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Exercise, Fibromyalgia, and Fibrofog: A Pilot Study

Jennifer L. Etnier, William B. Karper, Jennifer I. Gapin, Lisa A. Barella, Yu Kai Chang, and Karen J. Murphy

Background: This pilot study was designed to test the efficacy of a physical activity program for improving psychological variables and fibromyalgia syndrome (FMS) symptoms and to provide preliminary evidence regarding the effects on perceived cognitive symptoms and objectively measured cognitive performance by FMS patients. ***Methods:*** Sixteen women diagnosed with FMS were randomly assigned to an 18-week physical activity program or to a control condition. Psychological measures, FMS symptoms, perceived cognitive function, objective measures of cognition, and walking capacity were assessed at baseline and posttest. ***Results:*** At posttest, there were significant differences in fatigue (effect size, ES = 1.86), depression (ES = 1.27), FMS symptoms (ES = 1.56), self-reported cognitive symptoms (ES = 1.19), and delayed recall performance (ES = 1.16) between the physically active group and the control group, indicating that the FMS patients benefited from physical activity. Beneficial effects were also observed for 6 of the 7 objective measures of cognition and ranged from small to large (ESs = 0.26 to 1.06). ***Conclusions:*** Given that all FMS patients do not respond well to conventional treatments, these beneficial effects of physical activity are important. Future studies with larger samples are warranted to test the reliability of the findings for the objective measures of cognition.

Keywords: physical activity, cognition, mental health

Fibromyalgia syndrome (FMS) is a chronic pain syndrome that affects approximately 4.2% of the total population[1] and 7% of women 60- to 79-years-old.[2] Its characteristic physical symptoms include multiple tender points, widespread pain and stiffness, fatigue, and sleep disturbances. In addition, most people with FMS also experience depression[3–5] and many FMS patients report subjective decrements in cognitive functioning.[6,7] In particular, FMS patients have reported a co-occurring cluster of short-term memory problems, mental clarity disturbances, and dissociative symptoms that has been described in the vernacular as "fibrofog."[8] Fibrofog has been described by FMS patients as being the single most debilitating symptom and as the symptom that is of most concern to them.[9]

The evidence for fibrofog comes from both self-reported subjective complaints and from objective measures of cognitive performance. Leavitt et al[8] compared subjective reports of cognitive symptoms between FMS patients and patients with other rheumatic diseases. Results showed that 59.3% of FMS patients reported symptoms characteristic of fibrofog, including memory failure, mental confusion, and dissociation as compared with less than 10% of the comparison group. They also found that for FMS patients, 77% of the cognitive complaints involved declines in memory and mental confusion. Similarly, Katz et al[10] found that more FMS patients (51%) reported memory decline, mental confusion, and speech difficulties than did non-FMS controls (8.8%).

These self-reported perceptions of cognitive deficits must be interpreted cautiously because it has been shown that FMS patients exaggerate their cognitive symptoms relative to objective decrements in performance.[6] However, researchers have also compared objective measures of cognitive performance between FMS patients and control groups to objectify the concept of fibrofog.[11] When compared with non-FMS controls, FMS patients have been shown to perform more poorly on cognitive measures including working memory, free recall, verbal fluency, verbal knowledge,[12] concentration,[6] automatic processing and memory word recall,[13] and short-term memory.[14] Other researchers[7,15] have found that FMS patients performed similarly to a depressed control group and worse than a healthy control group on

The authors are with the Dept of Exercise and Sport Science, University of North Carolina at Greensboro, NC 27402.

tests of information processing, effortful memory tests, and word fluency tasks. Thus, the results of the extant literature generally support both subjective and objective cognitive decrements as a result of FMS.

Surprisingly, fibrofog has been largely ignored in the research, and fibrofog has not been targeted as an important outcome of interventions with FMS patients.[10] Physical activity interventions are no exception. Physical activity in the form of aerobic exercise and strength training has been implemented with FMS patients, and these studies have demonstrated the effectiveness of physical activity on a variety of physical and psychological outcomes.[16–18] Furthermore, using case study designs, Karper and colleagues[19–21] have demonstrated that physical activity participation generally has beneficial effects on the self-reported experience of fibrofog. However, there is no published study in which the effects of physical activity on cognitive function have been examined using a randomized trial specifically designed to examine the effects of physical activity on both self-reported cognitive symptoms and objective measures of cognitive performance in individuals with FMS.

In persons without FMS, there is evidence that physical activity benefits cognition such that regular physical activity is associated with better cognitive performance[22,23] and may protect against cognitive decline with advancing age.[24,25] Thus, it is plausible that regular participation in physical activity could also benefit the cognitive performance of FMS patients. The purpose of this pilot study was to test the efficacy of a walking and circuit training program for improving psychological variables and FMS symptoms and to provide preliminary evidence regarding the potential benefits of physical activity for perceived cognitive symptoms and objectively measured cognitive performance by FMS patients. Data from this pilot study are intended to provide guidance for future research examining the potential benefits of physical activity for cognitive functioning in FMS patients.

Methods

Participants

Local rheumatologists were invited to refer patients to the study. Participants were also recruited through advertisements in local newspapers. The diagnosis of FMS was made by the participant's physician and was based on the guidelines of the 1990 American College of Rheumatology criteria.[26] Most of the participants reported having symptoms as teenagers and receiving a medical diagnosis within the last 1 to 10 years. Assuming that soft tissue pain, fatigue, and sleep problems are part of FMS, the most prevalent comorbidities reported by the participants were anxiety/depression, cognitive deficits (fibrofog), osteoarthritis, irritable bowel syndrome, headache syndromes, neuropathies, auditory and chemical sensitivities, and low/high blood pressure. Inclusion criteria required that participants be over 18 years of age, be currently inactive (defined as participating in exercise 1 day or less per week), and satisfy the American College of Sports Medicine[27] criteria for the safe conduct of exercise. In addition, participants had to be willing to be assigned to either treatment condition. Eligibility with respect to these criteria was determined during an initial phone interview.

All participants were women and the age range was from 32 to 70 years. Twenty-five women volunteered for the study, 22 completed baseline testing, and 16 were randomized to the treatment group or the control group. All of these 16 participants remained in the study for its duration and were available for posttesting (see Figure 1). There were no significant differences between participants who stayed in the study and those who dropped out following baseline testing for age, walking capacity, any of the psychological measures, or any of the cognitive measures, $F_{1,20}$ values = 0.02 to 2.65, P values > .05. This study was approved by the Institutional Review Board, and informed consent was requested of all participants.

Measures

Psychological Measures. The Center for Epidemiology Scale—Depression was used to measure symptoms of depression.[28] Fatigue was assessed using the Fatigue Severity Scale,[29] which has been shown to have good psychometric properties.[30]

Fibromyalgia Syndrome Symptoms. Fibromyalgia syndrome symptoms were measured using the Fibromyalgia Impact Questionnaire, which has acceptable levels of internal consistency and test–retest reliability.[31] Because of its sensitivity to change, the Fibromyalgia Impact Questionnaire has been recommended for use in clinical trials relative to FMS.[32]

Walking Capacity. Walking capacity was assessed using a submaximal timed quarter-mile walk test[33] conducted in a gymnasium. Participants were asked to walk the quarter-mile distance as quickly as they could, and time to completion was recorded in seconds as the measure of walking capacity. Participants who were unable to complete the total distance (2 from the control group and 1 from the exercise group) received the maximum score for the sample as their performance measure.

Cognitive Measures. Cognitive measures were selected to assess areas of cognition that have been found to be impaired in FMS patients[6,12,34] and that were expected to be sensitive to the effects of a physical activity intervention.[22,23]

Subjective perceptions of cognitive ability were assessed using the Pincus Cognitive Symptoms Inventory.[35] Participants were asked to rate their ability to perform 21 everyday cognitive tasks on a scale from 1 (*never a problem*) to 4 (*a problem all the time—unable to do*). Examples of the cognitive abilities include

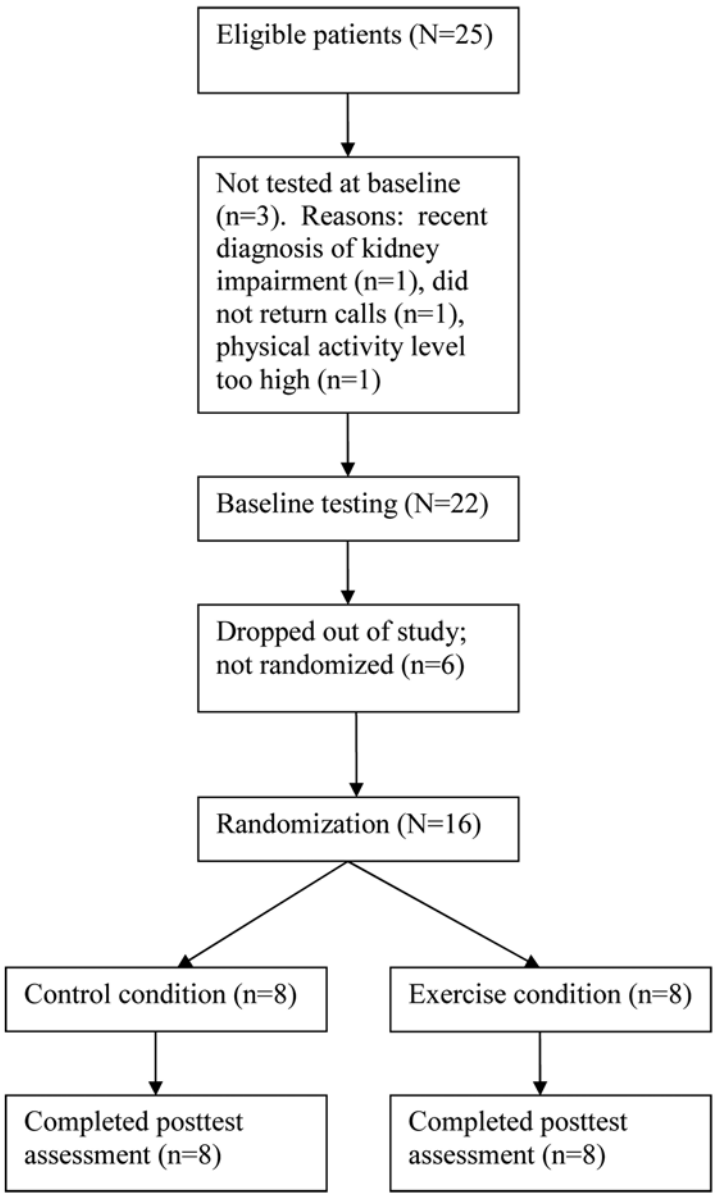

Figure 1 — Consort flow diagram.

"concentrate on a task you need to do," "remember why you came into a room," and "find your way while driving."

Memory was assessed using the Rey Auditory Verbal Learning Test (AVLT).[36] Participants were read a list of 15 words (list A) during 5 separate trials. Following each trial, participants were immediately asked to recall as many words as possible. The maximum number of words recalled on any of these 5 trials was used as the measure of immediate recall. Then, participants were read 15 additional words as a distraction (list B) and were immediately asked to recall these words and then to recall the words from list A. In addition, 30 minutes later, participants were asked to again recall the words from list A (delayed recall).

Attention was assessed using the Paced Addition Serial Attention Task.[37] Participants were read a series of single-digit numbers at the rate of 1 digit every 2.4 seconds, were asked to sequentially add pairs of these numbers, and were instructed to verbally respond with the appropriate sums. This task is indicative of selective attention, information processing, and mental tracking.

Executive function was measured using the Wisconsin Card Sorting Task.[38] Participants were given a stack of 60 unique cards. On each card was printed 1 of 4 symbols in 1 of 4 colors. The task requires that

participants place each card under 1 of 4 stimulus cards. Participants were asked to discern the guiding principle from the experimenter's feedback as to whether they had placed the card under the appropriate stimulus card. The guiding principle changed from color to form to number. Measures of performance were the number of categories achieved, perseverative errors, and the number of trials needed to complete the first category.

Executive function was also measured using the Stroop interference task.[39,40] This task consists of 3 different trials, all of which are to be performed as quickly as possible. In the first trial, participants were asked to identify the color of colored rectangles. In the second trial, participants were asked to read color names as quickly as possible. In the third trial, participants were asked to identify the color of ink in which color names were written. The measure of interference was the time to complete the third trial minus the average of trials 1 and 2.

Procedures

Participants were randomly assigned to either an experimental (N = 8) or a delayed-treatment (N = 8) condition. Experimental participants participated in exercise sessions for 18 weeks. Delayed-treatment participants were in a no-treatment control condition for 18 weeks and then were invited to join the exercise class for 18 weeks. Results from the first 18-week period are presented (Table 1).

At baseline and at 18 weeks (posttest), participants were asked to complete psychological measures, the measure of FMS symptoms, cognitive tests, and the walking capacity test. These tests were conducted on a nonexercise day for the experimental participants. In addition, these sessions were conducted at approximately the same time of day for each participant at baseline and posttest to minimize time-of-day effects.[41]

The exercise sessions were 60 minutes in duration 3 days per week. During the exercise sessions, participants walked, performed light resistance exercises, and performed static-bridging and stretching exercises. All exercise sessions were conducted and directly supervised by the second author who has experience conducting exercise interventions with FMS patients[9,19–21,42,43] and who tailored the exercise program to the abilities and responses of the participants. In terms of the walking portion, participants were encouraged to walk at a comfortable/brisk pace (55% to 65% of maximal heart rate reserve) for 15 minutes. Over the course of the intervention, they were encouraged to try to walk a greater distance in the 15-minute period and used this as a self-measure of aerobic fitness. In terms of the light resistance exercises, participants moved through an 8-station light resistance exercise circuit. When subjects were able to easily complete the required number of repetitions for a certain exercise, resistance was increased by 1 pound. Often, this caused subjects to reduce the number of repetitions for a short time followed by slowly working back to the required number. Static-bridging exercises require that the exerciser support her body (holding the body very still) in various positions to increase core (abdominal, back, and pelvic) muscle strength/endurance. For instance, to strengthen the lower back, subjects would lie on their backs on a mat with legs bent and knees up. On the "up" command, they would lift their back and hips off the mat so that only their head, shoulders, and feet would remain on the mat (forming a type of "bridge"). This position would be held for a number of seconds. When people who are pain-free do this, they usually hold the bridge position for 60 seconds or more. These FMS subjects could only tolerate holding the position for approximately 3 seconds. Therefore, after returning their back and hips to the mat on the "down" command, the move was repeated. Usually 10 repetitions were completed at each session. FMS symptom flare-ups frequently limited the participants' ability to progress in terms of increasing walking distance, repetitions, resistance, and endurance, and therefore, flexibility was required in terms of the goals of each session.

Statistical Analysis

The small sample size of this pilot study resulted in a general failure of the randomization process to result in equivalent means at baseline. Thus, analysis of covariance was used to examine group (control, exercise) differences in fitness, psychological outcomes, and cognitive performance at posttest. In these analyses, the baseline measures of the respective outcomes were used as the covariate. Because of the small sample size and concerns regarding the assumptions needed for parametric analyses, normality was tested for all dependent variables. When nonnormal distributions were observed, the data were converted to binary outcomes and logistic regression was used to test for significant differences. Alpha was set at .05; however, because this study was viewed as a pilot study, corrections for multiple comparisons were not made. In addition, because data for the cognitive outcomes were regarded as preliminary, statistical analyses were expected to be underpowered. Therefore, effect sizes for differences between the exercise group and the control group in estimated marginal means at posttest are presented to provide direction for future research (see Table 1).

Results

Participants

Twenty-two individuals met the inclusion criteria and agreed to participate in the study. All participants were women, and the age range was from 32 to 70 years (mean = 55.14, standard deviation = 8.88). Of these, 16 participants remained in the study for posttesting (age

Table 1 Estimated Marginal Means, Standard Errors, and Effect Sizes for the Exercise Group (N = 8) and the Control Group (N = 8) at Posttest

	Mean	SE	ES[a]
Walking capacity (s)[b]			
exercise	282.85	9.34	1.41
control	320.15	9.34	
Fatigue[b]			
exercise	4.17	0.42	1.65
control	6.13	0.42	
Depression[b]			
exercise	19.97	3.15	1.00
control	28.91	3.15	
FMS symptoms[b]			
exercise	41.40	6.43	1.48
control	66.58	6.43	
Cognitive symptoms[b]			
exercise	1.92	0.11	0.22
control	1.99	0.12	
Interference[b]			
exercise	19.77	2.20	0.00
control	19.73	2.20	
Perseverative errors[b]			
exercise	8.34	1.48	–0.16
control	7.66	1.48	
Number of categories			
exercise	5.68	0.32	0.41
control	5.32	0.32	
Trials to complete first category[b]			
exercise	14.66	1.11	0.50
control	16.22	1.11	
Maximum number of words			
exercise	13.95	0.42	0.86
control	12.92	0.42	
Delayed recall			
exercise	11.76	0.68	0.60
control	10.61	0.68	
Attention			
exercise	38.90	3.52	0.10
control	37.97	3.77	

Abbreviations: ES, effect size; FMS, fibromyalgia syndrome.
[a] All ESs (calculated using pooled SD) are presented such that a positive ES is indicative of the exercise group being "better" and a negative ES is indicative of the control group being "better."
[b] Higher mean indicates worse performance or worse in terms of the psychological construct.

range = 32 to 70 years, mean = 54.69, standard deviation = 9.25). Women in the exercise group completed an average of 65% of the possible exercise sessions (range = 48% to 80%).

Walking Capacity

There was a significant difference in fitness as a function of treatment, $F_{1,13} = 7.98$, $P < .02$. Examination of the means indicated that the exercise group had better fitness than did the control group.

Psychological Measures

There was a significant difference in fatigue, $F_{1,13} = 10.51$, $P < .01$, and a nearly significant difference in depression, $F_{1,13} = 3.78$, $P < .10$, as a function of treatment. Examination of the means indicated that the exercise group reported significantly less fatigue and less depression than did the control group.

Fibromyalgia Syndrome Symptoms

There were significant differences in FMS symptoms, $F_{1,11} = 6.92$, $P < .03$, as a function of treatment group. Examination of the means indicated that the exercise group reported significantly fewer FMS symptoms than did the control group.

Cognitive Outcomes

There were no significant differences in self-reported cognitive symptoms as a function of treatment group, $F_{1,13} = 0.00$, $P > .05$.

There were no significant differences in interference or perseverative errors as a function of treatment (F values < 0.99, P values > .05). The assumption of normality was violated for number of categories and for trials to complete the first category; thus, the dependent variable was converted to a binary variable such that approximately equal numbers of participants were considered "high" and "low" at baseline. Logistic regression with repeated measures[44] indicated that there were no significant changes in performance from baseline to posttest as a function of treatment group. There was no significant difference in performance on the Paced Addition Serial Attention Task, $F_{1,12} = 0.03$, $P > .05$, delayed recall, $F_{1,13} = 1.27$, $P > .05$, or immediate recall, $F_{1,13} = 2.88$, $P > .05$, as a function of treatment.

Discussion

It has been shown that individuals with FMS experience a variety of psychological disturbances, report perceptions of impaired cognitive abilities, and demonstrate worse cognitive performance than comparison groups on laboratory measures of cognition. Exercise has been found to benefit FMS patients in terms of psychological symptoms associated with the experience of FMS, and this study was designed to test the efficacy of a walking and resistance exercise program for improving both psychological variables and FMS symptoms. Furthermore, case studies suggest that benefits to cognitive

performance may also be realized from participation in exercise.[19–21] However, this is the first study to use a randomized trial to examine the effects of exercise on both self-reported cognitive symptoms and objective measures of cognitive performance in individuals with FMS. Thus, this study provides preliminary evidence relative to the efficacy of an 18-week physical activity intervention for cognitive symptoms and cognitive performance of FMS patients.

Results indicated that after participating in exercise for 18 weeks, participants experienced significant improvements in aerobic fitness and reported significantly less fatigue, less depression, and significantly fewer FMS symptoms than did control participants. These results are consistent with the findings of other researchers who have typically supported the beneficial effects of physical activity on psychological outcomes when interventions have been 4 months or longer in duration.[45–49] These findings are important in and of themselves because of the known health benefits associated with physical activity, the multitude of somatic and cognitive symptoms experienced by patients with FMS,[50] and the fact that some FMS patients do not respond well to conventional treatments.[17] Thus, our findings suggest that 18 weeks of exercise for 60 minutes per day, 3 days per week benefits aerobic fitness, fatigue, depression, and FMS symptoms for FMS patients.

Results indicated that there was not a significant difference in perceived cognitive symptoms as a function of treatment group. However, an examination of the effect size showed that the exercise group reported less difficulty performing everyday cognitive tasks than the control group (ES = 0.22). Although research has generally shown that subjective measures of cognitive performance are not predictive of objective measures of performance in community-dwelling older adults,[51] depressed older adults,[52,53] older adults with atherosclerotic vascular disease,[54] and FMS patients,[6] there is evidence that subjective memory complaints are predictive of subsequent declines in objectively measured cognitive performance[55–57] and that perceptions of change in cognitive abilities are predictive of actual change in cognitive abilities.[58] Furthermore, FMS patients report that the cognitive difficulties they experience are the single most distressing symptom of the syndrome.[9] Thus, the small effect of physical activity on self-reported cognitive symptoms may be meaningful to the FMS patients.

With respect to the objective measures of cognition, a significant effect for exercise was not evidenced for any of the cognitive measures. Although significant differences between the groups were not identified, it is important to emphasize that this study was designed to provide preliminary data relative to objective measures of cognitive function and was expected to be statistically underpowered. Examination of the effect sizes then becomes important for guiding subsequent research in this area. Examination of the effect sizes indicated that there were positive effects of exercise on cognitive performance for 5 of the 7 measures and that the size of the effect ranged from small for measures of attention (average effect size, ES = 0.10) and for measures of executive function, which were sensitive to the effects of exercise (average ES = 0.33) to large for measures of memory (average ES = 0.73). These findings suggest that the effects of exercise on objective measures of cognition are likely to be found statistically reliable with a study using a larger number of participants. In particular, for attention 788 participants would be needed, for executive function 76 participants would be needed, and for memory 18 participants would be needed to have sufficient statistical power (power = 0.80, alpha = .05) to ascertain the reliability of these results.

The relatively small effect size for measures of executive function is somewhat surprising given the findings from a recent meta-analytic review that showed that the effects of physical activity on cognition were moderate (ES = 0.68) for executive function tasks.[22] It is important to note, however, that Colcombe and Kramer[22] categorized the Rey Auditory Verbal Learning Test as an executive function test, whereas we considered the AVLT to be a memory task. If we had considered the AVLT to be an executive function task, our overall ES for this cognitive category would have been 0.49, which is essentially a moderate effect size and is consistent with the findings reported by Colcombe and Kramer.[22]

Should future research confirm the reliability of these preliminary findings in a larger sample of FMS patients, then the next important step would be to identify the mechanisms underlying this relationship. Based on findings with other populations of older adults (eg, healthy older adults, older adults with chronic obstructive pulmonary disease), several mechanisms have been proposed to explain this relationship, and animal studies and studies using neuroimaging techniques have been designed to test these mechanisms. In particular, mechanisms for this relationship include changes in cerebral structure (angiogenesis and neurogenesis), increases in cerebral blood flow, increases in neurotransmitters (eg, dopamine, serotonin), and increases in neurotrophic factors (eg, brain-derived neurotrophic factor, insulin-like growth factor). Identification of the mechanisms that explain the relationship between physical activity and cognitive performance will be important so that physical activity interventions can be prescribed (either alone or as an adjunct to traditional treatments) to benefit the cognitive symptoms of FMS patients.

In conclusion, the results from this study demonstrate that an 18-week physical activity intervention has significant large effects on psychological measures and on FMS symptoms. Although the small sample size means that these significant effects should be judged cautiously, the consistency of our results with past literature suggests that these are not spurious findings. Furthermore, because small to moderate effects were observed for measures of executive function, immediate recall, and attention and because the past

literature supports the potential for physical activity to have a positive effect on cognitive performance in FMS patients, it is our belief that future studies with larger sample sizes will confirm a positive effect of physical activity on cognitive performance for FMS patients. Last, given that fibrofog is reported by many patients to be the most debilitating symptom of FMS, the fact that traditional interventions are not completely effective in alleviating fibrofog, the potential link between perceived cognitive abilities and subsequent changes in cognition, and the health benefits that accompany exercise participation, this preliminary evidence in support of exercise for cognitive function in FMS patients is important and will hopefully provide the impetus for more research in this area.

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