CLINICAL SCIENCE

The association of major depressive episode and personality traits in patients with fibromyalgia

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INTRODUCTION: Personality traits have been associated with primary depression. However, it is not known whether this association takes place in the case of depression comorbid with fibromyalgia.

OBJECTIVE: The authors investigated the association between a current major depressive episode and temperament traits (e.g., harm avoidance).

METHOD: A sample of 69 adult female patients with fibromyalgia was assessed with the Temperament and Character Inventory. Psychiatric diagnoses were assessed with the Mini-International Neuropsychiatric Interview severity of depressive symptomatology with the Beck Depression Inventory, and anxiety symptomatology with the IDATE-state and pain intensity with a visual analog scale.

RESULTS: A current major depressive episode was diagnosed in 28 (40.5%) of the patients. They presented higher levels of harm avoidance and lower levels of cooperativeness and self-directedness compared with non-depressed patients, which is consistent with the Temperament and Character Inventory profile of subjects with primary depression. However, in contrast to previous results in primary depression, no association between a major depressive episode and self-transcendence was found.

CONCLUSIONS: The results highlight specific features of depression in fibromyalgia subjects and may prove important for enhancing the diagnosis and prognosis of depression in fibromyalgia patients.

KEYWORDS: Fibromyalgia; Personality; Depression; Temperament; Character.

Santos DM, Lage LV, Jabur EK, Kaziyama HHS, Iosifescu DV, Lucia MCS, et al. The association of major depressive episode and personality traits in patients with fibromyalgia. Clinics. 2011;66(6):973-978.

Received for publication on December 14, 2010; **First review completed on** January 6, 2011; **Accepted for publication on** February 28, 2011

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INTRODUCTION

Fibromyalgia (FMS) is a syndrome characterized by chronic widespread musculoskeletal pain and stiffness in association with fatigue and poor sleep. The classification of the American College of Rheumatology Criteria for FMS[1] includes the presence of pain in all four body quadrants in combination with excess tenderness to manual palpation in at least 11 of 18 muscle–tendon sites, in the absence of clinically demonstrable peripheral nociceptive causes. Although some biological mechanisms have been identified, the etiology and pathogenesis of FMS remain unclear.[2,3] The prevalence of FMS in the general population is estimated to be between 1.3% and 4.8%.[4] Patients with FMS also frequently suffer from emotional distress and/or psychiatric disorders.[5,6]

Depression in a medical setting or comorbid with medical conditions has been reported to be frequent, difficult for general practitioners to recognize ,[7–9] associated with increased morbidity and to have different psychopathological presentation.[10] Of note, the prevalence of depression is increased in fibromyalgia patients compared with medically healthy individuals.[11,12] Among patients with fibromyalgia, the current and 12-month prevalence of major depression (MDD) has been reported to be between 20% and 30%[13,14] in various studies, but also from 30% to 80% in others,[15] compared with 4% to 6%, respectively, for current and 12-month prevalence of MDD in the general population.[16,17] The prevalence of MDD appears to be higher in FMS patients than in rheumatoid arthritis patients, according to some[18,19] but not all[20] reports. An epidemiological study placed fibromyalgia as the second most common general

medical condition associated with MDD, with an odds ratio (OR) of 3.4.[21] In addition to this increased prevalence, depression in FMS has been reported to be associated with sexual dysfunction,[22] lower rates of physical therapy[23] and vitamin D deficiency.[24] Considering the relevance of the association between personality and MDD in the general population, it is pertinent to investigate whether this association extends to patients with fibromyalgia or not. Studying the association between a specific personality trait (harm avoidance) and the depression comorbid with FMS may bring inputs about the nature of such depression and its potential response to treatment.

Several studies have reported a specific pattern of personality traits in MDD subjects (primary depression), as assessed using Cloninger's Temperament and Character Inventory (TCI).[25] The TCI is based on a psychobiological model of personality and evaluates 7 traits referring to temperament and character. Temperament evaluation includes 4 dimensions: novelty seeking (NS), harm avoidance (HA), reward dependence (RD) and persistence (P). The assessment of the character includes the evaluation of self-transcendence (ST), self-directedness (SD) and cooperativeness (C). Prior studies have consistently reported that MDD was associated with higher HA, but not NS and RD dimensions.[26,27] HA scores appear to be directly correlated with the severity of depressive symptomatology. In addition, other studies investigating the character personality traits (ST, SD and C) have suggested that MDD subjects tend to have higher scores of HA and ST and lower scores of SD and C compared with healthy volunteers.[28–30]

Altered personality traits have also been described in chronic pain patients by some but not all authors.[31] A pattern close to that described in MDD (i.e., increased HA scores and decreased SD scores) has been reported in patients with non-specific musculoskeletal disorders,[32] tension-type headache[33] and migraine.[33,34] Moreover, a correlation of HA, SD and C with depression severity has been reported in tension-type headache patients,[33] and some authors have suggested that the association of chronic pain with TCI dimensions is caused, at least in part, by the presence of comorbid depression.[34] Two studies have previously reported[35,36] an association between higher HA and higher Beck Depression Inventory scores in neurological and cardiac patients. The association between depression and HA has physiological and clinical implications. Physiologically, HA has been associated with serotonergic dysfunction[37] and, clinically, HA independent of the other dimensions has been related to an increased risk of developing depression[38,39] and to the response to antidepressant treatment.[27]

Three studies[40–42] have previously investigated the association between depression and personality aspects in FMS patients. Johnson et al. (1997)[40] evaluated the self-esteem structure in 61 female FMS patients; they found that depressed FMS patients present a self-esteem structure with lower sense of self-esteem, lower self-assertiveness and less emotional candor, different from the non-depressed FMS patients. Nordahl and Stiles (2007)[42] reported a sociotropic personality style similar to MDD only in FMS patients with current or lifetime history of MDD. In another study, Mazza et al. (2008),[41] using the Beck Depression Inventory and the TCI, reported a depressive state and trait correlation with HA and strong depressive state association with SD in FMS patients. None of the above-mentioned studies used an instrument that captures parameters similar to those captured by the TCI; and, to our knowledge, no study has specifically investigated the association of TCI personality traits with a current major depressive episode (MDE) in FMS patients. Thus, our main hypothesis was that a current MDE in FMS patients is associated with harm avoidance (HA); secondarily, we investigated the association of current MDE with other TCI dimensions.

MATERIALS AND METHODS

Patients

Patients included in this study were recruited between June 2006 and September 2008 from the Rheumatology and Neurology departments of the Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, Brazil. The neurology unit specializes in chronic pain patients, and the rheumatology unit specializes in the diagnosis and treatment of FMS. Patients were referred to a screening interview by their neurologist or rheumatologist. Physicians were instructed to refer all female patients aged 18 years or older with FMS according to the American College of Rheumatology Criteria.[1] Only females were included in the study because FMS is 10 times more prevalent in women.

The exclusion criteria included major medical conditions, debilitating neurological conditions, bipolar disorder, dysthymic disorder, psychosis and other DSM-IV Axis I disorders, except anxiety and major depressive episode, because of the high prevalence of these diagnoses. Patients with inability to comprehend the instruments were also excluded.

During the study period, 279 patients were referred to the screening visit. Forty-nine patients refused to participate in the study or missed the scheduled appointment. Fifty-nine patients were excluded because of medical comorbidities, 29 due to psychiatric conditions and 73 because of inability to comprehend the instrument instructions. Sixty-nine patients were included in the study analysis.

Measures

A questionnaire was used to collect sociodemographic data including age, marital status, educational level, employment status and total family income. Recorded clinical characteristics included length of history of FMS symptomatology (years) and current psychopharmacological treatment (antidepressant, benzodiazepine, antipsychotic).

Psychiatric disorders were diagnosed by a psychologist (D.M.S.) using the Brazilian version[43] of the Mini-International Neuropsychiatric Interview (M.I.N.I.).[44] The M.I.N.I. is a structured interview designed to access the psychiatric diagnosis in accordance with the DSM-IV and ICD-10 criteria.[44]

The Beck Depression Inventory (BDI)[45] was used to assess the severity of depression. BDI is a 21-item self-report questionnaire that has been widely used to evaluate medically ill depressed patients. The Brazilian version was validated by Gorenstein et al. (1996).[46]

The IDATE-state,[47] a 20-item self-report questionnaire, was used to measure anxiety severity; we used the Brazilian version validated by Gorenstein et al. (1996).[46]

Comorbid medical conditions were evaluated with the Cumulative Illness Rating Scale (CIRS),[48] a questionnaire that measures the severity of all comorbid illnesses and groups

them into 13 organ systems: cardiac, hypertension, vascular, respiratory, EENT (eye, ear, nose, throat, larynx), upper gastrointestinal (GI), lower GI, hepatic, renal, other GU, musculoskeletal–integumentary, neurological, endocrine–metabolic. The interviewer (D.M.S.) asked the patient about the 13 organ systems and rated the severity of illnesses for each organ as none, mild, moderate, severe or extremely severe.

Pain severity was evaluated with a visual analog scale (VAS). The scale anchors were ''no pain'' and ''pain as bad as it could be'', and with a numeric range from 0 to 10 centimeters. Patients were questioned about pain intensity in the previous week.

Personality traits were assessed using the self-administrated Brazilian version of TCI[49] consisting of 240 self-descriptive, true/false items, assessing 4 temperament dimensions (NS, HA, RD, P) and 3 character dimensions (SD, C, ST). NS includes 4 subdimensions: NS1, exploratory excitability versus stoic rigidity; NS2, impulsiveness versus reflection; NS3, extravagance versus reserve; NS4, disorderliness versus regimentation. HA consists of 4 subdimensions: HA1, anticipatory worry and pessimism versus uninhibited optimism; HA2, fear or uncertainty versus confidence; HA3, shyness with stranger versus gregariousness; HA4, fatigability versus vigor. The third dimension of temperament, RD, includes 2 subdimensions: RD1, sentimentality; and RD3, dependence versus independence. P expresses the preservation of a form of behavior as resistance to frustration. The first character dimension of SD has a further 5 subdimensions: SD1, responsibility versus blame; SD2, purposefulness versus lack of goal or direction; SD3, resourcefulness; SD4, acceptance versus self-striving; and SD5, congruent second nature. C includes 5 subdimensions: C1, social acceptance versus social intolerance; C2, empathy versus social disinterest; C3, helpfulness versus unhelpfulness; C4, compassion versus revengefulness; and C5, integrated conscience. ST includes 3 subdimensions: ST1, self-forgetfulness versus self-conscious experience; ST2, transpersonal identification versus self-isolation; ST3, spiritual acceptance versus rational materialism.[25,50]

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

Statistics

Comparisons between FMS patients with and without current MDE were performed with t-tests (for normally distributed variables), with Mann–Whitney U-tests (for variables without normal distribution) and with chi-square tests (for categorical variables). The TCI dimensions did not show normality; consequently, we used the Mann–Whitney U-test to investigate our main hypothesis (association of current MDE with HA) and our secondary hypotheses (association of current MDE with other TCI dimensions). We used Spearman's correlation tests to investigate correlation between TCI dimensions and BDI and IDATE scores. All tests were performed with an alpha of 0.05, two-tailed.

RESULTS

The 69 FMS patients included in this study had a mean age of 46.3 ($\pm$8.9) years, 9.8 ($\pm$3.7) years of schooling, 65.2% were married and 65.2% were Caucasian. The mean length of FMS symptomatology was 8.9 ($\pm$6.5) years, and the mean pain intensity on the VAS was 7 ($\pm$1.9). Sixty-six percent of the patients were using antidepressants, 8.6% were using benzodiazepine and 23.1% were using antipsychotics. Current MDE was diagnosed in 28 (40.5%) and anxiety disorder in 11 (15.9%) patients (Table 1).

We found no significant differences on sociodemographic or clinical characteristics between FMS patients with or without a diagnosis of MDE (Table 1).

Compared with non-depressed subjects, patients with MDE had higher HA scores on the main HA scale ($p = 0.002$) and on 3 out of 4 HA subscales: HA1 ($p < 0.001$), HA3 ($p = 0.040$) and HA4 ($p = 0.023$) (Table 2). Patients with MDE exhibited lower SD ($p = 0.001$) and lower C ($p = 0.027$) compared with non-depressed patients. There were no significant differences on the other TCI scales (NS, P, RD and ST) between depressed and non-depressed FMS patients (Table 2).

Among MDE patients, the BDI was positively correlated with HA ($\rho = 0.384$) and ST ($\rho = 0.466$) scores. A negative correlation was found between SD and BDI ($\rho = -0.646$). The IDATE-state was negatively correlated with the SD ($\rho = -0.397$) and C ($\rho = -0.446$) scales, and positively correlated with HA ($\rho = 0.367$). There was no significant association between pain intensity and TCI traits.

DISCUSSION

In this study of 69 FMS patients, we found that current MDE was associated with higher HA scores than in non-depressed subjects, and that HA scores were positively correlated with the severity of depressive symptoms (measured by the BDI). In addition, in a post hoc analysis (two-way ANOVA) using HA as the dependent variable and including anxiety disorders as a potential confounder, we found that MDE was associated with HA independently of anxiety disorders. High HA scores indicate a tendency to be cautious, pessimistic, insecure and fearful; these subjects present shyness in most social situations, feel chronically tired and fatigued.[51] In addition, MDE patients had lower SD and C scores than non-depressed FMS patients. Those with low SD scores are characterized by difficulties in accepting responsibility, lack of long-term goals, low self-esteem and are often dependent, whereas individuals with low C scores are characterized by social intolerance, social disinterest and always seeking their own profit.[51] These results suggest that MDE in FMS patients resembles primary depression described in non-medically ill psychiatric patients. However, besides the same three traits described above in our depressed FMS patients, previous studies with psychiatric patient samples have revealed that patients with primary MDD also have increased ST scores compared with healthy control subjects.[28–30] In our sample, ST scores were no different in depressed compared with non-depressed FMS patients. It is possible that normal levels of ST may be a characteristic of MDE associated with FMS, in contrast to primary depression.

To our knowledge, two studies used the TCI in FMS patients,[41,52] and only one evaluated the association of TCI with depressive symptoms.[41] In that study, Mazza et al. (2009) investigated the effect of selective serotonin reuptake inhibitors (SSRI) on TCI dimensions over a period of 6 months in 60 FMS patients compared with 80 healthy control subjects.[41] They reported a significant decrease in BDI scores with treatment and a depressive state and trait dependence of HA and strong depressive state dependence

Table 1 - Sociodemographic and clinical characteristics of female FMS patients with and without a current major depressive episode.

Sociodemographic and clinical characteristics	Total sample (N = 69)	MDE absent (N = 41)	MDE present (N = 28)	*p* value
Categorical variables*	**N (%)**	**N (%)**	**N (%)**	
Marital status (married)	45 (65.2)	27 (65.9)	18 (64.3)	0.788
Ethnicity (Caucasian)	45 (65.2)	28 (68.3)	17 (60.7)	0.623
Benzodiazepine (using)	6 (8.6)	3 (7.3)	3 (10.7)	0.623
Antidepressant (using)	46 (66.6)	27 (65.9)	19 (67.9)	0.862
Antipsychotic (using)	16 (23.1)	10 (24.4)	6 (21.4)	0.775
Musculoskeletal comorbidities (presence)	42 (60.8)	25 (60.9%)	17 (60.7)	0.092
Anxiety disorders	11 (15.9)	6 (14.6)	5 (17.8)	0.748
Numerical variables†	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Age	46.33 (±8.9)	47.85 (±8.6)	44.11 (±9.1)	0.088
Total family income	1794.7(±1311.8)	1843.66(±1335)	1723.21(±1297)	0.711
Educational level	9.85 (±3.7)	9.88 (±3.9)	9.82 (±3.6)	0.952
Comorbidities (CIRS)	16.10 (±3.4)	16.22 (±3.7)	15.93 (±2.8)	0.730
FMS history (years)	8.98 (±6.5)	8.73 (±0.9)	9.38 (±1.5)	0.701
Pain intensity	7.04 (±1.9)	6.87 (±0.2)	7.28 (±0.4)	0.129‡

*Chi-square.
†t-test.
‡Mann–Whitney.
CIRS = Cumulative Illness Rating Scale; MDE = major depressive episode.

Table 2 - Comparison between temperament and character inventory dimensions of female FMS patients with and without a current major depressive episode.

	MDE absent (N = 41)	MDE present (N = 28)	*p* value
Novelty seeking	16.63±5.24	15.18±4.73	0.364
NS1	6.00±2.10	4.68±2.50	0.032
NS2	3.51±2.17	3.61±1.77	0.785
NS3	4.66±2.33	4.36±2.31	0.639
NS4	2.46±1.91	2.54±1.75	0.813
Harm avoidance	18.37±6.85	23.79±6.90	0.001*
HA1	4.59±2.62	7.25±2.61	0.000
HA2	5.54±1.38	5.71±1.38	0.481
HA3	3.95±2.31	5.11±2.33	0.040
HA4	4.29±2.51	5.71±2.46	0.023
Reward dependence	14.32±3.62	13.39±3.52	0.201
RD1	7.10±1.73	7.43±1.95	0.452
RD3	4.54±2.32	3.18±2.16	0.018
RD4	2.68±1.39	2.79±1.60	0.900
Persistence	5.34±1.39	4.75±1.94	0.167
Self-directedness	31.34±6.86	25.39±7.21	0.001*
SD1	6.00±1.43	4.29±2.09	0.001
SD2	5.80±1.66	4.29±1.98	0.000
SD3	3.29±1.50	2.25±1.43	0.004
SD4	7.61±1.86	6.82±2.14	0.099
SD5	8.63±2.33	7.75±2.34	0.095
Cooperativeness	33.66±5.17	31.57±4.04	0.027*
C1	6.24±1.91	6.00±1.81	0.474
C2	5.00±1.30	4.54±1.17	0.186
C3	6.12±1.12	5.75±1.08	0.128
C4	9.07±1.21	8.75±1.27	0.229
C5	7.02±1.44	6.57±1.23	0.111
Self-transcendence	18.46±4.54	18.79±7.07	0.717
ST1	6.29±1.83	6.32±2.68	0.629
ST2	4.73±1.76	5.00±2.14	0.577
ST3	7.46±2.65	7.46±3.61	0.644

The Mann–Whitney test was used to compare the temperament and character inventory dimensions between FMS patients with and without current MDE.
*Indicates significant differences $p < 0.05$.
MDE, major depressive episode.

of SD in FMS patients. Consistent with our results, Mazza et al. (2009) also did not find an association between ST and depression trait or state.

Regarding the investigation of other aspects of depression comorbid with FMS, we found 3 studies that compared depressed with non-depressed FMS patients. In their study, Nordahl and Stiles (2007)[42] compared 25 depressed with 19 non-depressed FMS patients and also with two other groups, one with 43 psychiatric outpatients with MDD and another with 41 healthy control subjects. They found that the cognitive personality style that is typical of MDD (higher levels of sociotropy and dysfunctional attitudes) was only present in FMS patients if they met the criteria for a concurrent or lifetime history of MDD. This is a finding in line with ours, reinforcing the relevance of depression for the dysfunctional aspects of FMS patients. Johnson et al. (1997)[40] investigated the self-esteem structure in 61 female FMS patients compared with 40 healthy control subjects and 37 non-depressed patients with rheumatoid arthritis. Depressed FMS patients presented a self-esteem structure characterized by low basic self-esteem combined with a demanding need to earn self-esteem, which is a distinct pattern compared with non-depressed FMS patients, rheumatoid arthritis patients and healthy control subjects. The authors proposed that depressed FMS patients represent a specific group of FMS patients.[40] Okifuji et al. (2000)[23] reported that depressed FMS patients reported more maladaptative thoughts and functional limitations than non-depressed FMS patients.

Studies[32–34] that have investigated the association of chronic pain with TCI dimensions have reported that the TCI differences from healthy control subjects could not be explained totally by the pain condition and were explained, at least in part, by a greater presence of depressive and anxiety symptoms among FMS patients. In this particular, IDATE-state scores were positively correlated with HA and negatively correlated with SD and C. In addition, in the post hoc analysis using HA as the dependent variable, including MDE and anxiety disorders as independent variables, we found that anxiety disorders were associated with HA

independently of MDE. The prevalence of 15.9% for anxiety disorders may be considered relatively low; however, it is in accordance with the reported prevalence rates of anxiety disorders (current and lifetime) among FMS patients ranging from 11% to 65%.[5,12,53] Sixty-six percent of our patients were using antidepressants, 23.1% were using antipsychotics and 8.6% were using benzodiazepines, which could have been enough to treat some cases of anxiety disorder, but not depressive ones, and possibly, at least in part, explain the relatively low prevalence of anxiety disorders in our sample.

Two studies[35,36] have investigated the association between TCI and depression comorbid with other medical conditions (in one study, MDD comorbid with heart disease; in the other, MDD comorbid with Parkinson's disease). In both studies, the depression was only associated with HA. Together with our findings, these data suggest that depression comorbid with medical conditions has some similarities when compared with primary depression. None of these studies reported a difference in ST comparing patients and control subjects. These results suggest that several forms of depression comorbid with chronic pain may be associated with normal ST levels.

Our findings of HA dysfunction in depression associated with FMS does not preclude the possibility that non-depressed FMS may also be associated with some degree of HA dysfunction, as has been proposed by some authors. Indeed, HA may be an essential trait in the perception of pain. Pud et al. (2006)[54] studied pain perception in healthy volunteers and evaluated temperament traits with the Cloninger's tridimensional personality theory. Their results showed that HA correlated with pain responsiveness, and a higher HA was likely to predict a heightened pain response. These data support the view that treating depression, and consequently reducing HA, may be relevant to regularize pain perceptions and achieve pain control in these patients.

Some limitations of our study should be considered. Regarding the secondary hypotheses, while investigating the association of MDE with the various dimensions of the TCI, we performed multiple comparisons, increasing the probability of a type I error. We evaluated only current MDE and were not able to appraise a possible influence of previous episodes of MDD on TCI dimensions. Our sample comprised patients in a tertiary hospital; consequently, generalization of our results for less severely affected patients should be considered with prudence. We performed a cross-sectional evaluation, and it is difficult to determinate to what extent the evaluation of HA is biased by a depressive state. Studies have demonstrated that HA scores are higher during an episode of major depression compared with the periods before and after remission of the episode with successful treatment with antidepressants.[26,55] However, patients with a diagnosis of MDD even before the first episode or in a remission state after an episode have higher HA scores than the general population. A recent study treating depression in FMS patients revealed that HA was state and trait dependent on depression.[41] We compared the association between HA and MDE found in our FMS patients with literature data about the association of TCI with primary depression. The inclusion of a control group without fibromyalgia would offer more accurate information for this comparison. However, it should be remembered that our objective was to investigate the association of TCI and depression in FMS patients and not a comparison of TCI between FMS patients and those without FMS. The TCI requires a minimum of schooling; for Brazilian samples, it has been reported that at least 4 years of instruction are necessary.[49] Because of this, in our screening phase, 73 patients were excluded for inability to comprehend the TCI instructions. Consequently, it is difficult to infer whether the results of our study are applicable for patients with poor schooling.

In conclusion, although several studies have evaluated the coexistence of FMS and psychiatric disorders, data about the specific characteristics of comorbid depression are sparse. Our data support the view that patients with FMS are heterogeneous, particularly regarding the existence of a subgroup with comorbid depression. The association of depression with increased levels of HA and also with decreased levels of SD and C, found in our sample, suggests that depression in FMS patients may deserve special focus considering the clinical and psychophysiological implications of TCI dimensions. New research should consider the relevance of depression and its association with TCI dimensions with respect to fibromyalgia treatment and prognosis.

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