
Hearing loss in fibromyalgia?

Somatic sensory and non-sensory symptoms in patients with fibromyalgia and other rheumatic disorders

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ABSTRACT

Objective. It has been proposed that fibromyalgia can be understood as a disorder of central sensitisation and dysregulation (CD) and that characteristic somatic symptoms are the result of “central augmentation”. We examined this hypothesis by analysing sensory and non-sensory variables in the context of the updated (2010) American College of Rheumatology definition of fibromyalgia and the fibromyalgianess (polysymptomatic distress) scale.

Methods. We studied 11,288 patients, including those with fibromyalgia, rheumatoid arthritis (RA) and osteoarthritis (OA). We divided somatic symptoms into sensory (hearing difficulties) and evaluative (easy bruising and hair loss) non-sensory symptoms, and included a non-symptom that was neutral as to psychological content or meaning (influenza vaccination). Data were analysed by logistic regression and adjusted for age and sex.

Results. Fibromyalgia patients reported more sensory and non-sensory symptoms than patients with RA and OA, but not more non-symptoms. At all levels of fibromyalgianess (or fibromyalgia intensity) the probability of sensory and non-sensory symptoms was similar across all rheumatic diseases, and this association occurred in FM criteria (+) and criteria (-) patients. No association was noted with the non-symptom control question.

Conclusions. While the CD hypothesis is consistent with hearing problems in fibromyalgia, there is no medical explanation for the evaluative symptoms of hair loss and bruising being increased. The associations between fibromyalgia/fibromyalgianess and evaluative (not sensory) symptoms must occur through mechanisms other than central sensitisation and augmentation, and are consistent with over-reporting that has a

psychological basis. However, augmentation of sensory symptoms does not preclude simultaneous over-reporting.

Introduction

Recent advances in the understanding of fibromyalgia and its mechanisms have suggested an important role for central pain dysregulation in the genesis of the fibromyalgia phenotype (1-4, 5-10). The current central dysregulation model of fibromyalgia holds that central nervous system sensitisation leads to decreased pain threshold and to consequent increased pain that is observed clinically. But fibromyalgia is concerned with more than pain, and a signal feature of the syndrome is an increase in the number and intensity of clinical symptoms (11, 12). According to the central dysregulation model, fibromyalgia symptoms are explained by “central nervous system augmentation of sensory information (13).” As an example of this mechanism, fibromyalgia patients were shown to have “significantly greater sensitivity to all levels of auditory stimulation ...” as well as to “everyday sounds (13).” But in another study of 12,495 healthy workers, “Psychosomatic status ...” was found to affect “the relationship between subjective hearing difficulties and the results of audiometry (14).

To investigate and further clarify the central dysregulation (and augmentation) hypothesis and how it affects the fibromyalgia concept, we studied three types of self-report symptoms in patients with rheumatoid arthritis (RA), osteoarthritis (OA) and fibromyalgia: symptoms that were characterised by sensory perceptions, symptoms that were perceived but were not related to sensory perceptions (non-sensory symptoms), and reports of neutral events (non-symptoms) that were unrelated to sensory input. In addition, we inves-

Competing interests:

W. Häuser received one consultancy honorarium for study design from Daiichi Sankyo;
the other co-authors have declared no competing interests.

tigated the degree to which the fibromyalgians scale (Fig. 1), a measure of polysymptomatic distress, predicted study symptoms. We used the fibromyalgians scale to examine whether the central characteristic of fibromyalgia would be associated with specific symptoms. In this investigation we hypothesized that symptoms not associated with sensory input would be increased in fibromyalgia, a finding not consistent with the central augmentation hypothesis for symptoms, but consistent with a psychological basis; and that general symptom increases would be found as a function of fibromyalgians in patients with and without fibromyalgia, suggesting that fibromyalgia could be considered to a spectrum disorder rather than a discrete condition.

Methods

Patients and diagnoses

Beginning in 2009, we studied participants with fibromyalgia, rheumatoid arthritis and osteoarthritis who were participants in the National Data Bank for Rheumatic Diseases (NDB) longitudinal study of rheumatic diseases outcomes (15). Participants were volunteers, recruited primarily from the practices of US rheumatologists, who complete mailed or Internet questionnaires at 6-month intervals (January and July). They were not compensated for their participation. The NDB utilises an open cohort design in which patients are enrolled continuously. For patients with more than one questionnaire during the study period we randomly selected a single observation for study. Diagnoses were made by the patient's rheumatologist or confirmed by the patient's physician in cases that were self-referred (15). In this report many patients with an initial diagnosis of fibromyalgia on entry into the NDB no longer satisfy fibromyalgia criteria, a change that occurred primarily because of symptom improvement (16).

Entry criteria

Patients were designated as having criteria positive fibromyalgia if they satisfied survey criteria for fibromyalgia (17). The survey fibromyalgia criteria were modified from the American Col-

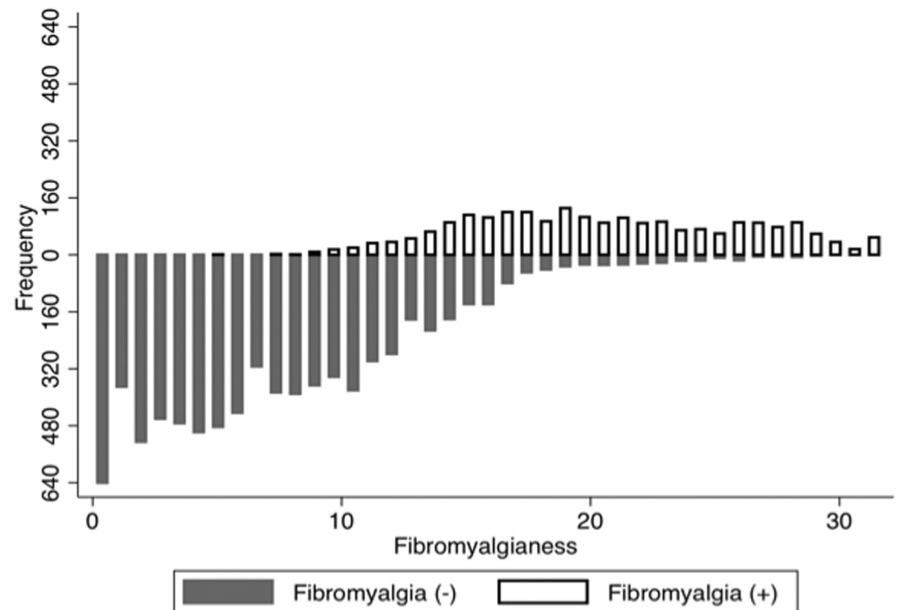


Fig. 1. Distribution of fibromyalgians scores among fibromyalgia criteria positive and negative patients with RA and osteoarthritis.

lege of Rheumatology preliminary diagnostic criteria for fibromyalgia (18) to allow the use of self-report questionnaires. For patients to be diagnosed with fibromyalgia they had to have either a Widespread Pain Index ≥ 7 and Symptom Severity Score ≥ 5 or a Widespread Pain Index between 3-6 and Symptom Severity Score ≥ 9 (17). The widespread pain index is a 0-19 count of painful body regions. The Symptom Severity Score is the sum of the severity (0-3) of the 3 symptoms (fatigue, waking unrefreshed, cognitive symptoms) plus the sum of the number of the following symptoms occurring during the previous 6 months: headaches, abdominal pain, depression (0-3). The final score is between 0 and 12.

Study variables

We examined a series of symptom variables associated with fibromyalgia and used in the ACR 2010 preliminary fibromyalgia criteria study (18). For the purpose of this study, we concentrated on 3 symptom variables and 1 control variable that allowed us to examine the central augmentation hypothesis. These variables were self-reported as yes or no by the patient and included "hearing difficulties, easy bruising" and "hair loss" within the last 6 months. We designated hearing difficulties as a sensory

somatic symptom and easy bruising and hair loss as non-sensory somatic symptoms. In addition, influenza vaccination within the last year was included as a non-symptom control variable. As influenza ("flu") vaccination is recommended by US public health authorities (19, 20), is widely used, and has no known associations with fibromyalgia, we would expect that it is not associated with fibromyalgians or increased in fibromyalgia.

The other main variables in the study were diagnosis and fibromyalgians. Fibromyalgians is the sum of the Widespread Pain Index and the Symptom Severity Score. Ranging from 0 to 31, it is an observable measure of the latent variable, polysymptomatic distress. It contains the content of all of the variables present in the survey fibromyalgia criteria and provides a full measure of the intensity of fibromyalgia symptoms (21, 22).

Statistical methods

The relations between the 3 symptom variables and the influenza vaccination variable (dependent variables) and the diagnostic groups and fibromyalgians score (predictor variables) were analysed by logistic regression, adjusted for age and sex, and reported primarily as graphics of predicted variables based

on the average marginal effect (AME). Pairwise differences between the diagnostic groups in the adjusted models utilised Bonferroni's test for multiple comparisons. Data were analysed using Stata, version 12.0 (23).

Ethical approval

Subjects' written consent was obtained according to the Declaration of Helsinki (most recently at the General Assembly in October 2008), and (2) the study has been approved by the Via Christ Institutional Review Board, Wichita, Kansas.

Results

Of the 11,288 patients, 1,199 had fibromyalgia, 8,533 had RA and 1,556 had osteoarthritis. Given the large sample size, there were statistically significant differences among diagnostic groups for all of the study variables in Table I. As noted in the table, patients with fibromyalgia were younger, more likely to be women, current smokers, and obese. Education levels were similar across groups.

Controlling for age and sex (Table II), a significantly greater percent of patients with fibromyalgia had hair loss (23.4 vs. 18.1 & 15.8), hearing difficulties (36.2 vs. 21.4 and 15.8), and easy bruising (47.6 vs. 41.5 and 38.5); and influenza vaccination was less common (57.1 vs. 63.6 and 60.9). In addition, as expected, fibromyalgianess scores were substantially higher in patients diagnosed with fibromyalgia (Table I). Figure 1 shows the distribution of fibromyalgianess scores in RA and OA and the location and number of patients satisfying modified ACR 2010 criteria in these groups. Both sensory (hearing difficulties) and non sensory (hair loss and easy bruising) symptoms are more common in fibromyalgia than in RA or OA (Table II).

Figure 2 shows the level of symptoms as a function of age for each of the 3 symptom variables and also the control variable, influenza vaccination. Importantly, both predicted means (Table II) and age-related sensory symptoms and non-sensory symptoms (Fig. 2) are greater in fibromyalgia patients than in those with other rheumatic disorders.

Figure 3 shows that the relation between sensory and non-sensory symp-

Table I. Characteristics of patients with fibromyalgia, RA and osteoarthritis.

Variable	Fibromyalgia	RA	OA
Number of subjects	1,199	8,533	1,556
Age (years)	57.8 (12.2)	62.3 (12.9)	66.5 (12.8)
Sex (% male)	4.2	19.4	18.3
Education category			
0–8 (%)	1.3	1.5	1.2
8–11 (%)	3.4	4.4	3.5
12 (%)	25.3	30.6	24.6
13–15 (%)	33.5	28.8	29.7
16 or > (%)	36.5	34.6	41.1
Current smoker (%)	14.9	11.6	7.7
Body mass index	30.9 (7.6)	28.6 (6.8)	29.5 (7.3)
WHO BMI Categories			
Underweight (BMI 18.5 kg/m ²) (%)	1.5	1.9	0.9
Normal weight (BMI 18.5–24.9 kg/m ²) (%)	20.6	31.7	28.5
Overweight (BMI 25.0–29.9 kg/m ²) (%)	28.5	32.0	30.7
Obese (BMI >30.0 kg/m ²) (%)	49.4	34.4	39.9
Polysymptomatic distress (fibromyalgianess)%	16.9 (7.6)	10.2 (7.7)	9.7 (7.1)
ACR 2010 fibromyalgia criteria positive (%)	58.7	22.4	18.3

WHO: World Health Organisation; BMI: Body Mass Index; ACR: American College of Rheumatology.

Table II. Predicted symptom prevalence and 95% confidence intervals among patients with fibromyalgia, RA and osteoarthritis, adjusted for age and sex.

Variable	Fibromyalgia	RA	OA
Number of subjects	1,199	8,533	1,556
Hearing difficulties (%)	36.2 (33.4, 39.0) ^{a,b}	21.4 (20.6, 22.3)	24.1 (22.1, 26.1)
Hair loss (%)	23.4 (20.1, 25.9) ^{a,b}	18.1 (17.1, 19.0)	15.8 (13.9, 17.7)
Easy bruising (%)	47.6 (44.7, 50.4) ^{a,b}	41.5 (40.4, 42.5)	38.5 (36.1, 40.9)
Flu vaccination (%)	57.1 (54.1, 60.1) ^a	63.6 (62.6, 64.6)	60.9 (58.3, 63.5)

^aFibromyalgia significantly different from RA; ^bFibromyalgia significantly different from OA. RA is not significantly different from OA for any variable.

toms and polysymptomatic distress is similar across all groups. That is, once polysymptomatic distress is accounted for, patients with fibromyalgia, RA and OA do not differ in the levels of symptom reporting. However, influenza rates continue to differ among the groups and are not associated with fibromyalgianess. Controlling for age, sex, and diagnostic group in logistic regression analyses, a one-unit increase in fibromyalgianess increased the risk of hair loss by 7% (Odds ratio 1.07 (95% CI 1.06, 1.08)), hearing difficulties by 7% (OR 1.07 (1.06, 1.08)), easy bruising by 8% (OR 1.08 (1.07, 1.08)), but did not increase the risk of flu vaccination (OR 1.00 (1.00, 1.01)).

Discussion

The primary purpose of this study was to explore the nature of somatic symptoms and symptom reporting in

fibromyalgia. From the time fibromyalgia was first characterised clinically, somatic symptoms have been recognised as being an integral feature of the syndrome. Fibromyalgia patients generally report more symptoms, more diagnoses and more distress associated with symptoms than patients with other rheumatic disorders (11, 12). Various psychiatric terms have been applied to increased symptom reporting (24), including excess symptom reporting, somatisation, somatising, somatoform disorders and hypochondriasis, and fibromyalgia has been categorised as a "somatoform-associated disorder (25)." Excess symptom reporting has major health economic consequences (26), but is difficult to categorise meaningfully, as symptom reporting is common in the population (27–29), the line between ordinary symptom reporting and too much symptom reporting is difficult

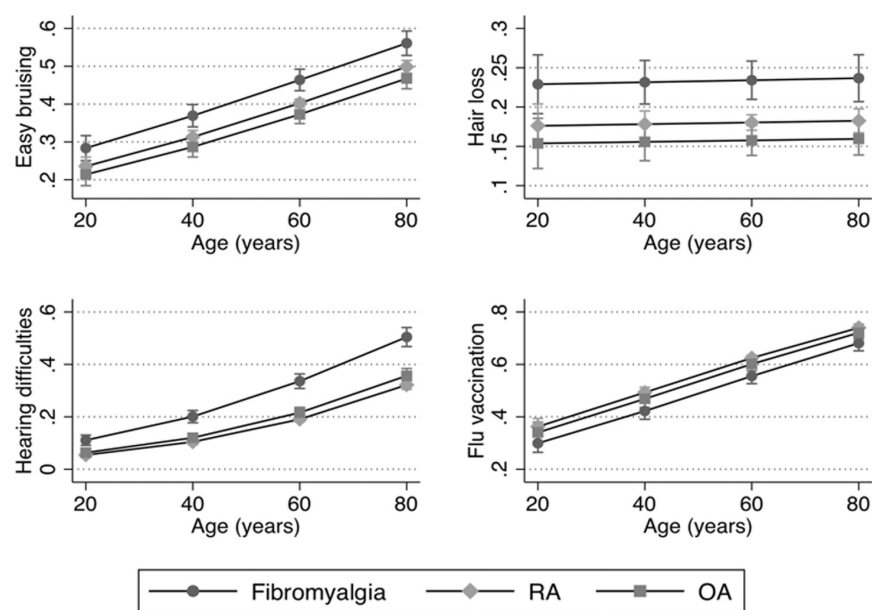


Fig. 2. The relationship between diagnostic groups and study symptoms at different ages, adjusted for sex. Symptoms are significantly more common in patients with fibromyalgia. However, influenza vaccination is slightly less common in the fibromyalgia group.

to define, and classical DSM-IV (30) somatisation disorders are rare (27). It is now recognised that increased symptom reporting can have a (neuro) biologic basis (25, 31).

The work of Clauw and others have suggested that fibromyalgia and associated disorders such as irritable bowel syndrome have similar pathophysiological underpinnings, involving what is believed to be a single common set of aberrant CNS processes (7). These disorders are held to be dysregulated “centrally-driven” conditions in which most individuals have a diffuse CNS hyperalgesia state identifiable using experimental sensory testing, and corroborated by functional neuroimaging (1-4), and somatic symptoms that include not only pain but also fatigue, insomnia, memory difficulties, and mood disorders (5, 6). Fibromyalgia symptoms are seen as representative of “generalised neurobiological amplification (7) and “central augmentation (7-9).”

Following on the observations of Wessely and Hotopf that fibromyalgia “lie[s] at the extreme end of the spectrum of polysymptomatic distress (32),” we have shown that fibromyalgia-related polysymptomatic distress can be measured by the fibromyalgianess scale (Fig. 1) (17), a measure derived from the 2010 American College of Rheu-

matology preliminary diagnostic criteria for fibromyalgia (18). We used this scale and the study symptom reports to investigate aspects of the validity of the central augmentation hypothesis. The fibromyalgianess scale allowed us to study the relation between the level of fibromyalgianess intensity (and fibromyalgia) and symptom reporting. Central to this concern is the degree to which psychological factors contribute to the pathogenesis of fibromyalgia.

The idea that intrinsic psychological factors as well as central sensitisation might play separate roles was underscored by a systematic review of the comorbidity in patients with irritable bowel syndrome (IBS). Whitehead *et al.* showed that that IBS patients were heterogeneous, with some having a predominant psychological etiology and some a predominantly biologic etiology (33). They considered the presence of multiple comorbid disorders to be a marker for psychological influences on etiology. Wilhemsen further refined this idea, indicating that “the dual-etiology hypothesis of functional somatic syndromes implies that in some patients with somatoform disorders there is a predominant biological etiology, whereas in others there is a predominant psychological etiology (31).”

In the current study we found that

non-sensory somatic symptoms were increased in fibromyalgia patients compared with RA and OA patients (Table III), but also that in all patients – regardless of diagnosis, non-sensory symptoms increased with fibromyalgianess scores. As there is no clear or hypothesized reason for increased hair loss or bruising in fibromyalgia, this suggests that this reporting is a manifestation of “over reporting” or a psychological effect.

Although the literature of functional somatic syndromes and somatoform disorders deals with symptom reporting (24), it is most always concerned with somatic symptoms and somatic symptom interpretation. Non-sensory symptom over reporting is important because it would appear to reflect primarily psychological processes in contradistinction central augmentation. Patients who for different reasons scan their body for symptoms of disease are bound to discover more symptoms than they otherwise would notice, representing a hypochondriacal belief that all symptoms are important (31). Salkovskis and Bass propose that people experience particularly severe and persistent health anxiety (‘Hypochondriasis’) because they have an enduring tendency to misinterpret bodily variations and other ambiguous health-related information (34).

While hair loss and bruising do not represent somatic symptoms, the classification of hearing loss is not as simple. Patients with FM displayed significantly greater sensitivity to all levels of auditory stimulation and were more sensitive to everyday sounds (13, 35). This increased sensitivity has been ascribed to central augmentation. But hearing loss could also represent a response to increased sensitivity and, therefore, also to central augmentation. Thus tinnitus and hyperacusis is hypothesized to be caused by central augmentation. Even so, Hashimoto (14) and colleagues, who studied audiometry in 12,495 healthy workers in Japan without excess noise exposure, noted that “Psychosomatic status...” was found to affect “the relationship between subjective hearing difficulties and the results of audiometry”, and noted that self-re-

Table III. Characteristics of study symptoms and their association with central augmentation, fibromyalgia and fibromyalgiansess.

	Symptom Class	Hypothesized Association with Central augmentation	Associated with FM	Associated with fibromyalgiansess in FM, RA and OA
Hearing loss	Sensory	±	+	+
Bruising	Non-sensory	-	+	+
Hair loss	Non-sensory	-	+	+
Influenza vaccination	Non-symptom	-	-	-

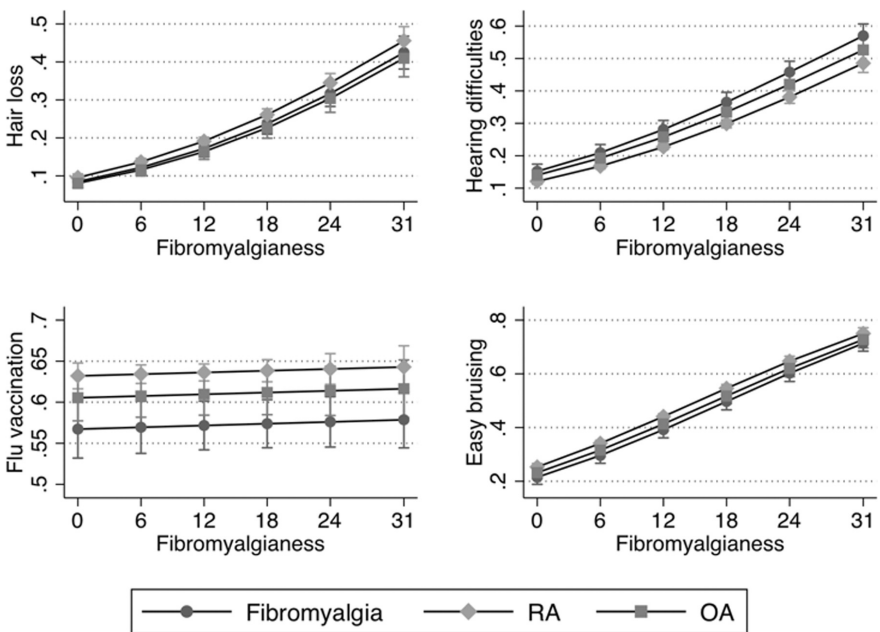


Fig. 3. The effect of fibromyalgiansess on study symptoms. The effect of fibromyalgiansess on study symptoms is similar in the 3 diagnostic groups and at all levels of fibromyalgiansess. By contrast, vaccination reporting is not affected by fibromyalgiansess, and reflects values seen in Figure 2.

port of hearing loss was associated with increased symptom reporting. In the current report all sensory symptoms were increased in patients with fibromyalgia and also in those with higher levels of fibromyalgiansess. However, influenza vaccination was not over reported (Table III). This indicates that patient responses were not generally increased, but for only increased for symptoms. Although we only reported the results of 3 symptom variables, we analysed many other symptoms that were reported in the American College of Rheumatology study (18), and found the result to be remarkably similar to what we reported here. These variables were omitted for reasons of space and clarity. The issue of psychological abnormality in fibromyalgia is complex. Multiple

studies have found more psychological illness in fibromyalgia than in control subjects. Depression in fibromyalgia may be secondary to pain. On the other hand familial studies show evidence of depression in family members (36, 37). Fibromyalgia has been linked to a series of specific conditions including anxiety (38, 39), alexithymia (40, 41), hypervigilance (35), hypochondriasis (42, 43), and somatisation (43-46). Hypochondriasis is associated with health anxiety and responds to cognitive behavioural therapy (CBT), as does fibromyalgia. Whitehead's review of IBS concluded that there was evidence of psychological abnormality in patients with multiple comorbid conditions (33), also a frequent finding in fibromyalgia (11, 12). Despite many suggestions, there is no clear single

psychological abnormality that links all fibromyalgia patients. While our data are consistent with the central augmentation hypothesis, they are also consistent with other interpretations, in particularly over-reporting unrelated to central augmentation. The fibromyalgiansess scale provides a measure of polysymptomatic distress, and was derived from the 2010 American College of Rheumatology criteria (18). When we applied this scale to the study symptoms (Fig. 3) we noted that higher levels of fibromyalgiansess were associated with increased probability of symptom reporting. In addition, it was not necessary for criteria positive fibromyalgia to be present for the scale to predict symptoms. Thus one interpretation of the symptoms is that they are a measure of polysymptomatic distress. We found this association with both sensory and non-sensory symptoms, but not with our neutral control reporting variable, influenza vaccination. This indicates that not all reporting is increased in fibromyalgia, but only reporting that has intrinsic (psychological) meaning to the patient. These finding suggest to us two important problems with the fibromyalgia concept and the central augmentation hypothesis. First, the fibromyalgiansess scale and its performance suggest that the division into fibromyalgia positive and negative cases is artificial. Rather, the concept of fibromyalgia and fibromyalgiansess exists as a continuum. Second, while there is substantial evidence in support of the central augmentation hypothesis (7, 9, 47-49) it is clearly insufficient to explain all of the observed data. Finally, we believe that studies of fibromyalgia that compare the end of the spectrum of polysymptomatic distress with "normals" distort the reality of the nature of polysymptomatic distress. In summary, our data find evidence of general over reporting in patients with fibromyalgia and do not suggest the central augmentation model is sufficient. Symptoms linked to fibromyalgia are identified across the entire spectrum of fibromyalgia, and do not require a diagnosis of fibromyalgia. It seems likely that psychological factors that are independent of the central sensitisation play a role in this disorder.

Key messages

- Fibromyalgia patients report more sensory and non-sensory symptoms, but not more non-symptoms.
- Controlling for fibromyalgianess, sensory/non-sensory symptoms are similar across all rheumatic diseases, including fibromyalgia.
- Fibromyalgia symptoms may bypass central sensitisation mechanisms, and are consistent with psychologically-based over-reporting.

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