Exercise in warm water decreases pain and improves cognitive function in middle-aged women with fibromyalgia

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Abstract

Objectives

To compare the cognitive function performance in patients with fibromyalgia (FM) with respect healthy controls and to evaluate the short-term efficacy of exercise therapy in a warm, chest-high pool on pain and cognitive function in women with FM.

Methods

Sixty middle-aged women with FM were randomly assigned to either an exercise training group (n = 35) to perform 3 sessions per week of aquatic training (32ºC) including mobility, aerobic, strengthening, and relaxation exercises for 16 weeks, or a control group (n = 25). Twenty-five healthy women matched for age, weight, body mass index, and educational and physical activity levels were recruited. Pain was assessed in patients using a syringe calibrated like a pressure dolorimeter, and a visual analog scale. The severity of FM was evaluated using the Fibromyalgia Impact Questionnaire. Cognitive function was measured in healthy individuals and patients using several standardized neuropsychological tests. All patients were measured at baseline and post-treatment.

Results

At baseline, the healthy group evidenced cognitive performance that was significantly superior to the group of patients with FM in all of the neuropsychological tests. The exercise group significantly improved their pain threshold, tender point count, self-reported pain, severity of FM, and cognitive function, while in the control group the differences were not significant.

Conclusion

An exercise therapy three times per week for 16 weeks in a warm-water pool is an adequate treatment to decrease the pain and severity of FM well as to improve cognitive function in previously unfit women with FM and heightened painful symptomatology.

Key words

Fibromyalgia, exercise, pain, cognitive dysfunction, neuropsychological assessment, fibromyalgia impact questionnaire.

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Introduction

Fibromyalgia (FM) is a chronic musculoskeletal pain syndrome which is associated with a wide variety of symptoms such as headaches, sleep disturbances, fatigue, anxiety and depressive mood (1). Most of these symptoms have been closely analyzed in several studies (2, 3). Patients with FM frequently tend to have subjective cognitive complaints (4, 5). However, few studies have examined objective cognitive impairment in FM. From these studies, there are inconsistent findings of subtle problems in complex attention, word fluency, and memory in persons with FM relative to healthy controls (5, 6). Nevertheless, it is not clear whether these subtle deficits can be attributed to central nervous system dysfunction. Existing data suggest that the influence of psychological variables such as depression, pain, and fatigue contribute to neuropsychological presentation in FM (7).

The etiology of FM is unknown, and the pathogenesis is unclear. Thus, causal treatment is not possible. Of the symptomatic treatments, antidepressants and sedatives have been found to have some pain-modulating effect (8). A variety of other pharmacologic and nonmedical treatment modalities have been tried and several controlled studies have shown that different kinds of exercise programs may modulate pain in patients with FM (9, 10). For these and another reasons a growing body of evidence suggests that exercise is beneficial for individuals with FM (11).

A large quantity of studies suggests that there is a positive effect of moderated physical exercise on the cognitive function of several healthy (12) and clinical populations (13).

Although the number of studies examining the benefit of exercise for FM has steadily increased in the last 20 years, no study has addressed the benefits of exercise alone on cognitive function. To date, only 2 studies on the treatment of FM with controlled cognitive function have been published (14, 15). Both studies showed improved cognitive function in FM patients, but they were multidisciplinary, including exercise and education, and therefore we can not discern if the effects were due to exercise, education or to both.

The purpose of this study was: 1) to compare the cognitive function performance in patients with FM with respect to healthy controls and 2) to evaluate the effect of 16 weeks of moderated exercise therapy in a chest-high pool of warm water on pain and cognitive function in women with FM.

Materials and methods

Participants

An invitation to participate in the study was sent to female members, between ages 18 and 60 years, of a local FM association in Spain (n = 250). Sixty-eight potentially eligible subjects responded and sought more information. Those 68 eligible patients gave their written informed consent after the study protocol was explained to them. The study flow of patients is presented in Figure 1. Patients' personal medical records were examined by a physician and their diagnosis of FM was confirmed according to ACR-1990 criteria (16). In order to determine the differences among patients with FM and healthy people, a group of 25 healthy female volunteers matched for age, weight, body mass index, and educational and physical activity levels were recruited and all of them gave their written informed consent.

The exclusion criteria included the presence of subjects with a history of morbid obesity, known cardiopulmonary diseases, uncontrolled endocrine or allergic disturbances, severe trauma, frequent migraines, inflammatory rheumatic diseases, and severe psychiatric illness. Subjects with other diseases that prevented physical loading and those who were pregnant were omitted. Finally, those women with FM who attended another physical or psychological therapy were excluded to avoid possible interactions with the present trial. Patients with a history of regular physical activity more strenuous than slow-paced walking a maximum of 2 times a week over 4 months prior to study entry were excluded from the final analysis according to the criteria of Schachter *et al.* (17). The Spanish version of the revised Physical Activity Readiness Questionnaire (18) was administered to identify persons at risk for adverse events while

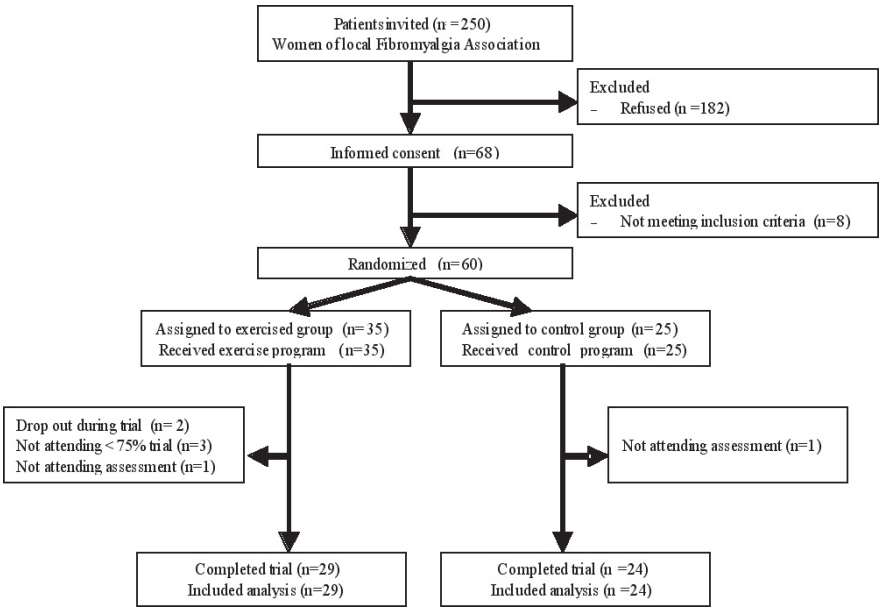

Fig. 1. Flow of patients throughout trial.

exercising. On the whole, 8 patients were excluded from the study because they were attending a psychological therapy program (n = 2), exercised regularly (n = 2), or had history of severe trauma (n = 1), arrhythmia (n = 1), inflammatory rheumatic disease (n = 1) or psychiatric illness (n = 1). According to the applied criteria, a final sample of 60 women with FM was randomly assigned to either an exercise group or a control group. Six patients in the exercise group and 1 from the control group were not included in the analysis for diverse reasons. Finally, twenty-nine women from the exercise group and twenty-four from the control group fully completed the study and were included in the analysis (Fig. 1).

The evaluation of the results was carried out immediately after the training period consisting of 16 weeks. The initial measurements before the training period were designated as baseline values.

The Committee on Biomedical Ethics of the Aragon Government (Spain) gave approval for the study.

Pain

Pressure pain thresholds in all tender points, according to ACR-1990 criteria (16), were measured using a syringe calibrated like pressure dolorimeter (19). The syringe was calibrated to obtain the equivalency of cm^3 in Kg of pressure in order to determine the amount of tender points positive to the exploration according to the guidelines that ACR recommends for the diagnosis of FM. A tender point is considered positive to the exploration when the patient manifests pain with a pressure ≤ 13 cm^3. Estimates of pain severity were reported using information from a 100 mm visual analog scale (VAS) that was included in the Fibromyalgia Impact Questionnaire (FIQ). The scale was scored 0-100 mm, with higher scores reflecting greater levels of pain. This scale was anchored at 0 with "no pain" and at 100 mm with "the most severe pain".

For each patient, the number of examined points positive to the exploration, that is to say, sore to a pressure ≤ 4 Kg (13 cm^3), the forces required to produce pain over the 18 points examined, and the self-reported pain severity were recorded.

Severity of FM

The influence of FM on functional status was assessed for each patient with the validated Spanish version of the FIQ (20). The original version of the FIQ was designed by Burckhardt *et al.* (21) to evaluate the severity of the effect of FM on daily activities. This instrument measures physical functioning and symptoms of pain, fatigue, morning tiredness, stiffness, depression and anxiety, along with job difficulty and overall well-being in the past week. Previous research has shown adequate reliability, validity, and sensitivity to change as a result of treatment with this instrument (22). The questionnaire is scored from 0 to 100, where a higher score indicates a greater impact of the syndrome on the person.

Cognitive function

All participants were asked to complete several standardized neuropsychological tests that examined a variety of cognitive domains.

The Paced Auditory Serial Addition Task (PASAT) measures sustained and divided attention, auditory information processing speed, and stimulus competition filtering skill (23). In this study, the PASAT was administered only at the slowest presentation rate of 2.4 seconds. The score is the number of correct responses over 60 trials.

Repetition of digits and Reversal of digits tests assess full attention and concentration. These tests are administered by giving a score of 1 point for each trial passed (24).

The Trail Making Test (TMT) (25) provides information on visual search, motor function, scanning, speed of processing, mental flexibility and executive functions. Trails A and B were administered according to the guidelines presented by Spreen and Strauss (24). The time required to complete each part was recorded.

The Controlled Oral Word Association test (COWA) assesses verbal fluency. The COWA test was administered according to the instructions used by Spreen and Benton (26) and described in detail by Spreen and Strauss (24). The total number of words generated in 1 minute for the letters F, A, and S (phonemic fluency) was recorded.

The Rey Auditory Verbal Learning Test (RAVLT) (27) measures immediate free recall, delayed free recall, delayed recognition, and verbal learning. This is a multiple-trial verbal list learning test and was given on an individual basis.

Exercise therapy

The exercise group trained in a chest-high warm pool (32ºC) 3 times per week

for 16 weeks. Each session included 10 minutes of warm-up with slow walks and mobility exercises; 10-20 minutes of strength exercises developed at slow pace using water and aquatic materials as resistance, including a stepped progression during the program (Table I); 20-30 minutes of aerobic exercises developed progressively at intensity sufficient to achieve 50-80% of predicted maximum heart rate (220 – age) (Table II); and 10 minutes of cooling down with low-intensity and relaxation exercises. Heart rate was monitored with a pulse meter (Polar Accurex Plus; Polar Electro Oy, Kempele, Finland). The intervention program met the minimum training standards of the American College of Sports Medicine (28).

Statistical analysis

The normality of the variables was evaluated by the Kolmogorov-Smirnov test. Data are expressed as mean (SD). Differences in baseline characteristics and cognitive function among the groups were compared using non-parametric one-way ANOVA. The effects of the intervention program on pain, severity of FM, and cognitive function were evaluated using the paired Student's *t* test and Wilcoxon signed ranks test. Pearson analysis was performed to examine relations of interest. Spearman analysis was applied when data were not normally distributed. The α level was set at 0.05.

Table I. Strength training progression during the program.

Period, weeks	Repetitions	Weekly routines	Sets	Exercises	Duration, minutes	Weekly frequency
1 - 2	10-15	A	1	8	8-10	3
3 - 4	10-15	A	1-2	8-10	10-15	3
5 - 8	10-12	B1,B2	1-2	8-10	10-15	3
9 - 12	10-12	B1,B2	2-3	8-10	15-20	3
13 - 16	8-10	C1,C2,C3	2-3	8-10	15-20	3

A: all major muscular groups; B1: trapezius, latissimus-dorsi, biceps brachii, abductors, adductors and torso muscles *(i.e.* abdominals, oblique and lumbar); B2: pectoralis, triceps brachii, deltoids, gluteus, quadriceps, knee flexors (*i.e.* biceps femoris, semimembranosus and semitendinosus) and gastrocnemius muscles; C1: trapezius, latissimus-dorsi, biceps brachii and torso muscles; C2: gluteus, quadriceps, knee flexors, gastrocnemius, abductors and adductors muscles; C3: pectoralis, triceps brachii, deltoids and torso muscles.

Table II. Aerobic training progression during the program.

Period, weeks	Intensity, % HR_{max}	Duration, minutes	Weekly frequency
1 - 2	50-60	20-25	3
3 - 4	55-65	20-25	3
5 - 8	60-70	20-25	3
9 - 12	65-75	25-30	3
13 - 16	70-80	25-30	3

HR_{max}: Maximum age-related heart rate (220 – age).

Table III. Characteristics of women with fibromyalgia who followed the pool-based exercise program, controls and healthy group*.

Group	Exercise (n = 29)	Control (n = 24)	Healthy (n = 25)	*P* value
Ethnicity, %				
Caucasian	100	100	100	NS
Age, years	50 (7)	46 (8)	47 (10)	NS
Body mass index, kg/m^2	27 (5)	27 (4)	26 (4)	NS
Duration of symptoms, years	14 (10)	14 (9)		NS
Tender point count, 1-18	15.1 (3.9)	16.1 (2.9)		NS
Occupation, %				
Domestic labor	52	67	60	
Operatives	21	17	12	NS
Office or store worker	17	13	20	
Manager	10	4	8	
Highest education, %				
Elementary school	59	63	60	
High school	31	29	24	NS
College/University	10	8	16	

*Values are the mean (SD) unless otherwise indicated; NS: not significant.

Results

Thirty (86%) of the 35 exercisers who attended > 36 of the 48 sessions completed the follow-up at 16 weeks (Fig. 1). Two women (6%) from the exercise group dropped out during the program due to transportation problems and employment commitments.

Table III shows similar baseline characteristics for the exercise, control and healthy groups. Nevertheless, even though no differences in the FIQ score and VAS for pain were found, the exercise group demonstrated a significantly lower pain threshold than the control group in 5 tender points ($p < 0.05$).

The healthy group demonstrated a cognitive performance significantly superior to patient's group with FM in all of the neuropsychological parameters assessed. In addition, the group of patients showed a proportion of subjects that were unable to correctly execute the trial B of TMT at a level that was significantly superior to the healthy group ($p < 0.01$) (Table IV).

The exercise group presented a significant increment of the pain threshold in the 18 tender points and a significant reduction of tender point count and VAS for pain between the pre-program and post-program evaluations. By contrast, in the control group the differ-

Table IV. Cognitive function of patients with fibromyalgia syndrome (n = 53) and healthy subjects (n = 25)*.

	FM Group (n = 53)	Healthy Group (n = 25)	*P* value
Repetition of digits, 0-18	7.2 (2.2)	9.1 (2.1)	< 0.01
Reversal of digits, 0-18	5.3 (1.7)	7.2 (1.9)	< 0.001
TMT trial A, s	73.1 (33.5)	54.1 (25.2)	< 0.05
TMT trial B, s	131.4 (55.0)	81.5 (37.6)	< 0.001
PASAT Test 2.4´´, 0-60	26.8 (14.2)	40.5 (12.6)	< 0.001
RAVLT ΣA1-A5, 0-75	41.5 (9.7)	48.3 (8.4)	< 0.01
RAVLT B1, 0-15	4.5 (1.4)	5.8 (1.7)	< 0.01
RAVLT A6, 0-15	8.5 (2.7)	10.5 (2.3)	< 0.001
RAVLT A7, 0-15	8.0 (2.7)	10.4 (3.0)	< 0.001
RAVLT Matrix, 0-50	35.0 (7.6)	40.7 (4.8)	< 0.01
COWA ΣF, A, S, words	26.7 (11.1)	36.1 (13.5)	< 0.01

*Values are the mean (SD); 95% CI: confidence interval; NS: not significant; TMT: Trail Making Test; PASAT: Paced Auditory Serial Addition Task; RAVLT: Rey Auditory Verbal Learning Test; COWA: Controlled Oral Word Association; One subject of the FM group and one of the healthy group were unable to correctly execute trial A of TMT. Twenty-three subjects of the FM group and three of the healthy group were unable to correctly execute trial B of TMT.

ences were not significant (Table V).

Fourteen (48%) of the 29 exercisers presented less than 11 tender points after the therapeutic program. However, none of the patients from the control group supported this finding.

The exercise group showed statistically significant improvements in FIQ score and in all neuropsychological tests between pre-program and post-program evaluations. The control group did not demonstrate significant differences (Table V).

Discussion

Compared to other works, the sample analyzed in this study is representative of FM, both in the average of pressure pain threshold (29, 30) and the tender point count (31, 32), as well as in the coefficient of variation of both variables (33-35).

An important finding of the study is the increase of pain threshold and the decrease of tender point count produced by the aquatic exercise program. These results support the conclusions of other authors (9, 10, 31, 36, 37). Nevertheless, these findings have not been found in other studies of exercise therapy (15, 35, 38-40). These discrepancies could be attributed to differences in the exercise program and to the assessment of pain quantification. It is relevant that the patients have confirmed the decrease of pain through the self-reported VAS. The perception of improvement is fundamental for continuation of the therapy.

The improvements observed in pain threshold and FIQ with an exercise therapy could be attributed to a central mechanism such as the endogenous opioid system, by increasing peripheral levels of β-endorphins (41), multiple analgesia systems, mediated by other substances such as growth hormone and corticotrophin (42), and the monoamine-serotonergic system, by promoting a decrease of sympathetic activity (43). Some peripheral mechanisms such as an increased capillary density of skeletal muscle and decreased susceptibility to muscle microtrauma would also be able to improve painful symptomatolgy. If performed in water, this exercise therapy could improve the results because of the water's buoyancy and warm temperature. The buoyancy of the water limits the impact of exercise on weight-bearing joints because the external gravity load applied to the lower extremities is reduced in comparison with the load produced in land-based exercise. This potentially limits exercise-induced pain. Since movements and exercise load can be easily adjusted to each patient's limitations, this mode of exercise could be recommended for patients experiencing severe symptoms, exhibiting low function, or those at risk of exercise-induced pain. Regarding warm-water temperature, several studies have found that temperature ranging from 30 to 34ºC reduces stiffness and pain in patients with FM (44). Therefore, we suggest that warm therapeutic pools have the benefit of providing immediate treatment for any exercise-induced pain. This is because the vasodilatory effect of heating may improve muscular ischemia and help to clear algesic mediators in FM. We suggest that warm pools with a water temperature of ≥ 32ºC are better tolerated by individuals with FM because such patients tend to be more sensitive to cold (16).

The principal finding of this study is that the exercise therapy significantly improved cognitive function in patients with FM. Even though the improvement in cognitive function with an exercise therapy has been reported for healthy (12) and clinical populations (13), this is the first non-educational program which demonstrates the positive effect on patients with FM. To date, the two studies of aquatic exercise and education programs have found similar results. These studies have not been able to discern if the improvement was due to physical or psychological training.

Even though there is not a consensus in the literature, a deficiency in cognitive function in patients with FM has been reported (4, 5, 32, 45, 46). This cognitive deficiency could be attributed to a dysfunction of the central nervous system (47-49) or to attentional deficit associated with the painful symptomatology (5, 45). We consider that the cognitive improvement after exercise therapy is fundamentally due to an increase in pain threshold. In this sense, our study demonstrates significant correlation between some neuropsychological tests (repetition of digits test $r = 0.325$ $p < 0.05$; reversal of digits test $r = 0.303$ $p < 0.05$) and the pain threshold. When we compared TMT results between FM and healthy groups, we found that a significant proportion of patients were unable to accomplish the trial B of TMT. This trial appraises the executive and attentional function. In addition, it is unlikely that a short exercise therapy could improve central nervous system

Table V. Effects of a 16-week warm water exercise program in a therapeutic pool on pain and cognitive function in women with fibromyalgia syndrome assigned to the exercise group (n = 29) or control group (n =24)*.

		Exercise Group (n = 29)			Control Group (n = 24)		
		Pre-program	Post-program	*P* value	Pre-program	Post-program	*P* value
Pressure pain thresholds over tender points, cm²							
Trapezius	Dominant	9.5 (2.6)	12.7 (2.4)	< 0.001	10.9 (1.9)	11.1 (2.7)	NS
	Nondominant	10.6 (2.9)	12.8 (2.5)	< 0.001	11.5 (2.3)	11.2 (2.5)	NS
Occiput	Dominant	8.6 (3.3)	11.3 (2.1)	< 0.001	9.5 (1.8)	9.7 (2.5)	NS
	Nondominant	8.6 (3.5)	10.3 (2.2)	< 0.01	9.8 (2.0)	9.6 (2.6)	NS
Ant. cervical	Dominant	5.5 (1.9)	8.5 (1.4)	< 0.001	6.9 (1.4)	7.0 (1.2)	NS
	Nondominant	5.4 (2.0)	8.6 (1.3)	< 0.001	7.3 (1.6)	7.1 (1.7)	NS
Supraspinatus	Dominant	10.1 (3.2)	13.2 (2.7)	< 0.001	11.5 (2.2)	11.4 (2.4)	NS
	Nondominant	10.7 (2.9)	13.6 (2.4)	< 0.001	11.7 (2.1)	11.5 (2.2)	NS
Second rib	Dominant	8.2 (2.7)	11.7 (2.4)	< 0.001	9.9 (1.6)	10.3 (2.2)	NS
	Nondominant	8.3 (3.2)	11.9 (1.9)	< 0.001	10.0 (1.6)	10.5 (2.3)	NS
Lateral epicondyle	Dominant	11.0 (3.5)	13.4 (2.6)	< 0.001	11.8 (1.5)	11.9 (2.2)	NS
	Nondominant	11.1 (3.6)	13.5 (2.3)	< 0.001	11.8 (1.7)	11.8 (2.3)	NS
Gluteal	Dominant	11.2 (2.5)	14.1 (2.1)	< 0.001	11.7 (2.1)	11.7 (2.8)	NS
	Nondominant	11.6 (2.7)	14.3 (2.1)	< 0.001	11.9 (2.3)	11.8 (2.8)	NS
Greater trochanter	Dominant	10.9 (3.5)	13.7 (2.6)	< 0.001	11.9 (1.7)	12.1 (2.2)	NS
	Nondominant	11.5 (3.1)	13.7 (2.5)	< 0.001	12.0 (1.7)	12.2 (2.1)	NS
Knee	Dominant	10.2 (3.7)	12.7 (3.1)	< 0.001	11.8 (1.8)	11.9 (2.1)	NS
	Nondominant	10.8 (3.8)	13.2 (2.6)	< 0.001	11.5 (2.4)	11.4 (2.9)	NS
Tender point count, 1-18		15.1 (3.9)	10.8 (5.1)	< 0.001	16.1 (2.9)	15.8 (3.3)	NS
Fibromyalgia Impact Questionnaire							
Total score, 0-100		68.2 (13.4)	63.1 (10.3)	< 0.05	63.6 (16.7)	62.7 (14.1)	NS
VAS pain, 0-100		78.3 (18.5)	66.9 (14.7)	< 0.01	72.5 (24.7)	75.8 (20.0)	NS
Neuropsychological tests							
Repetition of digits, 0-18		6.6 (2.3)	8.2 (2.4)	< 0.001	8.0 (1.9)	7.9 (2.5)	NS
Reversal of digits, 0-18		5.0 (2.0)	5.7 (2.0)	< 0.001	5.6 (1.2)	5.8 (1.6)	NS
TMT trial A, s		81 (35)	65 (42)	< 0.001	63 (29)	60 (32)	NS
TMT trial B, s		141 (56)	110 (42)	< 0.001	110 (48)	104 (28)	NS
PASAT Test 2.4´´, 0-60		25.7 (15.5)	32.3 (15.1)	< 0.001	28.2 (12.7)	29.3 (13.5)	NS
RAVLT ΣA1-A5, 0-75		39.9 (10.9)	48.2 (11.9)	< 0.001	43.4 (7.5)	44.9 (10.3)	NS
RAVLT B1, 0-15		4.6 (1.4)	4.9 (1.8)	NS	4.5 (1.4)	4.3 (1.3)	NS
RAVLT A6, 0-15		8.3 (3.0)	9.7 (2.9)	< 0.01	8.7 (2.5)	9.7 (2.9)	NS
RAVLT A7, 0-15		7.8 (3.0)	9.8 (3.1)	< 0.001	8.1 (2.4)	9.1 (3.2)	NS
RAVLT Matrix, 0-50		33.5 (7.4)	37.9 (6.6)	< 0.001	36.8 (7.6)	34.6 (6.4)	NS
COWA ΣF, A, S, words		23.1 (11.1)	29.0 (11.9)	< 0.001	31.0 (9.7)	35.2 (11.8)	NS

*Values are the mean (SD); 95% CI: confidence interval; NS: not significant; VAS: visual analog scale; TMT: Trail Making Test; PASAT: Paced Auditory Serial Addition Task; RAVLT: Rey Auditory Verbal Learning Test; COWA: Controlled Oral Word Association; In pre-program assessment, one subject of the exercise group and one of the control group were unable to correctly execute trial A of TMT, eight subjects of the exercise group and fifteen of the control group were unable to correctly execute trial B of TMT. In post-program assessment, one subject of the exercise group was unable to correctly execute trial A of TMT, ten subjects of the exercise group and nine of the control group were unable to correctly execute trial B of TMT.

pain-modulation. For this reason, we reject this hypothesis.

Furthermore, other benefits associated with the exercise therapy, such as the increase of blood flow, and consequently, the availability of cerebral nutrients (50), endothelial nitric oxide production, cerebral perfusion (51), trophic factors stimulation and neuronal growth (52), could contribute to the improvement of cognitive function.

The findings obtained in this study should be verified with larger samples and longer therapies. The significant differences in baseline pain thresholds between groups in 5 of the 18 tender points may have increased the improvements observed in the pain threshold of these 5 tender points. Nevertheless, this limitation can not justify the important longitudinal changes found in the pain threshold of all of the tender points, VAS for pain, total score FIQ, and all neuropsychological tests. For these reasons, we can conclude that exercise therapy three times per week for 16 weeks in a chest-high pool of warm water increased pain threshold, reduced the number of tender points, self-reported pain intensity, and severity of FM. Moreover, we conclude that it improved cognitive function in previously unfit women with FM and heightened

painful symptomatology. The observed changes provide additional evidence that supports the efficacy of exercise for individuals with FM.

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