Are psychological distress symptoms different in fibromyalgia patients compared to relatives with and without fibromyalgia?

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ABSTRACT

Objectives. *Investigating psychological distress symptoms in the context of fibromyalgia (FM) is important due to their role in pain perception, and in the development of pain related disability. Although* The Symptom Check-List-90-Revised *(SCL-90-R)* (1) *questionnaire was used to evaluate psychological distress symptoms in FM patients, it was not applied in a familial context in families of FM patients. Our aim was to identify possible differences between FM patients and their relatives with and without FM regarding psychological distress symptoms.*

Methods. *The participants of the current investigation included 127 diagnosed female patients with FM, and 57 of their first degree relatives, 27 of whom had previously undiagnosed FM. Psychological distress was measured using* The Symptom Check-List-90-Revised *(SCL-90-R), a self report symptom inventory that addresses 9 distress dimensions reflecting various types of psychopathology.*

Results. *FM patients reported significantly higher severity in 6 of the 9 distress symptoms compared to relatives without FM: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety and psychoticism. Similar results were observed among relatives with FM, compared to the healthy group, except for anxiety. No differences were observed between FM patients and relatives with FM in the report of psychological distress.*

Conclusions. *FM patients and relatives with FM expressed similar symptoms of psychological distress compared to the healthy group.*

Introduction

The American College of Rheumatology (ACR) published in 1990 unified criteria for the classification of the fibromyalgia (FM) syndrome (2): a presence of chronic widespread pain (for at least 3 months) accompanied by minimum 11 tender points from a total of 18 defined body sites. Using these criteria, FM can be identified with a sensitivity of 88% and a specificity of 81% (2). FM is frequently accompanied by symptoms such as depression, anxiety, sleep disturbances, fatigue, chronic headaches, irritable bowel syndrome (IBS), morning stiffness, paresthesias and sensitivity to weather changes (3). It is associated with a negative effect on the quality of life and physical functioning (3-4) and with frequent use of health services (5). The prevalence of FM in the general population is 2%, and it is predominant among women (5).

The etiology of FM is still not fully understood. However, since chronic widespread pain is a major component in this illness, it is assumed that FM is a central pain disorder. This assumption is based primarily on physiological findings of elevated level of substance P in the cerebrospinal fluid (6) and low levels in concentrations of serotonin, norepinephrine and dopamine meta-bolism in FM patients compared to healthy controls (7).

Like other chronic pain conditions, FM is thought to involve psychological and social factors. The basis of this hypothesis is that mainly pre-existing personality and psychological characteristics of the individual are responsible for a variety of emotional reactions following a painful event (8). A three-stage theory (9) that may be relevant also for FM, and was based on studies of low back pain patients (10-11), suggests that chronic pain patients carry a unique personality and psychological characteristics, which may be exacerbated by the stress of attempting to cope with an enduring pain. This model describes a mental "chain reaction" deconditioning due to pain or a harmful event, which ends in acceptance of a "sick role" and in strengthening abnormal illness behavior. The first stage starts with an

acute phase, in which initial psychological reactions such as anxiety and fear appear as a result of pain occurrence. After 2 to 4 months begins the second stage. In this stage, behavioral and psychological reactions expand to the more chronic shape of the pain. As a consequence, depression, distress, somatization and other reactions, start to develop, depending on the personality or psychological characteristics and environmental conditions of the individual. As these problems continue, one enters into the last, chronic stage that is expressed by excuse from normal responsibilities and social obligations, which is known as a "sick role" (9).

Pathogenic mechanisms may be involved in chronic pain conditions as well (12). According to this theory, some circumstances like genetic predisposition are responsible for susceptibility to systemic conditions including FM. An exposure to stressors may deteriorate these illnesses, due to inadequate function of the stress response that result in various symptoms and possible psychiatric disorders.

Several epidemiologic (13-16) and genetic investigations (17-20) support familial aggregation in FM. The former studies were based on findings regarding a high prevalence of undiagnosed FM in families of patients with FM, and the later, on differences in genes polymorphism in the serotonergic (18), dopaminergic (19) and catecholaminergic (21) systems of FM patients compared to controls.

In addition, depression and anxiety that frequently go together with FM, also are explained in part by genetic factors (22-23); and depression was associated with low serotonin as well as FM. Other psychological components like somatization (24) and obsessive compulsiveness (25) were found to be associated with FM as well. Therefore, such components should be explored in the context of FM patients, and their families.

Bradley *et al*. indicated that a thorough assessment of chronic pain must include an evaluation of psychological and social factors associated with individual's subjective experience and pain behaviors (26). There are several psychological screening tests oriented toward the assessment of psychological disturbance in chronic pain conditions like the Symptom Checklist 90-Revised (SCL-90-R) (1). This questionnaire enables to measure a presence of psychopathology in chronic pain patients including FM patients (5, 27-31).

The objective of the current investigation was to identify possible differences between FM patients and their relatives with and without FM regarding psychological distress symptoms.

Patients and methods

Study population

The present study was part of a genetic study of 549 participants, which was conducted during 2003-2007 in Israel, and focused on FM diagnosed patients and their family members. For the use of the genetic study, only FM patients and relatives that fulfilled the ACR criteria or were previously diagnosed answered a structured questionnaire, which included the SCL-90-R. However, for the purpose of comparing psychological distress symptoms between FM patients and relatives without FM, we asked healthy sisters with the nearest birth date to diagnosed female patients with FM (Index cases – IC), to fulfill a structured questionnaire as well. Overall, data on the SCL-90-R were available for 127 ICs out of 131, and 57 of their female relatives from a total of 418 first-degree relatives from both sexes. Most of the ICs were out-patients at the Soroka University Medical Center in the southern part of the country. Through the ICs, we located their blood relatives. We used a cross sectional design to compare different variables in the families, and therefore, divided the relatives into 2 groups according to the 1990 ACR criteria. Finally, there were three study groups: 127 ICs (FM patients); 27 mothers, sisters and daughters with previously undiagnosed FM (relatives with FM); and 30 healthy sisters (relatives without FM). Six female relatives that were diagnosed previously to this investigation were excluded from the analysis since we did not expect to find any differences between them and other diagnosed FM patients.

All the participants signed an informed consent consistent with the Helsinki committee before they went through a physical examination and fulfilled a structured questionnaire at their homes. The interviews were administrated by a trained interviewer and were conducted, whenever possible, in a separate area in the house, in order to avoid any distractions from other family members.

Measurements

In addition to the tender points assessment, which was used for the classification of the relatives into 2 groups, the participants' tenderness threshold was measured by a dolorimeter that was applied by a pressure of about 4 kg/cm^2 on 9 tender points of the 18 sites. A trained examiner conducted both measurements. Then, the participants fulfilled a structured questionnaire concerning their socio-demographic background, health behavior, personality characteristics and psychological distress, as well as information regarding chronic widespread pain. The socio-demographic background and behavior measurements contained questions about age, education, marital status, professional status, employment, BMI and smoking. The psychological distress was evaluated by the Hopkins Symptom Checklist Revised (SCL-90-R) (1).

The SCL-90-R instrument is a self-report symptom inventory (1), which was originally oriented toward assessment of psychopathology in psychiatric and medical out-patients, and was further extended to measure psychological distress in a wide range of populations, from nonpatients "normal" populations, to medical patients (32). The SCL-90-R was validated in Hebrew (33). This questionnaire consists of 90 items regarding the last "7 days, including today". Each item has a five point scale of distress, ranging from "not at all" to "extremely" (0 to 4, respectively). These items are summarized into nine symptom dimensions: somatization, obsessive-compulsiveness, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism (34).

Statistical analysis

All the statistical analyses were conducted in SPSS 14.0. For categorical

Table I. Socio-demographic background of female patients with FM, relatives with FM and relatives without FM.

Variable		FM patients[1] n=127	Relatives with FM[2] n=27	Relatives without FM[3] n=30	*p*-value
Socio-demographic background					
Age (years)*	Range	20-78	20-74	21-68	
	Median	50	50	40	0.017
	Mean (SD)	47.5 (11.7)	47.5 (13.9)	40.4 (12.5)	
Education	Range	0-25	0-22	2-17	
	Median	12	12	12	*0.177
	Mean (SD)	13.2 (3.8)	12.2 (3.4)	12.9 (3.3)	
Marital status					
single / widow	Number (%)	25 (19.8)	6 (22.2)	7 (23.3)	^0.872
married		82 (65.1)	15 (55.6)	18 (60.0)	
divorced / separated		19 (15.1)	6 (22.2)	5 (16.7)	
Professional status					
working	Number (%)	58 (46.0)	15 (55.6)	20 (66.7)	^0.110
Employment					
Full time	Number (%)	21 (36.2)	9 (60.0)	15 (75.0)	^0.007

*Kruskal-Wallis test, (with Bonferonni correction) alpha=0.017, for an overall comparison of 3 groups. ^Chi-square test 1,2,3 – group numbers, for significance level in Mann-Whitney test, for pairwise comparisons.

Table II. Health behaviour measures of female patients with FM, relatives with FM and relatives without FM.

Variable		FM patients[1] n=127	Relatives with FM[2] n=27	Relatives without FM[3] n=30	*p*-value
Health behaviour measures					
BMI (kg/m^2)	Range	16.9-54.6&	21.7-45.9	18.9-37.9	
	Median	26.8	30.4	25.8	*0.258
	Mean (SD)	28.2 (6.3)	29.9 (6.0)	27.2 (5.4)	
Smoking	Number (%)				
current		34 (27.0)	10 (37.0)	7 (23.3)	^0.476
past		32 (32.7)	2 (11.8)	4 (16.0)	^0.078

*Kruskal-Wallis test, (with Bonferroni correction) alpha=0.017, for an overall comparison of 3 groups. ^Chi-square test & Includes a person with 177cm height and weight of 171 kg. 1,2,3 – group numbers, for significance level in Mann-Whitney test, for pairwise comparisons.

variables we used the Chi-square test in order to compare proportions in the three groups. An alpha of 0.017 was used to reject the null hypothesis (Bonferroni correction). For quantitative variables with asymmetric distribution, nonparametric Kruskal-Wallis test was used for overall comparisons of 3 groups, and pairwise comparisons were done by the nonparametric Mann-Whitney test.

Results

The present investigation included 127 female FM patients, 27 female relatives with FM and 30 female relatives without FM. Their mean ages were 47.5, 47.5 and 40.4 years, respectively, and most of them were married. The mean educational level of the three groups was similar as well as their BMI and smoking status (Tables I and II). The ICs were significantly lower regarding full time employment.

The mean tender points of FM patients, relatives with FM and relatives without FM were 15.7 (2.2), 13.5 (2.0) and 7.3 (3.4), respectively. FM patients were significantly more sensitive compared to relatives with and without FM. The same trend was observed among relatives with FM compared to relatives without FM. The dolorimetry results were similar, including lower pain threshold in FM patients than in relatives with and without FM; and of relatives with FM compared to relatives without FM.

The differences between the three groups in the SCL-90-R scores were analyzed by the Kruskal-Wallis and pairwise comparisons were done by Mann-Whitney tests, due to non-normal distribution of the psychological measures (Table III, Graph 1). The reported distress symptoms of FM patients were more severe than those of relatives without FM on somatization (P1-3<0.001), obsessive-compulsiveness (P1-3<0.001), interpersonal sensitivity (P1-3=0.006), depression (P13<0.001), anxiety (P1-3=0.002) and psychoticism (P1-3<0.001). Relatives with FM expressed higher distress in somatization (P2-3<0.001), obsessive-compulsiveness (P2-3=0.001), interpersonal sensitivity (P1-3=0.040), depression (P2-3<0.001) and psychoticism (P1-3<0.016) compared to the healthy group. There were no differences between FM patients and relatives with FM.

Discussion

In the current study, we explored psychological distress symptoms in families of FM patients. In total, we analyzed the data of 127 FM patients, 27 of their relatives with FM and 30, without FM. Our aim was to identify possible differences between FM patients and their relatives with and without FM regarding psychological distress symptoms.

In our study, FM patients had significantly more severe symptoms of somatization, depression, obsessive-compulsiveness, interpersonal sensitivity, anxiety and psychoticism compared to relatives without FM. These findings are supported by Wolfe *et al*. (5) that explored FM in the population of Whichita, KS, USA and found an association between FM and most of the SCL-90-R items, mainly somatization, depression and anxiety (5). Our findings are also supported by Sperber and coworkers that explored clinical implications of FM in

Table III. Psychological distress symptoms in FM patients, relatives with FM and relatives without FM.

Symptom*	FM patients[1] n=127 Mean (SD)	Relatives with FM[2] n=27 Mean (SD)	Relatives without FM[3] n=30 Mean (SD)	*p*-value**
Somatization	2.2 (0.9)	2.2 (0.8)	0.9 (0.7)	<0.001
Obsessive-compulsive	1.6 (0.9)	1.5 (0.9)	0.8 (0.6)	<0.001
Interpersonal sensitivity	0.8 (0.7)	0.7 (0.6)	0.5 (0.6)	0.019
Depression	1.5 (0.9)	1.3 (0.7)	0.7 (0.6)	<0.001
Anxiety	1.2 (0.9)	1.1 (0.7)	0.7 (0.6)	0.009
Hostility	0.8 (0.8)	0.6 (0.6)	0.5 (0.5)	0.291
Phobic anxiety	0.5 (0.8)	0.5 (0.7)	0.3 (0.6)	0.115
Paranoid ideation	0.7 (0.7)	0.8 (0.7)	0.5 (0.6)	0.219
Psychoticism	0.6 (0.7)	0.6 (0.6)	0.3 (0.4)	0.002
GSI	1.7 (1.7)	2.0 (1.5)	1.7 (1.4)	0.689

*Possible range of the 9 symptom dimensions: 0-"not at all" to 4- "extremely"; **Kruskal-Wallis test, (with Bonferroni correction) alpha=0.017, for an overall comparison of 3 groups; [1,2,3] Group numbers, for significance level in Mann-Whitney test, for pairwise comparisons.

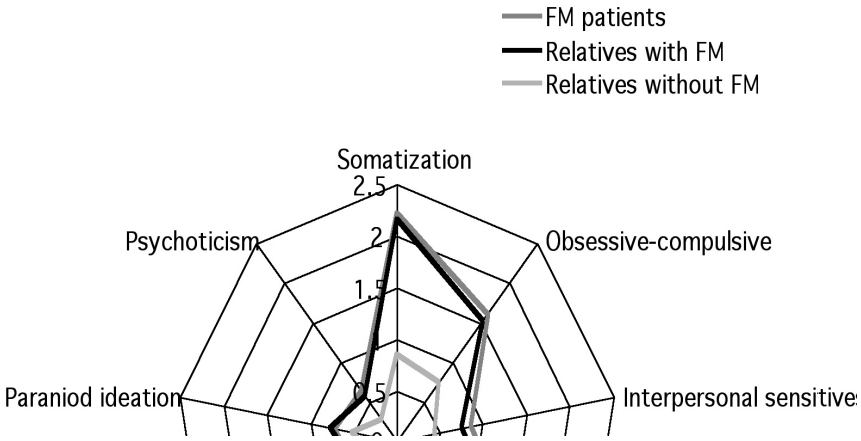

Fig. 1. Mean scores of psychological distress symptoms in FM patients, relatives with FM and relatives without FM.

IBS patients and controls and reported a severity gradient of the 9 psychological distress symptoms from controls from the general population, to IBS non-patients, IBS-only patients, and IBS-patients with concomitant FM (35).

There is a wide documentation regarding an evidence of psychiatric comorbidity in FM (16, 36-38) in addition to a familial component to this syndrome (13-20). Both were seen in our dataset, where the psychological profile of FM patients and relatives with FM was similar. This result reinforces previous findings of Arnold *et al*. (37) who investigated the co-occurrence of FM with psychiatric disorders in a familial study of FM, among FM pro-bands and their relatives, compared to rheumatoid arthritis pro-bands and their relatives. They reported an evaluated higher risk to bipolar disorder, major depressive disorder and anxiety disorder in individuals with FM relatively to those without FM (37). Hudson *et al*. observed OR of 2.0 to find co-aggregation of FM with other forms of affective spectrum disorder (ASD) (38). Our finding is also consistent with Epstein *et al*. that reported a high lifetime and current prevalence of major depression among FM patients from four tertiary-care centers in the USA (39).

However, Buckelew *et al* (40), suggested that there are differences between chronic pain conditions, such as FM, and psychiatric patients regarding SCL-90-R symptoms. Their indication was based on findings of different patterns of response to the SCL-90-R items among psychiatric inpatients compared to chronic pain patients. Whereas the former tend to endorse equivalent levels of somatic and cognitive distress items, the others were restricted to somatic signs of anxiety and depression (40).

We also found that compared to relatives with FM, the ICs were different from the healthy group on the symptom of anxiety. This finding may indicate a longer duration of pain experience as disease continues (9) among FM patients as opposed to relatives who have been diagnosed as having FM just recently, during the present study. This resemblance between FM patients and relatives with FM may be due to their common widespread chronic pain experience. In contrast to other pain conditions, a triggering event is frequently reported in the development of FM. A recent investigation has reported significantly higher levels of various forms of traumatization and dissociation among patients with FM compared to rheumatoid arthritis (41). It appears that relatives with FM are going through similar pathways as FM patients did. However, FM patients seem to adopt the "sick role" (9) as only 36.2% of them reported full time work compared to 60% among relatives with FM.

This investigation has several limitations. One limitation, concerning the study design is a selection bias. Most of the ICs that were enrolled from a list of the rheumatology outpatients of a university hospital were middle aged. As a result, many parents and siblings were deceased, or were too ill to participate. Therefore, we recruited younger FM patients that had at least one alive parent who was willing to participate in the study. In addition, drug use was ignored in the analysis. Drugs may affect the severity and number of reported psychological distress symptoms, and lead to underestimation of these symptoms.

In summary, relatives with FM were different from the healthy relatives in five psychological distress symptoms, whereas FM patients were different from this group in six distress symptoms. These findings suggest that relatives with FM tend to develop FM in the future, "given" an environmental trigger or a psychological trauma if they did not developed it already. However, as the present study is cross-sectional, no risk of disease can be inferred. Prospective

longitudinal studies of unaffected first-degree relatives of index FM cases are needed, in order to determine onset risks of the condition and the risk factors of environmental triggers of psychological traumas.

These findings raise the need for intervention strategies of the health services, such as administrating updated unified instructions for health care providers, caring for individuals with a familial background of FM. Identifying blood relatives with symptoms that may evolve into FM may have a positive effect on their quality of life and on their chances to better deal with a possible future diagnosis of FM.

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