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RESEARCH ARTICLE

Mindfulness levels in patients with fibromyalgia following recommended pharmacological treatment: A multicenter, uncontrolled, one-year follow-up study

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KEYWORDS
Fibromyalgia;
Follow-up;
Mindfulness;
Pain

Abstract
Objectives. To assess the change in mindfulness levels at a one-year follow-up visit in patients with fibromyalgia (FM) who were following recommended pharmacological treatment and to identify the variables related to that change.
Methods. A one-year, uncontrolled, two-wave longitudinal multicentre study design. The study sample consisted of patients (n=269) with FM in primary care settings. Patients received the recommended pharmacological treatment for FM (pregabalin and, if they were diagnosed with depression, duloxetine). The main outcome variable was mindfulness, as measured by the Mindful Attention Awareness Scale (MAAS). Other psychological variables evaluated in this study included pain catastrophising, pain acceptance, mental defeat, psychological inflexibility, perceived injustice, and positive and negative affect. Spirituality, anxiety, depression, global function, pain and quality of life were also assessed.
Results. FM patients who followed recommended pharmacological treatment in primary care settings improved with regard to general function and pain (Cohen's d, 0.52 and 0.50, respectively) but decreased with regard to their mindfulness levels (d=0.49). After controlling for baseline mindfulness values, the variables included in the model that explained changes in mindfulness (r2=0.958, r2 change=0.140, $p<0.001$) were anxiety, pain acceptance, spirituality and psychological inflexibility. The final equation was significant, $F(6,193)=21.96$, $p<0.001$, and the model explained 95.83% of the variance.
Conclusion. This investigation is the first study to confirm that mindfulness levels decrease in FM patients who receive recommended pharmacological treatment. The identification of psychological variables that are related to this decrease can help to modify FM treatment protocols to increase treatment efficacy.

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PALABRAS CLAVE
Fibromialgia;
Seguimiento;
Mindfulness;
Dolor

Nivel de *mindfulness* en pacientes con fibromialgia tras el tratamiento farmacológico recomendado: estudio multicéntrico, no controlado y con un año de seguimiento

Resumen
Objetivos. Evaluar el cambio en el nivel de *mindfulness* al año de seguimiento en pacientes con fibromialgia (FM) que siguieron el tratamiento farmacológico recomendado e identificar las variables relacionadas con dicho cambio.
Métodos. Estudio multicéntrico, no controlado, longitudinal, de un año de seguimiento. La muestra consistió en n=269 pacientes con FM, procedentes de atención primaria. Los pacientes recibieron el tratamiento farmacológico recomendado para la FM (pregabalina, y si habían sido diagnosticados de depresión, duloxetina). La variable principal fue *mindfulness*, medida mediante la escala *Mindful Attention Awareness Scale* (MAAS). Otras variables psicológicas evaluadas en este estudio fueron la «catastrofización» ante el dolor, la aceptación del dolor, el hundimiento mental, la inflexibilidad psicológica, la injusticia percibida, y el afecto negativo y positivo. También fueron evaluadas la espiritualidad, la ansiedad, la depresión, la función global, el dolor y la calidad de vida.
Resultados. Los pacientes con FM que siguieron el tratamiento farmacológico recomendado en atención primaria mejoraron respecto a la función general y el dolor (*d* de Cohen, 0,52 y 0,50, respectivamente) pero disminuyeron los niveles de *mindfulness* (*d*=0,49). Tras controlar para los valores iniciales de *mindfulness*, las variables incluidas en el modelo que explicaban los cambios en *mindfulness* (r2=0,958, r2 cambio=0,140, $p<0,001$) fueron la ansiedad, la aceptación del dolor, la espiritualidad y la flexibilidad psicológica. La ecuación final fue significativa $F(6.193)=21,96$, $p<0,001$), y el modelo explicaba el 95,83% de la varianza.
Conclusión. Este es el primer estudio que confirma que los niveles de *mindfulness* disminuyen en los pacientes con FM que reciben el tratamiento farmacológico recomendado. Identificar las variables psicológicas relacionadas con esta disminución puede ayudar a modificar el protocolo terapéutico de la FM para aumentar la eficacia del tratamiento.

Introduction

Fibromyalgia (FM) is a disabling syndrome that is characterised by a history of widespread pain, experienced for at least three months, and tenderness in at least 11 of 18 predefined tender points following digital palpation with a force of approximately 4 kg/cm^2. FM is associated with a myriad of symptoms, such as generalised muscle ache, stiffness, fatigue and non-restorative sleep (Wolfe, Smythe, Yunus, 1990). FM is a common disorder with a European prevalence ranging from 2.2 to 6.6% and predominantly occurs in women in their thirties to fifties (Branco, Bannwarth, Failde, et al., 2010). FM is at least twice as common as rheumatoid arthritis and is considered to be a significant public health problem. The aetiology of FM is uncertain; however, the existence of central sensitisation is widely accepted (Smith, Harris, Clauw, 2011).

A recent FM treatment network meta-analysis (Nüesch, Häuser, Bernardy, et al., 2013) indicated statistically significant advantages of pharmacological interventions (i.e., SNRIs and pregabalin) over placebo with respect to pain and quality of life. Cognitive Behavioural Therapy (CBT) appears to be the best psychological intervention, although Bernardy et al. (Bernardy, Füber, Köllner, et al., 2010) noted the absence of any positive effects from CBT on the key symptoms of FM (pain, fatigue, or sleep) in patients.

Burgeoning evidence from randomised controlled trials supports the effectiveness of mindfulness-based therapies for the treatment of chronic pain conditions (Veehof, Oskam, Schreurs, et al., 2011; Zeidan, Gordon, Merchant, et al., 2010; Zeidan, Martucci, Kraft, et al., 2011). The diverse mechanisms that underlie the effects of mindfulness training on health and well-being include increased control of attention, awareness of inner experiences, emotional regulation, and changes in the concept of self or body awareness (Hölzel, Lazar, Gard, et al., 2011). Some studies have suggested that mindfulness alters the contextual evaluation of pain (Zeidan, Gordon, Merchant, et al., 2010) and reduces pain catastrophising and pain sensitivity (Zeidan, Martucci, Kraft, et al., 2011). For these reasons, mindfulness training is considered to be a promising alternative or supplement to current interventions for FM (Goldenberg, Kaplan, Nadeau, et al., 1994; Grossman, Tiefenthaler-Gilmer, et al., 2007; Schmidt, Grossman, Schwarzer, et al., 2011).

Mindfulness-based therapies may be particularly effective as an early intervention for at-risk patients and may play an important role in chronic pain screening and early intervention (Schütze, Rees, Preece, et al., 2010). This postulation suggests an early inclusion of mindfulness within the fear-avoidance model and argues that low levels of mindfulness could be a vulnerability factor in early pain management (Schütze, Rees, Preece, et al., 2010). Quick measures of

mindfulness are a potentially useful screening tool during acute pain episodes (Crombie, Davies, Macrae, 1998).

To our knowledge, no previously study has examined whether mindfulness levels change over time in FM patients following pharmacological treatments. The aim of this study was to assess changes in mindfulness levels at a one-year follow-up visit in patients with FM that followed the recommended pharmacological treatment and identify the psychological variables involved in those changes.

Materials and Methods

Study Design: This investigation was a one-year, two-wave longitudinal, uncontrolled, multicentre study.

Setting and Study Sample: Patients were recruited from the 24 primary care health centres in Zaragoza, Spain. General practitioners recruited FM patients who met the inclusion criteria until the required sample was obtained. We did not assign a quota of patients for each centre. Patients who were considered for inclusion were adults between 18 and 65 years of age who were able to understand and read the Spanish language and met the criteria for FM according to the American College of Rheumatology (Alda, Luciano, Andrés, Serrano-Blanco, Rodero B, del Hoyo, et al., 2011). Additionally, the participants must not have received psychological treatment during the 2 years prior to the study, and must have agreed to follow the recommended pharmacological treatment for FM while not receiving psychological or non-pharmacological non-psychological FM treatment for the one-year duration of the study. Participants also provided written informed consent. We excluded patients with severe Axis I psychiatric disorders (e.g., dementia, schizophrenia, paranoid disorder, alcohol and/or drug use disorders), severe Axis II disorders, somatic disorders when a clinician determined that the patient was unable to complete a psychological assessment, and women who were pregnant or nursing. Some of the patients were recruited from the control groups (recommended pharmacological treatment) of previous studies that assessed the efficacy of psychological treatments in FM (Luciano, Guallar, Aguado, López-Del-Hoyo, Olivan, Magallón, 2014; Briley, 2010). According to the Ethics Committee, a controlled study with a placebo arm was unacceptable when investigating a disorder with a recommended pharmacological treatment.

Recommended Pharmacological Treatment: In 2007, the United States Food and Drug Administration (FDA) approved pregabalin as the first-line drug to manage the symptoms of FM. Within 18 months, the FDA also approved duloxetine and milnacipran for the same purpose. Although these drugs are currently marketed in Europe for other purposes, European regulatory authorities recently rejected proposals to extend their approval of these drugs to include the treatment of FM (Briley, 2010). On the basis of the FDA recommendations and the Spanish Consensus for the Treatment of Fibromyalgia (Alegre de Miquel, García-Campayo, Tomás Florez, Gómez Argüeles, Blanco Tarrio, Gobbo Montoya, 2010), treatment with pregabalin (300 to 600 mg/day) and duloxetine (60 to 120 mg/day) was administered to patients in this study that had major depressive disorder diagnosed according to their psychiatric interview. When pregabalin and/or duloxetine are not tolerated, the clinical guide recommends substituting these medications with gabapentin and/or venlafaxine, respectively. Small and occasional doses of non-opioid analgesics for pain and benzodiazepines for anxiety and/or insomnia were permitted. Non-pharmacological non-psychological therapies were not allowed during the study.

Measurements

Socio-demographic and Clinical Variables: The following socio-demographic data were collected: gender, age, marital status (single, married/in a relationship, separated/divorced, or widowed), educational level (no formal studies, primary, lower secondary, upper secondary, or university) and occupation. We recorded relevant clinical variables (i.e., years since diagnosis and main clinical symptoms), pharmacological and psychological treatment data and referrals to other medical specialties. Finally, self-reported spirituality was assessed utilising a 0-100 analogue visual scale.

Main Outcome Variable

Mindfulness: This study employed the Mindful Attention Awareness Scale (Brown, Ryan, 2003), which is one of the most widely utilised instruments to assess mindfulness traits. Respondents completed the 15-item self-administered scale to indicate the frequency of the experience described in each statement on the scale. Respondents answered with a 6-point Likert-type scale ranging from 1 (almost always) to 6 (almost never); higher scores reflect greater mindfulness. To monitor for socially desirable responses, respondents were asked to answer according to what 'really reflects' their experience rather than what they believe their experience should be. The items are distributed across cognitive, emotional, physical, interpersonal and general domains. The psychometric properties of the questionnaire are adequate (Brown, Ryan, 2003). We utilised a Spanish version of this instrument (Soler, Tejedor, Feliu-Soler, et al., 2012) that has previously demonstrated adequate psychometric properties for FM (Cebolla, Luciano, Piva Demarzo, et al., 2013).

Pain-related Psychological Constructs

- *Pain catastrophising:* One of the most frequently utilised questionnaires for measuring this construct is the Pain Catastrophising Scale (PCS) (Sullivan, Bishop, Pivik, 1995). This instrument is a 13-item self-administered questionnaire that assesses the following three dimensions: rumination, magnification and helplessness. Each item is scored from 0 (not at all) to 4 (always); total scores range from 0 to 52. This instrument has good temporal stability, internal consistency and construct validity. The Spanish version of this scale was utilised (García-Campayo, Rodero, Alda, et al., 2008).
- *Pain acceptance:* This variable was assessed with the Chronic Pain Acceptance Questionnaire (CPAQ) (Vowles, Eccleston, 2004). This instrument is a 20-item self-administered questionnaire. All items are rated on a scale from 0 (never true) to 6 (always true). The maximum total

score is 120; higher scores indicate greater acceptance. The Spanish version of this questionnaire was utilised (Rodero, García-Campayo, Casanueva, et al., 2010).

- *Mental defeat* (Tang, Salkovskis, Hanna, 2007): This concept was evaluated with the Pain Self-Perception Scale (PSPS). This instrument is a 24-item self-administered scale. The statements are rated on a 5-point scale (0=Not at all/Never, 1=Very little, 2=Moderately, 3=Strongly, 4=Very strongly), generating a total score that ranges from 0 to 96; higher scores indicate elevated levels of mental defeat. The validated Spanish version was utilised (García-Campayo, Rodero, del Hoyo, et al., 2010).
- *Pain psychological inflexibility* (Wicksell, Renöfält, Olsson, et al., 2008): The Psychological Inflexibility in Pain Scale (PIPS) was developed to assess this core construct in Acceptance and Commitment Therapy (ACT). This instrument is a 16-item self-administered questionnaire. Participants are asked to rate how true certain statements are utilising a 7-point Likert-type scale that ranges from '1=never true' to '7= always true'; higher scores indicate more psychological inflexibility. The psychometric properties of this instrument are considered to be adequate. The validated Spanish version of this test was utilised in this study (Rodero, Pereira, Pérez-Yus, et al., 2013).
- *Perceived injustice:* The Injustice Experience Questionnaire (IEQ) (Sullivan, Adams, Horan, et al., 2008) is a 12-item self-report measure that was developed to measure this concept. This instrument addresses the degree to which individuals perceive their post-disorder life as being characterised by injustice. The psychometric properties of the IEQ are considered to be adequate. The Spanish version of this test was utilised in this study (Rodero, Luciano, Montero-Marín, et al., 2012).
- *Positive and negative affect:* Both dimensions were measured utilising the Positive and Negative Affect Scale (PANAS) (Watson, Clark, Tellegen, 1988). The PANAS consists of two mood scales with 10 items each that assess positive and negative affects. The scores for each scale range from 0 to 50. These scales have shown adequate psychometric properties. The Spanish version of the PANAS was utilised in this study (Sandín, Chorot, Lostao, et al., 1999).

Other Variables

- *Hospital Anxiety and Depression Scale (HADS):* This instrument is a self-reported scale that is designed to screen for the presence of depression and anxiety disorders in medically ill patients. The instrument contains 14 items that are rated on a four-point Likert-type scale. Two subscales independently assess depression and anxiety (HADS-Dep and HADS-Anx, respectively) (Zigmond, Snaith, 1983). Patients with 14 or more points on the entire scale (or more than eight points on either of the two subscales) are considered to be 'probable cases' of anxiety and/or depression. In addition to anxiety and depression, we utilised a composite outcome of anxiety-depression because some authors have recommended using the total score to indicate emotional distress (Vallejo, Rivera, Esteve-Vives, et al., 2012). The Spanish version of this questionnaire was utilised in this study (Herrero, Blanch, Peri, et al., 2003).
- *Fibromyalgia Impact Questionnaire (FIQ)* (Burckhardt, Clark, Bennet, 1991): The FIQ is a 10-item self-report questionnaire that was developed to measure the functional status of FM patients. The first item focuses on the patient's ability to participate in muscle movement activities. The next two items ask patients to specify the number of days within the past week that they felt good and to indicate how often they missed work. Finally, the last seven questions (which address job ability, pain, fatigue, morning tiredness, stiffness, anxiety and depression) are measured utilising a Visual Analogue Scale (VAS). The total score on the FIQ ranges from 0 to 100; a higher score indicates a poorer functional status. The Spanish validated version was utilised in this study (Rivera, Gonzalez, 2004).
- *Pain Visual Analogue Scale (PVAS):* The PVAS was designed to allow for a thorough and comprehensible subjective assessment of pain. A visual analogue scale is typically a 10 cm horizontal line with perpendicular lines on each edge that define the extreme limits of the pain experience. Anchoring points at each edge are characterised by verbal expressions such as 'no pain' (accompanied by the number '0') at one end and 'the maximum pain ever experienced' (accompanied by the number '100') at the other end. Previous studies have demonstrated sound psychometric properties of the PVAS (Huskisson, 1983).
- *The EuroQol-5D questionnaire (EQ-5D):* The EQ-5D is a generic two-section instrument utilised to assess health-related quality of life (Brooks, Rabin, De Charro, 2003). Section 1 records the patient's self-reported problems in the following five domains: mobility, self-care, routine activities, pain and/or discomfort and anxiety and/or depression. Each domain is divided into three levels of severity that correspond to the following: no problems, some problems or extreme problems. Section 2 records the patient's self-assessed health on a VAS, which is a 10 cm vertical line on which the best and worst imaginable health states are scored as 100 and 0, respectively. We utilised the validated Spanish version of the EQ-5D in this study (Badía, Roset, Montserrat, Herdman, Segura, 1999).
- *The Mini International Neuropsychiatric Interview (MINI)* (Lecrubier, Sheehan, Weiller, et al., 1997) is a short, structured psychiatric interview that allows for the diagnosis of a patient's main psychiatric diagnosis according to the DSM-IV and ICD-10 classifications. It is divided into several modules that assess different diagnostic categories. This psychiatric interview has been translated and validated in numerous languages including Spanish (Ferrando, Soto, Bobes, Soto, Franco, Gubert, 1998).

Procedures

General practitioners recruited newly diagnosed FM patients from the selected health centres until the required sample size was reached. Trained researchers administered the questionnaires at baseline to assess socio-demographic variables, main outcomes, other variables, and pain-related psychological constructs. At the one-year follow-up visit, researchers that were unaware of the baseline results administered the main outcome variable measures to the same patients. The doctors that participated in the study received specialised training on the Spanish consensus for the treatment of FM (Alegre de Miquel, García-Campayo, Tomás Florez, Gómez Argüeles, Blanco Tarrio, Gobbo Montoya, et al., 2010). This con-

sensus includes the need to refer the patient to a rheumatologist to confirm their diagnosis. Data collection was conducted between January 2012 and June 2014.

Sample Size

To calculate the required sample size, we considered the population of patients suffering from FM only in the region of Aragón, Spain. Epidemiological studies (Branco, Bannwarth, Failde, et al., 2010) indicate that the prevalence of FM in Spain is approximately 2-3%. The population of Aragón is estimated to be 1,150,000 persons; therefore, prevalence data suggest that approximately 25,000 inhabitants of Aragón have FM. Assuming a confidence level of 95%, an estimated error of 5%, and the most unfavourable assumption (p=0.5), a sample size of 265 patients was necessary in this study for an accuracy of 3%. EPIDAT 3.1 was utilised to calculate the sample size.

Statistical Analyses

At baseline, the mean and standard deviation values were calculated for continuous variables that displayed normality; the median values and interquartile periods were calculated when this criterion was not fulfilled. The Kolmogorov-Smirnov test was applied to adjust the data to a normal distribution. We analysed the differences in socio-demographic variables, main outcomes and other pain-related psychological construct variables. These differences were calculated using the Chi-squared test for categorical variables or Fisher's exact test when appropriate. To determine the relationships between categorical variables and one- or two-level variables or quantitative variables, Student's t-test or an ANOVA were utilised, respectively, for all variables that fulfilled the normality assumption. For the remaining variables, non-parametric tests such as the Mann-Whitney U test or the Kruskall-Wallis test were utilised. The outcomes were illustrated as the means of the effect sizes; Cohen's d was reported for each comparison. The convention for Cohen's d states that a value of 0.20 is small, 0.50 is medium, and 0.80 is large.

A Spearman's rho non-parametric correlation matrix was developed to determine the relationships and possible overlap between pain-related psychological constructs. We included these constructs and other variables in the analyses of the significance of this matrix as well as in each of the calculated correlations.

Finally, we conducted hierarchical multiple regression analyses (adjusted for baseline values) to assess the predictive validity of the different variables in the study on the main outcome (mindfulness) at the one-year follow-up visit. The R squared value measured the goodness of fit and the validity of the model was assessed utilising the following three parameters: (a) absence of heteroskedasticity (using the Breusch-Pagan statistic); (b) absence of collinearity among independent variables (using the Variance Inflation Factor, VIF, which should be <10), and (c) residual analysis (a normal distribution should be presented with a mean=0) (Kline, 2005). The data were analysed utilising the SPSS 19 statistical package.

Ethical Considerations

Informed consent was obtained from all participants prior to the study. Prior to giving their consent, the patients received a general overview of the objectives and characteristics of the study. The respondents were informed that their participation was voluntary and that they could choose to withdraw from the study at any time, with a guarantee that they would continue to receive the treatment that their doctor considered to be the most appropriate. The study followed the norms of the Helsinki Convention and its subsequent modifications and adhered to the Declaration of Madrid of the World Psychiatric Association. The study protocol was approved by the ethical review board of the regional health authority.

Results

Characteristics of the study sample

A total of 292 patients were interviewed during the recruitment period. A rheumatologist had not diagnosed 5 patients (1.7%); 2 patients (0.6%) were excluded due to a severe Axis I psychiatric disorders (opioid use disorder); 5 patients (1.7%) were excluded because they did not understand Spanish; and 11 patients (3.7%) decided to withdraw from the study. The final sample included 269 patients.

The majority of the patients were female (258 patients, 95.9%), middle-aged (mean age=52.1 years, SD=8.5), of European ethnic descent (N=269, 100%), married or in a relationship (199, 73.9%), and had reached a medium educational level (187, 69.5% primary or secondary education). A total of 58 patients (21.5%) received a disability pension. The mean duration of their illness was 17.9 months (SD=11.5). Their mean spirituality score, on a 0-100 scale, was 52.34 (SD=30.53).

Pharmacological and non-pharmacological treatments

At the one-year follow-up visit, no patients had received psychological or non-psychological non-pharmacological treatment. All of the FM patients had received pharmacological treatment, which mainly consisted of analgesics such as pregabalin (226, 84.02%) or gabapentin (43, 15.98%) and antidepressants such as duloxetine (143, 53.1%) or venlafaxine (18, 6.69%). The patients were also given benzodiazepines (69, 25.6%) or other allowed analgesics (141, 52.4%).

Differences in study variables at the one-year follow-up

The mean and standard deviation values of the studied variables at baseline and the one-year follow-up visit are shown in Table 1. Mindfulness significantly decreased (with moderate size effect) at the one-year follow-up visit. Some outcome variables significantly improved, such as pain measured with sphygmomanometer (large size effect), the pain visual analogue scale (moderate size effect) and the FIQ (moderate size effect). Finally, some pain-related variables such as mental defeat, perceived injustice and psychological inflexibility improved with a small size effect.

Table 1 Mean (M) and standard deviation (SD) of the study variables at baseline and the 1-year follow-up visit (N=269)

Psychological variables	Baseline Mean (SD)	1-year follow-up Mean (SD)	*p*-value (Cohen's *d*)
Mindfulness (MAAS)	57.47 (17.42)	49.43 (14.91)	0.001* (0.49)
Spirituality	52.34 (30.53)	51.86 (29.94)	0.853
Pain catastrophising (PCS)	24.53 (13.64)	23.26 (13.14)	0.142
Pain acceptance (CPAQ)	47.62 (23.16)	48.43 (21.33)	0.232
Mental defeat (PSPS)	48.07 (32.51)	40.75 (28.43)	0.001* (0.23)
Perceived injustice (IEQ)	30.17 (12.12)	27.58 (10.97)	0.001* (0.22)
Psychological inflexibility (PIPS)	57.29 (18.18)	53.46 (15.44)	0.001* (0.22)
Anxiety (HADS-A)	10.81 (4.94)	10.38 (4.63)	0.632
Depression (HADS-D)	7.80 (4.68)	7.24 (4.34)	0.072
Emotional distress (HADS)	18.61 (8.71)	17.63 (7.83)	0.179
Positive affect (PANAS-PA)	25.19 (8.42)	24.53 (7.72)	0.343
Negative affect (PANAS-NA)	24.19 (9.03)	24.45 (8.21)	0.726
Pain sphygmomanometer	112.72(47.07)	77.88 (40.47)	0.001* (0.79)
Pain (PVAS)	66.57 (20.36)	55.82 (22.21)	0.001* (0.50)
Functional impairment (FIQ)	59.23 (14.97)	51.43 (14.63)	0.001* (0.52)
Quality of life (EQ-5D)	47.42 (19.74)	49.87 (20.18)	0.186

*Significant differences.

Psychological predictors of mindfulness in fibromyalgia

A longitudinal model of mindfulness in fibromyalgia was constructed with a hierarchical multiple regression analysis. The results of this analysis are displayed in Table 2. As expected, mindfulness at baseline explained a significant amount of the variance (r2=0.813, $p<0.001$) in mindfulness one year later. After controlling for the baseline MAAS value, the independent variables that we finally entered into the model (r2=0.958, r2 change=0.140, $p<0.001$) were as follows: anxiety, pain acceptance, spirituality and psychological inflexibility. The final equation was significant, $F(6,193)=21.96$, $p<0.001$, and the model explained 95.83% of the overall variance. The Breusch-Pagan *p*-value was 0.967.

Discussion

This uncontrolled one-year follow-up study confirms that FM patients who follow the recommended pharmacological treatment (pregabalin for pain and, if they have been diagnosed with depression, duloxetine) present with a significant and clinically moderate decrease in mindfulness levels. This is the first study to demonstrate this finding. The other results presented in this study were expected. Pharmacological treatment significantly improves most of the following outcome variables: global function measured by FIQ (moderate size effect), pain measured by the VAS (moderate size effect), and pain measured by sphygmomanometer (large size effect). Quality of life, measured by the EQ-5D, was the only variable that was not modified. This result may be expected because some meta-analyses have confirmed that most treatments are not effective at improving EQ-5D scores in FM (Bernardy, Füber, Köllner, et al., 2010). Finally, most of the psychological variables were not improved except, at a small level, the following three items: psychological inflexibility, mental defeat and perceived injustice. This is also conceivable, as no psychological treatments were used.

Because this investigation was not a controlled study, we cannot be certain that the significant and moderate improvements in the outcome variables were due to the prescribed treatment. Other potential explanations include the natural evolution of this disorder. However, a recent meta-analysis on the efficacy of pharmacological and psychological treatments for FM in primary care also showed moderate improvements in the outcome variables measured in our study (Garcia-Campayo, Magdalena, Magallón, et al., 2008); therefore, the observed improvements can be reasonably attributed to the treatment.

The occurrence of decreased mindfulness scores alongside improvements in global function and pain seems to be counterintuitive. We have previously demonstrated that patients with fibromyalgia show significantly lower levels of mindfulness compared to healthy controls (Cebolla, Luciano, Piva Demarzo, et al., 2013). However, this decrease in mindfulness levels after one year of standard treatment could be explained by several reasons. This decrease could be a side effect of the pharmacological treatments for FM (e.g., antidepressants, benzodiazepines and analgesics); however, we are not aware of any specific studies that demonstrate the association between psychopharmacological treatments and mindfulness (Berger, Sadosky, Dukes, et al., 2010). A second probable reason could be the cognitive impairment associated with FM (Glass, 2008), as a consequence of the brain changes that are produced by this disorder. Research has indicated that the amount of glutamate, an important mediator in the neurotransmission of chronic pain sensitisation and cognitive dysfunction (Dickenson, 2002), significantly increases in the posterior cingu-

Table 2 Psychological variables that predict mindfulness in fibromyalgia patients

Psychological variables (baseline values)	Coefficient	*p*-value	95% Confidence interval
Adjusted variable			
Mindfulness (MAAS)	0.38	0.000	0.26 to 0.51
Predictors			
Anxiety (HADS-A)	-0.59	0.013	-1.05 to -0.12
Pain acceptance (CPAQ)	0.19	0.001	0.07 to 0.30
Spirituality	0.06	0.029	0.01 to 0.12
Psychological inflexibility (IEQ)	0.22	0.003	0.08 to 0.37

A hierarchical multiple regression model was used to predict mindfulness at the 1-year follow-up visit. Only significant variables at 5% are shown.

late of patients with FM (Fayed, Andres, Rojas, et al., 2012). On the contrary, glutamate levels significantly decrease in long-term meditators compared with healthy non-meditators; this reduction is associated with years of meditation (Fayed, Andres, Rojas, et al., 2012). A third possible explanation suggests that distraction is a potentially useful strategy for decreasing acute pain intensity (Kohl, 2013), making mindfulness a skill that is more difficult to develop in chronic pain patients.

Regardless of the aetiology of the mindfulness score decrease in FM patients, mindfulness is a relevant factor that affects the outcome of these patients (Veehof, Oskam, Schreurs, et al., 2011; Grossman, Tiefenthaler-Gilmer, et al., 2007- Schütze, Rees, Preece, et al., 2010); strategies for improving mindfulness in this population would be useful. Knowing the long-term variables that are related to mindfulness in patients with FM can be useful to modify and improve the treatment of these patients. In our study, anxiety, pain acceptance, spirituality and psychological inflexibility were related to mindfulness at the one-year follow-up visit.

The inverse relationship between anxiety and mindfulness is well known. Mindfulness-based approaches have been shown to be effective treatments for anxiety disorders (Hofmann, Sawyer, Witt, et al., 2010). Mindfulness techniques must be adapted to accommodate the difficulties in clinical practice among patients with anxiety (Orsillo, Roemer, 2005). Previous studies have shown that pain acceptance plays an important role in the treatment of FM (Rodero, Casanueva, Luciano, et al., 2011) and explains 24% of the variance in the general health of patients with chronic pain, whereas pain itself only accounts for 9% of the variance (McCracken, Velleman, 2010). Previous research has demonstrated the relevant role of pain acceptance in the treatment of FM (Luciano, Guallar, Aguado, López-Del-Hoyo, Olivan, Magallón, et al., 2014); however, this study suggests that this effect could be related to mindfulness levels.

The relationship between mindfulness and spirituality is not new. Previous studies have demonstrated that the practice of mindfulness increases spirituality and that both mindfulness and spirituality increase as psychological and medical symptoms improve (Carmody, Reed, Kristeller, et al., 2008). Other studies have utilised structural equation modelling to suggest that increased daily spiritual experiences following mindfulness techniques may partially explain improved mental health as a function of greater mindfulness (Greeson, Webber, Smoski, et al., 2011). However, our investigation is the first that shows that baseline spirituality is associated with a higher mindfulness score at a one-year follow-up.

The main limitation of this study is that it is not controlled; therefore, outcomes cannot be exclusively attributed to the prescribed treatment. Another study limitation is the possibility that not all of the relevant pain-related constructs were included. Some constructs are unknown or difficult to measure. Another limitation is that some experts have criticised the concept of constructs such as catastrophising (Tang, Salkovskis, Poplavskaya, et al., 2007) and even mindfulness (Grossman, 2011); these critics suggest the need for new assessment tools. Finally, spirituality is a complex concept and the VAS may be considered to be an oversimplified method of measurement.

In conclusion, mindfulness seems to decrease over time in FM patients who have received the recommended pharmacological treatment, even when significant improvements in relevant outcome variables (e.g., global function or pain) were observed. This study identified the variables that best predict mindfulness levels in these patients. These findings should be replicated in controlled studies. FM treatment protocols should consider these variables and act upon them when possible. Mindfulness-based therapies may be particularly effective as early interventions for at-risk individuals.

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