Differences in the personality profile of fibromyalgia patients and their relatives with and without fibromyalgia

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Abbreviations:
FM: fibromyalgia
TPQ: Tridimensional Personality Questionnaire
NS: novelty seeking
HA: harm avoidance
RD: reward dependence
P: persistence

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ABSTRACT

Objectives. *To investigate whether Fibromyalgia (FM) patients differ from their first-degree relatives with and without FM regarding the four personality traits, based on Cloninger's TPQ questionnaire (1).*

Methods. *The study population was obtained from a genetic study from 2003-2007 and included 129 female FM patients, 27 female relatives with undiagnosed FM and 30 female relatives without FM. All participants completed a socio-demographic questionnaire and the Tridimensional Personality Questionnaire (TPQ) (1) that refers to four personality dimensions: "novelty seeking", "harm avoidance", "reward dependence" and "persistence". Non-articular tenderness was evaluated by tender point count and by dolorimetry.*

Results. *FM patients and their relatives with FM had higher scores on "harm avoidance" than relatives without FM ($p<0.001$, $p=0.017$ respectively). Furthermore, the mean point counts of FM patients were significantly higher and their tenderness thresholds were significantly lower than that of their relatives in the other two groups ($p<0.001$; $p<0.001$, respectively).*

Conclusions. *The findings suggest that relatives with FM display personality resemblance to FM patients especially in the personality trait harm avoidance. It appears that there are factors in this personality trait that are hereditary and that may contribute to the development of FM. However, the results could not differentiate between factors from a genetic or a non-genetic origin, due to the study design. In addition, FM's place as an independent component among genetic disorders such as pain, depression and anxiety is still unclear.*

Introduction

Fibromyalgia (FM) is a syndrome of diffuse chronic pain accompanied by specific tender points on physical examination, with unknown etiology. There are several symptoms that are frequently associated with FM, including depression, anxiety, irritable bowel syndrome (IBS), and sleep disturbances (2-4). The estimated prevalence of FM in the general population is 2%. FM is up to 7 times more prevalent among women than men (5, 6) and increases with age.

During the past few years, several studies have reported a familial aggregation in FM. Buskila *et al*. found FM among 28% of the children of women with FM (7), and 26% FM in first-degree relatives of diagnosed FM women (8). Roizenblatt *et al*. found in a study of 34 children with FM that 71% of their mothers had FM (9). An odds ratio of 8.5 of FM was found among first-degree relatives of FM patients, compared to relatives of patients with rheumatoid arthritis (10). In addition, two family studies suggested that FM might coaggregate with major mood disorders (major depressive disorder and bipolar disorder) in families of FM patients (11, 12).

This assumption is also supported by reports of genetic studies of an association between some neurotransmitters and FM. The serotonergic system is responsible for mood and deep sleep, and is involved in pain perception (13). Russell *et al*. found low levels of serotonin metabolites in FM patients compared to healthy controls (14). Moldofsky and Warsh found low levels of free plasma tryptophan in patients with FM, and a positive effect due to the use of tryptophan, on their sleep (15). Moreover, tricyclic antidepressant drugs were found to improve sleep (16), tender points measures and stiffness (17) in FM. There was also a positive effect of noradrenaline (or norepinephrine) on FM. This neurotransmitter prepares the body for appropriate response in stress-

ful situations, and affects depression. Noradrenergic selective reuptake inhibitors drugs that were designed to treat central depression and Attention-Deficit/Hyperactivity Disorder (ADHD) were also useful in the treatment of FM (18, 19). A third neurotransmitter that was associated with FM is dopamine, which is essential for normal functioning of the central nervous system, arousal and sleep, and is involved in pain modulation (20-22). A second-generation dopamine agonist that was proven to reduce the symptoms of restless legs syndrome (23, 24), improved assessment scores of pain, fatigue, functioning and global health status of FM patients (25).

These three neurotransmitters are also associated with personality traits. One of the models that enables to evaluate personality in the general population, links each of these neurotransmitter systems to a specific personality dimension. This model is called Tridimensional Personality Questionnaire (TPQ) (26). According to Cloninger, there are 3 personality dimensions: "novelty seeking" (NS), "harm avoidance" (HA) and "reward dependence" (RD) that are thought to reflect variations in three brain systems: behavioural activation, behavioural inhibition and behavioural maintenance, respectively. Each system involves a principal monoamine modulator: serotonin, dopamine and noradrenaline in that order. Genetic analysis has confirmed a hereditability component between 50% and 65% in each of the TPQ temperament factors (27). They are independently heritable, manifest in early childhood, and are moderately predictive of adolescent and adult behaviour (28). Persistence (P), a fourth temperament factor, was originally a sub-scale of the "reward dependence" dimension and was separated from it due to lack of correlation with the other sub-scales (1).

Based on this model, several investigations have already assessed the TPQ in FM. Cohen *et al*. investigated the association between FM and the serotonin transporter promoter region polymorphism, and the relationship to anxiety related personality traits in female FM patients compared to healthy subjects.

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

Variable		FM patients[1] n=129	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	
	Mean (SD)	47.5 (11.7)	47.5 (13.9)	40.4 (12.5)	*0.017
Education (years)	Range	0–25	0–22	2–17	
	Median	12	12	12	
	Mean (SD)	13.2 (3.8)	12.2 (3.4)	12.9 (3.3)	*0.177
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 (45.0)	15 (55.6)	20 (66.7)	^0.110

*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=129	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	
	Mean (SD)	28.2 (6.3)	29.9 (6.0)	27.2 (5.4)	*0.258
Smoking					
current	Number (%)	34 (26.4)	10 (37.0)	7 (23.3)	^0.476
past	Number (%)	32 (24.9)	2 (7.4)	4 (13.3)	^0.078

*Kruskal-Wallis test, (with Bonferonni 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.

FM patients had significantly lower scores on NS and higher scores on HA and P traits, and a significant difference was found in the frequency of the serotonin genotype of FM patients compared to healthy controls (29). They further investigated an association between FM and the dopamine D4 receptor gene and the relationship to NS trait in FM patients and controls with no genetic relation. They found a decreased frequency of this polymorphism in FM patients who scored low on the NS trait, compared to the controls (30).

As described above, personality traits in the context of FM were compared solely to controls with no familial relation. Therefore, the objective of the present study was to supply additional support to a familial aggregation of FM by investigating whether patients with FM differ from their first-degree relatives with and without FM regarding their personality profile, based on Cloninger's TPQ questionnaire.

Subjects and methods

Study sample

The present study was part of a genetic study of 549 participants, conducted during 2003-2007 in Israel. For the use of the genetic study, we approached 131 female FM diagnosed patients (Index cases – IC) mostly from the outpatient clinic of the Soroka University Medical Center in Beer-Sheva, and

Table III. Tenderness measurements of patients with FM, relatives with FM and relatives without FM.

Measure		Patients with FM[1] n=129	Relatives with FM[2] n=27	Relatives without FM[3] n=30	*p*-value[#]	*p*-value*
Point count	Range	9–18	11–18	0–13		p_{1-2}<0.001
	Median	16.0	13.0	7.5		p_{1-3}<0.001
	Mean (SD)	15.7 (2.2)	13.5 (2.0)	7.3 (3.4)	<0.001	p_{2-3}<0.001
Tenderness threshold	Range	0–4.7	0–6.4	2.7–7.3		p_{1-2}<0.001
	Median	2.5	3.2	4.0		p_{1-3}<0.001
	Mean (SD)	2.4 (0.9)	3.2 (1.2)	4.2 (1.3)	<0.001	p_{2-3}=0.008

[1,2,3] – group numbers.
*Kruskal-Wallis test, (with Bonferonni correction) alpha=0.017.
#pairwise comparisons by Mann-Whitney tests.

Table IV. The four personality traits of patients with FM, relatives with FM and relatives without FM.

Personality trait	Patients with FM[1] n=129 Mean (SD)	Relatives with FM[2] n=27 Mean (SD)	Relatives without FM[3] n=30 Mean (SD)	*p*-value[#]	*p*-value*
Novelty seeking (NS)	14.8 (4.2)	12.3 (4.5)	13.3 (5.2)	0.010	p_{1-2}=0.003 p_{1-3}=0.193 p_{2-3}=0.255
Harm avoidance (HA)	17.4 (6.8)	16.7 (7.5)	12.6 (6.3)	0.002	p_{1-2}=0.777 p_{1-3}<0.001 p_{2-3}=0.017
Reward dependence (RD)	13.1 (4.1)	12.5 (5.3)	12.6 (4.6)	0.865	p_{1-2}=0.647 p_{1-3}=0.719 p_{2-3}=0.936
Persistence (P)	4.0 (2.0)	3.4 (1.6)	3.6 (1.9)	0.330	p_{1-2}=0.160 p_{1-3}=0.469 p_{2-3}=0.558

[1,2,3] – group numbers.
*Kruskal-Wallis test, (with Bonferonni correction) alpha=0.017.
#pairwise comparisons by Mann-Whitney tests.

418 of their male and female first-degree relatives. FM patients and female relatives who fulfilled the 1990 ACR criteria for FM, or who were previously diagnosed, answered a structured questionnaire, including the TPQ. For comparison purposes, we administrated the structured questionnaire also to a healthy sister in each family with the closest age to the IC. Six female relatives were already diagnosed prior to this investigation and therefore were excluded from the analysis. In total, the present study included 129 ICs (*FM patients*), 27 mothers, sisters and daughters with previously undiagnosed FM (*relatives with FM*), and 30 healthy sisters (*relatives without FM*) who fulfilled the TPQ.

The interviews and physical examinations were performed by trained research assistants (interviewer and examiner) who went to each family home following the ICs approval and after having each family member's primary consent to participate, by telephone. At their homes, the participants fulfilled an informed consent, which was approved by the Helsinki committee, after receiving an explanation of the study objectives and privacy of the data.

Tenderness assessment

Tenderness was assessed by point count and by dolorimetry. A trained examiner performed both examinations. First, tender points were examined by thumb palpation at 18 tender point sites, as defined by the 1990 ACR criteria (31). Then, the tenderness threshold was measured with a dolorimeter by applying a pressure of about 4 kg/cm^2 on 9 tender point locations. The tenderness threshold is calculated as an average of the 9 tender points.

Questionnaires

We administrated a structured questionnaire concerning medical history, quality of life, physical functioning, psychological distress and personality traits to FM patients and diagnosed female relatives. Other relatives were asked a few questions about their socio-demographic background, and then whether they suffered from diffuse pain. If they did, we further inquired for how long. In case of fulfilling the first ACR criterion, this individual went through a tender point count examination. If she met the second criterion for the classification of FM this relative completed the same structured questionnaire. Due to the questionnaire's length and also in order to enable a comparison of personality traits with healthy relatives, we asked only one available healthy sister in each family with nearest age to the IC, to fulfil the questionnaire.

The current investigation included only female individuals since FM is more frequent among women (32) and rises significantly with age; and given that there are sex differences in personality traits. Women scored higher on harm avoidance and reward dependence, and lower in novelty seeking compared to men (33). Meta analysis confirmed the first two findings except for controversial findings in novelty seeking (34). In total, 186 female participants fulfilled the TPQ questionnaire. One hundred and twenty-nine of them were ICs, 27 were female relatives with undiagnosed FM, and 30 were relatives without FM.

The TPQ is a 100-item true/false instrument that takes about 15 minutes to complete (27). It is widely used worldwide, and was translated into Hebrew (35). The items are summarised into four personality dimensions, "novelty seeking" (NS), "harm avoidance" (HA), "reward dependence" (RD) and "persistence" (P). The first two traits contain 34 items each, RD – 21 items, and P – 9 items. Items 61 and 71 were dropped from scoring because of non-

specificity after an empirical item analysis in the general population (33). A low mean score represents a low expression of the trait.

Statistical analysis

Chi-square tests were used to compare proportions of qualitative variables in the 3 groups. In case of quantitative variables with asymmetric distribution, we used the nonparametric Kruskal-Wallis test to compare the three groups, and the Mann-Whitney test was used for pair-wise comparisons. A Bonferroni correction was used in comparison of the 3 groups, with a *p*-value of 0.017.

Results

The three groups were similar on most demographic and health variables, except for age and employment (Tables I, II). FM patients were approximately seven years older than relatives without FM ($p_{1\text{-}3}$= 0.013). Most of the participants were married and had an education of about 12 years. No statistical differences were found regarding country of birth, professional status, BMI or smoking.

The mean tender point count of FM patients was significantly higher compared to that of relatives with FM ($p_{1\text{-}2}$ <0.001), and without FM ($p_{1\text{-}3}$<0.001) (Table III). Similar results were found between relatives with and without FM ($p_{2\text{-}3}$<0.001). In addition, the tenderness thresholds of FM patients were significantly lower than that of their relatives in the other two groups ($p_{1\text{-}2}$ <0.001; $p_{1\text{-}3}$<0.001) (Table III), and the tenderness threshold of relatives with FM was lower than that of relatives without ($p_{2\text{-}3}$= 0.008).

The four personality traits of the TPQ were assessed and compared in the three groups (Table IV, Fig. 1). The main differences were seen in the HA and NS scores. FM patients and relatives with FM had higher scores on HA compared to the healthy relatives (p<0.001, p=0.017 respectively). With regards to NS, FM patients scored higher on NS compared to their relatives with undiagnosed FM ($p_{1\text{-}2}$= 0.003).

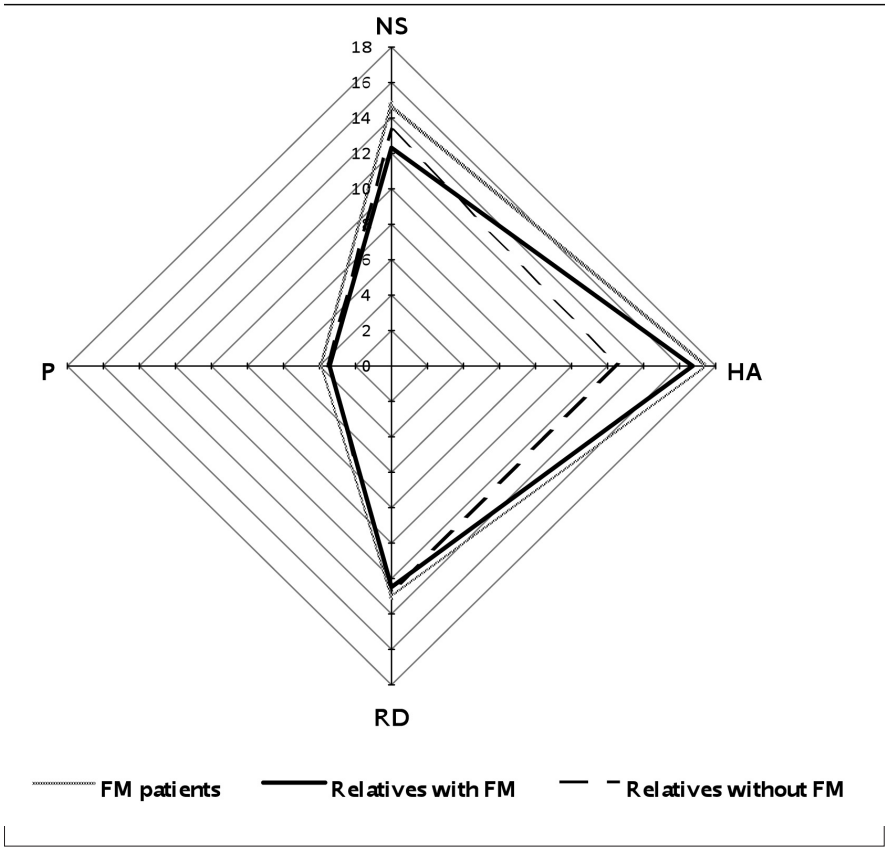

Fig 1. The four personality traits of patients with FM, relatives with FM and relatives without FM. NS: novelty seeking; HA: harm avoidance; RD: reward dependence; P: persistence.

Discussion

In the present study, we examined differences in personality profile of female FM-diagnosed patients, and their female relatives with and without FM, based on Cloninger's TPQ questionnaire.

FM patients had significantly higher mean tender point counts compared to both relatives with and without FM. In addition, the relatives with FM had significantly more tender points compared to relatives without FM. The same trend was seen in the tenderness threshold assessment. In the current study, the mean point count of both relatives with and without FM was 10.0, and their tenderness threshold was 3.9 kg. These results were similar to an earlier study that reported a mean of 10.3 tender points, and a mean tenderness threshold of 3.3 kg, in relatives of FM patients (36).

In the analysis of the TPQ, FM patients and their relatives with FM had higher scores on HA compared to relatives without FM. This finding supports a familial aggregation of FM. It is also consistent with the findings of Cohen *et al*. who investigated the association between FM and the serotonin transporter promoter region polymorphism. They found higher scores in the HA trait among female FM patients from Israeli and of Bedouin origin, compared to healthy subjects (29). Other supporting evidence comes from studies that have reported high HA in also other health conditions that are frequent in FM, such as pain (37), migraine (38), non-specific musculoskeletal disorders (39) and depression (40).

Study limitations

The ICs that were enrolled from the rheumatology outpatients of the university hospital were middle-aged women. As a result, many family members were not available for interview (were deceased or too ill to participate). Therefore, we interviewed FM patients with at least one live parent who was willing to participate in the study.

It was interesting to compare each group and especially the healthy relatives to the general population, since it is possible that even relatives without

FM are more sensitive than the general population. However, normative data are lacking in Israel and the only available sample includes male and female students and university staff members, thus representing educated individuals.

The present study cannot determine if harm avoidance behaviour leads to FM or *vice versa* since it was designed as a cross-sectional investigation. It is possible that one will develop harm-avoidance behaviour due to FM in order to reduce pain. However, it is possible that there is a pathogenic mechanism, which causes people who suffer from FM as well as other pain conditions, to react more severely in response to pain. For instance, there is a theory that pre-existing personality and psychological characteristics in an individual are responsible for a variety of emotional reactions following a painful event (41). Another theory suggests that some circumstances like genetic predisposition are responsible for susceptibility to systemic conditions like FM (42).

When people come from the same family or familial group it would be expected to find them sharing similar background such as education or habits which may have an affect on personality characteristics. Therefore, we would expect that healthy relatives will resemble individuals in the other groups in the expression of the HA trait as expressed in the RD or P traits. However, in the absence of such similarity, we suspect that genetic factors that are associated with this trait may contribute to the development of FM.

The findings of this study suggest that relatives with FM display personality resemblance to FM patients especially in the personality trait HA. Thus, relatives with FM may have a tendency to develop FM in the future, "given" an environmental trigger or a psychological trauma. It appears that there are factors in the personality trait HA that are hereditary, that may contribute to the development of FM. However, the results could not differentiate between factors from a genetic or a non-genetic origin, due to the study design. In addition, FM's place as an independent component among genetic disorders such as pain, depression and anxiety is still unclear. Therefore, further genetic investigation is necessary.

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