

**Title:** Association of sedentary time and physical activity with pain, fatigue and impact of fibromyalgia: the al-Ándalus project.

**Running head:** Fibromyalgia, physical activity and symptoms.

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## **Abstract**

We examined the association of objectively measured sedentary time (ST) and physical activity (PA) levels with pain, fatigue and the impact of the disease in women with fibromyalgia. Four hundred and nineteen (mean age $\pm$ SD = 51.7 $\pm$ 7.6 years old) women with fibromyalgia participated. ST and PA levels (light, moderate and moderate-to-vigorous [MVPA]) were measured with triaxial accelerometry. We assessed experimental pain with algometry, and clinical pain, fatigue and impact of fibromyalgia with a number of questionnaires. The association of ST and light PA with most of the pain- and fatigue-related outcomes and impact of fibromyalgia (all,  $P\leq 0.019$ ) was independent of moderate and vigorous PA. Furthermore, the association of vigorous PA with general and physical fatigue was independent of ST, light and moderate PA (all,  $P<0.001$ ). In conclusion, lower levels of ST or higher levels of light PA are associated with lower pain, fatigue and the overall impact of the disease independent of moderate and vigorous PA in women with fibromyalgia. Interestingly, higher vigorous PA is independently associated with lower general and physical fatigue. These results are significant for future ST and PA intervention studies in this population.

**Keywords:** GT3X+; accelerometry; sedentary behaviour; physical activity intensity levels; symptomatology; fibromyalgia severity.

## INTRODUCTION

Fibromyalgia has been recently defined as a complex multi-dimensional disorder (Segura-Jiménez et al., 2015a; Wolfe et al., 2011) with pain as its main symptom (Segura-Jiménez et al., 2015a; Wolfe et al., 2011) and a large variety of other important physical and psychological non-pain symptoms (Segura-Jiménez et al., 2015a, 2014b). Physical exercise promotes improvements on this vast symptomatology in fibromyalgia patients (Busch et al., 2011; Carbonell-Baeza et al., 2011; Clauw, 2014). However, the majority of studies have focused on the study of the effect of exercise interventions, whereas the objective quantification of physical activity (PA) in free-living condition has received poor attention in this population.

Sedentary time (ST) has been indirectly associated with health status in the general population (Matthews et al., 2012) and has been associated with higher risk of fibromyalgia (Mork et al., 2010). Little is known about the consequences of a sedentary lifestyle on fibromyalgia symptomatology. Ellingson et al. (2012b) observed a worsening in the regulation of pain by the central nervous system in fibromyalgia patients who were highly sedentary compared to those who spent less time in sedentary behaviours. It is known that fibromyalgia patients show reduced PA levels compared with their counterparts (McLoughlin et al., 2011a; Segura-Jiménez et al., 2015b). However, adopting this behaviour might, in fact, trigger a worsening of their condition (Busch et al., 2011; Ellingson et al., 2012b). A recent study has shown that increasing steps per day leads to improvements in physical function and pain in fibromyalgia patients (Kaleth et al., 2014). Also, it has been previously shown that there is a link between pain modulation and PA in this population, so that women who are physically active present increased ability to modulate their pain than those who are physically inactive (Ellingson et al., 2012b).

Overall, the study of the relationship between ST and PA with fibromyalgia symptoms is scarce, and the studies accomplishing this aim are focused on pain only (Ellingson et al., 2012b; Fontaine et al., 2010). Fatigue is the second most reported symptom in fibromyalgia patients and it is highly related with pain (Rongen-Van Dartel et al., 2014; Wolfe et al., 2013). There is an association between prolonged ST with fatigue in the general female population (Ellingson et al., 2014). Furthermore, higher PA levels are associated with higher levels of energy and lower levels of fatigue in female healthy adults (Ellingson et al., 2014) and in patients with rheumatoid arthritis (Rongen-Van Dartel et al., 2014). Indeed, improvements in energy and fatigue mood states seem consistent across a range of populations and conditions after engagement in PA behaviours (Puetz, 2006). This makes plausible the idea of a consistent relationship between ST and PA with fatigue in fibromyalgia patients.

Given the potentially deleterious impact of sustained ST and the promising benefit of PA for symptoms in fibromyalgia, it is clinically relevant to determine whether objectively assessed ST and PA are associated with key symptoms such as pain and fatigue in this population, and consequently with the overall impact of the disease. Since self-reported questionnaires usually provide misleading information in fibromyalgia population (Segura-Jiménez et al., 2014a, 2013b), objective measures of PA such as accelerometry has been proposed for this purpose due to its validity, reliability and feasibility (Freedson et al., 2012; Ozemek et al., 2014; Troiano et al., 2014). Therefore, we aimed to examine the individual (objective 1) and independent (objective 2) association of objectively measured ST and PA levels with pain, fatigue and the overall impact of the disease in women with fibromyalgia. We hypothesized that ST and PA would be separately and independently associated with fibromyalgia symptoms.

## **METHODS**

### **Participants**

In order to obtain a representative sample of fibromyalgia patients from the southern Spain (Andalusian) population, the sample size needed was calculated ( $n=300$ ). Then, a sex and province proportional recruitment was planned (Segura-Jiménez et al., 2015a). Women with fibromyalgia were recruited via fibromyalgia associations, Internet advertisement, flyers and e-mail. Written informed consent from all participants ( $n=617$ ) was obtained. A total of 568 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 (Wolfe et al., 1990), have neither acute or terminal illness nor severe cognitive impairment (Mini Mental State Examination (MMSE) score  $< 10$ ), and be  $\leq 65$  years old. Thirty-six women with fibromyalgia were not previously diagnosed, 81 did not meet the 1990 ACR criteria, 1 had severe cognitive impairment and 11 were older than 65 years old. Therefore, 439 women with fibromyalgia met the inclusion criteria. The Ethics Committee of the *Hospital Virgen de las Nieves* (Granada, Spain) reviewed and approved the study.

### **Measurements**

#### *Sedentary time and physical activity*

Activity counts were measured at a rate of 30 Hz and stored at an epoch length of 1 second (Aguilar-Farías et al., 2014; Sasaki et al., 2011) with a triaxial accelerometer GT3X+ (Actigraph, Pensacola, Florida, USA). Participants wore the device on the hip near to the centre of gravity, underneath clothing and secured with an elastic belt.

Accelerometer wearing time was calculated by subtracting the sleeping time from each day. Patients reported the time they went to bed and the time they woke up in a sleep diary. Bouts of 90 continuous minutes of 0 counts were excluded from the analysis, considered as non-wear periods (Choi et al., 2012). PA was recorded up to 9 days, starting from the day the participants received the accelerometers until the day that they were instructed to return the devices. PA data from the first recorded day (to avoid reactivity) and last day (return back device) were excluded. A total of 7 continuous days with a minimum of 10 valid hours per day was the criteria for being included in the study analysis.

As an overall measure of PA, average counts per minute (cpm) in each independent axis and the vector magnitude was calculated for each women. ST and light, moderate and vigorous PA intensity levels were calculated based upon recommended PA vector magnitude cut points (Aguilar-Farías et al., 2014; Sasaki et al., 2011): 0-199, 200-2689, 2690-6166 and  $\geq 6167$ , respectively, and were expressed as minutes per day. In addition, moderate-to-vigorous PA (min/day; MVPA) was calculated as the sum of moderate and vigorous PA. Total PA (min/day) was calculated as the sum of the light, moderate and vigorous intensity levels. Data download, reduction, cleaning and analyses were performed using the manufacturer software (Actilife™ 6 desktop).

### *Experimental pain*

Tender points were assessed according to the 1990 ACR fibromyalgia criteria (Wolfe et al., 1990) using a standard pressure algometer (FPK 20; Wagner Instruments, Greenwich, CT, USA). The mean pressure of two alternative measurements at each tender point was used. Tender point were positive if the patient noted pain at pressure  $\leq 4 \text{ kg/cm}^2$  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 (algometer score) was also calculated.

### *Clinical pain*

We used the Revised Fibromyalgia Impact Questionnaire (FIQR) pain sub-scale (Bennett et al., 2009b), the 36-item Short-Form health survey (SF-36) pain sub-scale (Alonso et al., 1995) and a pain visual analogue scale (PVAS) to assess clinical pain in the context of the last 7 days, the last month and the current pain, respectively. All scales presents a minimum score of 0 and a maximum scoring of 10, except for the SF-36 (0-100). In both the FIQR and the PVAS lower scores indicate lower pain, whereas in the SF-36 is the contrary.

### *Fatigue*

Fatigue severity was measured with the *Spanish version of the Multidimensional Fatigue Inventory (MFI-S)* (Munguía-Izquierdo et al., 2012; Schwarz et al., 2003). General fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation are the 5 scales composing this questionnaire. Each subscale includes four items with five-point Likert scales. Scores on each subscale range from 4 to 20, with higher scores indicating greater fatigue.

### *The impact 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 (Bennett et al., 2009b). The FIQR total score range from 0 to 100, with a higher score indicating greater effect of the condition on the person's life.

### *Anthropometry and body composition*

Weight (kg) and total body fat percentage were measured using a portable eight-polar tactile-electrode impedanciometer (InBody R20, Biospace, Seoul, Korea). Following the manufacturer's recommendations, we asked them not to have a shower, not to practice



intense PA and not to ingest large amounts of fluid and/or food in the 2 hours before the measurement. Patients were instructed not to wear clothing (except underwear) nor metal objects during the assessment.

#### *Medication for pain*

The consumption of painkillers (analgesics) was registered as a binary variable (yes/no).

### **Statistical analysis**

Descriptive statistic (mean±standard deviation) was used to describe the clinical characteristics of the group. To explore the association between ST and PA levels with pain, fatigue and the impact of fibromyalgia, we performed bivariate partial correlations. Age, total body fat percentage and pain medication were used as covariate, since these outcomes are associated with pain. Accelerometry-wear time was also used as covariate.

In order to study the differences in pain, fatigue and the impact of fibromyalgia across groups of ST, quintiles based on the distribution of the data for total ST were compared using one-way analysis of covariance (ANCOVA) with age, total body fat percentage, pain medication and accelerometry-wear time as covariates. Similarly, in order to study the differences in the outcomes across groups of light, MVPA and total PA, quintiles based on the distribution of the data for light, MVPA and total PA, respectively were compared using ANCOVA with the covariates above-mentioned. Post-hoc analysis with the Bonferroni's correction assessed the differences across quintiles.

The independent association of ST, light, moderate and vigorous PA with pain, fatigue and the impact of fibromyalgia was studied using linear regression analysis. ST and light PA

could not be included in the same model due to the existence of multicollinearity (variance inflation factor  $> 10$ ), which is an indicative of overlapping information between these variables. Therefore, we studied their association with fibromyalgia symptoms in separate regression models. In the first analysis, ST, moderate and vigorous PA were simultaneously introduced as independent variables. Pain, fatigue and the impact of fibromyalgia were introduced individually as dependent variables in separate models (we used only those variables which showed a previous association in the correlation analysis). Age, total body fat percentage, pain medication and accelerometry-wear time were included as covariates. In the second analysis, we used the same procedure to assess the independent association of light, moderate and vigorous PA with pain, fatigue and the impact of fibromyalgia.

We used the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). The statistical significance was set at  $P < 0.01$ , except when Bonferroni's adjustment was used ( $P < 0.05$ ).

## RESULTS

Accelerometer data from 4 patients were lost, due to malfunction when downloading data and 18 patients did not meet the accelerometer criteria. Patients with missing data were also excluded (n=11). The final sample included in the analyses comprised 408 women with fibromyalgia, whose clinical characteristics are shown in **table 1**.

### *Individual association of ST and PA levels with symptoms (objective 1).*

The association of ST and PA levels with pain, fatigue and overall impact of the disease in women with fibromyalgia are presented in **table 2**. There was a positive correlation between ST and FIQR pain, SF-36 pain, algometer score, general fatigue, physical fatigue, fatigue-related reduced activity, reduced motivation and FIQR total score ( $r_{\text{partial}}$  between 0.14 and 0.31; all,  $P<0.01$ ), however, there was no correlation between ST and PVAS, tender points nor mental fatigue. The association of ST with SF-36 pain and algometer score was inverse ( $r_{\text{partial}}$  between -0.17 and -0.22; all,  $P<0.01$ ). Light and total PA were inversely correlated with FIQR pain, SF-36 pain, algometer score, general fatigue, physical fatigue, fatigue-related reduced activity, reduced motivation and FIQR total score ( $r_{\text{partial}}$  between -0.13 and -0.29; all,  $P<0.01$ ), but not with PVAS, tender points nor mental fatigue. The association of light and total PA with SF-36 pain and algometer score was positive ( $r_{\text{partial}}$  between 0.17 and 0.22; all,  $P<0.01$ ). MVPA was positively correlated with SF-36 pain and negatively correlated with physical fatigue, fatigue-related reduced activity and FIQR total score ( $r_{\text{partial}}$  between 0.14 and 0.21; all,  $P<0.01$ ).

The impact of fibromyalgia across quintiles based on the distribution of the data for total ST are plotted in **figure 1**. There were differences in the FIQR total score between the quintiles of ST ( $F=13.650$ ,  $P<0.001$ ). The post-hoc analysis revealed that those with the highest ST (5<sup>th</sup> quintile) presented higher FIQR total score than the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> quintiles (74.5 vs.

64.9, 59.1, 62.7 and 58.1, respectively; all  $P \leq 0.001$ ). Overall, pain- and fatigue-related outcomes showed similar results that those observed with the FIQR total score (see **supplementary table 1**).

The impact of fibromyalgia across quintiles based on the distribution of the data for light, MVPA and total PA are plotted in **figure 2**. There were differences in the FIQR total score between the quintiles of light ( $F=8.983$ ,  $P<0.001$ ), MVPA ( $F=4.858$ ,  $P=0.001$ ) and total PA ( $F=9.157$ ,  $P<0.001$ ). The post-hoc analysis revealed that patients with the lowest light PA (1<sup>st</sup> quintile) presented higher FIQR total score than the 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> quintiles (73.5 vs. 66.5, 60.6, 59.7 and 61.3, respectively; all  $P<0.05$ ). Similarly, those with the lowest MVPA (1<sup>st</sup> quintile) presented higher FIQR total score than the 3<sup>rd</sup> and 5<sup>th</sup> quintiles (69.8 vs. 62.0 and 58.7, respectively; all  $P<0.05$ ). Finally, those patients with the lowest total PA (1<sup>st</sup> quintile) presented higher FIQR total score than the 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> quintile (73.6 vs. 65.6, 61.1, 60.5 and 59.8; all  $P \leq 0.01$ ). Overall, pain- and fatigue-related outcomes showed similar results that those observed with the FIQR total score (see **supplementary table 2**).

*Independent association of ST and PA levels with symptoms (objective 2).*

**Table 3** shows the independent association of sedentary time, moderate and vigorous PA with pain, fatigue and overall impact of the disease in women with fibromyalgia. ST was independently associated with SF-36 pain ( $B=-0.030$ ), general fatigue ( $B=0.004$ ), fatigue-related reduced activity ( $B=0.014$ ), reduced motivation ( $B=0.008$ ) and FIQR total score ( $B=0.048$ ) (all,  $P<0.01$ ). Vigorous PA was independently associated with general fatigue ( $B=-0.248$ ) and physical fatigue ( $B=-0.214$ ) (all,  $P<0.01$ ). Moderate PA was not independently associated with any outcome (all,  $P<0.05$ ).

**Table 4** shows the independent association of light, moderate and vigorous PA with pain, fatigue and overall impact of the disease in women with fibromyalgia. Light PA was

independently associated with SF-36 pain ( $B=0.030$ ), general fatigue ( $B=-0.004$ ), fatigue-related reduced activity ( $B=-0.014$ ), reduced motivation ( $B=-0.009$ ) and FIQR total score ( $B=-0.048$ ) (all,  $P<0.01$ ). Vigorous PA was independently associated with general fatigue ( $B=-0.260$ ) and physical fatigue ( $B=-0.218$ ) (all,  $P<0.01$ ). Moderate PA was independently associated with fatigue-related reduced activity ( $B=-0.022$ ;  $P=0.01$ ).

## **DISCUSSION**

The results of the present study highlight the association of ST and all PA levels (especially light PA) with pain, all fatigue dimensions except mental fatigue, and the overall impact of fibromyalgia in women affected by this disease. Lower levels of sedentary time and higher levels of light PA were associated with a better symptomology in fibromyalgia. Furthermore, the association of ST and light PA with symptoms is independent of moderate and vigorous PA. Of note is that vigorous PA was also independently associated with general and physical fatigue.

The wide negative consequences of a sedentary lifestyle on health have been previously reported (Matthews et al., 2012). However, the study of the association between ST and pain is scarce. Ellingson et al. (2012a), however, found no association between sedentary behaviour and pain in healthy women. Nonetheless, their study might have been underpowered to detect significant associations due to the small sample size (n=21). Additionally, this sample consisted of healthy women who were relatively active (Ellingson et al., 2012a) and their results might vary if the same procedure is replicated in a more sedentary group with lower overall PA. Therefore, the generalization of their results should not expand upon the general population or to those experiencing chronic pain. In fact, in fibromyalgia patients, Ellingson et al. (2012b) observed that fibromyalgia patients who were highly sedentary presented a dysregulation of pain compared to those who spent less time in sedentary behaviours. This is in concordance with the results of the current study, which showed an independent association between objectively measured ST and not only pain, but also different dimensions of fatigue and the overall impact of fibromyalgia.

The effect of diverse exercise interventions in fibromyalgia pain improvements is well documented (Rahman et al., 2014; Segura-Jiménez et al., 2013a, 2014c). The scientific

literature shows that conventional exercise interventions and complementary and alternative exercise programs lead to pain improvements in this population (Carbonell-Baeza et al., 2011; Segura-Jiménez et al., 2013a, 2014c). Despite the controversial low clinical relevance of these improvements, a recent study observed that exercise therapy might be even better than pharmacological interventions as a fibromyalgia treatment (Rahman et al., 2014), which highlights the strong link that seems to exist between fibromyalgia pain and physical exercise. In fact, both sensory and affective pain networks have been related to PA behaviours (Ellingson et al., 2012b; McLoughlin et al., 2011b) and a higher physical fitness has been associated with lower pain levels (Soriano-Maldonado et al., 2015). The results of the current study showed an association of all PA levels with different measures of pain, and the association of light PA with the outcomes was generally independent of moderate and vigorous PA. This disagrees with previous findings in healthy adult women, where participation in vigorous PA was the only PA level related to pain (Ellingson et al., 2012a). However, as aforementioned, this sample consisted of healthy women who were relatively active and the results should not extrapolate to other populations with less overall PA (Ellingson et al., 2012a). Nonetheless, we also observed that the association of vigorous PA with general and physical fatigue was independent of ST and light and moderate PA. Concurring with our findings, previous studies have shown an association of pain modulation with light and moderate PA in fibromyalgia (Ellingson et al., 2012b). This reinforces the importance of being physically active in this population, no matter the intensity of the PA performed. The larger effect associated with the SF-36 pain sub-scale was probably linked to the fact that this sub-scale is a well-established (cited in more than 2500 studies (Puetz, 2006)) multi-item scale focusing on the frequency of feelings of pain experienced over the last month. The other measures (PVAS and FIQR-pain) are single-item measures that might not represent the multi-dimensionality of pain. Otherwise, we also observed an association of

ST and PA with the algometer score but this was smaller than that with the SF-36 pain. This might be due to selection criteria (there was not a preselection of highly sedentary and/or low physically active patients) and restriction of range (tenderness was consistently high in the whole sample).

As in most fatiguing syndromes, in fibromyalgia, fatigue might depend on both peripheral and central mechanisms (Staud, 2012). Furthermore mood disorders are linked to chronic fatigue as well (Staud, 2012). Pain and fatigue are strongly linked and therefore, the attainment of similar findings to those observed in pain was expected. Fatigue is a highly reported symptom for most fibromyalgia patients and seems to contribute as much to these patients' dysfunction as pain itself (Staud, 2012). In this line, we might hypothesize that inactivity (via both neurobiological and psychological mechanisms) might result in pain and fatigue, and consequently aggravate the impact of the fibromyalgia. Recently, Ellingson et al. (2014) concluded that reductions in prolonged sedentary behaviour and meeting PA recommendations was associated with higher levels of energy and lower levels of fatigue in adult women. We found that ST, light and vigorous PA are independently associated with general and physical fatigue, and fatigue-related reduced activity and motivation. Our findings concur with other studies in the general population and other conditions (Rongen-Van Dartel et al., 2014).

The composition of groups of quintiles of ST allowed us to observe that those with the highest ST presented higher pain, fatigue and impact of fibromyalgia than the rest of the groups based on ST. Similarly, we observed that those with the lowest PA presented higher pain, fatigue and impact of fibromyalgia than the rest of the groups of PA. Furthermore, it is interesting that all the PA intensity levels presented this approach. Since a 14% change in the impact of fibromyalgia has been considered clinically relevant (Bennett et al., 2009a), the



differences observed in the FIQR between the first and last quintiles of ST (~22%) and total PA (~19%) in the current study might be considered clinically relevant. Our results are in agreement with the recent body of literature which suggests that even small increases in activity in inactive individuals may be beneficial to public health (Ekelund et al., 2015). For that purpose, our data suggest that women with fibromyalgia should avoid being in the quintile 5 of ST and quintile 1 of total PA. In other words, they should prevent engaging in very high sedentary behaviours (~9 hours/day) and spend ~6.5 hours/day in PA. It is likely that more than 6 hours per day of PA seems too much for this population, which have difficulty adhering to exercise. However, we must bear in mind that all types (e.g.: walking, housework, gardening, etc.) and levels of PA can be included in this overall achievement. The overlap of information in ST and light PA in the present study indicates that overall greater time spent in ST results in lower time spent in light PA, and vice versa. Therefore, we support in promoting decreases in ST, and this behaviour would likely result in increases in low-intensity (light) PA behaviours, thus making easier to achieve the total PA daily goal. This might be a reasonable strategy to diminish ST and increase PA. Another target might be promoting increased PA by asking fibromyalgia patients to accumulate short bouts of activity throughout the day. In fact, a previous study showed that accumulating 30 minutes of lifestyle PA throughout the day produced clinically relevant changes in perceived physical function and pain in fibromyalgia patients (Fontaine et al., 2010). However, concurring with the majority of studies in nearly any condition, the beneficial effects of PA in function and pain were not sustained over time (Fontaine et al., 2011). Therefore, it is wise to search for innovative methods that may prevent relapse into inactivity in this population. For this end, it might be appropriate to address fear avoidance of PA with behavioural change programs (Kop et al., 2005).

### *Limitations and strengths*

The cross-sectional design of the current study does not allow establishing causal relationships. It seems plausible to speculate that pain and fatigue might reduce participation in PA (Kop et al., 2005); however, it is equally plausible that fibromyalgia patients who are less sedentary and more physically active suffer less pain, fatigue and overall impact of fibromyalgia (Kaleth et al., 2014). Indeed, results from intervention studies support the later hypothesis. In fact, it has been suggested that a vicious cycle might exist, whereby symptoms may lead to inactivity, and inactivity leads to increased symptoms (Kop et al., 2005). On the other hand, the lack of relationships between self-reported PA and pain sensitivity highlight the importance of using objective measures of PA when possible in PA-related research (Ellingson et al., 2012a). A strength of the present study was the use of accelerometer measures of PA, which allowed us to objectively quantify ST and graded intensities of PA. The accelerometer criteria were higher than other studies which are usually less strict (Ellingson et al., 2012a, 2014, 2012b; Kop et al., 2005; McLoughlin et al., 2011a). Furthermore, we assessed a relatively large sample size of women with fibromyalgia representative from southern Spain (Andalusia) (Segura-Jiménez et al., 2015a).

## **CONCLUSIONS**

We found that ST is independently and positively associated with levels of pain, fatigue and impact of the disease in women with fibromyalgia. Importantly, from all PA levels, light PA showed the largest independent associations with pain, fatigue and the impact of fibromyalgia, although vigorous PA was also independently associated with general and physical fatigue. This is important when giving advice on PA in this population, suggesting that patients should avoid being highly sedentary and high physically inactive. Our results are supportive in including ST and PA assessment in fibromyalgia research.

## **Perspective**

This study is the first studying the association of ST with symptoms in women with fibromyalgia independently of physical activity intensity levels. We observed that higher ST is independently and positively associated with pain, fatigue and impact of fibromyalgia. In addition, the inverse association of vigorous PA with pain, fatigue and the impact of fibromyalgia was independent of ST. Overall, the results suggests that women with fibromyalgia who are highly sedentary and low physically active show greater disease severity than those who are low sedentary and high physically active.

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## **Competing interests**

None of the authors had any conflict of interests.

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**Table 1.** Clinical characteristics of fibromyalgia women,  $n=408$ .

Variable	Mean	SD
Age (years)	51.4	7.6
Weight (kg)	70.9	13.7
Height (cm)	158.0	5.9
Body mass index (kg/m <sup>2</sup> )	28.4	5.3
Total body fat percentage (%)	40.1	7.6
FIQR pain	7.5	1.9
SF-36 pain	21.1	14.7
Pain Visual Analogue Scale	6.0	2.2
Tender points count	16.7	2.0
Algometer score (kg/cm <sup>2</sup> )	43.3	13.4
MFI-S		
General fatigue	18.0	2.5
Physical fatigue	16.7	3.0
Reduced activity	13.0	4.9
Reduced motivation	13.2	3.9
Mental fatigue	14.3	2.4
FIQR total score	64.4	16.8
Sedentary time (min/day)	460	104
Light PA (min/day)	419	92
Moderate PA (min/day)	44	30
Vigorous PA (min/day)	0.4	2.0
MVPA (min/day)	44	30

FIQR, Revised Fibromyalgia Impact Questionnaire; MFI-S, Spanish version of the Multidimensional Fatigue Inventory; MVPA; moderate-vigorous physical activity; PA, physical activity; SD, standard deviation; SF-36, 36-item Short-Form health survey.

**Table 2.** Partial correlations between pain, fatigue and overall impact of the disease with sedentary time and physical activity (PA) levels in women with fibromyalgia,  $n=408$ .

Variables	Sedentary time	Light PA	Moderate PA	Vigorous PA	MVPA	Total PA
FIQR pain	0.14*	-0.13*	-0.08	-0.11	-0.09	-0.14*
SF-36 pain	-0.22**	0.20**	0.14*	0.15*	0.14*	0.22**
Pain Visual Analogue Scale	0.11	-0.11	-0.03	-0.10	-0.04	-0.11
Tender points count	0.12	-0.11	-0.05	-0.15*	-0.06	-0.12
Algometer score	-0.17*	0.17*	0.06	0.10	0.06	0.17*
MFI-S						
General fatigue	0.17*	-0.16*	-0.08	-0.22**	-0.10	-0.17*
Physical fatigue	0.18**	-0.15*	-0.14*	-0.17**	-0.15*	-0.18**
Reduced activity	0.31**	-0.29**	-0.21**	-0.07	-0.21**	-0.31**
Reduced motivation	0.21**	-0.21**	-0.09	-0.14*	-0.10	-0.21**
Mental fatigue	0.09	-0.09	-0.05	-0.06	-0.06	-0.09
FIQR total score	0.29**	-0.27**	-0.18**	-0.15*	-0.19**	-0.29**

Analyses controlled for age, total body fat percentage, pain medication and accelerometry-wear time. FIQR, Revised Fibromyalgia Impact Questionnaire; MFI-S, Spanish version of the Multidimensional Fatigue Inventory; MVPA, moderate-to-vigorous physical activity; SD, standard deviation; SF-36, 36-item Short-Form health survey. \* $P<0.01$ ; \*\* $P<0.001$ .

**Table 3.** Independent association of sedentary time, moderate and vigorous physical activity (PA) with pain, fatigue and overall impact of the disease in women with fibromyalgia, *n*=408.

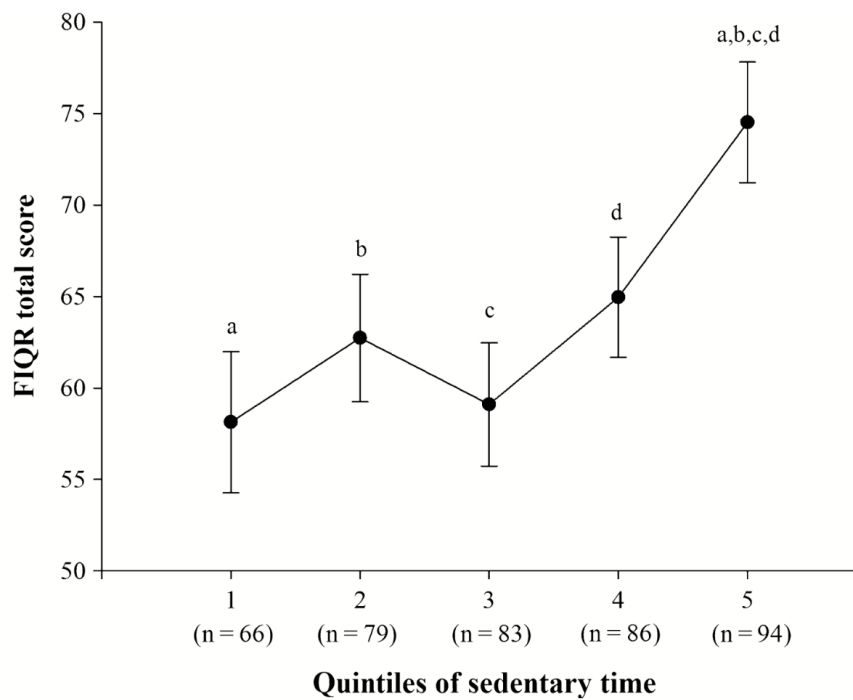
Variable	B	(95% CI)	$\beta$	P
<b>SF-36 pain</b>				
Sedentary time (min/day)	-0.030	-(0.048 ; -0.012)	-0.215	0.001
Moderate PA (min/day)	-0.001	-(0.061 ; 0.059)	-0.003	0.964
Vigorous PA (min/day)	0.866	(0.150 ; 1.582)	0.118	0.018
<b>General fatigue</b>				
Sedentary time (min/day)	0.004	(0.001 ; 0.006)	0.148	0.005
Vigorous PA (min/day)	-0.248	-(0.367 ; -0.129)	-0.197	<0.001
<b>Physical fatigue</b>				
Sedentary time (min/day)	0.004	(0.001 ; 0.008)	0.147	0.019
Moderate PA (min/day)	-0.003	-(0.015 ; 0.009)	-0.027	0.646
Vigorous PA (min/day)	-0.214	-(0.356 ; -0.072)	-0.143	0.003
<b>Reduced activity</b>				
Sedentary time (min/day)	0.014	(0.009 ; 0.020)	0.305	<0.001
Moderate PA (min/day)	-0.007	-(0.026 ; 0.012)	-0.042	0.468
<b>Reduced motivation</b>				
Sedentary time (min/day)	0.008	(0.004 ; 0.012)	0.208	<0.001
Vigorous PA (min/day)	-0.213	-(0.399 ; -0.026)	-0.110	0.026
<b>FIQR total score</b>				
Sedentary time (min/day)	0.048	(0.028 ; 0.067)	0.296	<0.001
Moderate PA (min/day)	0.003	-(0.063 ; 0.069)	0.005	0.933
Vigorous PA (min/day)	-0.949	-(1.741 ; -0.157)	-0.114	0.019

Analyses controlled for age, fat percentage, pain medication and accelerometry-wear time. B, unstandardized coefficient;  $\beta$ , standardized coefficient; CI, confidence interval; FIQR, Revised Fibromyalgia Impact Questionnaire; SE, standard error; SF-36, 36-item Short-Form health survey.

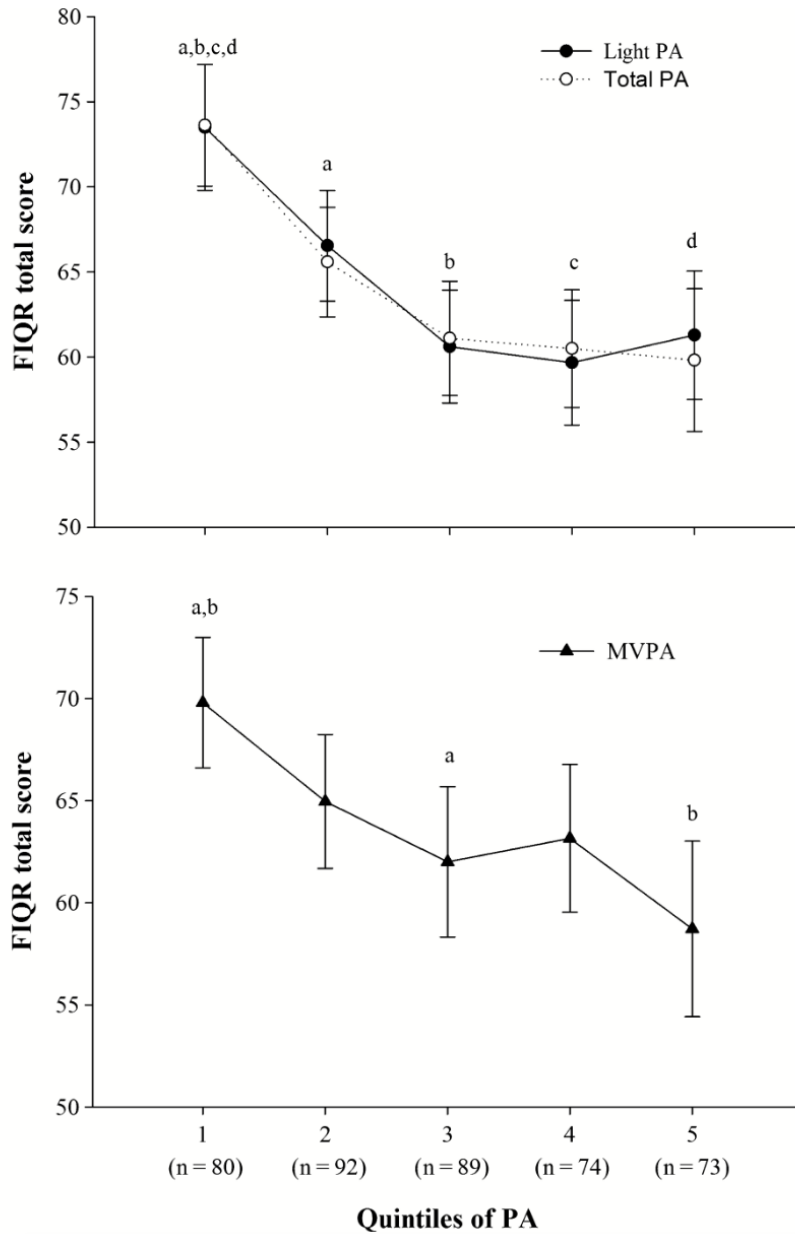
**Table 4.** Independent association of light, moderate and vigorous physical activity (PA) with pain, fatigue and overall impact of the disease in women with fibromyalgia,  $n=408$ .

Variable	B	(95% CI)	$\beta$	P
<b>SF-36 pain</b>				
Light PA (min/day)	0.030	(0.012 ; 0.048)	0.189	0.001
Moderate PA (min/day)	0.029	-(0.023 ; 0.081)	0.058	0.273
Vigorous PA (min/day)	0.896	(0.181 ; 1.612)	0.122	0.014
<b>General fatigue</b>				
Light PA (min/day)	-0.004	-(0.007 ; -0.002)	-0.159	0.003
Vigorous PA (min/day)	-0.260	-(0.379 ; -0.142)	-0.206	<0.001
<b>Physical fatigue</b>				
Light PA (min/day)	-0.004	-(0.008 ; -0.001)	-0.130	0.019
Moderate PA (min/day)	-0.007	-(0.017 ; 0.003)	-0.069	0.180
Vigorous PA (min/day)	-0.218	-(0.360 ; -0.076)	-0.146	0.003
<b>Reduced activity</b>				
Light PA (min/day)	-0.014	-(0.020 ; -0.009)	-0.269	<0.001
Moderate PA (min/day)	-0.022	-(0.038 ; -0.005)	-0.130	0.010
<b>Reduced motivation</b>				
Light PA (min/day)	-0.009	-(0.014 ; -0.005)	-0.219	<0.001
Vigorous PA (min/day)	-0.240	-(0.425 ; -0.055)	-0.124	0.011
<b>FIQR total score</b>				
Light PA (min/day)	-0.048	-(0.067 ; -0.028)	-0.261	<0.001
Moderate PA (min/day)	-0.045	-(0.102 ; 0.013)	-0.079	0.126
Vigorous PA (min/day)	-0.996	-(1.788 ; -0.205)	-0.119	0.014

Analyses controlled for age, fat percentage, pain medication and accelerometry-wear time. B, unstandardized coefficient;  $\beta$ , standardized coefficient; CI, confidence interval; FIQR, Revised Fibromyalgia Impact Questionnaire; SE, standard error; SF-36, 36-item Short-Form health survey.



**Figure 1.** Association between quintiles of sedentary time with the overall impact of fibromyalgia in female patients. Estimated mean (dots) and 95% confidence interval (error bars) represent values after adjustment for age, total body fat percentage, medication for pain and accelerometry-wear time (analysis of the covariance was used to test the group differences). Quintile 5 represents the group with the highest sedentary time. Common superscripts indicate significant ( $P \leq 0.001$ ) differences between the groups with the same letter after Bonferroni's correction. FIQR, Fibromyalgia Impact Questionnaire Revised.



**Figure 2.** Association between quintiles of light physical activity (PA), moderate-to-vigorous physical activity (MVPA) and total PA with the overall impact of fibromyalgia in female patients. Estimated mean (dots) and 95% confidence interval (error bars) represent values after adjustment for age, total body fat percentage, medication for pain and accelerometry-wear time (analysis of the covariance was used to test the group differences). Quintile 1 represents the group with the lowest PA. Common superscripts indicate significant ( $P < 0.05$ )



differences between the groups with the same letter after Bonferroni's correction. FIQR, Fibromyalgia Impact Questionnaire Revised.