Pain Medicine, 20(12), 2019, 2506–2515
doi: doi: 10.1093/pm/pny304
Advance Access Publication Date: 29 January 2019
Original research Article

OXFORD

MUSCULOSKELETAL SECTION

Lower Fatigue in Fit and Positive Women with Fibromyalgia: The al-Ándalus Project

Fernando Estévez-López, PhD,*[,†,‡] María Rodriguez-Ayllon, MSc,[§,a] Alberto Soriano-Maldonado, PhD,[¶,‖,a] Pedro Acosta-Manzano, MSc,* Víctor Segura-Jiménez, PhD,[‖] Inmaculada C. Álvarez-Gallardo, PhD,[‖] Manuel Pulido-Martos, PhD, Manuel Herrador-Colmenero, PhD,[§] Rinie Geenen, PhD,[‡] Ana Carbonell-Baeza, PhD,[‖] and Manuel Delgado-Fernández, PhD***

*Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Granada, Spain; †Institute of Nursing and Health Research, School of Health Sciences, Ulster University, Northern Ireland, UK; ‡Department of Psychology, Faculty of Social and Behavioural Sciences, Utrecht University, Utrecht, the Netherlands; §PROmoting FITness and Health Through Physical Activity (PROFITH) Research Group, Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Granada, Spain; ¶Department of Education, Faculty of Education Sciences, University of Almería, Almería, Spain; ‖SPORT Research Group (CTS-1024), CERNEP Research Center, University of Almería, Almería, Spain; ‖‖Department of Physical Education, Faculty of Education Sciences, University of Cádiz, Cádiz, Spain; **Department of Psychology, Faculty of Humanities and Sciences of Education, University of Jaén, Jaén, Spain

[a]Equal contribution

Correspondence to: Fernando Estévez-López, PhD, Faculty of Sport Sciences, Department of Physical Education and Sport, University of Granada, Granada, Spain, Carretera de Alfacar, s/n, 18011, Granada, Spain. Tel: (+34) 938-244-375; Fax: (+34) 958-244-369; E-mail: festevez@ugr.es.

Funding sources: This work was supported by the Spanish Ministry of Economy and Competitiveness (I+D+i DEP2010-15639, I+D+i DEP2013-40908-R to MDF; BES-2014-067612 to FEL); the University of Granada and CEI BioTic Granada (Mobility grant to FEL); the Consejería de Turismo, Comercio y Deporte, Junta de Andalucía (CTCD-201000019242-TRA to MDF); and the University of Granada, Plan Propio de Investigación 2016, Excellence Actions: Units of Excellence; Unit of Excellence on Exercise and Health (UCEES).

Disclaimer: The funders of the present study did not have any role in the study design, data collection and analyses, decision to publish, or preparation of the manuscript.

Conflicts of interest: The authors have no conflicts of interest to declare.

Abstract

Objective. To analyze 1) the independent association of physical fitness, positive affect, and negative affect with the different dimensions of fatigue (general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue) and 2) whether the interactions of physical fitness, positive affect, and negative affect were associated with fatigue over and above the independent association. **Design**. Cross-sectional study in 420 women with fibromyalgia. **Setting**. Fibromyalgia associations from southern Spain. **Methods**. Physical fitness was measured by performance-based tests, and questionnaires were used to measure positive affect, negative affect, and different dimensions of fatigue (general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue). Age, body mass index, and current pain level were included as potential confounders in all analyses. **Results**. Physical fitness was independently associated with general fatigue, physical fatigue, and reduced activity (all $P \leq 0.02$). Positive affect was independently associated with all fatigue dimensions (all $P < 0.001$). Negative affect was independently associated with general fatigue, physical fatigue, reduced motivation, and mental fatigue (all $P \leq 0.04$). The interaction of overall physical fitness and positive affect was related to general fatigue and physical fatigue (all $P \leq 0.02$). Women with fibromyalgia with higher levels of overall physical fitness and positive affect showed the lowest general fatigue and physical fatigue. **Conclusions**. In women with fibromyalgia, positive affect was independently and consistently associated with all dimensions of fatigue. The combination of higher levels of overall physical fitness and positive affect might serve as a buffer against general and physical fatigue in women with fibromyalgia.

Key Words: Chronic Pain; Multidimensional Fatigue Inventory; Positive and Negative Affect; Rheumatic and Musculoskeletal Diseases; Senior Fitness Test

Introduction

Fibromyalgia is a common disease [1] characterized by a genetic susceptibility [2,3] to chronic widespread pain and increased sensitivity to painful stimuli [4,5]. Fatigue is markedly prevalent in fibromyalgia. Up to 82% of people with fibromyalgia report severe fatigue [6], and more than 25% identify fatigue as their main complaint [7]. Fatigue is a distressing symptom [8] that negatively impacts the quality of life of people with the condition [9,10] and is recognized as a core symptom in the updated fibromyalgia diagnostic criteria [11]. In spite of the importance of fatigue in fibromyalgia, most previous research has focused on determinants and management of pain, with only limited investigation of fatigue [12,13]. Given that fatigue is a complex symptom that is difficult to manage, the current study aims to identify modifiable factors that are associated with fatigue and that may play a role in its treatment. It is noteworthy that, as we did in a previous study [14], most of the literature in fibromyalgia has assessed fatigue as a unidimensional construct using visual analog scales (VAS) or numeric rating scales (NRS) [6,15,16]. Nonetheless, the subjective experience of fatigue is multidimensional by nature because it involves physical (e.g., I want to but I can't) and psychological domains (e.g., I don't feel like doing anything) [12,17].

Previous literature, including one of our studies [18], has shown that single components of physical fitness (e.g., muscular strength) are inversely associated with fibromyalgia symptoms [18–20], including fatigue [14,21,22]. Although physical exercise is advised as a way to manage fatigue in fibromyalgia [23], physical activity guidelines tend to focus on improving physical fitness as a whole and meeting public health recommendations [24,25], but there is limited evidence about the association of overall physical fitness with fatigue in fibromyalgia. Recently, we have revealed that, independent of physical activity, overall physical fitness is associated with general fatigue, physical fatigue, reduced activity, and reduced motivation [26]. However, no psychological factors were included in the model, even though it is well known that they facilitate adaptation to chronic symptoms [27–29]. Previous literature has also shown that psychological factors (including positive affect and negative affect) are associated with adaptation to fibromyalgia-related symptoms. In fact, such factors may play a role in avoidance of and motivation to engage in exercise among people with fibromyalgia [30,31].

Positive and negative affect are defined as one's affective evaluation of life [32]. These components reflect two distinct (independent) but correlated dimensions of affect [33]. The role of both positive affect and negative affect on health is considered important [34], and indeed positive and negative affect are associated with fibromyalgia symptoms [35–37] and with fatigue in chronic diseases [38,39]. Although previous studies have demonstrated that positive and negative affect are associated with fatigue in fibromyalgia [31,40], they did not include the multidimensional domains of fatigue.

A comprehensive understanding of the associations of overall physical fitness, positive affect, and negative affect with the multiple dimensions of fatigue in fibromyalgia is imperative. Recently, it has been suggested that more sophisticated models are required to explain patient adaptation to chronic conditions such as fibromyalgia [41–43]. These models should account for the interplay of physical and psychological factors [37,44]. The individual associations of physical and psychological factors and their interactions with fatigue will suggest how to tailor therapy to the characteristics of patients when targeting the management of fatigue in fibromyalgia [45]. Among psychological factors, positive affect seems to be an important source of resilience (i.e., adaptive factor) in chronic pain conditions in general [30,36] and in fibromyalgia in particular [36,37,40]. Therefore, the strongest associations with dimensions of fatigue may be expected for positive affect.

The present study is aimed at analyzing 1) the independent associations of physical fitness, positive affect, and negative affect with the different dimensions of fatigue (general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue); and 2) whether the interactions of physical fitness, positive affect, and negative affect are associated with fatigue over and above the independent association.

Methods

Participants

To obtain a representative sample of people with fibromyalgia from Andalusia (southern Spain), a two-phase (sex and province) proportional sampling of people with fibromyalgia was planned, as described elsewhere [46]. A total of 646 potential participants were recruited from different local fibromyalgia associations throughout the eight provinces of Andalusia. Potential participants were recruited via e-mail, letter, telephone, and announcements in local mass media and university websites. All participants were assessed between November 2011 and January 2013. To be included, participants had to 1) have a medical diagnosis of fibromyalgia (the participants were requested to provide their medical records to

confirm this), 2) meet the 1990 American College of Rheumatology (ACR) fibromyalgia criteria [5], and 3) have neither acute/terminal disease nor severe cognitive impairment. The analysis only included women. The participants with incomplete questionnaires or with an incomplete physical performance evaluation were excluded.

Ethical Considerations

All participants were provided with written informed consent before taking part in the study. The al-Ándalus Project protocol was reviewed and approved by the Ethics Committee of the Virgen de las Nieves Hospital (Granada, Spain; registration number: 15/11/2013-N72). The ethical guidelines of the Declaration of Helsinki were followed.

Measures

Sociodemographic and Clinical Data

Participants completed a questionnaire about demographics and health: gender, date of birth, marital status, education level, and presence/absence of acute or terminal illness (such as cancer, stroke, recent cardiomyopathy, severe coronary disease, schizophrenia, or any other disabling injury).

Fibromyalgia Criteria

The 18 tender points according to the 1990 ACR fibromyalgia criteria [5] were assessed through physical examination using a manual algometer (FPK 20; Wagner Instruments, Greenwich, CT, USA). The mean of two alternative measurements at each tender point was used to determine whether each tender point was positive (i.e., patient reported pain at a pressure of $\leq 4\,kg/cm^2$) or negative.

Cognitive Performance

The Mini-Mental State Examination (MMSE) [47] was used as a screening instrument to determine cognitive impairment. Participants who failed to reach a score of at least 10 points on the MMSE were excluded.

Body Mass Index

Weight in kilograms (InBody R20, Biospace, Seoul, South Korea) and height in centimeters (Seca 22) were measured. Body mass index (BMI) was calculated as kg/m^2.

Current Pain Level

Current pain intensity was assessed on a 10-cm VAS, with higher scores representing higher pain intensity [48].

Physical Fitness

Physical fitness was assessed using a battery of performance-based tests, which included the Functional Senior Physical Fitness Test Battery [49] and the handgrip strength test. This battery is commonly used in people with fibromyalgia [14,50], and it has been shown to be feasible and reliable in fibromyalgia [51]. Briefly, we used the "30-second chair stand test" and the "arm curl test" to assess muscular strength. To assess flexibility, we used the "chair sit-and-reach test" and the "back scratch test." The "8-foot up-and-go test" and the "6-minute walk test" were used to assess motor agility and cardiorespiratory fitness, respectively. The standardized scoring of these tests is available elsewhere [14,18,52,53].

Positive Affect and Negative Affect

The Spanish version [54] of the Positive and Negative Affect Schedule (PANAS) [55] is a 20-item questionnaire that assesses positive affect and negative affect. The PANAS consists of 10 positive and 10 negative adjectives answered on a five-point Likert scale ranging from 1 = "very slightly or not at all" to 5 = "extremely." The two-factor structure (positive affect, negative affect) is also appropriate for people with fibromyalgia [56]. The PANAS scores range from 10 to 50 for both subscales, where higher scores reflect a more positive affect or negative affect. The time frame of the questionnaire was "in general."

Fatigue

The Spanish version [57] of the Multidimensional Fatigue Inventory (MFI) [58] is a 20-item questionnaire that evaluates five dimensions of fatigue: general fatigue, physical fatigue, reduced motivation, reduced activity, and mental fatigue. Each fatigue dimension is assessed with four items on a five-point Likert scale ranging from 1 = "yes, that is true" to 5 = "no, that is not true." Thus, the MFI scores for each fatigue dimension range from 4 to 20, where higher scores indicate more fatigue. The time frame of the fatigue scales is "lately."

Statistical Analyses

For physical fitness measures, we computed a set of normalized *z*-scores [(value-mean)/SD] for each participant. We used data from the 6-minute walk test to compute a "cardio-respiratory fitness *z*-score." The means of the *z*-scores of the chair sit-and-reach and back scratch tests were used to compute a "flexibility *z*-score." For a better representation of the performance of higher scores, we used inverted 8-foot up-and-go test scores to compute a "motor agility *z*-score." Also, the mean of the *z*-scores of the 30-second chair stand and arm curl tests were used to compute a "muscular strength *z*-score." Finally, we calculated an overall physical fitness score as the mean of the four *z*-scores (i.e., single components) of physical fitness. Although the present study focused on overall

physical fitness, additional analyses with single components of physical fitness (i.e., cardio-respiratory fitness, flexibility, motor agility, and muscular strength) were conducted (Supplementary Data).

All the analyses of the present study were adjusted for age, BMI, and current pain level, as they are known to be potential confounders of the association under study [59–63].

The analysis was conducted in a number of stages; first, we analyzed associations of overall physical fitness, positive affect, and negative affect with dimensions of fatigue (main aim) by partial correlations. Second, we conducted multiple linear regression analyses to weigh the potential unique contribution of independent variables per se (i.e., independent association) and their interactions on dimensions of fatigue (i.e., dependent variables) using separate analyses for each dependent variable. To compute the interaction term of each pair of variables, we centered the variables before computing the interaction. In a single step (using the *enter* method), we incorporated all the independent variables in the regression model: age, BMI, current pain level, overall physical fitness, positive affect, negative affect, overall physical fitness * positive affect, overall physical fitness * negative affect, and positive affect * negative affect.

To probe significant interactions, regression lines for individuals with low (–1 SD) and high (+1 SD) levels of overall physical fitness were plotted for low (–1 SD) and high (+1 SD) levels of positive affect [64]. All analyses were performed using the Statistical Package for Social Sciences (version 20.0; IBM SPSS Statistics, Armonk, NY, USA). The level of significance was set at $P < 0.05$ (two-tailed).

Table 1. Characteristics of the participants (N = 420)

Characteristics	Value	
Age, mean (SD), y	51.2	(7.4)
Marital status, No. (%)		
Married	321	(76.4)
Not married	99	(23.6)
Education level, No. (%)		
Unfinished studies	38	(9.0)
Primary school	207	(49.3)
Secondary school (including vocational training)	117	(27.9)
University degree	58	(13.8)
Years since clinical diagnosis, No. (%)		
<1 y	26	(6.4)
1–5 y	142	(34.9)
>5 y	239	(58.7)
Missing data	13	(3.1)
Body mass index, mean (SD), kg/m^2	28.4	(5.5)
Current pain level, mean (SD), VAS (0–10 cm)	5.9	(2.2)
Physical fitness tests, mean (SD)		
Chair sit-and-reach test, cm	–10.9	(11.8)
Back scratch test, cm	–13.5	(12.1)
30-sec chair stand test, repetitions	10.5	(3.1)
8-foot up-and-go test, sec	6.7	(1.7)
Arm curl test, repetitions	14.4	(4.9)
6-min walk test, m	490.3	(77.0)
Affect, mean (SD), PANAS (10–50)		
Positive affect	23.1	(6.8)
Negative affect	24.0	(8.5)
Dimensions of fatigue, mean (SD), MFI (4–20)		
General fatigue	18.0	(2.5)
Physical fatigue	16.6	(3.0)
Reduced activity	12.9	(4.9)
Reduced motivation	13.1	(3.8)
Mental fatigue	14.2	(2.3)

MFI = Multidimensional Fatigue Inventory; PANAS = Positive and Negative Affect Schedule; VAS = visual analog scale.

Results

From 646 potential participants, 226 were excluded because they did not provide evidence of a medical diagnosis of fibromyalgia from a rheumatologist (N = 39), did not meet the 1990 ACR criteria (N = 99), had acute or severe health conditions (N = 2), showed a severely impaired cognitive performance (N = 1), were men (N = 21), were older than age 65 years (N = 25), or did not complete all the assessments (N = 39). Descriptive characteristics of the 420 participants who composed the final study sample are presented in Table 1. Participants with and without missing data (N = 39 and N = 420, respectively) did not differ in terms of the dimensions of fatigue (*P* values range from 0.216 to 0.919).

All partial correlations of overall physical fitness, positive affect, and negative affect (adjusting for age, BMI, and current pain level) with dimensions of fatigue were significant (all $P < 0.001$, except for overall physical fitness and mental fatigue, $P = 0.006$; data not shown). Table 2 presents the results derived from the multiple linear regression analyses. Overall physical fitness was independently associated with general fatigue, physical fatigue, and reduced activity ($t = –4.08$, $P < 0.001$, $t = –3.79$, $P < 0.001$, and $t = –2.31$, $P = 0.021$, respectively). Independently of the other components, cardio-respiratory fitness and muscular strength were associated with general fatigue whereas flexibility was related to physical fatigue and reduced activity (Supplementary Data). Positive affect was independently associated with all the dimensions of fatigue (*t* from –4.25 to –9.53 for general fatigue and reduced motivation, respectively; all $P < 0.001$). Except with reduced activity, negative affect was independently associated with all dimensions of fatigue (*t* from 2.04 to 5.83 for general fatigue and reduced motivation, respectively; all $P \leq 0.042$). Additionally, the interactions of overall physical fitness and positive affect with general fatigue and physical fatigue were significant ($t = –2.30$, $P = 0.022$, and $t = –3.00$, $P = 0.003$, respectively). Figure 1 displays the estimated values of general fatigue and physical fatigue for participants having low (–1 SD) and high (+1 SD) scores on overall physical fitness and positive affect. The graph shows that those participants who had high overall physical fitness and positive affect in particular perceived the least general fatigue and physical fatigue.

Table 2. Multiple linear regression examining the independent associations of overall physical fitness, positive affect, and negative affect with dimensions of fatigue (N = 420)

	General Fatigue		Physical Fatigue		Reduced Activity		Reduced Motivation		Mental Fatigue	
	β	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*
Age	–0.15	0.002	–0.06	0.229	0.00	0.997	0.05	0.283	0.03	0.494
Body mass index	0.10	0.029	0.21	<0.001	0.12	0.007	0.05	0.209	0.02	0.611
Current pain level (VAS, 0–10 cm)	0.11	0.018	0.03	0.528	–0.03	0.568	0.01	0.870	0.00	0.936
OPF*	–0.20	<0.001	–0.18	<0.001	–0.11	0.021	–0.04	0.358	–0.03	0.593
Positive affect (PANAS)	–0.21	<0.001	–0.24	<0.001	–0.36	<0.001	–0.43	<0.001	–0.26	<0.001
Negative affect (PANAS)	0.10	0.042	0.10	0.039	0.06	0.254	0.26	<0.001	0.20	<0.001
Interaction OPF and PA	–0.11	0.022	–0.15	0.003	–0.04	0.458	0.01	0.828	–0.02	0.691
Interaction OPF and NA	0.06	0.254	0.02	0.716	0.02	0.754	0.06	0.213	–0.01	0.885
Interaction PA and NA	0.05	0.307	–0.06	0.190	–0.05	0.325	–0.05	0.232	0.10	0.052
Total adjusted R^2 of the model	0.21		0.22		0.19		0.34		0.16	

β indicates standardized regression coefficients with significance levels of *t*. All the analyses were adjusted for age, body mass index (kg/m^2), and current pain level (VAS, 0–10 cm). Fatigue was assessed with the Multidimensional Fatigue Inventory. All adjusted R^2 values were significant; all $P < 0.001$.

NA = negative affect; OPF = overall physical fitness; PA = positive affect; PANAS = Positive and Negative Affect Schedule; VAS = visual analog scale.

*Overall physical fitness was calculated as the average of the *z*-scores of the four physical fitness components: cardio-respiratory fitness, flexibility, motor agility, and muscular strength.

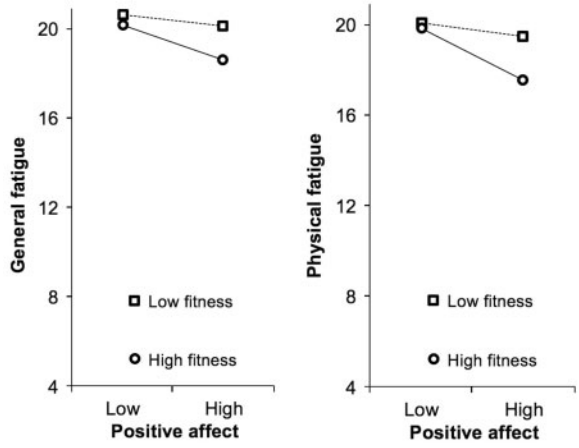

Figure 1. General fatigue (left) and physical fatigue (right) for participants with low (–1 SD) and high (+1 SD) levels of overall physical fitness (fitness) and positive affect (N = 420). Values were estimated adjusting for age, body mass index (kg/m^2), and current pain level (visual analog scale, 0–10 cm). Overall physical fitness was calculated as the average of *z*-scores of the four physical fitness components: cardio-respiratory fitness, flexibility, motor agility, and muscular strength. Positive affect and the dimensions of fatigue were assessed by means of the Positive and Negative Affect Schedule and Multidimensional Fatigue Inventory, respectively.

Our regression model explained between 16% and 34% of the variability in dimensions of fatigue (adjusted R^2 values were 0.21, $F(9, 409) = 13.67$, for general fatigue; 0.22, $F(9, 409) = 14.07$, for physical fatigue; 0.19, $F(9, 409) = 11.91$, for reduced activity; 0.34, $F(9, 409) = 24.16$, for reduced motivation; 0.16, and $F(9, 409) = 8.92$, for mental fatigue; all $P < 0.001$).

Discussion

The findings of the present study indicate that overall physical fitness, positive affect, and negative affect are independently associated with multiple dimensions of fatigue. Positive affect consistently demonstrated the strongest association with all dimensions of fatigue. In addition to these independent associations, we found that the interaction of overall physical fitness and positive affect was related to general fatigue and physical fatigue.

In fibromyalgia, a vicious cycle of reduced physical activity, physical deconditioning, and worsening physical fatigue may emerge [65]. Patients may avoid physical exercise programs and physical activity in daily life in order to avoid subsequent (short-term) fatigue and pain flares [13]. However, current opinion is that avoidance of physical activity exacerbates long-term fatigue. A previous randomized controlled trial indicated that resistance exercise training reduced long-term physical fatigue [66].

Our results reflect previous literature that observed correlations between specific physical fitness test performance, such as handgrip strength [14,21,22], and fatigue. Several previous studies in fibromyalgia aimed to improve single components of physical fitness, particularly cardiorespiratory fitness [66,67], and physical activity recommendations have focused on improving overall physical fitness [25]. In the present study, while taking account of positive affect and negative affect, overall physical fitness was independently associated with general fatigue, physical fatigue, and reduced activity, but not with reduced motivation and mental fatigue. Looking at the single components, we observed that cardio-respiratory fitness and muscular strength were associated with general fatigue, while flexibility was the only component of physical fitness that was associated with physical fatigue and reduced activity. Previous literature found that both flexibility and muscular strength were also related to pain in fibromyalgia [68]. This suggests that it might be worthwhile to consider not only cardiovascular fitness but also other components of

physical fitness in fibromyalgia in order to give a full account of fatigue as well as pain.

Previous literature has demonstrated that people with fibromyalgia usually experience deficits in the regulation of positive affect [69], and those patients with higher levels of positive affect experience lower pain and fibromyalgia severity [36,37,44]. Even while adjusting for overall physical fitness and negative affect, the present study showed that positive affect was consistently associated with all dimensions of fatigue. Our results again reflect previous studies that have highlighted the importance of positive affect as a source of resilience in fibromyalgia [36,37,44], but our results extend previous findings to all dimensions of fatigue.

Negative affect is not just the polar opposite of positive affect. Both affects are to a certain extent separate dimensions that are associated with distinct personality variables, cognitions, and behaviors [56,70]. High negative affect is a vulnerability factor that is closely associated with neuroticism and may promote alerts of danger and avoidance behavior [70,71]. It has been well documented in the literature that many people with fibromyalgia appear to live a life characterized by avoidance instead of approach behaviors [31]. In contrast, positive affect is closely associated with extraversion [70]. Positive affect appears to be a resilience factor that reflects an optimistic outlook and approach tendencies [72,73], including the pursuit of physical activity [74,75]. Through behavioral and cognitive changes, and perhaps also more directly, positive affect and negative affect may have a different impact on fatigue. In comparison with negative affect, we observed that positive affect had a stronger association with fatigue. The findings of the present study suggest that in the therapeutic environment, not only should negative affect be targeted, but promoting positive affect should also be considered.

In our study, we also found that the interaction of overall physical fitness and positive affect was associated with general fatigue and physical fatigue. This probably reflects at least three combined effects. First, positive affect enhances health in general [34], and more specifically adherence to healthy behaviors such as engaging in physical activity [74,75]. Second, more time engaged in physical activity (which is one of the determinants of overall physical fitness) is related to better mood [76,77], and time spent in physical activity more clearly enhances positive affect than negative affect [78]. Third, daily increases in fatigue are associated with a reduction in positive affect in women with fibromyalgia [40], which suggests that fatigue influences mood. Additionally, the broaden-and-build theory [79] predicts that positive affect helps to cope with stressful stimuli such as fatigue, which suggests that mood affects fatigue. In fact, it has been pointed out that positive affect could help people who experience chronic pain (e.g., fibromyalgia) to better manage the disease [30]. Therefore, a model specifying reciprocal influences among overall physical fitness, positive affect, negative affect, and fatigue seems the most plausible. Further prospective research is required to ascertain the assumed bidirectional causality between these factors in fibromyalgia.

Inspired by pain research [41–43] and recognizing that fatigue is a multidimensional symptom [80], we suggest that adaptation to fatigue requires a sophisticated model that includes the interplay of both physical and psychological factors. The findings of the present study suggest that, even after account was taken of the independent effects, the combination of high overall physical fitness and high positive affect was associated with even lower general fatigue and physical fatigue, which reflects the previous literature [37]. As previously reported [44,81], our study adds further evidence suggesting that fibromyalgia incorporates subgroups based on the combination of physical and psychological factors.

Clinical Applications

Fibromyalgia is a common condition in which most people experience severe levels of fatigue [6]. Because fibromyalgia is currently an incurable complex disease, adaptation is a clinical priority. The findings from the present study highlight the importance of considering the independent associations and the interaction of overall physical fitness and positive affect with fatigue.

Although our cross-sectional design precludes strong inferences about cause-and-effect directionality of the observed associations, our results have some clinical implications that need corroboration by clinical–experimental research. First, consistent with the 2016-updated European League Against Rheumatism recommendations for the management of fibromyalgia [45], physical exercise is advisable for people with fibromyalgia. Our results tentatively suggest that a multidisciplinary approach focused on enhancing both physical fitness and mood (by means of physical exercise and cognitive behavioral modalities, respectively) might reduce general fatigue or physical fatigue in women with fibromyalgia. Second, as the association with health outcomes seems to be particularly strong for positive affect [30,34,36], cognitive behavioral therapy increasing positive affect might be especially helpful in reducing levels of all dimensions of fatigue in fibromyalgia. Finally, the existence of fibromyalgia subgroups in terms of combination of (high or low) levels of overall physical fitness and positive affect suggests that "one size fits all" seems to be an inappropriate approach in fibromyalgia. For instance, in women with fibromyalgia with low overall physical fitness, monotherapy (i.e., physical exercise) or multicomponent therapy (i.e., to complement physical exercise with cognitive behavior modalities) might be advisable for those with women with high and low levels of positive affect, respectively. Given our cross-sectional design, future clinical-experimental research is required to support these potential implications.

Limitations and Strengths of the Study

This study has a number of limitations; first, the cross-sectional design of this study precludes inferences on causality. Second, the participants were recruited mostly via local fibromyalgia associations. Third, cultural differences in the experience of having fibromyalgia are plausible. Women with fibromyalgia from southern Spain might be more severely affected than their peers in other countries such as, for instance, the Netherlands [82] or the United States [83]. Fourth, the study included only adult (aged 18–65 years) women. These limitations question the generalizability of our findings to other populations with fibromyalgia. To confirm or refute our findings, future studies with independent samples would be of interest. The large sample size, on the other hand, is a strength of the present study. Additionally, the research team corroborated participants' fibromyalgia diagnoses. Taking into consideration the discordance between self-reported and performed measures among women with fibromyalgia [52,84,85], physical fitness was measured by a battery of performance-based tests, which is reliable and feasible in fibromyalgia [51]. Furthermore, we assessed several dimensions of fatigue, which provides a more comprehensive approach than traditional unidimensional measures of fatigue [80,86].

Conclusions

We found independent associations of overall physical fitness, positive affect, and negative affect with diverse dimensions of fatigue, with positive affect consistently showing the strongest association with all dimensions of fatigue. Additionally, women with fibromyalgia with a combination of high levels of both overall physical fitness and positive affect experienced the lowest general fatigue and physical fatigue. Overall, the findings indicate that the combination of high levels of both overall physical fitness and positive affect might be a buffer against fatigue. This suggestion requires corroboration in clinical–experimental research.

Acknowledgments

The authors gratefully acknowledge all participants for their collaboration and enthusiasm. We would like to thank the collaborators in the al-Ándalus project and all the members of the Physical Activity for Health Promotion (PA-HELP; CTS-1018) research group. We are grateful to Ms. Carmen Sainz-Quinn and Dr. Joseph McVeigh (University College Cork, Cork, Ireland) for assistance with the English language.

Supplementary Data

Supplementary data are available at *Pain Medicine* online.

References

1. Queiroz LP. Worldwide epidemiology of fibromyalgia. Curr Pain Headache Rep. 2013;17(8):356.
2. Estévez-López F, Aparicio VA, Ruiz JR, et al. The TT genotype of the rs6860 polymorphism of the charged multivesicular body protein 1A gene is associated with susceptibility to fibromyalgia in southern Spanish women. Rheumatol Int 2018;38(3):531–3.
3. Estévez-López F, Camiletti-Moirón D, Aparicio VA, et al. Identification of candidate genes associated with fibromyalgia susceptibility in southern Spanish women: The al-Ándalus Project. J Transl Med 2018;16(1):43.
4. Mork PJ, Vasseljen O, Nilsen TIL. Association between physical exercise, body mass index, and risk of fibromyalgia: Longitudinal data from the Norwegian Nord-Trøndelag Health Study. Arthritis Care Res (Hoboken) 2010;62(5):611–7.
5. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33(2):160–72.
6. Overman CL, Kool MB, Da Silva JA, Geenen R. The prevalence of severe fatigue in rheumatic diseases: An international study. Clin Rheumatol 2016;35 (2):409–15.
7. Bennett RM, Russell J, Cappelleri JC, et al. Identification of symptom and functional domains that fibromyalgia patients would like to see improved: A cluster analysis. BMC Musculoskelet Disord 2010; 11(1):134.
8. Shillam CR, Dupree Jones K, Miller L. Fibromyalgia symptoms, physical function, and comorbidity in middle-aged and older adults. Nurs Res 2011;60 (5):309–17.
9. Sallinen M, Kukkurainen ML, Peltokallio L, Mikkelsson M. "I'm tired of being tired"—fatigue as experienced by women with fibromyalgia. Adv Physiother 2011;13(1):11–7.
10. Humphrey L, Arbuckle R, Mease P, et al. Fatigue in fibromyalgia: A conceptual model informed by patient interviews. BMC Musculoskelet Disord 2010;11 (1):216.
11. Wolfe F, Clauw DJ, Fitzcharles M-A, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res (Hoboken) 2010;62(5):600–10.
12. Vincent A, Benzo RP, Whipple MO, et al. Beyond pain in fibromyalgia: Insights into the symptom of fatigue. Arthritis Res Ther 2013;15(6):221.
13. Russell D, Álvarez Gallardo IC, Wilson I, et al. "Exercise to me is a scary word": Perceptions of fatigue, sleep dysfunction, and exercise in people with fibromyalgia syndrome—a focus group study. Rheumatol Int 2018;38(3):507–15.

14. Aparicio VA, Segura-Jiménez V, Álvarez-Gallardo IC, et al. Fitness testing in the fibromyalgia diagnosis: The al-Ándalus Project. Med Sci Sports Exerc 2015; 47(3):451–9.
15. Dailey DL, Frey Law LA, Vance CGT, et al. Perceived function and physical performance are associated with pain and fatigue in women with fibromyalgia. Arthritis Res Ther 2015;18:68.
16. Bartley EJ, Robinson ME, Staud R. Pain and fatigue variability patterns distinguish subgroups of fibromyalgia patients. J Pain 2018;19(4):372–81.
17. Dupond J-L. Fatigue in patients with rheumatic diseases. Joint Bone Spine 2011;78(2):156–60.
18. Castro-Piñero J, Aparicio VA, Estévez-López F, et al. The potential of established fitness cut-off points for monitoring women with fibromyalgia: The al-Ándalus Project. Int J Sports Med 2017;38(5):359–69.
19. Soriano-Maldonado A, Estévez-López F, Segura-Jiménez V, et al. Association of physical fitness with depression in women with fibromyalgia. Pain Med 2016;17(8):1542–52.
20. Soriano-Maldonado A, Artero EG, Segura-Jiménez V, et al. Association of physical fitness and fatness with cognitive function in women with fibromyalgia. J Sports Sci 2016;34(18):1731–9.
21. Valkeinen H, Häkkinen A, Alen M, et al. Physical fitness in postmenopausal women with fibromyalgia. Int J Sports Med 2008;29(5):408–13.
22. Aparicio VA, Ortega FB, Heredia JM, et al. Handgrip strength test as a complementary tool in the assessment of fibromyalgia severity in women. Arch Phys Med Rehabil 2011;92(1):83–8.
23. Ericsson A, Mannerkorpi K. How to manage fatigue in fibromyalgia: Nonpharmacological options. Pain Manag 2016;6(4):331–8.
24. Reis RS, Salvo D, Ogilvie D, et al. Scaling up physical activity interventions worldwide: Stepping up to larger and smarter approaches to get people moving. Lancet 2016;388(10051):1337–48.
25. Haskell WL, Lee I-M, Pate RR, et al. Physical activity and public health: Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation 2007;116(9):1081–93.
26. Segura-Jiménez V, Soriano-Maldonado A, Estévez-López F, et al. Independent and joint associations of physical activity and fitness with fibromyalgia symptoms and severity: The al-Andalus Project. J Sports Sci 2017;35(15):1565–74.
27. de Ridder D, Geenen R, Kuijer R, van Middendorp H. Psychological adjustment to chronic disease. Lancet 2008;372(9634):246–55.
28. Turk DC, Okifuji A. Psychological factors in chronic pain: Evolution and revolution. J Consult Clin Psychol 2002;70(3):678–90.
29. van Middendorp H, Evers AWM. The role of psychological factors in inflammatory rheumatic diseases: From burden to tailored treatment. Best Pract Res Clin Rheumatol 2016;30(5):932–45.
30. Sturgeon JA, Zautra AJ. Resilience: A new paradigm for adaptation to chronic pain. Curr Pain Headache Rep 2010;14(2):105–12.
31. van Middendorp H, Lumley MA, Jacobs JW, et al. Emotions and emotional approach and avoidance strategies in fibromyalgia. J Psychosom Res 2008;64 (2):159–67.
32. Diener E, Suh EM, Lucas RE, Smith HL. Subjective well-being: Three decades of progress. Psychol Bull 1999;125(2):276–302.
33. Diener E, Lucas RE, Scollon CN. Beyond the hedonic treadmill: Revising the adaptation theory of well-being. Am Psychol 2006;61(4):305–14.
34. Pressman SD, Cohen S. Does positive affect influence health? Psychol Bull 2005;131(6):925–71.
35. Sturgeon JA, Zautra AJ, Arewasikporn A. A multilevel structural equation modeling analysis of vulnerabilities and resilience resources influencing affective adaptation to chronic pain. Pain 2014;155(2):292–8.
36. Zautra AJ, Johnson LM, Davis MC. Positive affect as a source of resilience for women in chronic pain. J Consult Clin Psychol 2005;73(2):212–20.
37. Estévez-López F, Gray CM, Segura-Jiménez V, Soriano-Maldonado A, Álvarez-Gallardo IC, Arrayás-Grajera MJ, et al. Independent and combined association of overall physical fitness and subjective well-being with fibromyalgia severity: The al-Ándalus Project. Qual Life Res 2015;24(8):1865–73.
38. Velvin G, Bathen T, Rand-Hendriksen S, Geirdal AØ. Satisfaction with life in adults with Marfan syndrome (MFS): Associations with health-related consequences of MFS, pain, fatigue, and demographic factors. Qual Life Res 2016;25(7):1779–90.
39. Moreno PI, Moskowitz AL, Ganz PA, Bower JE. Positive affect and inflammatory activity in breast cancer survivors. Psychosom Med 2016;78 (5):532–41.
40. Zautra AJ, Fasman R, Parish BP, Davis MC. Daily fatigue in women with osteoarthritis, rheumatoid arthritis, and fibromyalgia. Pain 2007;128(1):128–35.
41. Da Silva JAP, Geenen R, Jacobs JWG. Chronic widespread pain and increased mortality: Biopsychosocial interconnections. Ann Rheum Dis 2018;77(6):790–2.
42. Geenen R, Overman CL, Christensen R, et al. EULAR recommendations for the health professional's approach to pain management in inflammatory arthritis and osteoarthritis. Ann Rheum Dis 2018;77 (6):797–807.
43. Sturgeon JA, Zautra AJ. Psychological resilience, pain catastrophizing, and positive emotions: Perspectives on comprehensive modeling of individual pain adaptation. Curr Pain Headache Rep 2013;17(3):317.
44. Estévez-López F, Segura-Jiménez V, Álvarez-Gallardo IC, et al. Adaptation profiles comprising objective and subjective measures in fibromyalgia: The

al-Ándalus Project. Rheumatology (Oxford) 2017;56 (11):2015–24.
45. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis 2017;76(2):318–28.
46. Segura-Jiménez V, Álvarez-Gallardo IC, Carbonell-Baeza A, et al. Fibromyalgia has a larger impact on physical health than on psychological health, yet both are markedly affected: The al-Ándalus Project. Semin Arthritis Rheum 2015;44(5):563–70.
47. Blesa R, Pujol M, Aguilar M, et al. Clinical validity of the "mini-mental state" for Spanish speaking communities. Neuropsychologia 2001;39(11):1150–7.
48. Williams DA, Arnold LM. Measures of fibromyalgia: Fibromyalgia Impact Questionnaire (FIQ), Brief Pain Inventory (BPI), Multidimensional Fatigue Inventory (MFI-20), Medical Outcomes Study (MOS) Sleep Scale, and Multiple Ability Self-Report Questionnaire (MASQ). Arthritis Care Res (Hoboken) 2011;63 (S11):S86–97.
49. Rikli RE, Jones CJ. Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years. Gerontologist 2013;53(2):255–67.
50. Aparicio VA, Carbonell-Baeza A, Ruiz JR, et al. Fitness testing as a discriminative tool for the diagnosis and monitoring of fibromyalgia. Scand J Med Sci Sports 2013;23(4):415–23.
51. Carbonell-Baeza A, Álvarez-Gallardo IC, Segura-Jiménez V, et al. Reliability and feasibility of physical fitness tests in female fibromyalgia patients. Int J Sports Med 2015;36(2):157–62.
52. Estévez-López F, Álvarez-Gallardo IC, Segura-Jiménez V, et al. The discordance between subjectively and objectively measured physical function in women with fibromyalgia: Association with catastrophizing and self-efficacy cognitions. The al-Ándalus Project. Disabil Rehabil 2018;40(3):329–37.
53. Álvarez-Gallardo IC, Carbonell-Baeza A, Segura-Jiménez V, et al. Physical fitness reference standards in fibromyalgia: The al-Andalus Project. Scand J Med Sci Sports 2017;27(11):1477–88.
54. Sandin B, Chorort P, Lostao L, et al. Escala PANAS de afecto positivo y negativo: Validación factorial y convergencia transcultural. Psicothema 1999;11 (1):37–51.
55. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: The PANAS scales. J Pers Soc Psychol 1988;54 (6):1063–70.
56. Estévez-López F, Pulido-Martos M, Armitage CJ, et al. Factor structure of the Positive and Negative Affect Schedule (PANAS) in adult women with fibromyalgia from southern Spain: The al-Ándalus Project. PeerJ 2016;4(3):e1822.
57. Munguía-Izquierdo D, Segura-Jiménez V, Camiletti-Moirón D, et al. Multidimensional Fatigue Inventory: Spanish adaptation and psychometric properties for fibromyalgia patients. The al-Andalus Study. Clin Exp Rheumatol 2015;30(6 Suppl 74):94–102.
58. Smets EM, Garssen B, Bonke B, De Haes JC. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res 1995;39(3):315–25.
59. Segura-Jiménez V, Borges-Cosic M, Soriano-Maldonado A, et al. Association of sedentary time and physical activity with pain, fatigue, and impact of fibromyalgia: The al-Ándalus Study. Scand J Med Sci Sports 2017;27(1):83–92.
60. Segura-Jiménez V, Castro-Piñero J, Soriano-Maldonado A, et al. The association of total and central body fat with pain, fatigue and the impact of fibromyalgia in women; role of physical fitness. Eur J Pain 2016;20(5):811–21.
61. Aparicio VA, Ortega FB, Carbonell-Baeza A, et al. Relationship of weight status with mental and physical health in female fibromyalgia patients. Obes Facts 2011;4(6):443–8.
62. Aparicio VA, Segura-Jiménez V, Álvarez-Gallardo IC, et al. Are there differences in quality of life, symptomatology and functional capacity among different obesity classes in women with fibromyalgia? The al-Ándalus Project. Rheumatol Int 2014;34(6):811.
63. Ortega FB, Sui X, Lavie CJ, Blair SN. Body mass index, the most widely used but also widely criticized index: Would a criterion standard measure of total body fat be a better predictor of cardiovascular disease mortality? Mayo Clin Proc 2016;91 (4):443–55.
64. Aiken L, West S. Multiple Regression: Testing and Interpreting Interactions. Newbury Park, CA: SAGE; 1991.
65. Kop WJ, Lyden A, Berlin AA, et al. Ambulatory monitoring of physical activity and symptoms in fibromyalgia and chronic fatigue syndrome. Arthritis Rheum 2005;52(1):296–303.
66. Ericsson A, Palstam A, Larsson A, et al. Resistance exercise improves physical fatigue in women with fibromyalgia: A randomized controlled trial. Arthritis Res Ther 2016;18.
67. Busch AJ, Webber SC, Richards RS, et al. Resistance exercise training for fibromyalgia. Cochrane Database Syst Rev 2013;12(12):CD010884.
68. Soriano-Maldonado A, Ruiz JR, Aparicio VA, et al. Association of physical fitness with pain in women with fibromyalgia: The al-Ándalus Project. Arthritis Care Res 2015;67(11):1561–70.
69. Zautra AJ, Fasman R, Reich JW, et al. Fibromyalgia: Evidence for deficits in positive affect regulation. Psychosom Med 2005;67(1):147–55.
70. Watson D, Clark LA. On traits and temperament: General and specific factors of emotional experience and their relation to the five-factor model. J Pers 1992;60(2):441–76.

71. Howell RT, Kern ML, Lyubomirsky S. Health benefits: Meta-analytically determining the impact of well-being on objective health outcomes. Health Psychol Rev 2007;1(1):83–136.
72. Gable PA, Harmon-Jones E. Approach-motivated positive affect reduces breadth of attention. Psychol Sci 2008;19(5):476–82.
73. Domachowska I, Heitmann C, Deutsch R, et al. Approach-motivated positive affect reduces breadth of attention: Registered replication report of Gable and Harmon-Jones (2008). J Exp Soc Psychol 2016; 67:50–6.
74. Cameron DS, Bertenshaw EJ, Sheeran P. Positive affect and physical activity: Testing effects on goal setting, activation, prioritisation, and attainment. Psychol Health 2018;33(2):258–74.
75. Peterson JC. A randomized controlled trial of positive-affect induction to promote physical activity after percutaneous coronary intervention. Arch Intern Med 2012;172(4):329–36.
76. Aggio D, Wallace K, Boreham N, et al. Objectively measured daily physical activity and postural changes as related to positive and negative affect using ambulatory monitoring assessments. Psychosom Med 2017;79(7):792–7.
77. Kim J, Lee S, Chun S, Han A, Heo J. The effects of leisure-time physical activity for optimism, life satisfaction, psychological well-being, and positive affect among older adults with loneliness. Ann Leis Res 2017;20(4):406–15.
78. Wiese CW, Kuykendall L, Tay L. Get active? A meta-analysis of leisure-time physical activity and subjective well-being. J Posit Psychol 2018;13(1):57–66.
79. Fredrickson BL, Joiner T. Positive emotions trigger upward spirals toward emotional well-being. Psychol Sci 2002;13(2):172–5.
80. Ericsson A, Mannerkorpi K. Assessment of fatigue in patients with fibromyalgia and chronic widespread pain. Reliability and validity of the Swedish version of the MFI-20. Disabil Rehabil 2007;29 (22):1665–70.
81. Wilson HD, Robinson JP, Turk DC. Toward the identification of symptom patterns in people with fibromyalgia. Arthritis Rheum 2009;61(4):527–34.
82. Ruiz-Montero PJ, Van Wilgen CP, Segura-Jiménez V, Carbonell-Baeza A, Delgado-Fernández M. Illness perception and fibromyalgia impact on female patients from Spain and the Netherlands: Do cultural differences exist? Rheumatol Int 2015;35 (12):1985–93.
83. Toussaint LL, Vincent A, McAllister SJ, Oh TH, Hassett AL. A comparison of fibromyalgia symptoms in patients with healthy versus depressive, low and reactive affect balance styles. Scand J Pain 2014;5 (3):161–6.
84. Bandak E, Amris K, Bliddal H, Danneskiold-Samsøe B, Henriksen M. Muscle fatigue in fibromyalgia is in the brain, not in the muscles: A case-control study of perceived versus objective muscle fatigue. Ann Rheum Dis 2013;72(6):963–6.
85. Walitt B, Čeko M, Khatiwada M, et al. Characterizing "fibrofog": Subjective appraisal, objective performance, and task-related brain activity during a working memory task. NeuroImage Clin 2016;11:173–80.
86. Choy EH, Arnold LM, Clauw DJ, et al. Content and criterion validity of the preliminary core dataset for clinical trials in fibromyalgia syndrome. J Rheumatol 2009;36(10):2330–4.