The influence of depression on personality traits in patients with fibromyalgia: a case-control study

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ABSTRACT

Objective. *We developed this study to investigate the association of fibromyalgia with personality traits, controlling for depression and other potential confounders.*

Methods. *We assessed personality traits using the Cloninger's Temperament and Character Inventory (TCI) in 78 female patients with fibromyalgia and in a control group of 78 subjects without fibromyalgia. The Mini-International Neuropsychiatric Interview was used to assess depression and anxiety diagnoses. To investigate the association between fibromyalgia and the Cloninger's Temperament and Character Inventory we performed unadjusted and adjusted analyses of covariance, using the TCI score as dependent variable and adjusting the model for depression, anxiety and for clinical and socio-demographic variables. We used a backward selection method to choose the final model.*

Results. *In the unadjusted analysis, fibromyalgia was associated with all personality traits, except persistency. After adjusting for depression and anxiety, patients with fibromyalgia presented decreased novelty seeking compared to controls; the differences in other personality traits were no longer significant. Novelty seeking was also correlated with the length of history of fibromyalgia and pain intensity.*

Conclusion. *Decreased novelty seeking may be a personality trait associated with fibromyalgia. Depression and anxiety should be considered potential confounders in the evaluation of personality traits in this population.*

Introduction

The fibromyalgia syndrome (FMS) is characterised by a history of chronic widespread pain, tender points, fatigue, waking unrefreshed and cognitive symptoms (1). In 1991 the American College of Rheumatology (ACR) defined operational criteria to diagnose fibromyalgia, including the presence of widespread pain for at least three months, and pressure pain at a minimum of 11 of 18 pre-defined tender points (2). In 2010, the new ACR criteria removed the tender point examination and included a widespread pain index and a symptom severity scale, which takes into account cognitive symptoms, inadequate sleep patterns, fatigue, and a number of somatic symptoms (1). The fibromyalgia syndrome affects around 3% of population and has been associated with female gender, middle age, lower education, lower household income, being divorced, and being disabled (3).

Higher prevalence of various psychological characteristics, including alexitimia, neuroticism and difficulties in relationships, has been reported in patients with FMS (4-7). However, the literature is inconsistent regarding specific personality traits or psychological profiles in patients with FMS (4). Such inconsistencies are related to the use of distinct instruments to assess personality and psychological profiles, samples with different clinical and sociodemographic profiles, and lacking adjustments for potential confounders in analyses.

The Cloninger's Temperament and Character Inventory (TCI) has the advantage of being based on a psychobiological model of personality. Its temperament traits have been associated to specific neurotransmitter systems: harm avoidance with serotonergic, novelty seeking with dopaminergic and reward dependence with the noradrenergic system (8-11). Consequently, it is suitable to study integrative models for the biological and psychological aspects related to fibromyalgia. It has

7 temperament and character traits; the temperament traits are novelty seeking, harm avoidance, reward dependence and persistence, while character traits include self-transcendence, self-directedness and cooperativeness.

Previous studies using the TCI in FMS subjects have reported increased harm avoidance (12-17), self-transcendence (12, 16) and persistence (12, 13), and lower novelty seeking (13, 17) and self-directedness (12, 14, 16, 17) compared to controls.

Depressive symptoms are very common in FMS patients (7, 4, 18) and higher severity of depression has been associated with poor outcome in FMS (19). Cloninger's Temperament and Character Inventory traits have been significantly correlated with the severity of depressive and anxiety symptoms in FMS patients (16). Thus, it is possible that depressive and anxiety symptoms may not only mimic specific personality traits (confounding the evaluation of personality in FMS patients), but also confound the relationship between FMS and personality traits. This topic has not been adequately investigated to date. In this study, we investigated the association of fibromyalgia with personality traits (measured with TCI), focusing on the potential influence of depression and anxiety in such association.

Materials and methods

Sample size

We estimated we would need 78 subjects per group to detect a clinically meaningful difference of 3 points in the TCI scores (with a two-tailed alpha of 0.05 and a power of 90%). Based on the literature (20), we expected that harm avoidance would be 18±5.5 (SD) in the control group and 21±6.0 (SD) in FMS subjects.

Sample

Methodological details of this study have been previously described (21). In summary, patients were recruited from the Rheumatology and Neurology departments of the Clinics Hospital, affiliated with the Faculty of Medicine of the University of Sao Paulo (HC-FMUSP), Sao Paulo, Brazil. The Neurology unit is specialised in the treatment of chronic pain, and the Rheumatology unit in the diagnosis and treatment of FMS. Patients were referred to a screening interview by their respective neurologist or rheumatologist. Physicians were asked to refer all female patients aged 18 years or older diagnosed with FMS according to the American College of Rheumatology Criteria (2). We restricted the study to females because FMS is 10 times more prevalent in women than in men (2).

The exclusion criteria used for both FMS patients and control subjects included severe medical conditions; debilitating neurological conditions; bipolar disorder, psychosis and other DSM-IV Axis I disorders, except anxiety and unipolar depressive disorders, because of the high prevalence of these diagnoses in FMS patients. Subjects who were unable to understand the study instruments were also excluded.

We screened 279 FMS patients, 49 refused to participate in the study or missed the scheduled appointment. Fig. 1 shows the flowchart of the screening process resulting in 78 FMS patients satisfying the inclusion and exclusion criteria.

Control group

Seventy-eight female workers from the HC-FMUSP without a diagnosis of FMS or other pain conditions were enrolled in the control group. All control subjects met exclusion criteria listed above and were also matched with patients by age, given the impact of age on the TCI (22). To enrol 78 subjects in the control group, we screened 85 subjects; seven of them were excluded [due to psychiatric disorders (n=5), pain disorder (n=1) and did not complete the interview (n=1)].

Measures

We used both self-reported and clinician-rated instruments to assess the severity of depression and anxiety (see below); such approach allows the assessment of a more subjective (*i.e.* self-rated) and a more objective (*i.e.* clinician-rated) parameter. This procedure is critical, considering the high prevalence of depression and anxiety in FMS patients and the possibility that such conditions may confound the relationship between FMS and personality traits.

A questionnaire was used to collect sociodemographic data including age, marital status, race or ethnic group, educational level, employment status and total family income. Recorded clinical characteristics included time since FMS diagnosis (years) and current psychopharmacological treatment (*i.e.* antidepressant, benzodiazepine, antipsychotic).

Diagnosis of mental disorders

A psychologist (DMS) diagnosed mental disorders using the Brazilian version (23) of the Mini-International Neuropsychiatric Interview (M.I.N.I.) (24). The M.I.N.I. is a structured interview designed to assess psychiatric diagnoses in accordance with the DSM-IV and CID-10 criteria (24).

Severity of depression and anxiety symptoms

We assessed the severity of depressive symptoms with the Beck Depression Inventory (BDI) (25, 26) and the 17-item version of the Hamilton Depression Rating Scale (HAM-D-17) (27). The BDI is a 21-item self-reported questionnaire widely used to evaluate medically ill-depressed subjects; its total score ranges from 0 to 63 and a total score <10 is usually interpreted as absence of clinical depression. The HAM-D-17 (27) is rater-administered and has been frequently used to evaluate severity of depression in clinical trials (27); its total score ranges from 0 to 50 and scores <7 usually indicate the absence of clinical depression.

The severity of anxiety was assessed with the State-Trait Anxiety Inventory – STATE (STAI-STATE) (28, 26) and the Hamilton Anxiety Rating Scale (HAM-A). The STAI-STATE is a 20-item self-reported questionnaire measuring the severity of state (*i.e.* current) anxiety, the total score ranges from 20 to 80 and scores >40 are interpreted as clinically significant anxiety. The HAM-A (29) is a 14-item rater-administered instrument, total scores range from 0 to 56 and total scores <17 usually represent mild severity of anxiety.

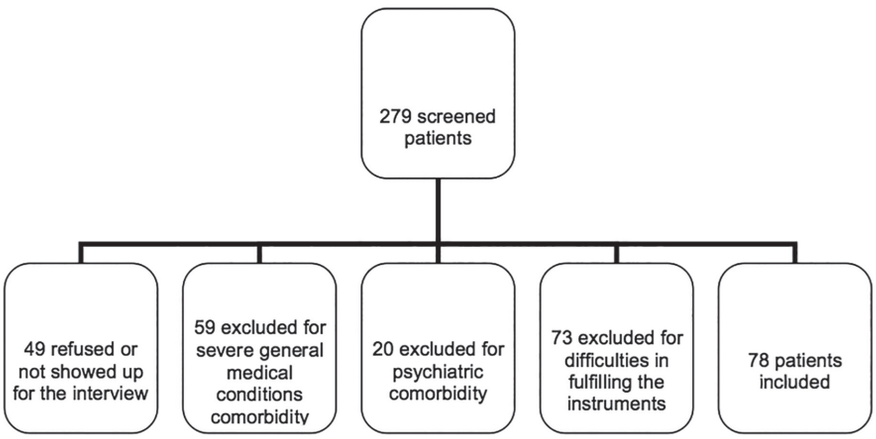

Fig. 1. Recruitment diagram for the FMS group.

Table I. Sociodemographic characteristics of patients with fibromyalgia and controls.

Sociodemographic characteristics	Groups		
	Fibromyalgia (n=78)	Control (n=78)	*p*-value
Categorical variables	n (%)	n (%)	
Marital status (married)	51 (65.4)	40 (51.3)	0.172
Race or ethnic group			
White/Caucasian	53 (67.9)	56 (71.8)	
Black	7 (9)	12 (15.4)	
Asians	0	4 (5.1)	0.010[a]
Brown/mixed race	18 (23.1)	6 (7.7)	
Continuous variables	Mean (SD)	Mean (SD)	
Age (years)	46.65 (±8.98)	46.21 (±9.03)	0.822
Educational level (years)	9.92 (±3.71)	13.78 (±2.81)	0.000[a]
Total family income ($ Reais)	1.821 (±1.314)	4.014 (±2.254)	0.000[a]

[a]Statistic significance *p*-value <0.05.

Comorbid conditions

We used the Cumulative Illness Rating Scale (CIRS) (30), to measure the severity of all comorbid illnesses, grouping them into 14 organ systems: cardiac, hypertension, vascular, respiratory, EENT (eye, ear, nose, throat, larynx), upper gastrointestinal, lower gastrointestinal, hepatic, renal, other genitourinary, musculoskeletal-integumentary, neurological, endocrine-metabolic and psychiatric. For this study, we did not rate the psychiatric conditions, which were either excluded or otherwise accounted for in the analysis. The severity of illnesses within each organ system is rated as: none, mild, moderate, severe, extremely severe.

Pain severity

Pain severity in the previous week was evaluated with a visual analog scale (VAS). The scale anchors "no pain" (numerically = 0) and "pain as bad as it could be" (10).

Personality traits

Personality traits were assessed using the self-administrated Brazilian version (31) of the TCI (32). It consists of 240 self-descriptive true/false items. It takes about 30 min to complete and assesses temperament (n=4) and character (n=3) traits. The temperament traits include novelty seeking (40 items), harm avoidance (35 items), reward dependence (24 items) and persistence (8 items); and the character traits are: self-directedness (44 items), cooperativeness (42 items) and self-transcendence (33 items). For each trait, total scores are calculated by summing the true answers. Cut-offs defining pathologic levels are generally not used; instead analyses have compared TCI traits scores between groups of interest (17). Studies have also investigated correlations between TCI trait scores and clinical, psychosocial or biological factors (9, 8).

Ethics

The research project was approved by the ethics committee of the HC-FMUSP, and all subjects provided written informed consent.

Statistical analysis

For comparisons between groups, we used the Student *t*-tests or non-parametric Mann-Whitney tests, respectively, for data with normal or non-normal distribution (assessed with the Kolmogorov-Smirnov test).

We compared the clinical and socio-demographic characteristics of the FMS and control groups with Mann-Whitney tests for continuous variables (income, education, and CIRS) and with Chi-square tests for categorical variables (marital status and ethnicity). For all statistically significant differences between groups, we investigated potential associations of the specific variables with the TCI (using Spearman correlation tests and Mann-Whitney tests). We then performed an analysis of covariance using TCI as dependent variable and as covariates the BDI, HAM-D-17, STAI, HAM-A scores, presence of depressive disorders diagnosis (*i.e.* major depressive disorder (MDD) and dysthymia), and all clinical and socio-demographic variables associated with FMS. We used a backward selection to choose the final model.

Results

Socio-economic variables were similar in FMS patients and controls, except for differences in race, higher educational levels and higher incomes among controls (Table I).

FMS patients also experienced increased rates and severity of depressive and anxiety disorders, as well as increased use of antidepressants and antipsychotics (Table II).

In non-adjusted comparisons, we found significant associations between FMS and all personality traits except persistence. However, only the association with novelty seeking remained statis-

Table II. Clinical characteristics of patients with fibromyalgia and controls.

	Groups		
Clinical Characteristics	Fibromyalgia (n=78)	Control (n=78)	*p*-value
Categorical variables	n (%)	n (%)	
Depressive disorders, (current)	37 (47)	5 (6)	0.000[a]
Anxiety disorders, (current)	11 (14)	2 (2.5)	0.009[a]
Benzodiazepines, (current use)	8 (10)	3 (4)	0.118
Antidepressant, (current use)	53 (68)	11 (14)	0.000[a]
Antipsychotic, (current use)	17 (21)	0	0.000[a]
Numeric variables	Mean (SD)	Mean (SD)	
BDI	17.28 (±9.2)	5.82 (±5.2)	0.000[a]
HAM-D-17	10.22 (±5.0)	2.35 (±2.8)	0.000[a]
STAI-STATE	41.77 (±9.8)	34.79 (±8.2)	0.000[a]
HAM-A	10.77 (±5.3)	1.92 (±2.4)	0.000[a]
CIRS	16 (±2.7)	13.4 (±0.8)	0.000[a]
VAS	7 (±2.0)	–	–
Fibromyalgia history, (years)	9 (±6.6)	–	–

BDI: Beck Depression Inventory; HAM-D-17: 17-item of the Hamilton Depression Rating Scale; STAI-STATE: State-Trait Anxiety Inventory; HAM-A: Hamilton Anxiety Rating Scale; CIRS: Cumulative Illness Rating Scale; VAS: Visual Analogue Scale measuring pain severity.
[a]Statistic significant *p*-value <0.05.

Table III. Comparison of the factors of the Cloninger's Temperament and Character Inventory between patients with fibromyalgia and controls.

	Groups			
	Fibromyalgia (n=78)	Control (n=78)	*p*-value non adjusted	*p*-value adjusted[a]
Factors of the Temperament and Character Inventory	Mean (SD)	Mean (SD)		
Novelty seeking	16.13 (±5.09)	18.59 (±4.74)	0.002[b]	0.002[b]
Harm avoidance	20.77 (±7.02)	15.67 (±4.87)	0.000[b]	0.856
Reward dependence	13.83 (±3.51)	14.96 (±4)	0.043[b]	0.543
Persistence	4.92 (±1.79)	4.55 (±1.56)	0.082	-
Self-directedness	28.85 (±7.37)	33.04 (±6.26)	0.000[b]	0.092
Cooperativeness	32.47 (±4.88)	33.71 (±4.25)	0.045[b]	0.105
Self-transcendence	18.10 (±5.86)	15.36 (±5.53)	0.002[b]	0.744

[a]For the adjusted values, we performed an analysis of covariance including the scores of the 17-item of the Hamilton Depression Rating Scale (HAM-D-17), Beck Depression Inventory (BDI), Hamilton Anxiety Rating Scale (HAM-A), State-Trait Anxiety Inventory (STAI-STATE); current diagnosis of depressive disorder; income; educational level; use of antidepressant and use of antipsychotic medicines. Adjusted *p*-values are those from the final model after excluding covariate variables without significant association from the model in backward approach.
[b]Statistic significant *p*-value <0.05.

tically significant after adjusting for the severity of depressive and anxiety symptoms (Table III). Novelty seeking was negatively correlated with the time since FMS diagnosis (p=0.026) and with pain intensity (p=0.002).

Discussion

In our sample of 78 women with FMS we found increased levels of harm avoidance and self-transcendence, and decreased levels of novelty seeking, self-directedness, cooperativeness and reward dependence compared to a control group without FMS, consistent with previous studies (13-17). Of note, only lower novelty seeking remained significantly associated with FMS after adjusting for depression and other confounders. Major depressive disorder and increased levels of anxiety are very common in FMS (18, 33) and have been associated with temperament and character (16); therefore it is not surprising that they can be potential confounders, as in our data. Consequently, it becomes imperative to co-vary the association between personality traits and fibromyalgia by depression and anxiety. Accordingly, previous reports of increased harm avoidance and self-transcendence and decreased self-directedness in FMS patients (34, 12-15) could also be, at least in part, explained by comorbid depression and anxiety. In line with our findings, depressive diagnoses have been shown to mediate the association of FMS with high sociotropic traits and increased dysfunctional attitudes (35).

The severity of pain in FMS patients has been previously related to a history of depressive and manic symptoms (36), in our data it was negatively correlated with novelty seeking. This is not surprising considering that novelty seeking and mania are both related to the dopaminergic neurotransmission (37). These results highlight the relevance of recognising and measuring the interaction of mood symptoms (i.e. depression, mania) with personality traits in FMS patients.

Novelty seeking and personality aspects previously described in FMS patients

Individuals with lower novelty seeking tend to be reflective, rigid, loyal, stoic, slow-tempered and frugal (38). Studies using other instruments have reported personality traits in FMS subjects that overlap the concept of novelty seeking including: a) hypoactivity in the Behavioral Approach System (39) (*i.e.* poorer response to environmental incentives resulting in a decrease of exploratory behaviours; b) alexithymia (40, 41) (*i.e.* novelty seeking has been significantly associated with the factor 2 of the alexithymia scale (*i.e.* ability to describe other people's feelings) (42); c) lower levels of the sociability component of extraversion and high prevalence of Type D (*i.e.* distressed) personality, which includes social inhibition as its central concept (43).

Mechanisms for the association between novelty seeking and fibromyalgia

The cross-sectional design of our study precludes any conclusions regarding the directionality of the association between novelty seeking and FMS.

Various mechanisms may explain the association of FMS with personality traits; a) both may share common genetic determinants, common biological risk factors (44, 13) or common stressors; b) personality traits may increase the risk for the development of FMS or for some of its clinical manifestations (45); c) FMS may lead to changes in personality. Additionally, subgroups of FMS patients with personality traits or psychopathologic presentations have been described (46).

Common biological factors

Among biological factors, inflammation may represent a common denominator between fibromyalgia and novelty seeking. Inflammation may impair motivation and novelty exploration through actions on information processing within brainstem dopaminergic structures (47). Increased levels of pro-inflammatory cytokines and a pro-inflammatory state have also been proposed to be a common factor (48) in the pathogenesis of fibromyalgia (49) and depression (50). Consequently, increased inflammation may explain the association between novelty seeking, fibromyalgia and depression. However, our results highlight that novelty seeking may be related to FMS independently of depression.

Regarding neurotransmitters, both novelty seeking and FMS have been associated with the dopaminergic system (11, 51). Thus, changes in the dopaminergic system may be the link between novelty seeking and FMS, which we described.

Common genetic determinants

A common genetic vulnerability is suggested by a genetic marker for the regulation of the dopaminergic system in FMS patients (44), particularly in a group of FMS patients with decreased novelty seeking (13). Of note, other non-biological factors including common environmental triggers, individual habits and stressors might also contribute to the association between FMS and decreased novelty seeking.

Novelty seeking influencing FMS

Certain personalities may facilitate the translation of stressors into physiological responses, triggering the fibromyalgia mechanism (45). Such personality factors and behavioural styles could lead to FMS by dysregulating the sympathetic nervous system, via neuronal, neurohormonal and neuroimmunological mechanisms, consistently with the stress model (52). A prospective study including the evaluation of novelty seeking in the general population and prospectively assessing the risk of developing FMS would be needed to test whether decreased levels of novelty seeking in FMS in our data reflect an increased risk for FMS in subjects with low novelty seeking.

Fibromyalgia influencing novelty seeking

Personality traits described in FMS patients in cross-sectional studies could also be a consequence of pain chronicity and/or other adverse factors associated with FMS (43). Thus, it is possible that the lower scores in novelty seeking in our FMS patients reflect a personality adjustment to the restriction imposed by the chronic pain and other disabling aspects of FMS. To confirm such hypothesis, a study should investigate prospectively in general population if subjects who just received the diagnosis of FMS will prospectively have decreased novelty seeking compared to those without FMS.

Various subtypes of fibromyalgia patients?

Subgrouping FMS patients have been recommended to allow a more personalized approach (53). The authors have proposed the existence of two (46, 54), three (55, 56) and four (57) subtypes of FMS patients according to personality traits, associated signs and symptoms and clinical comorbidity. Our study did not address this topic, but in this regard, our results may suggest the existence of three subtypes of FMS patients, one with depression with or without novelty seeking, one with low novelty seeking without depression, and a third group without significant mental health conditions.

Therapeutic implications

There are several important considerations regarding our data and mental health symptoms in FMS patients. First, the presence of low novelty seeking does not mean that patients intentionally decrease their novelty seeking behaviour; nor is this an evidence that low novelty seeking causes FMS, or even transform patients into "psychiatric" cases. The presence of depression and anxiety may contribute to a more "dramatic" presentation of FMS symptoms; this presentation indicates increased suffering and not that patients are lying or symptoms are imaginary.

Low novelty seeking may require psychotherapy (58) or even combinations of psychotherapy and antidepressants (59). Additionally, the treatment of depression should include its prevention and early detection as well as its treatment. In sum, the presence of mental health symptoms in FMS patients requires integrative care. However, we believe that rheumatologists should use their clinical judgment to decide whether to refer FMS patients for antidepressant treatment and/or psychotherapy (to improve personality aspects and to develop coping strategies), rather than automatically referring based exclusively on the presence of personality traits, symptoms or complaints. Additionally, rheumatologists should continue to monitor the outcome of such referrals in future appointments, ensuring that somatic and mental health symptoms are equally addressed on an on-going basis.

Study limitations

We should note several limitations of our study. First, our FMS and control groups had significant differences in schooling, income, depressive and anxiety symptoms. However, we performed a multivariate analysis controlling for these factors. The cross-sectional nature of our study precludes conclusions about the direction of the relationship. As we mentioned earlier, we do not know whether a) decreased novelty seeking increases the risk of developing FMS, b) FMS leads to a decrease of novelty seeking, or c) a common genetic, environmental or health factors contributes to the development of both FMS and novelty seeking.

Moreover, we did not control for the use of antidepressants, and antidepressants may impact personality traits, particularly harm avoidance (14). Due to exclusion criteria and other factors, our sample included only 23% of the initially screened subjects. Thus, our results may not be generalisable to FMS patients not included in our study because of our inclusion/exclusion criteria (*i.e.* illiterate subjects or those with low cognitive skills and unable to fill in study instruments, or subjects with other comorbid medical conditions including major psychiatric disorders). Also, since we only included women recruited from a tertiary teaching hospital, generalising our results to males and to other patients from the general population is questionable.

Conclusions

Our findings support the importance of an integrated approach for FMS patients, including a focus on depression, anxiety and personality traits, such as novelty seeking. We particularly demonstrated the relevance of controlling for anxiety, depression and other potential confounders in studies investigating the association between personality traits and FMS. The increased harm avoidance and self-transcendence and low self-directedness previously reported in FMS patients may in fact be explained by their association with depression and anxiety symptoms, as described here. Studies prospectively investigating a causal relationship and potential common risk factors (*i.e.* stressors and genetic factors) for the association between FMS and personality aspects are warranted. Also necessary are studies investigating the reduction of FMS symptoms by enhancing personality traits, improving coping strategies and treating depression and anxiety.

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