on retesting).
† $P < 0.06$.
‡ $P < 0.05$.
EX = exercise subjects; CTL = control subjects.

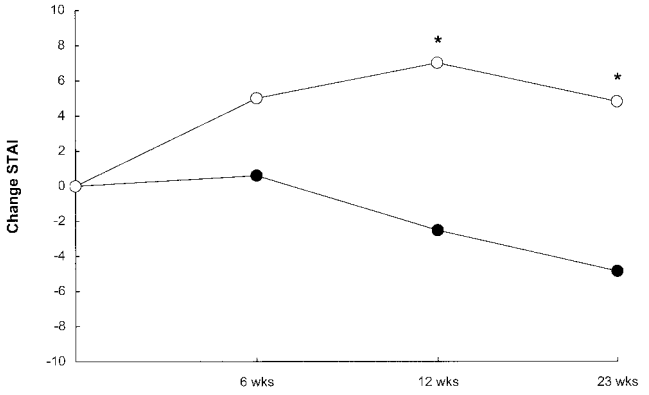


**Figure 3.** Changes (testing point–entry) in State-Trait Anxiety Inventory (STAI) scores for Exercise (●) and Control (○) subjects in the efficacy study. *$P < 0.05$, *t*-test on change scores (EX vs. CTL).

than CTL subjects (EX 44.6 years, CTL 49.8 years) and were more likely to speak English as their first language. Mean attendance at exercise classes over the 23-week study period by the 27 EX subjects was 55% (range 7–91%).

**Primary outcomes.** EX and CTL subjects showed significant differences on both primary outcomes at 23 weeks, although the magnitude of these changes was attenuated compared with efficacy analyses. BDI total scores were significantly lower in EX versus CTL subjects at 23 weeks, relative to their respective scores at entry, whether these scores were analyzed as continuous or categorical data (see Tables 3 and 5). Differences in BDI total change scores between EX and CTL subjects at 23 weeks reflected significant differences in both BDI cognitive/affective and BDI somatic change subscores at 23 weeks. As Table 5 indicates, 6-minute walk distances at 23 weeks were increased in EX subjects (+50 meters versus entry), in the absence of any change in their reported rate of perceived exertion, and minimally decreased in CTL subjects (−6 meters versus entry). All correlations between primary outcome change scores at 23 weeks and class attendance were significant (walk, r = 0.54; BDI total, r = −0.34; BDI cognitive/affective, r = −0.38).

**Secondary outcomes.** Differences in secondary outcomes, originally seen in the efficacy analyses, were replicated in the intent-to-treat analyses at 23 weeks (see Table 5). Specifically, anxiety, as measured by the STAI, again decreased in EX subjects, generating significant differences in change scores between EX and CTL subjects at 23 weeks. MHI depression, positive affect, and behavioral control subscales improved in EX subjects and mimimally deteriorated in CTL subjects, leading to significant differences in their change scores at 23 weeks. EX subjects' self-efficacy scores for pain, function, and other symptoms also increased, while the same scores decreased in CTL subjects, leading to significant differences between EX and CTL subjects at 23 weeks. Finally, FIQ total scores were again decreased in both EX and CTL subjects at 23 weeks, but these decreases were larger in EX subjects, and thus FIQ change scores were significantly different at 23 weeks.

Significant correlations were found between BDI cognitive/affective change scores and all subscales of the ASES (see Table 4). Like efficacy analyses, changes in 6-minute walk distance at 23 weeks were correlated only with changes in the ASES (function) subscale.

## DISCUSSION

This study demonstrates that 23 weeks of supervised exercise can improve the mood and physical function of

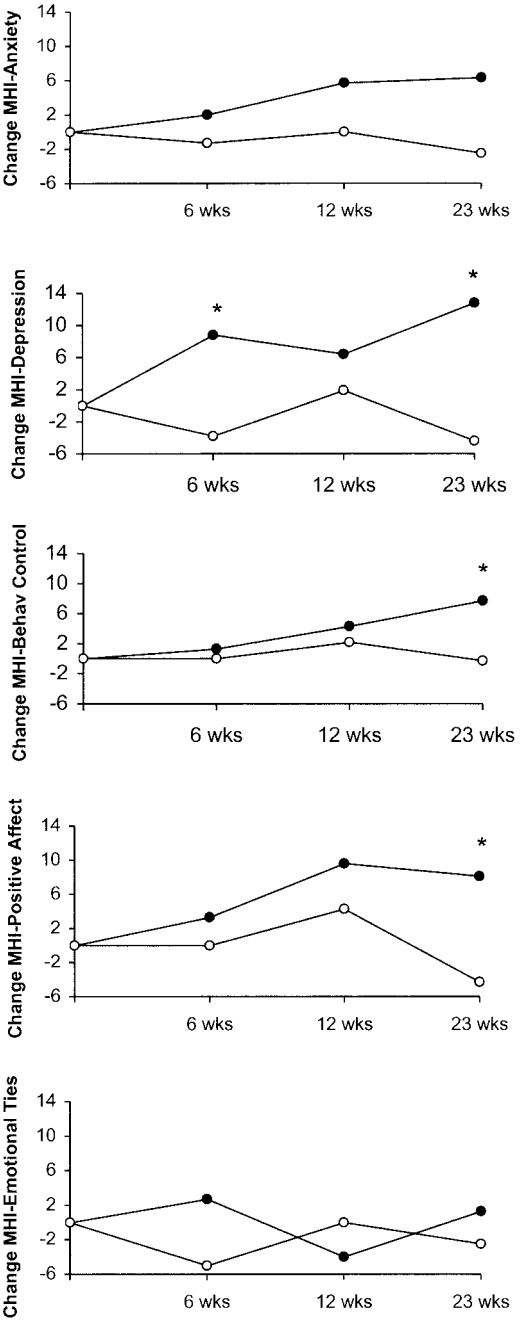


**Figure 4.** Changes (testing point–entry) in Mental Health Inventory (MHI) scores for Exercise (●) and Control (○) subjects in the efficacy study. *$P < 0.05$, *t*-test on change scores (EX vs. CTL).

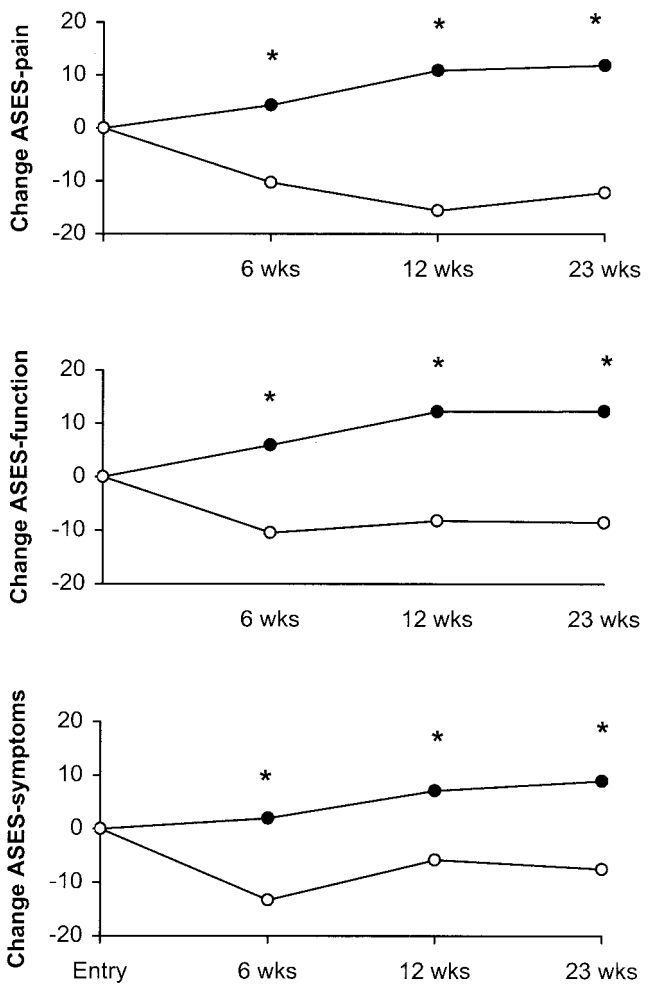


**Figure 5.** Changes (testing point–entry) in Arthritis Self-Efficacy Scale (ASES) scores for Exercise (●) and Control (○) subjects in the efficacy study. *$P < 0.05$, *t*-test on change scores (EX vs. CTL). EX = exercise group; CTL = control group.

patients with fibromyalgia. Improvements in mood and physical function, originally seen in the efficacy analyses, were sustained when data were analyzed on an intent-to-treat basis. Finally, these changes were observed in a predominantly tertiary-care sample of patients with long-standing fibromyalgia symptoms who were largely unemployed due to health reasons and took multiple medications for fibromyalgia; such subjects may be more recalcitrant to treatment.

Because some of the somatic symptoms of fibromyalgia (e.g., fatigue, sleep disturbances) can parallel the vegetative symptoms of depression, it is important that the changes we noted in depression were sustained when only the cognitive/affective items of the Beck Depression Inventory were analyzed. This strongly suggests that exercise can produce changes in subjects' level of depression, not merely their somatic symptoms of fibromylagia. The magnitude of the changes in BDI scores is also comparable to that achieved with a more extensive multidisciplinary intervention (22) that included individual and group counseling, when warranted. Finally, multiple other measures for depression, anxiety, and positive affect improved following exercise, which provides confirmatory evidence that exercise can improve the mood of individuals with fibromyalgia.

The gains we observed in physical function were also clinically significant. Changes in the 6-minute walk distance of EX subjects are equivalent to an average gain in walking speed of 0.47 miles per hour (efficacy study) or 0.31 miles per hour (intent-to-treat study). These improvements in physical function agree with gains we observed in exercise tolerance during the program where subjects were progressed from gentle whole-body exercise in a warm pool at week 1 to short bursts of jogging in a gymnasium by week 23. What is unclear is why gains in walking were not accompanied by gains in isokinetic knee extensor strength, because knee extensors are a large muscle group that is used during walking. Perhaps subjects performed below capacity on strength testing because of fear of exacerbating pain but at, or near, capacity on walking because walking was practiced during the program and known to be well tolerated. This failure to improve isokinetic strength in individuals enrolled in an exercise program has also been seen by others (14).

Our observation that class attendance, a surrogate for exercise compliance, was correlated with changes in BDI total and BDI cognitive/affective scores is consistent with meta-analyses that indicate that the effect of exercise on mood is dependent on the number of exercise sessions (19). However, this correlation was performed as a post-hoc analysis and is not a true test for a dose–response relationship between exercise and study outcomes. The only unbiased way to test for a dose–response relationship between exercise and outcomes is to independently manipulate the amount of exercise that subjects receive (i.e., to randomly assign subjects to one of several EX groups that vary in exercise intensity). Although clinically relevant, this additional manipulation was beyond the resources available to us for this study.

The fact that the number of tender points did not change following exercise is compatible with other exercise and educational studies (9,14) that failed to show a change in tender points when tender points were measured as a dichotomous variable (present/absent). Further, the one study to date that found a change in the number of tender points following exercise (11) found only a modest change (12.8 tender points to 10.2 tender points). In retrospect, perhaps a myalgic score that sums or averages the intensity ratings for tender points or readings from a dolorimeter would have been more sensitive to the effect of exercise on tender points. Such approaches have yielded changes immediately following exercise in most (7–9,11) but not all exercise studies (15). Alternatively, physical function and mood may improve following exercise while tender points do not. Although others have suggested that the number of tender points is an important correlate of fibromyalgia symptoms, particularly of the distress associated with fibromyalgia (45,46), the functional significance of tender points is unclear. We found a significant correlation at 23 weeks between FIQ total scores (a measure of fibromyalgia symptom severity) and the number of tender points ($r = 0.30$, $P < 0.05$, all subjects [n = 50], intent-to-treat analyses) but also observed that FIQ total scores declined in EX

**Table 4. Correlations between change scores* for self-efficacy and primary outcomes from the efficacy or intent-to-treat analyses**

| | BDI (cognitive/affective) | | 6-minute walk | |
|---|---|---|---|---|
| | Efficacy study (n = 31) | Intent-to-treat study (n = 50) | Efficacy study (n = 31) | Intent-to-treat study (n = 50) |
| ASES pain | −0.37† | −0.49‡ | 0.31 | 0.22 |
| ASES function | −0.67‡ | −0.60‡ | 0.65‡ | 0.54‡ |
| ASES symptoms | −0.33 | −0.31† | 0.31 | 0.24 |

BDI = Beck Depression Inventory; ASES = Arthritis Self-Efficacy Scale.
* Calculated as (23-week value−entry value).
† $P < 0.05$ (2-tailed).
‡ $P < 0.001$ (2-tailed) when correlations were tested for statistical significance.

subjects over the study period while number of tender points clearly did not. This suggests that changes in fibromyalgia symptoms may be independent of changes in the number of tender points, and further, that programs that fail to change the number of tender points may nonetheless be effective.

Our observation that self-efficacy (all scales) was enhanced in EX subjects over the study period replicates the work of others who showed that self-efficacy can be enhanced in individuals with fibromyalgia who participate in exercise (8) or exercise and educational programs (9). Further, changes in self-efficacy, particularly self-efficacy for function, were correlated with changes in primary outcomes. This raises the possibility that changes in self-efficacy may mediate the changes we observed in mood and function. But it is also possible that changes in function and/or mood improve subjects' self-efficacy for function (not vice versa) and/or that a third variable improved both self-efficacy and subjects' mood and function.

Although some may be concerned about the significant decline in subject numbers between the intent-to-treat (n = 50) and the efficacy analyses (n = 31) in this study, our intent was to minimize potential confounds in the efficacy analyses. Thus, we excluded subjects from the efficacy analyses who changed medications that could potentially alter mood and also subjects who sought treat-

**Table 5. Mean values (SD) on outcome measures in the intent-to-treat study**

| | | CTL subjects (n = 23) | | EX subjects (n = 27) | | |
|---|---|---|---|---|---|---|
| Scale | Subscale | Entry | 23 weeks | Entry | 23 weeks | Significance* |
| BDI | Total | 21.3 (9.8) | 21.3 (10.3) | 22.9 (12.2) | 16.9 (10.8) | $P < 0.05$ |
| | Cognitive/affective | 13.2 (7.1) | 12.7 (7.8) | 13.6 (9.4) | 9.1 (8.5) | $P < 0.05$ |
| | Somatic | 8.1 (3.6) | 8.6 (3.1) | 9.4 (3.4) | 7.8 (3.3) | $P < 0.05$ |
| Walk | 6-min walk distance (meters) | 414.1 (81.6) | 408.0 (82.1) | 427.8 (89.0) | 477.3 (104.5) | $P < 0.05$ |
| RPE | Exertion rate (during 6-min walk) | 12.6 (2.2) | 13.0 (3.0) | 12.8 (2.6) | 12.4 (2.7) | NS |
| STAI | State anxiety | 47.0 (14.6) | 51.7 (13.1) | 47.4 (15.9) | 41.3 (14.2) | $P < 0.05$ |
| MHI | Anxiety | 43.5 (18.9) | 41.3 (25.0) | 56.3 (27.7) | 59.6 (25.2) | NS |
| | Depression | 47.0 (24.2) | 44.8 (27.7) | 54.2 (26.1) | 65.9 (24.2) | $P < 0.05$ |
| | Behavioral/emotional control | 52.4 (24.1) | 51.7 (26.4) | 59.4 (24.3) | 69.1 (26.1) | $P < 0.05$ |
| | Positive affect | 38.4 (18.3) | 36.5 (20.4) | 41.3 (20.0) | 49.0 (23.1) | $P < 0.05$ |
| | Emotional ties | 48.7 (28.2) | 47.0 (32.3) | 57.0 (29.2) | 63.7 (32.8) | NS |
| Tender points | | 14.8 (2.6) | 15.3 (2.3) | 15.1 (2.4) | 15.1 (2.6) | NS |
| Knee strength | Extension @ 60°/sec (Nm) | 64.2 (32.3) | 64.6 (28.2) | 67.4 (35.4) | 74.6 (35.1) | NS |
| | Extension @ 120°/sec (Nm) | 51.5 (26.8) | 50.1 (23.5) | 54.9 (30.0) | 58.3 (30.1) | NS |
| FIQ | Total | 56.6 (12.9) | 54.9 (13.0) | 57.7 (11.7) | 48.6 (16.2) | $P < 0.05$ |
| ASES | Pain | 50.7 (22.0) | 39.7 (20.9) | 46.9 (23.9) | 56.0 (26.1) | $P < 0.05$ |
| | Function | 66.2 (18.8) | 58.7 (27.6) | 60.6 (21.6) | 72.3 (22.1) | $P < 0.05$ |
| | Symptoms | 47.8 (21.1) | 44.5 (22.9) | 47.9 (23.9) | 55.2 (23.6) | $P < 0.05$ |

* From independent *t*-tests (EX vs. CTL) of change scores (23 weeks−entry), NS = nonsignificant; BDI = Beck Depression Inventory; RPE = rate of perceived exertion; STAI = State-Trait Anxiety Inventory, MHI = Mental Health Inventory; FIQ = Fibromyalgia Impact Questionnaire; ASES = Arthritis Self-Efficacy Scale.

ment for stress. Because these strict criteria excluded similar numbers of subjects from both EX and CTL groups, it is unlikely that these exclusions were biased. Further, the fact that we still found group differences between EX and CTL subjects in the efficacy analyses when we imposed these strict conditions that lowered subject numbers suggests that the effects of exercise on physical function and mood were robust. The relatively high number of subjects who changed medications is also not necessarily surprising given that fibromyalgia is a chronic disorder associated with high medication usage (47).

It is also possible that, because resources did not permit us to run a separate attentional control group, some of the effects, particularly the mood effects we observed in the EX subjects, reflect the effect of belonging to a group rather than the effect of exercise per se. However, meta-analyses on the effect of exercise and depression have shown that exercise is a more effective intervention for depression than is participating in an "enjoyable (nonexercise) activity" (19).

In conclusion, with the aforementioned caveats, the changes that we observed in mood and physical function are encouraging and provide additional evidence supporting the efficacy of exercise for individuals with fibromyalgia. These results are particularly encouraging, because exercise is a simple and relatively inexpensive treatment that can be offered to patients outside of specialized treatment centers.

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