Alexithymia is associated with mood disorders, impairment in quality of life and disability in women with fibromyalgia

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ABSTRACT

Objective. *Alexithymia is a personality trait related to the quality of life of women with fibromyalgia (FM). It is still unknown whether alexithymia is associated with the clinical manifestations of FM. The present study describes the relationship between alexithymia and the domains included in the core set recommended by the Outcome Measures in Rheumatology (OMERACT) for FM evaluation.*

Methods. *One hundred and two women with FM were enrolled in the cross-sectional study. The domains evaluated were alexithymia, pain, fatigue, health-related quality of life, sleep quality, depression, anxiety, and disability. Univariate and multivariate (Kernel Regularized Least Squares method) analyses were performed to assess the relationship between alexithymia and the domains included in the core set recommended by the OMERACT.*

Results. *Alexithymia prevalence was 64.5% (95% Confidence Interval [CI], 54.6%–73.9%) and higher in women with depression (76.1%; 95%CI, 63.8%-86%). Female patients with FM and alexithymia showed higher pain intensity, anxiety and depression levels, and disability perception and lower quality of life, as compared to those with FM without alexithymia. Size effect differences ranged from medium to large and all of them were statistically significant ($p<0.05$). Using multivariate analysis, alexithymia was significantly associated with worse perceptions of quality of life (except physical health domain) and more disability perception, independently of other variables. However, alexithymia was not significantly associated with pain intensity.*

Conclusion. *Alexithymia plays an important role in clinical manifestations of FM, mainly in the psychological and social dimensions of quality of life and the degree of perceived disability.*

Introduction

Fibromyalgia (FM) is a chronic disease defined by musculoskeletal pain and hyperalgesia, coupled with medically unexplained symptoms (1, 2). Although it is not considered a psychiatric disease, there is evidence demonstrating a high prevalence of psychiatric comorbidity, mainly in stress and mood disorders (3, 4). In FM patients, psychological distress and psychiatric disorders could play an important role in symptom emergence, intensification, or maintenance; these factors could even negatively influence functional ability and pain perception (4, 5). Cognition and emotional regulation in people with FM could be relevant for pain management, adjustment to FM impact, and quality of life (1). Several psychological conditions, such as depression, anxiety, and stress, have been associated with disability (6-11). Among these psychological conditions, the relationship between alexithymia and disability is the least explored.

The alexithymia construct is comprised of four components: difficulty identifying feelings and distinguishing between feelings and the bodily sensations of emotional arousal; difficulty describing feelings to others; a stimulus-bound, externally orientated cognitive style; and constricted imaginal processes (12-14). Alexithymia is not considered a disease by itself; it does not even describe any disease, but it is conceived as a personality trait associated with higher vulnerability to mental disorders (mainly depression and anxiety), and it is also related to psychosomatics and medical disorders (*e.g.* chronic pain and FM) (4, 13, 15-17).

The study of alexithymia and FM is important since alexithymia could interfere with the perception of emotional sensations, causing an excessive perception of psychosomatic symptoms, as well as an excessive use of medical care (1, 4, 18, 19). Most studies have revealed a higher prevalence of alexithymia in people with FM, as compared to the general population and to other reasons for chronic pain (3, 17, 19-23); nevertheless, other studies have not shown these differences (15, 24). In fact, the exact role of alexithymia in FM has not been completely elucidated. The first studies about this relationship reported correlations with affective pain, depression, anxiety, neuroticism, and health-related quality of life (17, 25). However, other reports have brought into question an association between somatic symptoms and alexithymia (17, 20).

Since the association between alexithymia and FM is debatable, its evaluation is not a common practice (16). The aim of the present study is to describe the relationship between alexithymia and the domains included in the core set (pain, fatigue, health-related quality of life, physical function, sleep, depression, and anxiety) recommended by the Outcome Measures in Rheumatology (OMERACT) to evaluate FM (26) in a sample of patients from an outpatient care clinic. In order to define alexithymia's role of in FM, a group of FM subjects with alexithymia and another group of FM patients without alexithymia were compared. It was hypothesised that the presence of alexithymia would be associated with higher pain scores, pain catastrophising, anxiety, depression, insomnia, fatigue, disability, and reduced quality of life.

Table I. Sociodemographic and clinical data of patients.

	Nonalexithymic group (n=36)	Alexithymic group (n=66)	*p*-value effect	Size (n=102)	All patients
Age (years)	50.13 ± 6.22	47.40 ± 7.06	0.05	0.40	48.37±6.87
Years of education	10 ± 4.14	10.31 ± 2.91	0.66	0.09	10.20±3.37
Body Mass Index	28.39 ± 3.65	28.72 ± 3.39	0.65	0.09	28.59±3.47
Pain duration (months)	60 (48)	36 (36)	0.01	0.25	48 (48)
Time since fibromyalgia diagnosis (months)	36 (46.5)	24 (34)	0.03	0.22	24 (44.5)
		Frequency (n)	Percentage (%)		
Socioeconomic level					
High		6	5.8		
Medium		57	55.8		
Low		39	38.2		
Occupation					
Unemployed		4	4.9		
Employee		49	48		
Retired		2	1.9		
Housewife		46	45.1		
Comorbidity					
None		57	55.9		
Obesity		34	33.3		
Hypertension		8	7.2		
Hypothyroidism		5	4.9		
Osteoarthritis		3	2.9		
Hyperlipidaemia		2	1.9		
Diabetes		2	1.9		
Hiatal hernia		1	0.9		
Glaucoma		1	0.9		
Epilepsy		1	0.9		
Temporomandibular joint dysfunction		1	0.9		

Data: Mean ± standard deviation. Median (interquartile range)

Materials and methods

A cross-sectional study was carried out from May 2015 to December 2017 using a non-probabilistic sampling of consecutive cases at the outpatient clinic of rheumatology at a secondary care hospital. Patients included recent and previously FM diagnosed subjects, invited to participate while they checked-in. Women aged 18 years and older who fulfilled the preliminary criteria of an FM diagnosis (27) were included in the study. Men with FM (n=3) and patients with an acute disease that could modify their symptoms (*e.g.* fracture, trauma, fever, infection), a coexisting rheumatic disease (*e.g.* rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis), psychosis, or suicide attempts in the last three months were not included. The study was approved by the research and ethics committee (R-2014-1503-88), and patients signed an informed consent to participate.

A sample size of 60 was set, assuming about a 20% dropout rate, α error of 0.05, and 95% power to detect an effect size of 1.06 on pain score (27 subjects on anxiety score, effect size of 1.70; 36 subjects on depression score, effect size of 1.41) as found by Di Tella *et al*. (2). Within the study period, 108 women with FM were evaluated, and six of them (5.5%) were excluded due to incomplete surveys (5 patients with more than 2 incomplete questionnaires, especially Hospital Anxiety and Depression Scale (HADS), Pain Catastrophizing Scale, and Insomnia Severity Index. One more patient did not answer HADS).

Self-Reported Outcome Measures

The questionnaires used fulfilled 2 criteria: 1) Spanish version available and 2) assessment of some of the domains included in OMERACT core-set (26). They were answered by patients themselves in a printed format, previous to medical consultation with no limitation in time to answer, they are described as follows:

Pain intensity was determined using the Visual Analogue Scale (VAS) and the Medical Outcomes Study (MOS) Pain Severity Scale. VAS is a horizontal 10 cm line, where the beginning is pain absence (0) and the end is the worst imaginable pain (10). The MOS Pain Severity Scale is a 5-item scale to assess pain intensity (average and at the most), frequency, and duration over the last 7 days. Scores range from 0–100; higher score indicates more pain (28, 29).

Alexithymia was evaluated using the Modified Toronto Alexithymia Scale

Table II. Questionnaire scales in both study groups.

Normal distribution data					
	Nonalexithymic group (n=36)	Alexithymic group (n=66)	*p*-value[1]	Size effect	All patients (n=102)
WHOQOL-BREF					
Physical health	44.24±11.99	39.33±14.12	0.08	0.36	41.07±13.55
Psychological	57.63±14.24	45.32±18.81	<0.001	0.70	49.67±18.24
Social relationships	49.76±22.13	39.64±20.83	0.02	0.49	43.21±21.74
Environment	50.69±10.29	44.27±11.44	0.006	0.58	46.53±11.42
WHODAS 2.0	34.35±13.30	50.14±14.98	<0.001	1.0	44.57±16.40
ISI	14.05±5.95	16.39±5.32	0.04	0.42	15.56±5.32
FATIGUE					
General fatigue	11.17±3.45	11.09±2.37	0.90	0.02	11.12±2.79
Physical fatigue	11.67±3.24	11.16±2.92	0.44	0.16	11.35±2.92
HADS					
Anxiety	8.19±3.49	11.63±3.84	<0.001	0.92	10.42±3.95
Depression	6.72±3.99	9.66±3.87	<0.001	0.75	8.62±4.14
Non normal distribution data					
	Nonalexithymic group (n=36)	Alexithymic group (n=66)	*p*-value[2]	Size effect	All patients (n=102)
Pain					
Visual Analogue Scale	7 (3)	8 (3)	0.11	0.15	8 (3)
MOS Pain Severity Scale	72.85 (28.57)	82.85 (25.71)	0.05	0.19	77.14 (28.57)
Pain Catastrophising Scale					
Global	16 (16)	28.5 (20)	<0.001	0.35	24 (23.5)
Rumination	5 (5)	9 (8)	<0.001	0.36	7.5 (8)
Magnification	4 (4)	7 (5)	0.001	0.33	6 (6)
Helplessness	7 (10)	11 (10)	0.002	0.30	10 (10)
Fatigue					
Mental fatigue	11.5 (5)	9 (4)	0.07	0.18	10 (6)
Reduced motivation	10.5 (4)	8.5 (3)	0.12	0.15	9 (3)

ISI: Insomnia Severity Index; HADS: Hospital Anxiety and Depression Scale; MOS: Medical Outcomes Study.
Data: Mean ± Standard Deviation. Median (interquartile range).
[1]T test. [2]Mann Whitney test.

(TAS-20) (30). The scale's global score measures three different aspects of alexithymia: difficulty identifying feelings and distinguishing between feelings and bodily sensations, difficulty describing feelings, and externally oriented thinking. The cut-off points used to divide patients were those without alexithymia (global score ≤60) and those with alexithymia (global score ≥61).

The presence of depressive symptoms and anxiety were evaluated using the Hospital Anxiety and Depression Scale. It comprises 14 items in a range 0–3, and it is divided into two subscales, one for depression and the other for anxiety. The cut-off point to classify subjects with clinically relevant symptomatology was eight in both subscales (31).

Disability was evaluated using the generic instrument from the World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0), which measures people's activity limitations and participation restrictions. WHODAS 2.0 evaluates the six dimensions of an individual's function and defines disability per the constructs included in the International Classification of Functioning, Disability, and Health (ICF) (32). The global score was obtained by the complex method (33), with a range from 0 (no disability) to 100 (total disability).

To measure health-related quality of life, the World Health Organisation Quality Of Life-BREF (WHOQOL-BREF), which measures quality of life across cultures, was used (34). This instrument measures four quality of life dimensions: physical health, psychological health, social relationships, and environment. It is scored from 0 (low quality of life) to 100 (high quality of life), and a higher score in each domain indicates a better quality of life.

Fatigue was assessed by the Multidimensional Fatigue Inventory (MFI-20), which examines five dimensions: general fatigue, physical fatigue, decreased activity, reduced motivation, and mental fatigue. Each dimension comprises four items, which are scored from 4 to 20; higher scores indicate higher fatigue levels (35).

Sleep quality was measured through the Insomnia Severity Index (ISI). The ISI is a 7-item self-report questionnaire assessing the nature, severity, and impact of insomnia. The dimensions evaluated include the severity of sleep onset, sleep maintenance, early morning awakening problems, sleep satisfaction, the interference of sleep difficulties with daytime functioning, the noticeability of sleep problems by others, and distress caused by sleep difficulties (36). It is scored from 0 (absence of insomnia) to 28 (acute clinical insomnia).

The evaluation of pain catastrophising was performed using the Pain Catastrophising Scale (PCS), which has three dimensions: rumination, magnification, and helplessness. Scores range from 13 to 62; low or high scores mean poor or high catastrophising, respectively (37).

Statistical analysis

Variables with normal distribution in age, education level, WHOQOL-BREF, WHODAS 2.0, ISI, and HADS scores were shown using mean and standard deviation. Pain, fatigue, and pain catastrophising were reported in the median and interquartile range. In order to evaluate mean differences among the groups with and without alexithymia in variables with normal distribution, a Student's *t*-test for independent samples was used. The effect size was determined using Cohen's d, considering 0.2, 0.5, and 0.8 as threshold values to estimate low, medium, and large size

effects, respectively (38). For non-normal distribution variables, the Mann-Whitney U-test was used, and a size effect estimation was reported with a z statistic, considering 0.1, 0.3, and 0.5 as threshold values to estimate low, medium, and large size effects, respectively (38). Since assumptions to warrant multiple linear regression were not fulfilled, the Kernel Regularized Least Squares (KRLS) method was employed (39). KRLS borrows form machine learning methods designed to solve regression and classification problems without relying on linearity or additivity assumption, yet allows interpretation in ways analogous to generalised linear models while also permitting more complex interpretation to examine nonlinearities, interactions, and heterogeneous effects(39). KRLS analyses provides an estimate of the average pointwise marginal effect (like β coefficient from linear regression and could be interpreted as the average marginal effect) for each independent variable along with heterogeneity in the marginal effect expressed as an interquartile range (25th–75th). Statistical analysis was carried out with the Stata-14 program (2015; StataCorp, College Station, TX, USA).

Table III. Predictors of Pain Intensity (MOS Pain Severity Scale score). Pointwise marginal effects of predictors from Kernel-based Regularized Least Squares and standard errors in parentheses.

	Average	*p*-value	1st Quartile	Median	3rd. Quartile	R^2
Model 1						
Age	0.10 (0.06)	0.10	0.04	0.11	0.18	0.04
TAS-20 score	0.06 (0.02)	0.017	0.008	0.05	0.14	
Model 2						
Age	0.11 (0.07)	0.10	0.01	0.09	0.20	0.07
TAS-20 score	0.05 (0.02)	0.05	0.001	0.05	0.11	
HADS-anxiety score	0.08 (0.11)	0.48	-0.11	0.06	0.29	
Model 3						
Age	0.25 (0.12)	0.035	0.03	0.29	0.50	0.20
TAS-20 score	0.09 (0.05)	0.09	0.01	0.09	0.20	
HADS-anxiety score	-0.26 (0.22)	0.23	-0.64	-0.27	0.14	
HADS-depression score	0.69 (0.21)	0.001	0.34	0.66	1.07	
Model 4						
Age	0.31 (0.13)	0.024	-0.01	0.32	0.66	0.42
TAS-20 score	0.09 (0.06)	0.12	-0.03	0.09	0.23	
HADS-anxiety score	-0.79 (0.26)	0.004	-1.24	-0.85	-0.30	
HADS-depression score	0.65 (0.24)	0.01	0.24	0.60	1.10	
Insomia Severity Index score	0.93 (0.19)	<0.001	0.62	0.98	1.38	

Average and quartiles distribution of the pointwise marginal effects are shown in this table. Dependent variable is a continuous indicator for pain intensity. Column 2 reports the average pointwise marginal effect for each variable; columns 3 report the *p*-value for each estimate, and columns 4 through 6 report the first quartile, median, and the third quartile of the pointwise marginal effect for each variable. TAS-20 score: 20-item Toronto Alexithymia Scale; HADS: Hospital Anxiety and Depression Scale.

Results

The sample mainly included people with middle-low socioeconomic status and a mean education of 10.2 years. Among the participants, 48% had a remunerated activity and 45.1% were housewives. The median for pain duration was 48 months and 24 months for FM diagnosis. The main comorbidities were obesity (33.3%), followed by hypertension (7.2%) (Table I). The prevalence of alexithymia was 64.5% (95%CI, 54.6–73.9%). In addition, 70.6% (95%CI, 60.7–79.1%) showed anxiety levels and 61.8% (95%CI, 51.6–71.2%) showed depression levels, both of which were clinically relevant. In patients with depression, the prevalence of alexithymia was 76.1% (95%CI, 63.8–86%), and in patients without depression, it was 46.1% (95%CI, 30.1–62.9%).

Compared to FM patients without alexithymia, patients with alexithymia had significantly lower quality of life scores (except in the physical health dimension) and significantly higher scores in WHODAS 2.0, the ISI, and HADS (Table II). The effect size for the differences was large (d= 0.92) among the WHODAS 2.0 scores and the HADS anxiety subscale. The scores for the HADS depression subscale; the WHOQOL-BREF psychological health, environment, and global dimensions; and the Pain Catastrophising Scale subscales each had a medium effect size. There was a small effect size for the social and physical health dimensions of WHOQOL-BREF and the ISI (Table II). No statistically significant differences and small or no effect sizes were found when comparing age, education level, visual analogue scale, and fatigue. The MOS pain intensity results were inconclusive (p=0.05), with a small effect size (d=0.19).

When using multivariate analysis, alexithymia only explained a 2.5% variance in pain intensity. The overall model was able to explain 42% of pain intensity, including age, TAS-20, HADS, and the ISI. The results show a statistically significant relationship among pain intensity, age, anxiety-depression, and insomnia. Nevertheless, after including anxiety and depression in the model, alexithymia was not independently associated with pain intensity (p=0.12) (Table III). Alexithymia was independently associated with psychological health, but not the physical health dimensions of quality of life (Table IV) and disability (Table V). The main explanatory variables of the WHOQOL-BREF physical health score were the ISI and pain intensity, both of which explained 42% of the variance. The final model, which included age, anxiety, depression, alexithymia, and pain intensity, explained 60% of the variance within the physical health domain (Table IV). Related to the psychological health dimension, the main predictors were alexithymia, anxiety, depression, and the ISI, explaining 61% of the variance, while the final model explained 80% of the variance (Table IV). Moreover, alexithymia, pain intensity, and the ISI explained 44% of the variance in the WHODAS 2.0 score; the final model explained 49% of the variance (Table V). Based on these results, it is suggested that a one-point increase in the TAS-20 scale was associated with

Table IV. Predictors of health-related quality of life (World Health Organisation Quality of Life-BREF score). Pointwise marginal effects of predictors from Kernel-based Regularized Least Squares and standard errors in parentheses.

	Average	*p*-value	1st Quartile	Median	3rd. Quartile	R^2
Psychological health						
Model 1						
Age	0.12 (0.15)	0.44	-0.17	0.16	0.47	0.22
TAS-20 score	-0.36 (0.07)	<0.001	-0.60	-0.40	-0.13	
Model 2						
Age	-0.02 (0.14)	0.86	-0.33	-0.10	0.33	0.50
TAS-20 score	-0.19 (0.06)	0.006	-0.29	-0.19	-0.08	
HADS-anxiety score	-1.47 (0.25)	<0.001	-2.26	-1.45	-0.72	
MOS Pain Severity Scale score	-0.05 (0.05)	0.27	-0.13	-0.06	0.003	
Model 3						
Age	-0.16 (0.11)	0.13	-0.68	-0.37	0.37	0.80
TAS-20 score	-0.16 (0.05)	0.007	-0.30	-0.18	-0.03	
HADS-anxiety score	-0.98 (0.25)	<0.001	-1.90	-0.88	0.16	
HADS-depression score	-1.09 (0.22)	<0.001	-1.90	-0.93	-0.16	
MOS Pain Severity Scale score	0.02 (0.04)	0.61	-0.10	0.01	0.12	
Insomnia Severity Index Score	-0.64 (0.17)	<0.001	-1.01	-0.61	-0.07	
Physical health						
Model 1						
Age	0.006 (0.05)	0.90	-0.04	0.01	0.05	0.05
TAS-20 score	-0.06 (0.02)	0.003	-0.10	-0.08	-0.03	
Model 2						
Age	-0.003 (0.09)	0.96	-0.18	0.008	0.18	0.36
TAS-20 score	-0.05 (0.04)	0.26	-0.10	-0.05	-0.002	
HADS-anxiety score	- 0.53 (0.17)	0.003	-0.90	-0.58	-0.12	
MOS Pain Severity Scale score	- 0.18 (0.03)	<0.001	-0.26	-0.21	-0.10	
Model 3						
Age	-0.06 (0.09)	0.47	-0.28	-0.04	0.12	0.60
TAS-20 score	-0.03 (0.04)	0.38	-0.12	-0.05	0.05	
HADS-anxiety score	-0.09 (0.18)	0.61	-0.40	-0.03	0.31	
HADS-depression score	-0.15 (0.17)	0.37	-0.51	-0.15	0.25	
MOS Pain Severity Scale score	-0.13 (0.03)	0.001	-0.22	-0.13	-0.09	
Insomnia Severity Index score	-0.60 (0.13)	<0.001	-0.89	-0.58	-0.31	

Average and quartiles distribution of the pointwise marginal effects are shown in this table. Dependent variable is a continuous indicator for pain intensity. Column 2 reports the average pointwise marginal effect of each variable; column 3 reports the *p*-value for each estimate, and columns 4 through 6 report the first quartile, median, and the third quartile of the pointwise marginal effect of each variable.
TAS-20 score: 20-item Toronto Alexithymia Scale; HADS: Hospital Anxiety and Depression Scale; MOS: Medical Outcomes Study.

an average decrease of 0.15 points in the WHOQOL-BREF psychological health dimension (indicating a lower quality of life) and with an average increase of 0.16 points in the WHODAS 2.0 global score (indicating a higher disability level).

Discussion

Alexithymia has been found to be increased in adults with chronic pain compared with healthy ones, moreover, they might be associated with a greater pain intensity, depression, anxiety and disability symptoms (40). Our findings support the hypothesis that FM patients with alexithymia have a higher insomnia severity, greater levels of pain catastrophising, anxiety and depression, more disability perception, and lower quality of life than FM patients without alexithymia. Fatigue dimensions and pain intensity were not associated with alexithymia.

One of the main differences between the present study and the available studies on this topic is the statistical model used to adjust the predictors. The results revealed that alexithymia's punctuation effect is heterogeneous in marginal effects (Tables IV and V, columns 4-6). Hence, an absence of linearity is demonstrated in alexithymia's effect on quality of life and disability.

Similar to hypochondriacs, alexithymic people focus excessively on their body and tend to misinterpret body sensations of emotional arousal as symptoms of physical disease (18). Alexithymia could promote maladaptive illness behaviours, defined as a patient's ideas, affects, attitudes, and behaviours in relation to illness and the sick role, since alexithymic individuals may focus on, amplify, or overreact to unpleasant physical sensations (4). Alexithymia could result in a negative effect that causes hypervigilance, increasing somatic sensations and inducing high levels of anxiety and depression (33, 41). Alexithymia has a strong relationship with depressive symptoms as they both share the same affective origin; therefore, their manifestations could be overlapped or confused (19, 24, 41). Alexithymia could exacerbate depressive symptoms and pain through the misinterpretation of bodily sensations. Meanwhile, pain and depressive symptoms by themselves could reduce the ability to mentalise emotions and lead to secondary alexithymia (19).

There is inconsistent evidence about the relationship between alexithymia and pain intensity in FM patients; some studies have demonstrated a positive correlation, while others have not (24). In the present study, only a small proportion of pain intensity variance was explained by alexithymia, indicating that pain intensity in people with FM depends mostly on other factors. In agreement with previous studies (3, 16, 25, 40), pain intensity and alexithymia were independent events. A possible interpretation of this result could be that mood disorders might mediate the link between alexithymia and pain intensity. Pain severity is determined by the intensity of nociceptive stimulation and by psychological factors (emotional and motivational state) (42). It is possible to assess the sensory and/or affective components of pain. Discrimination between these two components of pain is important as they are regulated by different mechanisms (2). The central sensitisation mechanism in FM is understood as an emotional disorder that produces a dysregulation in pain perception, mainly on its affective com-

Table V. Predictors of disability (World Health Organisation Disability Assessment Schedule 2 score). Pointwise marginal effects of predictors from Kernel-based Regularized Least Squares and standard errors in parentheses.

	Average	*p*-value	1st Quartile	Median	3rd. Quartile	R^2
Model 1						
Age	0.06 (0.12)	0.58	-0.06	0.10	0.24	0.22
TAS-20 score	0.26 (0.05)	<0.001	0.12	0.26	0.44	
Model 2						
Age	0.07 (0.11)	0.49	-0.10	0.15	0.28	0.41
TAS-20 score	0.16 (0.05)	0.002	0.04	0.18	0.27	
HADS-anxiety score	0.53 (0.20)	0.009	0.18	0.59	0.91	
MOS Pain Severity Scale score	0.19 (0.04)	<0.001	0.09	0.19	0.30	
Model 3						
Age	0.12 (0.10)	0.25	-0.02	0.21	0.35	0.46
TAS-20 score	0.16 (0.04)	0.001	0.06	0.18	0.26	
HADS-anxiety score	0.35 (0.19)	0.08	0.003	0.41	0.69	
MOS Pain Severity Scale score	0.17 (0.04)	<0.001	0.10	0.17	0.27	
HADS-depression score	0.39 (0.18)	0.042	-0.02	0.40	0.83	

Average and quartiles distribution of the pointwise marginal effects are shown in this Table. Dependent variable is a continuous indicator for pain intensity. Column 2 reports the average pointwise marginal effect of each variable; column 3 reports the *p*-value for each estimate, and columns 4 through 6 report the first quartile, median, and the third quartile of the pointwise marginal effect of each variable.

ponent (1). Studies that considered this difference have reported that alexithymia was related to the affective dimension of pain (not assessed in the present study) more than sensory pain; furthermore, this link could be coordinated by psychological disorders, especially depression (1-3, 18, 24). Depression has been correlated bidirectionally with chronic pain (1). Besides, the relationship between mood disorders and pain intensity might be explained by the association of anxiety severity with a decrease in the perception of pain tolerance, together with an increase in pain perception. Anxiety is related to increased pain reports in clinical settings (anxiety-induced hyperalgesia) (42). Anxiety is an emotion described by negative affect and apprehensive anticipation of potential threats, and results in hypervigilance, somatic tension, and enhanced pain (42).

The available evidence demonstrates a clear relationship between the presence of alexithymia and a decreased perception of quality of life, regardless of the instrument used to define quality of life. Alexithymia *per se* had a negative impact on the health-related quality of life of the patients evaluated by the instrument SF-36 (13, 25), the Nottingham health profile (43), and, nowadays, WHOQOL-BREF. Even when alexithymia's role in the physical dimension of quality of life seemed to be regulated by mood disorders, alexithymia was not an independent predictor of the WHOQOL-BREF physical dimension after including anxiety and depression as covariates. This is similar to other reports (13, 44), alexithymia ceased to be a predictive factor of the physical component (SF-36) when depression was entered into the analysis. Pain intensity and mood disorders were main the predictors of the physical dimension of health-related quality of life in people with FM (13).

Scarce information is available about the relationship between disability and alexithymia. A study demonstrated(16) that people with alexithymia showed higher disability scores due to pain, as assessed by the Pain Disability Scale. Alexithymia was not an independent predictor, since depression was a complete mediator between the TAS-20 score and the Pain Disability Scale(16). Despite this result, when using a generic instrument to assess disability, alexithymia was significantly associated with disability, even after adjustments for pain intensity, anxiety, and depression.

Alexithymia levels in FM patients in daily practice might be important when determining ideal treatment options (3). FM is usually evaluated and treated by rheumatologists, even if it is characterised by a broad variety of clinical manifestations that involve many specialties (1). The information presented here validates the importance of a psychological and/or psychiatric evaluation to assess the best treatment strategy, together with an evaluation by a rheumatologist. Clinical observations and controlled studies have shown that psychotherapeutic treatments in patients with alexithymia are difficult (15). A psychotherapeutic treatment focused on alexithymia might lead FM patients to break down this vicious circle, not only decreasing depressive symptoms but also decreasing pain sensations by improving their ability to better distinguish emotional states from bodily sensations (19). Patients with both FM and alexithymia might benefit from psychological interventions that directly target emotional awareness processes, such as cognitive-behavioural therapy (CBT) and Mindfulness-Based Therapies (MBT) (3, 15, 45). CBT focuses on coping strategies, emotional control and cognitive psychology and has shown successful results in counteracting mood disorders and disability in FM patients (46). MBT could be effective in reducing alexithymia (47). FM patients treated with MBT have reported pain, sleep or psychological distress improvement (48).

Although the results support the present study's hypotheses and add to the existing evidence about alexithymia's role in FM, some limitations should be considered; because our patients were drawn from a referral hospital, they may represent the most severely afflicted patients and hence not be representative of most patients with FM. TAS-20 usage could have a limited ability to detect the most severe cases of alexithymia, and some reports have argued about the reproducibility of its factorial structure (4). Furthermore, the use of self-report questionnaires as an exclusive measure to assess alexithymia has been questioned (32). Explicit self-reports require respondents to be aware of their lack of emotional awareness and reduced capacity to describe and identify feelings. A better way to understand the alexithymia construct could be the parallel use of a performance-based instrument or a structured interview (4, 25). In addi-

tion, the present study's cross-sectional design does not allow for the establishment of causal relationships. These limitations could be improved in future research by assessing alexithymia with a mixed methods approach, such as a qualitative methodology including interview techniques and self-reporting, as well as a quantitative methodology, including longitudinal studies to evaluate the relationship between alexithymia and FM symptoms from the patient's and the health physician's viewpoints. Further longitudinal studies, are needed to clarify if the multidimensional treatment of alexithymia leads to the improvement of symptoms, quality of life, and disability related to FM.

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