RHEUMATOLOGY

Original article

Adaptation profiles comprising objective and subjective measures in fibromyalgia: the al-Ándalus project

Fernando Estévez-López^{1,2}, Víctor Segura-Jiménez^{1,3}, Inmaculada C. Álvarez-Gallardo^{1,3}, Milkana Borges-Cosic¹, Manuel Pulido-Martos⁴, Ana Carbonell-Baeza³, Virginia A. Aparicio⁵, Rinie Geenen^{2,*} and Manuel Delgado-Fernández^{1,*}

Abstract

Objectives. The aim of this study was to identify subgroups in terms of adaptation to FM and to test differences in FM severity between these subgroups.

Methods. The al-Ándalus project made it possible to perform a comprehensive population-based crosssectional study in 486 FM patients including multiple assessments of modifiable (could be targeted in therapy) resilience and vulnerability factors, measured by objective and subjective assessments, related to psychological and physical function. FM severity was assessed by means of FM impact (total score of the Revised Fibromyalgia Impact Questionnaire) and distress (Polysymptomatic Distress Scale of the modified 2011 preliminary criteria for FM). Exploratory factor analysis, cluster analysis and analysis of variance were conducted.

Results. Factor analysis yielded eight factors: three included objective measures (declarative memory, active lifestyle and objective physical fitness) and five included subjective measures (fatigue, psychological distress, catastrophizing, resilience and subjective physical fitness). Cluster analysis based on these eight factors identified five profiles: Adapted (16%), Fit (18%), Poor performer (20%), Positive (20%) and Maladapted (26%). Most profile comparisons revealed different levels of FM severity varying from Adapted (the most favourable profile) to Maladapted (the most unfavourable profile) with Fit, Poor performer and Positive obtaining intermediate positions.

Conclusions. Heterogeneity of FM was shown by five clinically meaningful profiles of modifiable factors that were associated with FM severity. It is of clinical interest to examine whether these profiles are associated with FM prognosis and the effectiveness of interventions, which would enhance the development of customized interventions based on adaptation profiles in FM.

Key words: accelerometry, chronic pain, cognitive performance, coping, epidemiology, functional capacity, patient subgroups, quality of life, resilience (psychological), vulnerability (psychological)

Rheumatology key messages

- Patients with fibromyalgia are heterogeneous with respect to modifiable resilience and vulnerability factors (adaptation profiles).
- Adaptation profiles of patient-reported (subjective) and performance-based (objective) measurements are associated with severity of fibromyalgia.
- The identified adaptation profiles may help to enhance the development of customized interventions in fibromyalgia.

¹Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Granada, Spain, ²Department of Psychology, Faculty of Social and Behavioural Sciences, Utrecht University, Utrecht, The Netherlands, ³Department of Physical Education, Faculty of Education Sciences, University of Cádiz, Cádiz, ⁴Department of Psychology, Faculty of Humanities and Sciences of Education, University of Jaén, Jaén and ⁵Department of Physiology, Faculty of Pharmacy, Faculty of Sport Sciences, and Institute of Nutrition and Food Technology, University of Granada, Spain

Submitted 4 November 2016; revised version accepted 3 July 2017 *Rinie Geenen and Manuel Delgado-Fernández contributed equally to this study

Correspondence to: Fernando Estévez-López, Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Carretera de Alfacar, s/n, 18011, Granada, Spain. E-mail: festevez@ugr.es

Introduction

FM is a heterogeneous and poorly understood disease [1–3]. The first diagnostic criteria for FM, launched by the ACR, focused on chronic widespread pain [4]. The modified 2011 preliminary criteria additionally included cognitive symptoms, unrefreshed sleep, fatigue and several somatic symptoms [5]. Thus, the clinical picture of FM might be now even more heterogeneous than two decades ago.

FM is frustrating [2], among other reasons because there is no uniform treatment that significantly and in the long term reduces its impact [6]. Therefore, to study modifiable factors that are associated with better outcomes in FM is of interest [7, 8]. Considering that there is no cure, it is adaptation to FM that is strived for. Adaptation reflects a dynamic process to healthily rebalance to new circumstances by maintaining appropriate psychological and physical functioning [9]. Traditionally, efforts were focused on maladaptive responses (vulnerability factors), such as catastrophizing. However, understanding factors that are related with long-term adaptive responses (resilience factors) is also essential in adaptation to FM [7, 10], for instance, positive affect.

The most recent recommendations for the management of FM involve a stepped approach that is tailored to the specific needs of the individual [6]. To suggest and evaluate tailored therapies, insight into heterogeneous profiles of patients is needed [11]. Obtaining a comprehensive understanding of FM subgroups requires multiple assessments of modifiable (could be targeted in therapy) resilience and vulnerability factors, measured by objective and subjective assessments, related to psychological and physical function, especially since in this population there is a discordance between objective measurements (what is observed in performance-based tests) and the patient's subjective appraisal (how people feel) when psychological or physical function is assessed [12-14]. Only a few previous studies, conducted with low sample sizes of 57 [15] and 107 [16], examined FM profiles using objective measurements; one study included physical performance measures [15] and the other biomedical measures [16]. However, to date most of the suggested profiles have not included objective measurements [17-25].

Therefore, the aims of the present study in patients with FM were (i) to define subgroups in terms of adaptation profiles and (ii) to test differences in FM severity between these subgroups, in order to tentatively gain insight into their clinical meaningfulness.

Methods

Participants

Detailed description of the methods and sampling procedures followed are provided elsewhere [26]. Briefly, participants were recruited mainly via FM associations from the eight provinces of Andalusia (southern Spain). Additional participants were recruited via e-mail, letter, telephone and mass-media advertisements. All interested participants (n = 646) gave their written informed consent after receiving detailed information about the study aims and procedures. The al-Ándalus project was reviewed and approved by the Ethics Committee of the Hospital Virgen de las Nieves (Granada, Spain); registration number: 15/11/2013-N72. The ethical guidelines of the Declaration of Helsinki (modified in 2000) were followed.

Measures

The Mini-Mental State Examination [27] was used to assess the presence of severe cognitive impairment (exclusion criterion). Participants with scores <10 were excluded. A standard sociodemographic questionnaire was completed by the participants, including the question, 'Have you ever been diagnosed with an acute or terminal illness?' (an exclusion criterion). Current pain intensity was assessed on a 10-cm visual analogue scale. The Beck Depression Inventory-II [28] was used to assess depression. Bioelectrical impedance (InBody R20; Biospace, Seoul, South Korea) measured body fat (%) and muscular mass.

A physical examination of the tender points with algometry was conducted, according to the 1990 ACR criteria for classification of FM [4]. This was done to confirm the diagnosis of FM and obtain an 'algometer score' (sum of the minimum pain-pressure values obtained for each tender point). The 36-item Short-Form Health Survey (SF-36) [29] was used to assess physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role and mental health.

General fatigue, physical fatigue, mental fatigue, reduced activity and reduced motivation were assessed using the Multidimensional Fatigue Inventory [30]. The Pittsburgh Sleep Quality Index (PSQI) questionnaire [31], Sedentary Behaviour Questionnaire [32], State Trait Anxiety Inventory-S [33], Satisfaction With Life Scale [34] and Trait Meta-Mood Scale-24 (emotional repair subscale) were used to assess sleep quality (PSQI global score), subjective sedentary time, current anxiety, satisfaction with life and emotional repair, respectively.

Participants' believed ability to manage pain, cope with symptoms and function physically was assessed using the Chronic Pain Self-efficacy Scale [35]. The Pain Catastrophizing Scale [36] was used to assess rumination, magnification and helplessness. The Life Orientation Test Revised [37] was used to assess optimism and pessimism.

The Positive and Negative Affect Schedule [38] was used to assess positive affect and negative affect. The International Fitness Scale [39] was used to subjectively assess cardiorespiratory fitness, muscular strength, speed-agility and flexibility. The Leisure Time Physical Activity Instrument [40] and Physical Activity at Homework or Workplace Instrument were used to subjectively assess light, moderate and vigorous physical activity. The Revised Fibromyalgia Impact Questionnaire (FIQR) [41] was used to assess FM impact (FIQR total The Senior Fitness Test battery [45] was used to objectively measure physical fitness by the following tests: the 30-s chair and stand, arm curl, chair sit-and-reach, back scratch, 8-foot up-and-go and 6-min walk tests. Triaxial GT3X+ accelerometers (Actigraph, Pensacola, FL, USA) were used to objectively measure sedentary time as well as light, moderate and vigorous physical activity (for further details, [8]).

Procedure

Assessments were conducted over three consecutive days. On day 1, participants were interviewed using the Mini-Mental State Examination and completed sociode-mographic data, clinical data (including current pain intensity) and the Beck Depression Inventory-II. Then, measurements of body composition and tender points were made. Subsequently, participants received several questionnaires to be completed at home on day 2. On day 3, participants returned the questionnaires and performed the PASAT, RAVLT and Senior Fitness Test. Afterwards, participants received the accelerometer to be worn for 9 days.

Statistical analyses

A higher order principal axis factor analysis with oblimin rotation was conducted to reduce the number of variables. Variables whose loadings were either <0.40 on all factors or >0.32 on at least two factors [46] were excluded in factor analysis. The decision about the number of factors was based on inspection of the scree plot [46] and heuristic interpretation of the factors.

To compute factor scores, standardized z-scores were computed for the score of each participant at each variable using the mean (s.b.) of the total sample as reference values: z = (score - mean)/s.b.; those variables in which higher scores represent worse health status (e.g. catastrophizing) were inverted; and factor scores were calculated by averaging z-scores of variables included in the same factor. As a result higher factor scores indicated better health status. Internal consistency of factors was analysed by Cronbach's α .

Using factor scores, a hierarchical cluster analysis with Ward's method was conducted to identify the optimal number of clusters (profiles) of participants. Visual inspection of the dendrogram was done to indicate the number of clusters that should be considered. Next, an optimization clustering (i.e. k-means cluster analysis) was performed to parsimoniously allocate participants to clusters. The number of clusters was decided by practical considerations (the least frequent cluster should include a minimum of 15% of the total sample [22]) and by heuristic interpretability of mean factor scores within clusters [47]. By using this combination of interpretability and hierarchical and k-means cluster analyses, the developed cluster solution minimizes the within-group variability and maximizes the betweengroup differences [48, 49].

Differences between profiles (independent variable) in categorical and continuous data (dependent variables) were analysed by a series of chi-square tests or one-way analysis of variance (ANOVA), respectively. Significance of the chi-square test was based on the z-scores of the difference between observed and expected frequency; a z-score >|1.96| was considered significant [50]. Post hoc analysis to test the significance of ANOVA pairwise comparisons was performed using the Student-Newman-Keuls test. For FM impact and polysymptomatic distress, we calculated an effect size using Cohen's d (standardized mean differences) to compare the most favourable and the most unfavourable profiles (using the mean and s.p. of these two profile subgroups). Cohen's d values were interpreted as small (0.2), medium (0.5) or large (0.8) effects. Analyses were performed using SPSS Statistics for Mac version 20.0 (IBM Corp., Armonk, NY, USA) and the level of significance was set at P < 0.05.

Results

From 646 interested participants, 88 were excluded because they did not have a previous FM diagnosis (n = 39), did not fulfil FM diagnosis on either the 1990 ACR criteria or the modified 2011 preliminary criteria (n = 47), or had an acute or terminal illness (n = 2). Of the remaining 558 participants, 486 participants that completed all the assessments were included in the present study; their characteristics are showed in Table 1 ('All participants' column). Participants with and without missing data (n = 72 and 486, respectively) did not differ in terms of sociodemographic and clinical characteristics with only one exception: people in the group without missing data were more often married (75% vs 64%).

Before conducting exploratory factor analysis, the score distributions of the variables were checked. Three variables showed skewed distributions (skewness > 2 [50]): the 8foot up-and-go test, objective vigorous physical activity and subjective vigorous physical activity. Data transformations did not solve this skewness, and consequently, these variables were not included in factor analysis. Multicollinearity, r > |0.80| [50], between variables obtained from a same instrument were observed for the PASAT (not answered and correct answers, r = -0.88) and RAVLT (immediate memory and verbal learning, r = 0.98). Therefore, PASAT not answered and RAVLT immediate memory were not included in factor analysis. After excluding those variables with skewness or multicollinearity, the Kaiser-Meyer-Olkin measure of sampling adequacy was 0.9 indicating that the patterns of correlations are relatively compact [50]. Bartlett's test of sphericity was significant

	TABLE 1	Sociodemographic and	clinical charac	cteristics of all the	participants and	of the p	articipants	within each	profile
--	---------	----------------------	-----------------	-----------------------	------------------	----------	-------------	-------------	---------

Characteristics	All participants (n = 486)	Adapted (n = 77)	Fit (n = 90)	Poor performer (n = 95)	Positive (n = 97)	Maladapted (n = 127)	l P-value
Age, mean (s.ɒ.), years Gender, n (%)	51.8 (8.1)	52.0 (8.2)	48.5 (7.5)	56.4 (7.8)	51.4 (7.5)	50.8 (7.9)	<0.001 0.61
Male	24 (4.9)	1 (1.3)	5 (5.6)	5 (5.3)	6 (6.2)	7 (5.5)	
Female	462 (95.1)	76 (98.7)	85 (94.4)	90 (94.7)	91 (93.8)	120 (94.5)	
Education level, n (%)					. (,)b		<0.001
Unfinished studies	50 (10.3)	12 (15.6)	3 (3.3)	22 (23.2) ^a	4 (4.1) ^b	9 (7.1)	
Primary	246 (50.6)	34 (44.2)	51 (56.7)	52 (54.7)	39 (40.2)	70 (55.1)	
Secondary (and vocational)	124 (25.5)	19 (24.7)	26 (28.9)	18 (18.9)	33 (34.0)	28 (22.0)	
University	66 (13.6)	12 (15.6)	10 (11.1)	3 (3.2) ⁵	21 (21.6)ª	20 (15.7)	
Marital status, n (%)		>					0.77
Married	364 (74.9)	60 (77.9)	66 (72.2)	71 (74.7)	70 (72.2)	97 (76.4)	
Single	44 (9.1)	6 (7.8)	12 (12.4)	6 (6.3)	12 (12.4)	11 (8.7)	
Separated/divorced	58 (11.9)	7 (9.1)	11 (11.3)	11 (11.6)	11 (11.3)	17 (13.4)	
Widow(ed)	20 (4.1)	4 (5.2)	4 (4.1)	7 (7.4)	4 (4.1)	2 (1.6)	
Working status, n (%)							0.006
Working	129 (26.5)	24 (31.2)	38 (42.2) ^a	21 (22.1)	26 (26.8)	20 (15.7) ⁵	
Houseworker	150 (30.9)	24 (31.2)	23 (25.6)	32 (33.7)	30 (30.9)	41 (32.3)	
Incapacity pension or sick leave	9 104 (21.4)	11 (14.3)	10 (11.1) ⁵	22 (23.2)	24 (24.7)	37 (29.1)	
Unemployed	80 (16.5)	12 (15.6)	16 (17.8)	13 (13.7)	14 (14.4)	25 (19.7)	
Others	23 (4.7)	6 (7.8)	3 (3.3)	7 (7.4)	3 (3.1)	4 (3.1)	
Fulfilment of the FM criteria, n (%)		-				h	<0.001
Only the 1990 ACR criteria	43 (8.8)	20 (26.0) ^a	9 (10.0)	7 (6.4)	5 (5.2)	2 (1.6) ⁵	
Only the m-2011 criteria	67 (13.8)	11 (14.3)	14 (15.6)	13 (13.7)	11 (11.3)	18 (14.2)	
Both the 1990 and 2011 criteria	376 (77.4)	46 (59.7)	67 (74.4)	75 (78.9)	81 (83.5)	107 (84.3)	
Years since diagnosis, n (%)							0.41
A year or less	35 (7.2)	5 (6.5)	9 (10.0)	3 (3.2)	6 (6.2)	12 (9.4)	
Between 1 and 5 years	160 (32.9)	25 (32.5)	27 (30.0)	30 (31.6)	29 (29.9)	49 (38.6)	
>5 years	280 (57.6)	45 (58.4)	52 (57.8)	61 (64.2)	59 (60.8)	63 (49.6)	
Missing data	11 (2.3)	2 (2.6)	2 (2.2)	1 (1.1)	3 (3.1)	3 (2.4)	
Years since first symptoms, n (%)							0.20
A year or less	44 (9.1)	8 (10.4)	11 (12.2)	10 (10.5)	6 (6.2)	9 (7.1)	
Between 1 and 5 years	202 (41.6)	27 (35.1)	45 (50.0)	35 (36.8)	36 (37.1)	59 (46.5)	
>5 years	228 (46.9)	40 (51.9)	32 (35.6)	48 (50.5)	52 (51.6)	56 (44.1)	
Missing data	12 (2.5)	2 (2.6)	2 (2.2)	2 (2.1)	3 (2.2)	3 (2.4)	

^aMore frequent than expected in chi-square test. ^bLess frequent than expected in chi-square test. m-2011: the modified 2011 preliminary criteria questionnaire for FM diagnosis.

 $(\chi^2$ =11630.0, P<0.001) indicating that variables were (overall) significantly correlated [50]. Additionally, our data lacked bivariate outliers as indicated by Cook's distances (all <1.0) [47]. Considering the large sample size, the quite normal score distributions of included variables, Cook's distances that suggested linear relations without bivariate outliers, and Kaiser-Meyer-Olkin and Bartlett's tests that indicated factorability (adequate correlation patterns), our data reasonably met the assumptions of exploratory factor analysis.

The scree plot suggested a solution between four and eight factors. On grounds of factor interpretability, we considered the eight-factor solution as the best solution; the seven-factor solution yielded a factor that involves subjective physical fitness and fatigue, while the eight-factor solution split them into two different factors. Twenty-one variables were not included in the factor solution because their factor loadings were either <0.40 on all factors or >0.32 on at least two factors [46]. As a result, we obtained factors that were robustly different from each other. Table 2 shows the 31 variables that were included in the eight factors and the appropriateness of internal consistency of these factors (all Cronbach's $\alpha > 0.70$). For further information, see supplementary Table S1, available at *Rheumatology* Online, where a pattern matrix of factor loadings is shown.

Visual inspection of the dendrogram resulting from hierarchical cluster analysis indicated that two-, three- or fivecluster solutions should be considered. The dendrogram is shown in supplementary Fig. S2, available at *Rheumatology* Online. Interpretation of the cluster means after k-means cluster analysis suggested a five-cluster solution as follows: Adapted (n=77, 16%), Fit (n=90, 18%), Poor performer

Factor	Cronbach's α	Scales/measurements
Fatigue	0.78	Physical fatigue ^a (MFI), general fatigue ^a (MFI), vitality (SF-36), reduced activity ^a (MFI) and physical role (SF-36)
Psychological distress	0.85	Anxiety state ^a (STAI), mental health (SF-36), negative affect ^a (PANAS), emotional role (SF-36), depression ^a (BDI-II) and sleep quality ^a (PSQI)
Declarative memory	0.80	Verbal learning, delayed recall and recognition memory (all RAVLT)
Active lifestyle	0.77	Sedentary time ^a , light physical activity, moderate physical activity (all accelerometer)
Catastrophizing	0.91	Rumination ^a , magnification ^a and helplessness ^a (all PCS)
Resilience	0.76	Emotional repair (TMMS-24), positive affect (PANAS) and optimism (LOT-R)
Objective fitness	0.81	The 30-s arm curl, 30-s chair stand, 6-min walk and chair sit-and-reach tests (all SFT)
Subjective fitness	0.72	Speed-agility, muscular strength, flexibility and cardiorespiratory fitness (all IFIS)

TABLE 2 Factors emerged from higher order principal axis factor analysis (n = 486)

Factors are described in order of their appearance from the factor analyses and scales/measurements in order of their factor loadings. ^aReversed scores, and therefore higher scores indicated better health status in all the scales/measurements. IFIS: International Fitness Scale; LOT-R: Life Orientation Test Revised; MFI: Multidimensional Fatigue Inventory; PCS: Pain Catastrophizing Scale; PANAS: Positive and Negative Affect Schedule; RAVLT: Rey Auditory Verbal Learning Test; SF-36: Short Form 36 health survey; SFT: Senior Fitness Test battery; STAI: State-Trait Anxiety Inventory; TMMS-24: Trait Meta-Mood Scale.

(n=95, 20%), Positive (n=97, 20%) and Maladapted (n=127, 26%). Figure 1 illustrates the mean factor scores at the five profiles, whose scores are compared in Table 3. The Adapted profile showed markedly favourable (z-scores ≥ 0.75) psychological distress, resilience, catastrophizing, fatigue and subjective physical fitness, and favourable $(0.25 \le z\text{-scores} < 0.75)$ declarative memory, active lifestyle and objective physical fitness. The Fit profile was characterized by favourable declarative memory, active lifestyle and objective physical fitness. The Poor performer profile showed average scores (-0.25 < z-scores < 0.25) on all factors except for declarative memory and objective fitness, which were markedly unfavourable (z-score \leq -0.75) and unfavourable (-0.75 < z-scores ≤ -0.25), respectively. The Positive profile showed favourable scores on psychological factors (except average on resilience and markedly favourable on catastrophizing) and average scores on physical factors (except unfavourable scores on active lifestyle). The Maladapted profile was characterized by unfavourable scores on most of the factors, with markedly unfavourable scores for resilience and catastrophizing, and average scores for declarative memory.

Table 1 shows the characteristics of the participants in the five profiles. Significant differences emerged in age, education level, working status and fulfilment of the FM criteria; all $P \leq 0.006$. *Post hoc* comparisons indicated that Poor performer and Fit profiles were the oldest and the youngest groups, respectively (P < 0.001). Poor performer profile included more people with unfinished studies and fewer with a university degree while the contrary was observed in the Positive profile (P = 0.002). People grouped in the Fit profile were more prone to be workers and not to be in a work incapacity or sick leave state, while people in the Maladapted profile were less prone to be workers (P < 0.001). Regarding clinical data, in the Adapted profile there was an increased percentage of people that met the 1990 ACR criteria but not the modified

2011 preliminary criteria; in contrast the Maladapted profile included fewer people who only met the 1990 ACR criteria (P < 0.001).

ANOVA showed that profiles were significantly different in FM impact and polysymptomatic distress; F(4, 481) = 65.50 and F(4, 481) = 17.07, both P < 0.001. Figure 2 illustrates *post hoc* comparisons between profiles. Overall, Adapted and Maladapted profiles showed the lowest and highest FM severity, respectively. Effect sizes of the mean differences between Adapted and Maladapted profiles were large for FM impact and polysymptomatic distress; Cohen's d (95% CI) was 2.50 (2.13, 2.87) and 1.25 (0.95, 1.56), respectively.

Discussion

The present study provided a comprehensive understanding of FM heterogeneity by including modifiable resilience and vulnerability factors, measured by objective and subjective assessments, related to psychological and physical function in a large sample of FM patients that fulfil different criteria of FM diagnosis. Five profiles emerged: Adapted, Fit, Poor performer, Positive and Maladapted. Significant differences in FM severity were observed between these adaptation profiles.

One rationale underlying our choice of variables was that resilience and vulnerability factors are fundamental in FM [7, 10]. Inclusion of such factors leads us to a more comprehensive characterization of FM profiles. For instance, previous research showed that levels of psychological distress are key to distinguishing between the most favourable and unfavourable profiles [19, 20]. The present study indicates that successful adaptation to FM not only involves the mere absence of negative signs but also high levels of emotional repair, positive affect and optimism. Among resilience factors, the beneficial role of positive affect was particularly supported in adaptation to FM Fig. 1 The five FM profiles comprising eight factors (n = 486)



Higher z-scores reflect better adaptation for all the factors. Thus higher z-scores reflect lower psychological distress, catastrophizing and fatigue as well as higher resilience, declarative memory, active lifestyle, objective fitness and subjective fitness.

TABLE 3 Differences in factors between subgroups (n = 486)

Factors	Post hoc differences testing by Student-Newman-Keuls	<i>F</i> (4, 481)	P-value
Fatigue	Adapted > Fit, Poor performer > Positive > Maladapted	94.83	<0.001
Psychological distress	Adapted > Positive > Poor performer, Fit > Maladapted	130.20	< 0.001
Declarative memory	Positive, Adapted, Fit > Maladapted > Poor performer	81.98	< 0.001
Active lifestyle	Fit, Adapted > Poor performer > Maladapted, Positive	42.83	< 0.001
Catastrophizing	Adapted, Positive > Poor performer, Fit > Maladapted	147.23	< 0.001
Resilience	Adapted > Positive, Poor performer > Fit > Maladapted	99.33	< 0.001
Objective fitness	Fit, Adapted > Positive > Poor performer, Maladapted	60.10	< 0.001
Subjective fitness	Adapted > Fit > Poor performer > Positive > Maladapted	55.66	< 0.001

Higher scores reflect better adaptation for all the factors. Thus higher scores reflect lower fatigue, psychological distress and catastrophizing as well as higher declarative memory, active lifestyle, resilience, objective fitness and subjective fitness.

Fig. 2 FM impact (left side) and polysymptomatic distress (right side) according to each profile (n = 486)



One-way analysis of variance; letters in common indicate significant differences between FM profiles in *post hoc* comparisons using the Student-Newman-Keuls test. FIQR: Fibromyalgia Impact Questionnaire-Revised; PSD m-2011c Q: PolySymptomatic Distress scale from the modified 2011 preliminary criteria Questionnaire for FM diagnosis.

[7, 10]. Additionally, catastrophizing was markedly low in our Adapted and Positive profiles. Catastrophizing also emerged as a distinctive factor among FM profiles in previous studies [3, 51, 52]. Resilience factors were a distinguishing feature in our study. Additionally, cognitivebehavioural approaches increasing helpful thoughts and activities that bring pleasure and satisfaction were shown to be successful [53]. Therefore, it is valuable to include resilience factors when pursuing information about adaptation to FM.

Our study corroborated the agreed key roles of the psychological [3, 17-20, 51] and physical [17, 18, 51] function in FM. Previous research reported similar profiles to our Adapted [3, 17, 51], Positive [17] and Maladapted [3, 17-22, 51, 52] profiles. Inclusion of objective and subjective data was a distinguishing feature of our study, only performed in two previous studies with smaller sample sizes: n=57 [15] and n=107 [16]. The Maladapted profile showed unfavourable scores on all measures but not in declarative memory performance. This may reflect the same as a previous study demonstrating that subjective appraisal of memory rather than cognitive performance is related to adaptation to FM [13]. Moreover, our results suggest that cognitive performance deficits are specific to the Poor performer profile instead of a common feature of FM [13, 26]. Finally, also the Fit profile with relatively more favourable performance scores than subjective scores suggested the usefulness of distinguishing between objective and subjective scores. To summarize, inclusion of objective and subjective assessments of psychological and physical function yield information supplementary to previous profile studies. Specifically, inclusion of objective measurements helped us to further characterize profiles already suggested

previously (Adapted, Positive and Maladapted), and to find new profiles (Fit and Poor performer).

Although the profiles were determined based only on modifiable factors, the patients that were included in the profiles also reflected differences in hardly or non-modifiable characteristics (i.e. age, education level and working status). For instance. Fit and Poor performer included more vounger and older patients, respectively. Additionally, patients included in profiles also differ in the fulfilment of the FM criteria (i.e. clinical data). In the Adapted profile there was an increased percentage of people meeting the 1990 ACR criteria but not the modified 2011 preliminary FM criteria, while this percentage was decreased in the Maladapted profile. This suggests that the change in focus of the criteria from pain towards a broader view on multiple symptoms and features of FM [24] may lead to an inclusion of more patients with a Maladapted profile. Additionally, our profiles, overall, reflected a continuum in adaptation to FM, with the Adapted and Maladapted profiles located at the opposite ends, which is in agreement with previous literature [18, 20, 21, 23, 51], and with Fit, Poor performer and Positive profiles showing averaged scores on FM severity. This finding was consistent for FM impact and polysymptomatic distress. which suggests the clinical meaningfulness of our profiles in terms of adaptation.

Our profiles were based on eight factors that included a total of 31 variables. Obviously, it is not possible to assess all variables in the limited time that clinicians have in their daily practice. Ideally, one assessment of each factor should be taken. A very brief assessment of profiles could be to only assess catastrophizing (with the Pain Catastrophizing Scale that includes 13 items) and the 30-s chair stand test (a fast and easy test that only

requires 30 s to be performed). The factors catastrophizing and objective fitness showed the highest internal consistency, and differentiated quite well between the five clusters: markedly favourable catastrophizing and favourable physical performance for Adapted, average catastrophizing and favourable physical performance for Fit, average catastrophizing and unfavourable physical performance for Poor performer, markedly favourable catastrophizing and average physical performance for Positive, and markedly unfavourable catastrophizing and unfavourable physical performance for Maladapted. Research is required to empirically assess the heuristic inference that catastrophizing and the 30-s chair stand test provide an adequate reflection of the five clusters.

A core starting point of our study was that the profiles of the present study were based on modifiable factors (susceptible to targeting with therapies). Although clinical implications of these results need longitudinal and clinical experimental research, the results suggest that therapies might be tailored to the different profiles in FM [54]. Our profiles seem to indicate that it is especially important to improve the poor psychological function of patients with Fit and Maladaptive profiles, and to enhance the deteriorated physical function of people allocated in Positive, Poor performer and Maladapted profiles. Therefore, monotherapy (for Fit and Positive) or multi-component therapy (for Maladapted) may be indicated for different profiles. The worrisome cognitive performance deficit observed in Poor performer profile patients should be targeted in therapy. There is strong evidence of the effectiveness of physical exercise on FM symptoms [6]. Cognitive-behaviour therapy seems to be a most promising psychological approach to this disease [6]. The, at first glance, positive adaptation to FM of 16% of the sample (Adapted profile) seems to be a particular challenge. It would be interesting to test whether this subgroup differs from the general population to determine potential daily recommendations for patients allocated in such a profile. Keeping a healthy and positive lifestyle and attitude appears indeed the best way of dealing with FM. Consequently, future research should examine the inference from the current study that patients with specific adaptation profiles fit better to specific therapies.

In particular two limitations of the present study must be acknowledged. Its cross-sectional design impedes determination of causal relationships and we did not include a replication sample. Further research using longitudinal and clinical experimental designs and replicating our profiles in other samples is warranted. This study also has strengths. A large sample of FM patients was included. We performed an in-depth characterization of the clinical picture of FM including resilience and vulnerability factors, measured by objective and subjective assessments in a large sample, which is unique in regard to the literature.

To conclude, the present study suggests that heterogeneity of FM can be specified using a number of modifiable (could be targeted in therapy) resilience and vulnerability (adaptive and maladaptive) factors, measured by objective and subjective assessments, related to psychological and physical function. Five clinically meaningful profiles were found that seem to be on a continuum of symptom severity from Adapted (the most favourable) to Maladapted (the most unfavourable). Future research should aim to replicate our profiles in other samples, examine whether these profiles are predictive of health outcomes in longitudinal observational studies, analyse whether the effectiveness of interventions is different across these profiles and design profile-specific interventions.

Acknowledgements

The authors gratefully acknowledge all participants for their collaboration and enthusiasm. We would like to thank collaborators in the al-Ándalus project and all the members of the Physical Activity for Health Promotion (PA-HELP; CTS-1018) research group.

Funding: This work was supported by the Spanish Ministry of Economy and Competitiveness [I+D+i DEP2010-15639, I+D+i DEP2013-40908-R to M.D.-F.; BES-2014-067612 to F.E.-L.]; the University of Granada and CEI BioTic Granada [Mobility grant to F.E.-L.], the Consejería de Turismo, Comercio y Deporte, Junta de Andalucía [CTCD-201000019242-TRA to M.D.-F.]; the Spanish Ministry of Education [FPU2014/02518 to M.B.-C.]. The funders of the present study did not have any role in study design, data collection and analyses, decision to publish or preparation of the manuscript.

Disclosure statement: The authors have declared no conflicts of interest.

Supplementary data

Supplementary data are available at *Rheumatology* Online.

References

- 1 Sarzi-Puttini P, Atzeni F, Perrot S. Fibromyalgia syndrome: still a medical dilemma. Reumatismo 2012;64:183–5.
- 2 Choy EHS. The role of sleep in pain and fibromyalgia. Nat Rev Rheumatol 2015;11:513-20.
- 3 Giesecke T, Williams DA, Harris RE *et al.* Subgrouping of fibromyalgia patients on the basis of pressure-pain thresholds and psychological factors. Arthritis Rheum 2003;48:2916-22.
- 4 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;33:160–72.
- 5 Wolfe F, Clauw DJ, Fitzcharles M-A *et al.* Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia. J Rheumatol 2011;38:1113-22.
- 6 Macfarlane GJ, Kronisch C, Dean LE *et al*. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis 2017;76:318–28.

- 7 Estévez-López F, Gray CM, Segura-Jiménez V *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;24:1865–73.
- 8 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;27:83–92.
- 9 Stanton AL, Revenson TA, Tennen H. Health psychology: psychological adjustment to chronic disease. Annu Rev Psychol 2007;58:565–92.
- 10 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;155:292–8.
- 11 Turk DC. The potential of treatment matching for subgroups of patients with chronic pain: lumping versus splitting. Clin J Pain 2016;21:44–55.
- 12 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;72:963–6.
- 13 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.
- 14 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 2017 (in press) doi: 10.1080/09638288.2016.1258737.
- 15 Follick BT, Cherry BJ, Rutledge DN, Zettel-Watson L, Jones CJ. Heterogeneity in fibromyalgia based upon cognitive and physical performance and psychological symptomology. J Am Assoc Nurse Pract 2016;28:19–30.
- 16 Loevinger BL, Shirtcliff EA, Muller D, Alonso C, Coe CL. Delineating psychological and biomedical profiles in a heterogeneous fibromyalgia population using cluster analysis. Clin Rheumatol 2012;31:677–85.
- 17 Wilson HD, Robinson JP, Turk DC. Toward the identification of symptom patterns in people with fibromyalgia. Arthritis Rheum 2009;61:527–34.
- 18 Vincent A, Hoskin TLL, Whipple MOO *et al*. OMERACTbased fibromyalgia symptom subgroups: an exploratory cluster analysis. Arthritis Res Ther 2014;16:463.
- 19 de Souza JB, Goffaux P, Julien N *et al.* Fibromyalgia subgroups: profiling distinct subgroups using the Fibromyalgia Impact Questionnaire. A preliminary study. Rheumatol Int 2009;29:509–15.
- 20 Calandre EP, Garcia-Carrillo J, Garcia-Leiva JM *et al*. Subgrouping patients with fibromyalgia according to the results of the Fibromyalgia Impact Questionnaire: a replication study. Rheumatol Int 2011;31:1555-9.
- 21 Docampo E, Collado A, Escaramís G et al. Cluster analysis of clinical data identifies fibromyalgia subgroups. PLoS One 2013;8:e74873.
- 22 Rehm SE, Koroschetz J, Gockel U et al. A cross-sectional survey of 3035 patients with fibromyalgia: subgroups of

patients with typical comorbidities and sensory symptom profiles. Rheumatology 2010;49:1146-52.

- 23 Salaffi F, Mozzani F, Draghessi A *et al*. Identifying the symptom and functional domains in patients with fibro-myalgia: results of a cross-sectional Internet-based survey in Italy. J Pain Res 2016;9:279–86.
- 24 Segura-Jiménez V, Soriano-Maldonado A, Álvarez-Gallardo IC *et al*. Subgroups of fibromyalgia patients using the 1990 American College of Rheumatology criteria and the modified 2010 preliminary diagnostic criteria: the al-Ándalus project. Clin Exp Rheumatol 2016;34(2 Suppl 96):S26-33.
- 25 Yim Y-R, Lee K-E, Park D-J et al. Identifying fibromyalgia subgroups using cluster analysis: relationships with clinical variables. Eur J Pain 2016;21:374–84.
- 26 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;44:563–70.
- 27 Lobo A, Ezquerra J, Gómez Burgada F, Sala JM, Seva Díaz A. [Cognocitive mini-test (a simple practical test to detect intellectual changes in medical patients)]. Actas Luso Esp Neurol Psiquiatr Cienc Afines 1979;7:189-202.
- 28 Wiebe JS, Penley JA. A psychometric comparison of the Beck Depression Inventory-II in English and Spanish. Psychol Assess 2005;17:481–5.
- 29 Alonso J, Prieto L, Antó JM. [The Spanish version of the SF-36 Health Survey (the SF-36 health questionnaire): an instrument for measuring clinical results]. Med Clin 1995;104:771–6.
- 30 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.
- 31 Hita-Contreras F, Martínez-López E, Latorre-Román PA et al. Reliability and validity of the Spanish version of the Pittsburgh Sleep Quality Index (PSQI) in patients with fibromyalgia. Rheumatol Int 2014;34:929–36.
- 32 Munguia-Izquierdo D, Segura-Jiménez V, Camiletti-Moirón D *et al.* Spanish adaptation and psychometric properties of the Sedentary Behaviour Questionnaire for fibromyalgia patients: the al-Andalus study. Clin Exp Rheumatol 2013;31(6 Suppl 79):S22-33.
- 33 Guillén-Riquelme A, Buela-Casal G. [Psychometric revision and differential item functioning in the State Trait Anxiety Inventory (STAI)]. Psicothema 2011;23:510–5.
- 34 Vázquez C, Duque A, Hervás G. Satisfaction with life scale in a representative sample of spanish adults: validation and normative data. Span J Psychol 2013;16:E82.
- 35 Martín-Aragón M, Pastor MA, Rodríguez-Marín J *et al.* [Self-efficacy perception in chronic pain. Adaptation and validation of the chronic pain self-efficacy scale]. Rev Psicol la Salud 1999;11:53–75.
- 36 García Campayo J, Rodero B, Alda M *et al.* [Validation of the Spanish version of the Pain Catastrophizing Scale in fibromyalgia]. Med Clin 2008;131:487-93.
- 37 Librán E, Tous J. [Psychometric properties of the "Life Orientation Test" (LOT)]. Psicothema 2002;14:673–80.

- 38 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. Peer J 2016;4:e1822.
- 39 Álvarez-Gallardo IC, Soriano-Maldonado A, Segura-Jiménez V et al. International Fltness Scale (IFIS): construct validity and reliability in women with fibromyalgia: The al-Ándalus Project. Arch Phys Med Rehabil 2016;97:395-404.
- 40 Segura-Jiménez V, Alvarez-Gallardo IC, Romero-Zurita A *et al.* Comparison of physical activity using questionnaires (leisure time physical activity instrument and physical activity at home and work instrument) and accelerometry in fibromyalgia patients: the Al-Ándalus project. Arch Phys Med Rehabil 2014;95:1903–11.e2.
- 41 Salgueiro M, García-Leiva JM, Ballesteros J *et al.* Validation of a Spanish version of the Revised Fibromyalgia Impact Questionnaire (FIQR). Health Qual Life Outcomes 2013;11:132.
- 42 Segura-Jiménez V, Aparicio VA, Álvarez-Gallardo IC *et al.* Validation of the modified 2010 American College of Rheumatology diagnostic criteria for fibromyalgia in a Spanish population. Rheumatology 2014;53:1803–11.
- 43 Gronwall DMA. Paced auditory serial-addition task: a measure of recovery from concussion. Percept Mot Skills 1977;44:367–73.
- 44 Teruya LC, Ortiz KZ, Minett TSC. Performance of normal adults on Rey Auditory Learning Test: a pilot study. Arq Neuropsiquiatr 2009;67:224–8.
- 45 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;36:157-62.

- 46 Stevens JP. Applied Multivariate Statistics for the Social Sciences. 5th edn. New York: Routledge, 2012.
- 47 van Leeuwen N, Bossema ER, Knoop H et al. Psychological profiles in patients with Sjogren's syndrome related to fatigue: a cluster analysis. Rheumatology 2015;54:776-83.
- 48 Cross CL. Statistical and methodological considerations when using cluster analysis in neuropsychological research. In: Allen DN, Goldstein G, eds. Cluster Analysis in Neuropsychological Research. New York: Springer, 2013, 13–35.
- 49 Basu N, Jones GT, Macfarlane GJ, Druce KL. Identification and validation of clinically relevant clusters of severe fatigue in rheumatoid arthritis. Psychosom Med 2017 (in press) doi: 10.1097/PSY.000000000000498.
- 50 Field A. Discovering Statistics using IBM SPSS Statistics (and sex and drugs and rock "n" roll). 4th edn. London: SAGE Publications, 2013.
- 51 Luciano JV, García-Forero C, Cerdà-Lafont M *et al*. Functional status, quality of life, and costs associated with fibromyalgia subgroups: a latent profile analysis. Clin J Pain 2016;32:829–40.
- 52 Lukkahatai N, Walitt B, Espina A, Gelio A, Saligan LN. Understanding the association of fatigue with other symptoms of fibromyalgia: development of a cluster model. Arthritis Care Res 2016;68:99–107.
- 53 Bennett R, Nelson D. Cognitive behavioral therapy for fibromyalgia. Nat Clin Pract Rheumatol 2006;2:416-24.
- 54 van Koulil S, van Lankveld W, Kraaimaat FW *et al.* Tailored cognitive-behavioral therapy and exercise training for high-risk patients with fibromyalgia. Arthritis Care Res 2010;62:1377-85.