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ORIGINAL RESEARCH

Association of Patterns of Moderate-to-Vigorous Physical Activity Bouts With Pain, Physical Fatigue, and Disease Severity in Women With Fibromyalgia: the al-Ándalus Project

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Abstract

Objectives: To examine the associations of non-bouted moderate-to-vigorous physical activity (MVPA) and patterns of MVPA in bouts ≥10 minutes with pain, physical fatigue, and disease severity in women with fibromyalgia, and test whether these associations are independent of sedentary time (ST) and physical fitness (PF).

Design: Cross-sectional study carried out from November 2011 to January 2013.

Setting: University facilities and fibromyalgia associations.

Participants: Women with fibromyalgia (N=439; 51.3±7.6y).

Interventions: Not applicable.

Main Outcome Measures: ST and MVPA were measured with triaxial accelerometry, and PF with the Senior Fitness test battery. We assessed pain, physical fatigue and disease severity with diverse questionnaires.

Results: Total time in non-bouted MVPA only was independently associated with lower physical fatigue (B=-0.012; P=.010) and disease severity (B=-0.068; P=.007) in women with fibromyalgia, regardless of PF but not of ST. Patterns of bouted MVPA were overall associated with symptoms independently of ST or PF. The strongest regressor was the maximum time in MVPA bout (min/bout), which was consistently and independently associated with pain, physical fatigue and disease severity after controlling for ST or PF (all, P≤.002). Patients meeting bouted physical activity guidelines displayed lower disease severity than those not meeting guidelines (bouted or non-bouted) and those meeting non-bouted physical activity guidelines (all, P≤.008).

Conclusions: Patterns of MVPA performed in bouts ≥10 minutes were overall consistently and independently associated with core symptoms (pain and fatigue) in fibromyalgia and the overall disease severity, regardless of ST or PF. The results suggest that longer bouts of continuous MVPA are associated with better symptoms profile in this population, which needs to be corroborated in longitudinal research.

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Fibromyalgia is a complex multi-dimensional disorder characterized by several symptoms, such as pain, fatigue, and stiffness.[1-4] Fear-avoidance beliefs lead patients with fibromyalgia to reduce their physical activity (PA) levels.[5,6] However, this reduction might worsen their affliction.[7,8] In fact, there is an association between PA and pain modulation in women with fibromyalgia, so that patients more physically active display greater ability to modulate their pain than physically inactive patients.[7] A recent study has also determined that an increase of steps per day promotes improved physical function and pain in patients with fibromyalgia.[9]

We have recently shown that higher time spent in light PA and vigorous PA is associated with lower core symptoms such as pain and physical-related fatigue in women with fibromyalgia.[10] However, the total time in moderate-to-vigorous physical activity (MVPA) was not associated with fibromyalgia symptoms when light or vigorous PA were accounted for.[10] According to the current PA guidelines, adults should engage in 150 minutes per week of MVPA in bouts of at least 10 minutes.[11] However, it is unclear whether MVPA accrued in bouts or not, is more beneficial for individuals' health. Determining if MVPA accrued in bouts $\geq$10 minutes (bouted MVPA) offers additional symptoms' improvement has important clinical relevance with respect to the promotion of PA in women with fibromyalgia.

Therefore, the purpose of the current study were (1) to check the association of objectively measured non-bouted MVPA and patterns of bouted MVPA with pain, physical fatigue, and disease severity in women with fibromyalgia; (2) to elucidate whether meeting the current PA guidelines for adults (bouted vs non-bouted MVPA) was associated with fewer symptoms in women with fibromyalgia. Given that sedentary time (ST) and physical fitness components seem to be consistently associated with fibromyalgia's symptoms,[7,12-14] we also tested whether the aforementioned associations were independent of ST and physical fitness.

Methods

Participants

We calculated the sample size needed (n=300) to obtain a representative sample of fibromyalgia patients from southern Spain (Andalusia).[2] A sex and province proportional recruitment of participants was carried out as described elsewhere.[2] We recruited fibromyalgia patients via associations, Internet advertisement, flyers, and e-mail, obtaining written informed consent from all participants interested in participating (n=646). From this sample, 595 participants agreed to wear an accelerometer. Patients were required to be previously diagnosed by a rheumatologist and meet the 1990 American College of Rheumatology (ACR) fibromyalgia criteria or the modified 2010 ACR preliminary diagnostic criteria.[4] Furthermore, patients were excluded if they had an acute illness, terminal illness, or severe cognitive impairment (Mini Mental State Examination [MMSE] score <10), were over 65 years old, or were men. The study assessments were carried out between November 2011 and January 2013. The Ethics Committee of the Hospital Virgen de las Nieves (Granada, Spain) reviewed and approved the study.

List of abbreviations:

ACR	**American College of Rheumatology**
FIQR	**Revised Fibromyalgia Impact Questionnaire**
MMSE	**Mini Mental State Examination**
MVPA	**moderate-to-vigorous physical activity**
PA	**physical activity**
PF	**global physical fitness**
ST	**sedentary time**

Procedures

In the first appointment, the MMSE was administered via interview, tender points were assessed according to the 1990 ACR criteria, and anthropometry and body composition were measured. Two days later (second appointment), participants received the accelerometer and the sleep diary and several questionnaires to be filled out. Furthermore, physical fitness was assessed. Nine days later (third appointment), participants returned the accelerometer and the sleep diary to the research team.

Measurements

Cognitive function

The MMSE[15] assesses 5 areas of cognitive functioning and was used for exclusion criteria purposes only.

Anthropometry and body composition

Weight (kg) and total body fat percentage were measured using a portable 8-polar tactile-electrode impedance analyzer (InBody R20).[a] We asked participants not to have a shower, not to practice intense PA, and not to ingest large amounts of fluid or food in the 2 hours before the measurement. Patients removed clothing (except underwear) and metal objects during the assessment. The validity and reliability of this instrument has been reported elsewhere.[16,17]

Medication for pain

We recorded consumption of painkillers (analgesics) in the last week with a binary variable (yes/no).

Time since diagnosis

Patients were required to include the time passed since their fibromyalgia diagnosis.

1990 ACR fibromyalgia diagnostic criteria

A trained researcher used a standard pressure algometer (FPK 20)[b] to assess tender points.[18] The mean pressure of 2 alternative measurements at each tender point was used. Tender point was positive if the patient reported pain at pressure $\leq$4 kg/cm^2 and the total count of positive tender points was recorded for each participant. The sum of the minimum pain-pressure values obtained from each tender point (pressure pain threshold) was also calculated.

Modified 2010 ACR fibromyalgia preliminary diagnostic criteria

These criteria are based on a self-reported questionnaire.[1,4] We obtained 2 scores from 2 different scales: (1) the Widespread Pain Index, which asked participants to grade whether they had experienced pain or tenderness in the previous week on 19 body areas; (2) the Symptom Severity scale, which asked participants to indicate the severity of fatigue, trouble thinking or remembering, and waking up tired (unrefreshed) over the previous week, and whether they had pain or cramps in the lower abdomen, depression, or headache during the previous 6 months. Patients were

diagnosed if they presented Widespread Pain Index ≥7 and Symptom Severity ≥5, or Widespread Pain Index 3-6 and Symptom Severity scale score ≥9. The Spanish version of the modified 2010 ACR fibromyalgia preliminary diagnostic criteria has shown high sensitivity and specificity as a diagnostic tool for fibromyalgia.[4]

Clinical pain

We used the 36-item Short-Form health survey multi-item pain subscale[19] to assess the frequency of feelings of pain experienced over the last month (minimum score of 0 and a maximum scoring of 100, where higher scores indicate lower pain). This subscale has been cited in more than 2500 studies.[20]

Physical fatigue

We used a subscale of the Spanish version of the Multidimensional Fatigue Inventory to assess physical fatigue.[21,22] This subscale includes 4 items with 5-point Likert scales. Scores on this subscale range from 4 to 20, with higher scores indicating greater fatigue.

The severity of fibromyalgia

The Revised Fibromyalgia Impact Questionnaire (FIQR) is a self-administered questionnaire, comprising 21 individual questions with a rating scale of 0 to 10.[23] The FIQR total score ranges from 0 to 100, with a higher score indicating greater effect of the condition on the person's life.

ST and MVPA

Activity counts were measured at a rate of 30 Hz and stored at an epoch length of 60 seconds[24,25] using a triaxial accelerometer (GT3X+).[c] Participants wore the device on the hip near to the center of gravity, underneath clothing and secured with an elastic belt. Accelerometer-wearing time was calculated by subtracting the sleeping time (through a diary where patients reported the time they went to bed and the time they woke up) from each day. Bouts of 90 continuous minutes (30min small window length and 2min skip tolerance) of 0 counts were considered as non-wear periods and excluded from the analysis.[26] Participants wore the accelerometer up to 9 days, however, the day they received the accelerometers and the day that they returned the devices were excluded from the analyses. A total of 7 continuous days (a minimum of 10 valid hours per day was required) was necessary for being included in the study analysis. ST and MVPA (min/d) were calculated based upon recommended vector magnitude cut point[24,25]: 0-199 and ≥2690 cpm, respectively. A bout of MVPA was defined as spending ≥10 continuous minutes in MVPA (up to 2min below the cut point allowance). Patterns of MVPA included in the present study were: time in bouted MVPA (min/wk), number of MVPA bouts (no./wk), average time per MVPA bout (min/bout), and maximum time in MVPA bout (the longest bout of MVPA, min/bout). Meeting bouted PA guidelines required engaging in 150 minutes per week of MVPA in bouts ≥10 minutes; whereas non-bouted PA guidelines did not need accumulate MVPA in bouts ≥10 minutes. We used the software Actilife v.6.11.7 desktop for data download, reduction, cleaning, and analysis purposes.[c]

Physical fitness

We used the chair sit and reach (lower-body flexibility), the back scratch (upper-body flexibility), the 30-second chair stand (lower-body strength), the arm curl (upper-body strength), the 8-foot up-and-go (motor agility), and the 6-minute walk (cardiorespiratory fitness) tests to measure physical fitness components.[27,28] The description of these tests is in supplemental appendix S1 (available online only at http://www.archives-pmr.org/).

Given that the diverse physical fitness components are associated with pain and fibromyalgia severity,[12-14] we used a composite of these physical fitness tests as a measure of global physical fitness (PF). To create this variable, we calculated a normalized index (z score) of each physical fitness test. The z score is calculated as (value − mean) / SD. The z-score values of the 8-foot up-and-go test were inverted, since higher score indicates worse performance. Finally, we calculated the weighted average of all these z scores together.

Statistical analysis

We used descriptive statistics, mean ± SD for continuous variables and n (%) for categorical data, to describe the clinical characteristics of the group. The differences in pain, physical fatigue, and disease severity across groups meeting or not meeting the current PA guidelines for adults (bouted and non-bouted MVPA) were compared using 1-way analysis of covariance with accelerometer-wearing time, age, total body fat percentage, and medication for pain as covariates. Post hoc analysis with Bonferroni correction assessed the differences across groups.

To explore the association of non-bouted MVPA and patterns of bouted MVPA with pain, physical fatigue and disease severity in women with fibromyalgia, we performed linear regression analysis. Non-bouted MVPA and patterns of bouted MVPA were introduced in separate models as independent variables. Pain, physical fatigue and disease severity were introduced individually as dependent variables in separate models. Different models were built. In model 1, accelerometer-wear time, age, total body fat percentage, and medication for pain were used as covariates. To test whether these associations were independent of ST, in model 2, we included all the covariates of model 1 together with ST. Similarly, to test whether the association of patterns of MVPA with the outcomes was independent of PF, in model 3, we included all the covariates of model 1 together with PF. The presence of multicollinearity was tested. Given that sociodemographic characteristics did not substantially modify the model parameters; they were not included as covariates.

We used IBM SPSS Statistics for Windows, version 22.0.[d] The statistical significance was set at $P<.05$.

Results

Thirty-seven women with fibromyalgia were not previously diagnosed, 16 did not meet the 1990 or modified 2010 ACR criteria, 1 had severe cognitive impairment, and 13 were older than 65 years old. Accelerometer data from 3 patients were lost due to malfunction when downloading data and 19 patients did not meet the accelerometer criteria. Patients with incomplete data (n=44) and men (n=23) were excluded from the analyses. The final sample comprised 439 women with fibromyalgia. Clinical and sociodemographic characteristics of the study participants are presented in table 1.

Differences in pain, physical fatigue, and disease severity across fibromyalgia groups not meeting PA guidelines, and meeting non-bouted and bouted PA guidelines is presented in figure 1. Post-hoc analyses showed that the patients meeting bouted PA guidelines displayed lower pain, physical fatigue, and disease severity than patients not meeting guidelines (bouted or non-bouted) (mean difference=8.3, -1.8, and -12.5, respectively;

Table 1 Clinical and sociodemographic characteristics of women with fibromyalgia, N = 439

Variable	Mean ± SD
Age	51.3±7.6
Weight (kg)	71.4±13.9
Height (cm)	158.3±5.9
Body mass index (kg/m^2)	28.5±5.4
Body fat (%)	40.1±7.7
Tender points (11-18)	15.2±4.6
Pressure pain threshold (kg/cm^2) (18-144)	49.9±22.0
Pain (0-100)	21.9±14.8
Physical fatigue (4-20)	18.0±2.6
Disease severity (0-100)	63.9±16.7
Sedentary time (min/d)	458.8±104.2
Total non-bouted MVPA (min/d)	45.2±30.1
Total bouted MVPA (min/wk)	87.4±112.8
No. of MVPA bouts (no./wk)	5.4±6.5
Average time per MVPA bout (min/bout)	12.3±8.5
Max time in MVPA bout (min/bout)	19.2±17.2
Min time in MVPA bout (min/bout)	8.8±5.2
	n (%)
Marital status	
Married	330 (75.2)
Not married	109 (24.8)
Educational level	
Non-university	378 (86.1)
University	61 (13.9)
Occupational status	
Working	123 (28.0)
Housekeeper	139 (31.7)
Not working	177 (40.3)
Time since clinical diagnosis	
<5 years	176 (40.5)
≥5 years	259 (59.5)
Comorbidities (yes)	
Asthma	57 (13.6)
Chronic cervical backache	335 (80.1)
Osteoporosis	88 (21.1)
Anemia	104 (24.9)

all $P<.001$) and patients meeting non-bouted PA guidelines (mean difference = 4.6, -1.1, and -6.6, respectively; all $P \leq .026$). Furthermore, patients meeting non-bouted PA guidelines displayed lower disease severity than patients not meeting PA guidelines (mean difference = -5.8; $P = .008$).

The association of non-bouted MVPA and patterns of bouted MVPA with pain is shown in table 2. Higher time in non-bouted MVPA ($\beta = 0.116$; $P = .017$), bouted MVPA ($\beta = 0.127$; $P = .007$), and number of MVPA bouts ($\beta = 0.103$; $P = .024$) were associated with better pain profile in women with fibromyalgia, however, these associations were no longer significant when ST or PF were included as covariates. The higher average time per MVPA bout ($\beta = 0.135$; $P = .004$) and maximum time in MVPA bout ($\beta = 0.184$; $P < .001$) were associated with a better pain profile in women with fibromyalgia, and these associations were independent of ST and PF (all $P < .05$).

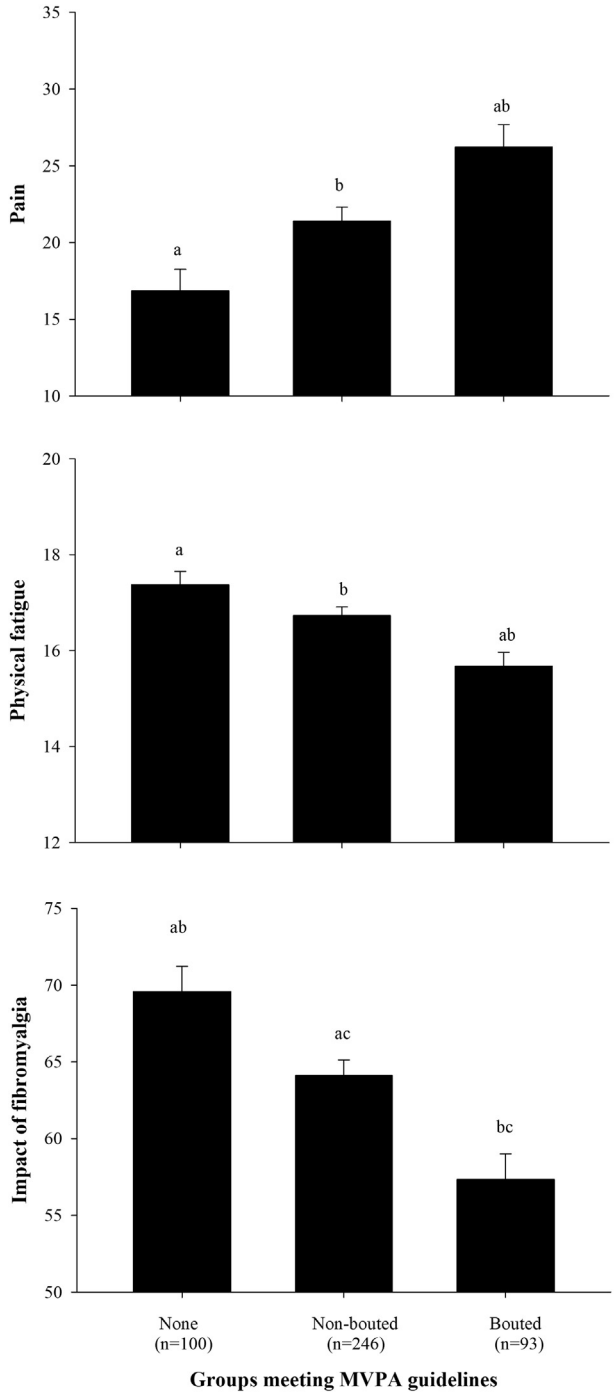

Fig 1 Association between the engagement in MVPA recommendations with or without accounting for a minimum of 10 min bouts with pain, physical fatigue and disease severity in female patients. None: <150 min/wk MVPA (either non-bouted or bouted); Non-bouted: meeting 150 min/wk non-bouted MVPA; Bouted: meeting 150 min/wk bouted MVPA. Bar (error bar) represents estimated mean and standard error after adjustment for age, total body fat percentage, medication for pain and accelerometer-wear time. One-way analysis of the covariance was used to test the group differences. Groups with the same superscript presented statistically significant differences after Bonferroni correction (all, $P < .05$).

Table 2 Association of non-bouted MVPA and patterns of MVPA bouts with pain in women with fibromyalgia, N = 439

Variable	B	(95% CI)	β	*P*
Time in non-bouted MVPA (min/d)				
Model 1	0.057	(0.010 to 0.103)	0.116	.017
Model 2	0.012	(-0.045 to 0.068)	0.024	.682
Model 3	0.036	(-0.010 to 0.081)	0.072	.127
Time in bouted MVPA (min/wk)				
Model 1	0.017	(0.005 to 0.029)	0.127	.007
Model 2	0.011	(-0.002 to 0.023)	0.080	.105
Model 3	0.014	(0.002 to 0.025)	0.103	.024
No. of MVPA bouts (no./wk)				
Model 1	0.245	(0.032 to 0.458)	0.107	.024
Model 2	0.127	(-0.097 to 0.352)	0.056	.266
Model 3	0.197	(-0.010 to 0.403)	0.086	.062
Average time per MVPA bout (min/bout)				
Model 1	0.235	(0.074 to 0.396)	0.135	.004
Model 2	0.173	(0.009 to 0.338)	0.099	.039
Model 3	0.158	(0.000 to 0.316)	0.091	.049
Max time in MVPA bout (min/bout)				
Model 1	0.158	(0.079 to 0.236)	0.184	<.001
Model 2	0.129	(0.048 to 0.209)	0.150	.002
Model 3	0.122	(0.045 to 0.199)	0.142	.002

NOTE. Model 1, analysis controlled for accelerometer-wear time, age, medication for pain and body fat percentage. Model 2, analysis controlled for model 1 + sedentary time. Model 3, analysis controlled for model 1 + physical fitness.
Abbreviation: CI, confidence interval.

The association of non-bouted MVPA and patterns of bouted MVPA with physical fatigue is shown in table 3. Higher time in non-bouted MVPA (β = -0.164; *P* < .001) and number of MVPA bouts (β = -0.137; *P* = .003) were associated with lower physical fatigue in women with fibromyalgia, however, these associations were no longer significant when ST was included as covariate. Higher time in MVPA bouts (β = -0.161, *P* < .001), average time per MVPA bout (β = -0.141; *P* < .002), and maximum time in MVPA bout (β = -0.194; *P* < .001) were associated with lower physical fatigue and these associations were independent of ST and PF (all, *P* < .05).

The association of non-bouted MVPA and patterns of bouted MVPA with disease severity in women with fibromyalgia is shown in table 4. Higher time in non-bouted MVPA (β = -0.180; *P* < .001) time in MVPA bouts (β = -0.169; *P* < .001) and number of MVPA bouts (β = -0.153; *P* = .001) were associated with lower disease severity, however, these associations were no longer significant when ST was included as covariate. The higher average time per MVPA bout (β = -0.167; *P* < .001) and maximum time in MVPA bout (β = -0.217; *P* < .001) were associated with lower severity of fibromyalgia and these associations were independent of ST and PF (all, *P* < .05). There was no evidence of multi-collinearity in any of the models mentioned above.

Discussion

In the current study, women with fibromyalgia meeting the bouted MVPA guidelines presented less pain, physical fatigue, and disease severity than patients meeting non-bouted MVPA guidelines. Furthermore, we found that the association of minute-by-minute basis MVPA with symptoms was not independent of ST in women with fibromyalgia. However, patterns of bouted MVPA were overall associated with lower pain, physical fatigue, and overall disease severity independently of ST or PF. Interestingly, the maximum time in bouts was the pattern that showed the strongest associations with symptoms, suggesting that MVPA should be performed in continuous bouts in this population.

According to the current PA guidelines for adults, MVPA should be accumulated in bouts of at least 10 minutes in order to count toward the recommended 150 minutes per week of MVPA required to meet these recommendations.[29] We showed that women with fibromyalgia who met current PA guidelines displayed lower pain, physical fatigue, and overall disease severity than those who engaged in ≥150 minutes per week of non-bouted MVPA and those with <150 minutes per week of (either bouted or non-bouted) MVPA. This supports the American College of Sports Medicine recommendation, which emphasizes that MVPA should be accumulated in bouts ≥10 minutes.[11] The observations of Fontaine et al[30] might be in line with our results, since they showed that accumulating 30 minutes of lifestyle PA throughout the day in short bouts produced clinically relevant changes in perceived physical function and pain in patients with fibromyalgia. However, they used the number of steps per day as a measure of PA, which cannot let us know the real intensity level and the total amount of PA (min/d) performed by patients.[30] In our previous pilot study, we did not find higher prevalence of meeting the non-bouted PA recommendations by patients grouped according to disease severity (total FIQ values <70 vs ≥70).[31] Differences in sample size, accelerometer model, and accelerometer criteria between studies might explain the discrepancies in the results obtained. It has been determined that 14% change in the FIQR total score might be considered clinically relevant,[32] thus, the differences observed in the FIQR total score, percentage difference = (group1 value − group2 value) / [(group1 value + group2 value) / 2)] × 100 = (69.7 − 57.3) / [(69.7 + 57.3) / 2)] × 100 = ∼19%, between women with fibromyalgia who met bouted PA guidelines and those who did not (bouted or non-bouted) in the

Table 3 Association of non-bouted MVPA and patterns of MVPA bouts with physical fatigue in women with fibromyalgia, N = 439

Variable	B	(95% CI)	β	*P*
Time in non-bouted MVPA (min/d)				
Model 1	-0.017	(-0.026 to -0.007)	-0.164	<.001
Model 2	-0.011	(-0.022 to 0.001)	-0.105	.063
Model 3	-0.012	(-0.021 to -0.003)	-0.117	.010
Time in bouted MVPA (min/wk)				
Model 1	-0.004	(-0.007 to -0.002)	-0.161	<.001
Model 2	-0.003	(-0.006 to -0.001)	-0.122	.011
Model 3	-0.004	(-0.006 to -0.001)	-0.135	.002
No. of MVPA bouts (no./wk)				
Model 1	-0.064	(-0.107 to -0.022)	-0.137	.003
Model 2	-0.044	(-0.089 to 0.001)	-0.093	.055
Model 3	-0.054	(-0.094 to -0.013)	-0.113	.010
Average time per MVPA bout (min/bout)				
Model 1	-0.051	(-0.083 to -0.018)	-0.141	.002
Model 2	-0.039	(-0.072 to -0.006)	-0.109	.020
Model 3	-0.033	(-0.065 to -0.002)	-0.093	.037
Max time in MVPA bout (min/bout)				
Model 1	-0.034	(-0.050 to -0.019)	-0.194	<.001
Model 2	-0.029	(-0.045 to -0.013)	-0.163	<.001
Model 3	-0.026	(-0.041 to -0.011)	-0.148	.001

NOTE. Model 1, analysis controlled for accelerometer-wear time, age, medication for pain and body fat percentage. Model 2, analysis controlled for model 1 + sedentary time. Model 3, analysis controlled for model 1 + physical fitness.
Abbreviation: CI, confidence interval.

current study merits highlighting. However, the differences in the FIQR total score between those meeting the non-bouted PA guidelines and those not meeting PA guidelines was ~9%. Interestingly, a 37% difference in pain perception between women with fibromyalgia who met bouted PA guidelines and those who did not (bouted or non-bouted) was observed, although this percentage was only 11% in the case of physical fatigue.

Previous studies investigating the effect of bouted and non-bouted MVPA in health have focused on the metabolic syndrome or cardiovascular disease risk factors. Clarke et al[33] argued that

Table 4 Association of non-bouted MVPA and patterns of MVPA bouts with disease severity in women with fibromyalgia, n = 368

Variable	B	(95% CI)	β	*P*
Time in non-bouted MVPA (min/d)				
Model 1	-0.101	(-0.153 to -0.048)	-0.180	<.001
Model 2	-0.022	(-0.085 to 0.040)	-0.040	.479
Model 3	-0.068	(-0.117 to -0.018)	-0.121	.007
Time in bouted MVPA (min/wk)				
Model 1	-0.025	(-0.039 to -0.012)	-0.169	<.001
Model 2	-0.014	(-0.028 to 0.000)	-0.094	.051
Model 3	-0.020	(-0.033 to -0.008)	-0.136	.002
No. of MVPA bouts (no./wk)				
Model 1	-0.399	(-0.639 to -0.160)	-0.153	.001
Model 2	-0.190	(-0.438 to 0.058)	-0.073	.133
Model 3	-0.324	(-0.547 to -0.100)	-0.124	.005
Average time per MVPA bout (min/bout)				
Model 1	-0.331	(-0.513 to -0.150)	-0.167	<.001
Model 2	-0.219	(-0.401 to -0.038)	-0.111	.018
Model 3	-0.211	(-0.383 to -0.040)	-0.107	.016
Max time in MVPA bout (min/bout)				
Model 1	-0.212	(-0.300 to -0.124)	-0.217	<.001
Model 2	-0.157	(-0.246 to -0.068)	-0.160	.001
Model 3	-0.156	(-0.239 to -0.072)	-0.159	<.001

NOTE. Model 1, analysis controlled for accelerometer-wear time, age, medication for pain and body fat percentage. Model 2, analysis controlled for model 1 + sedentary time. Model 3, analysis controlled for model 1 + physical fitness.
Abbreviation: CI, confidence interval.

total amount of MVPA accumulated throughout the week is important, whereas Tucker et al[34] concluded that it was unclear whether total MVPA or bouted MVPA was more beneficial for health. In the current study, we found that the patterns of bouted MVPA were generally associated with the severity of symptoms in women with fibromyalgia. In fact, the pattern that showed the greatest associations with pain, physical fatigue, and disease severity was the maximum time in MVPA bout (min/bout). This finding was particularly important since it suggests that greater bouted MVPA, rather than non-bouted MVPA, is overall associated with fewer fibromyalgia-related symptoms.

On the other hand, some studies have found that both the frequency of MVPA lasting longer than 10 minutes, but also the short bouts of MVPA (lower than 10 min) might have an important role in reducing the risk of metabolic syndrome.[35] This suggests that intensive bouts of PA, rather than the total amount of PA, seems to be inversely associated with metabolic syndrome.[33,35,36] Higher intensity short bouts is as beneficial to body mass index[37] and metabolic syndrome risk factors[38] as every minute in higher intensity long bouts. Alternatively, Strath et al[39] suggested that activity accumulated in bouts lasting $\geq$10 minutes appeared more predictive of lower levels of obesity markers and is potentially more effective for health promotion than non-bouted activity.[39] This lack of consensus reflects that there are insufficient data comparing the effects of short vs long bouts of PA on public health. The design of the present study did not allow testing whether shorter bouts of MVPA (sporadic) present similar associations with symptoms than longer bouts (10min) in women with fibromyalgia, so future studies are warranted.

The finding of the independent association of patterns of bouted MVPA with fibromyalgia symptoms, regardless of ST and PF, was interesting. This suggests that accumulating MVPA in bouts $\geq$10 minutes acts through a different pathway than those of ST and PF. In addition, when included in the model, ST and PF were generally associated with the outcomes (data not shown), which highlights the relevance of both ST and PF in this condition. Ellingson et al[7] showed that the central nervous system of women with fibromialgia, who were highly sedentary, regulated pain worse than patients who spent less time in sedentary behaviors[7]. Recently, we have also shown a consistent and independent association between objectively measured ST and core symptoms in women with fibromyalgia.[10] Similarly, higher flexibility, muscle strength, and cardiorespiratory fitness have been associated with pain, pain cognition, and the overall impact of fibromyalgia in female patients.[12-14]

Both sensory and affective pain networks have been related to PA behaviors.[7,40] However, the relationship between PA and central nervous system mechanisms of pain and overall symptoms in fibromyalgia is still unclear. Furthermore, it is still not clear what dose of PA is enough to affect pain modulatory mechanisms.[40] Our results seem to indicate that bouted MVPA might be associated with greater symptoms improvement in fibromyalgia. The complex integration of neural circuits makes difficult to ascertain this question. Due to the cross-sectional design of the present study, the mechanisms beyond our associations cannot be determined. However, we might hypothesize that bouted MVPA rather than non-bouted MVPA represents a continuous stimulus that leads to reduced affective responses to pain stimuli by reducing the distressing qualities of the stimulus, or to greater capacity to engage endogenous pain modulatory networks. Further research is warranted to ascertain the biological mechanisms behind these associations. Given that women with fibromyalgia are highly sedentary and not physically active,[41] their engagement in bouted MVPA seems unexpected. A wise intervention plan might address fear avoidance of PA with behavioral change programs.[42] At the same time, interventions aimed at increasing motivation to become less sedentary also seem plausible.[9] Furthermore, this behavior would likely result in increases in low-intensity PA behaviors, which is associated with key fibromyalgia symptoms.[7,30,40] Subsequently, engaging in non-bouted MVPA might be a prior step to undertake bouted MVPA as the ultimate goal, which must be taken into account in a rehabilitation setting. It is recommended searching for innovative strategies that may prevent relapse into inactivity in this population.

Study limitations

The cross-sectional design of the current study limits the determination of causal relationships. Women with fibromyalgia who are more physically active might display better symptom profile,[9] but also more symptoms might reduce participation in PA.[42] This vicious cycle has been previously described: symptoms may lead to inactivity, and inactivity leads to increased symptoms.[42] Patients were required to meet the 1990 ACR fibromyalgia criteria or the modified 2010 ACR preliminary diagnostic criteria;[4] which could have consequences for the heterogeneity of the study population and for the generalizability of the results. Nonetheless, analyses were repeated using the 1990 ACR fibromyalgia criteria as a diagnosis tool, and the results kept unchanged. Strength of the present study was the use of accelerometry to estimate PA, since self-reported questionnaires are discouraged in this population.[43,44] Nonetheless, accelerometry present limitations as difficulties capturing certain type of PA, such as cycling or weight-lifting. The accelerometer criteria for inclusion purpose was stricter than other previous studies, which provides a greater PA quality in the current study.[5,7,42] Furthermore, we adjusted for other healthy lifestyle factors, such as ST or PF. Finally, the relatively large sample size of women with fibromyalgia representative from southern Spain (Andalusia) was another strength.[2]

Conclusions

Interestingly, the association of non-bouted MVPA with symptoms was not independent of ST or PF in women with fibromyalgia. However, higher MVPA performed in bouts $\geq$10 minutes was independently associated with lower pain, physical fatigue, and overall disease severity in women with fibromyalgia. Our results show that longer bouts of continuous MVPA are associated with better symptoms profile in this population. Although causal relationship cannot be determined due to the study design, the results of the present study seem to support the current American College of Sports Medicine PA guidelines (at least 150min/wk of MVPA in bouts $\geq$10min) in women with fibromyalgia.

Suppliers

a. InBody R20; Biospace.
b. FPK 20; Wagner Instruments.
c. Actigraph LLC..
d. IBM SPSS Statistics for Windows, version 22.0; IBM.

Keywords

Chronic pain; Exercise; Fibromyalgia; Musculoskeletal diseases; Rehabilitation

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Supplemental Appendix S1
Description of physical fitness tests

The *chair sit and reach* test as measure of lower-body flexibility. The patients started in a sitting position with one leg extended, and slowly bended forward sliding the hands down the extended leg in an attempt to touch (or pass) the toes. The number of centimeters short of reaching the toe (negative score) or reaching beyond it (positive score) was recorded. The test was performed twice for each leg, and the average of the best score from each leg was used (28).

The *back scratch* test as measure of upper-body flexibility. It provides a measure of the overall shoulder range of motion, as the distance between (or overlap of) the middle fingers behind the back with a ruler. The participants performed the test twice, and the average of the best value from both hands was used (28).

The *30-s chair stand* as a measure of lower-body muscle strength. It measures the number of times an individual can rise to a full stand, starting from a seated position, with the back straight and feet flat on the floor within 30 seconds (28).

The *arm curl* test as a measure of upper-body muscle strength. It measures the number of times a hand weight (2.3 kg for women) can be curled through a full range of motion within 30 s. The test was performed once with each arm. The average number of repetitions was recorded (28).

The 8-foot up-and-go test as a measure of motor agility. It consists in standing up from a chair, walking 8 feet (2.44 m) to and around a cone, and returning to the chair in the shortest period of time. The best time from two trials was recorded (28).

The *6-min walk* test as a measure of cardiorespiratory fitness. This test measures the maximum distance (in meters) that the patient is able to walk in 6 min along a 45.7 m rectangular course (28).