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Generalized hypervigilance in fibromyalgia: evidence of perceptual amplification

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Summary The hypervigilance model of pain perception states that chronic pain patients have a heightened sensitivity to pain (e.g. low threshold and tolerance) because of increased attention to external stimulation and a preoccupation with pain sensations. This study tested the hypothesis that individuals with fibromyalgia, a chronic pain disorder of undetermined origin, have a generalized hypervigilant pattern of responding that extends beyond the pain domain. Twenty fibromyalgia out-patients, 20 rheumatoid arthritis (RA) patients, and 20 normal controls served as subjects. The RA and normal control subjects were age and sex matched to the fibromyalgia patients. Subjects were tested for pain tolerance, pain threshold, and noise tolerance and were asked to complete a number of questionnaires that assessed hypervigilance. As predicted, the responses of the fibromyalgia patients to both the pain and auditory stimuli were consistent with the generalized hypervigilance hypothesis. These patients had significantly lower threshold and tolerance values than the RA patients, who in turn, had lower values than the normal control subjects. The results of the psychological questionnaires revealed that the fibromyalgia and RA patients preferred lower levels of external stimulation than the control subjects. The outcome of this study supports the generalized hypervigilance hypothesis, suggesting that fibromyalgia patients have a perceptual style of amplification. The implications of these findings for understanding the role of biological, cognitive, and perceptual factors in pain disorders are discussed.

Key words: Fibromyalgia; Generalized hypervigilance; Pain perception

Introduction

Fibromyalgia is a chronic pain disorder of uncertain origin that affects the musculoskeletal system. Patients suffering from fibromyalgia report diffuse musculoskeletal aching and stiffness, a non-restorative sleep pattern, fatigue, and muscle stiffness upon awakening (Smythe 1986; Wolfe et al. 1990). Specific areas of localized tenderness, referred to as 'tender points', distinguish fibromyalgia from other soft tissue rheumatoid disorders (McCain and Scudds 1988).

Previous research has indicated that fibromyalgia patients have an increased sensitivity to painful stimulation (Scudds et al. 1987). These findings are in keeping with the hypervigilance model of pain perception (Chapman 1978; Rollman and Lautenbacher 1993) which states that certain chronic pain patients have heightened sensitivity to experimentally induced pain, showing increased attention to external stimulation and a preoccupation with pain sensations.

The present study examined whether the pattern of hypervigilance observed in response to painful somatosensory stimuli extends to other sensory domains. Rollman and Lautenbacher (1993) postulated that fibromyalgia involves a generalized pattern of hypervigilance, marked by increased attention to a variety of external and internal noxious sensations. They suggested that fibromyalgia patients are more observant of perceptual experiences with a negative quality, with pain being the one on which the most attention is focused. Thus, hypervigilance is viewed as an altered perceptual style, involving amplification of aversive stimuli.

Possible sources of hypervigilance

There has been speculation regarding factors that may contribute to an individual being hypervigilant. For example, Chapman (1978) proposed that hypervigilance may be mediated by cognitive factors, reflecting the in-

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fluence of past experience or present mental processes. Also, it may be that hypervigilance results from individuals paying attention to particular events or from a cognitive set or schema that leads the perceiver to search for somatic cues (Chapman 1978; Pennebaker 1982). For example, Pilowsky (1967) noted that in somatization disorders, patients may develop perceptual habits of hypervigilance for somatic distress signals. Other sorts of patients, such as those suffering from hypochondriasis, monitor bodily sensations closely, fearing that every noxious signal is indicative of disease. These behavior patterns are consistent with studies which suggest that body awareness may increase the probability that an individual will perceive internal sensations as being more noxious (Pennebaker and Lightner 1980).

With respect to fibromyalgia, it is possible that the nature of the disorder itself may augment hypervigilant behavior. Fibromyalgia patients have been diagnosed with a disorder that lacks a clearly identifiable organic cause, a disorder that physicians often cannot explain easily to their patients. The uncertainty and ambiguity surrounding the diagnosis of fibromyalgia may cause patients to worry that their symptoms might have been misdiagnosed and may be indicative of a much more serious condition. As a result, fibromyalgia patients may be even more likely to monitor bodily sensations and become preoccupied or 'vigilant' about such perceptual experiences (Robbins et al. 1990).

Generalized hypervigilance and fibromyalgia

Pain appears to be the hallmark symptom of fibromyalgia (Rollman 1989). Leavitt et al. (1986) determined that fibromyalgia patients selected significantly more words to describe their pain on the McGill Pain Questionnaire (MPQ) than arthritis patients. Perry et al. (1988) administered the MPQ, along with a visual analogue pain scale, to fibromyalgia and polyarthritis patients. For each of a number of measures, the fibromyalgia patients had significantly higher scores.

The clinical data suggest that fibromyalgia patients experience widespread and intense pain, not limited to tender point areas. Wolfe et al. (1990) reported that 59.5% of fibromyalgia patients said that they had pain in 15 or more body regions and that 68.8% of fibromyalgia patients described experiencing 'pain all over'. Moreover, there is evidence that fibromyalgia patients have a heightened response to other aversive sensory stimuli, not directly related to their disorder.

Block (1993) and Smythe (1986) observed that in addition to the pain and stiffness experienced by fibromyalgia patients, a substantial number report experiencing symptoms in various systems. For example, many fibromyalgia patients report numerous somatic complaints such as swelling feelings in soft tissues, paresthesias, chronic headache, irritable bowel syndrome, primary dysmenorrhea, temporomandibular dysfunction, and irritable bladder syndrome (Yunus et al. 1991). Another survey indicated additional problems and medical conditions that appear to be associated with the syndrome, including sensory symptoms, tinnitus, and aggravation of symptoms by noise, lights, stress, posture, and weather (Waylonis and Heck 1992). Consistent with these data are findings that revealed that three syndromes with uncertain etiologies: irritable bowel, chronic headache, and primary dysmenorrhea were significantly more common in fibromyalgia patients, compared with RA patients and normal control subjects (Yunus et al. 1989). These findings suggest that fibromyalgia patients find a variety of body experiences to be aversive. Smythe (1986) has described these patients as having an 'exquisite hypersensitivity' to a variety of external and internal stimuli and has referred to fibromyalgia as the 'irritable everything syndrome'.

Studies which have induced experimental pain indicate that fibromyalgia patients tend to have an exaggerated response to noxious stimuli when compared with other groups. Tunks et al. (1988) found that fibromyalgia patients had significantly lower pain thresholds than control subjects at both tender and non-tender points. Similar results have been reported by Granges et al. (1993), Granges and Littlejohn (1993b), Lautenschläger et al. (1991) and Scudds et al. (1987). Wolfe et al. (1995a) studied the incidence of fibromyalgia in the general population; decreased pressure pain threshold correlated with such symptoms of fibromyalgia as tender points, 'pain all over', fatigue, and irritable bowel symptoms, even in those who did not meet the standard criteria for the syndrome.

Lautenbacher et al. (1994) examined the responsiveness of fibromyalgia patients and matched healthy control subjects to a variety of noxious stimuli. Pressure, heat, and electrocutaneous thresholds were measured. The pressure pain thresholds were lower for the fibromyalgia group at both a tender and a non-tender control point. The same pattern of results was observed for the heat pain thresholds. The authors indicated that a 'pattern of pain hyperresponsiveness' appears to be associated with fibromyalgia and proposed that this pattern may consist of both central and peripheral factors.

Arroyo and Cohen (1993) also examined pain tolerance for electrocutaneous stimulation in the upper limbs of fibromyalgia patients and normal controls. Tolerance was markedly reduced in the patients (although there was no difference in detection thresholds), and all of them described a widespread sensation of tingling or burning, with tingling sensations around the electrodes lasting for seconds to minutes after stimulation.

The clinical and experimental studies cited above sug-

gest that fibromyalgia patients may have a hypervigilant pattern of perceiving. It appears that this pattern is not specific to muscular pain at tender points, but extends, at least, to other body areas and other forms of pain induction.

Research questions

Fibromyalgia patients, RA patients, and healthy volunteers were subjects in the present study. RA patients were selected as the control group because they also suffer from a painful rheumatological disorder. A fundamental difference between the two is that fibromyalgia does not have an established etiology, whereas rheumatoid arthritis has identifiable organic markers.

Pain tolerance and threshold were measured at a non-tender point using a pressure dolorimeter. Based on previous research (Scudds et al. 1987), it was predicted that fibromyalgia patients would have significantly lower pain threshold and tolerance levels when compared with the other groups. In addition, it was predicted that the RA patients would have lower levels than the control subjects.

Dolorimetry emphasizes pain assessment associated with soft tissue stimulation. To determine if fibromyalgia patients had a generalized hypervigilant pattern of responding, testing was extended to another domain, that of audition. Earlier studies have suggested that fibromyalgia patients may have altered auditory mechanisms (Gerster and Hadj-Djilani 1984; Hadj-Djilani and Gerster 1984). Changes in auditory processing have been examined in other pain states. Drummond and Woodhouse (1993) found that auditory discomfort thresholds did not differ between migraine sufferers and controls when tests were carried out during a headache-free interval, nor did they change during painful stimulation of the forehead with ice. However, during migraine attacks, auditory (and visual) discomfort thresholds decreased substantially (Woodhouse and Drummond 1993).

In the present study, all subjects were exposed to a white noise stimulus and noise tolerance levels were measured. The generalized hypervigilance hypothesis predicts that the fibromyalgia patients would overreact to this external stimulus and would have lower noise tolerance than the RA and normal control subjects. It was also of interest to see whether the RA patients would have lower noise tolerance levels than the normal control group.

In addition to perceptual measures, utilizing mechanical and auditory stimuli, we assessed hypervigilant behavior by means of questionnaires. All subjects were asked to complete three psychometric inventories: the Noise Sensitivity Scale, the Kohn Reactivity Scale, and the Pennebaker Inventory of Limbic Languidness.

Methods

Subjects

Sixty subjects participated in the study, with 20 subjects in each of the three groups. Patient groups were drawn from the Rheumatic Diseases Unit at University Hospital, London, Ontario, Canada. While the patients selected for this study might be expected to differ from patients seen by general practitioners, they are likely to be typical of those seen in rheumatology clinics.

Group 1 consisted of individuals diagnosed with fibromyalgia according to the criteria of Wolfe et al. (1990). Patients were contacted by telephone and the purpose of the study was explained to them. If a patient agreed to participate, an appointment for the testing session was arranged. The first twenty consecutive consenting patients were included in the study.

The response rate for this group was 69%. Twenty-nine patients were contacted (26 females and 3 males). Nineteen females and 1 male agreed to participate. The age range for the fibromyalgia subjects was 29–59 years, with a mean age of 46.1 years and a standard deviation of 7.6 years.

Group 2 consisted of 20 individuals who fulfilled the diagnostic criteria for either classical or definite rheumatoid arthritis. These patients were contacted in the same manner as were the fibromyalgia patients. The RA subjects were age and sex matched to the 20 fibromyalgia patients. The response rate for the rheumatoid arthritis group was 65%. Thirty-one patients (28 females and 3 males) were contacted. Again 19 females and 1 male participated. The ages of this group ranged from 21–66 years, with a mean age of 46.0 years and a standard deviation of 13.4 years.

Group 3 was composed of 20 healthy volunteers. This control group consisted of hospital staff, university graduate students, and volunteers from the community. These subjects did not have any chronic pain disorders. They were age and sex matched to the fibromyalgia patients. The age range of this group was from 25–60 years, with a mean age of 42.5 years and a standard deviation of 9.8 years. Normal control subjects were paid $10 for their participation.

There was no difference between the fibromyalgia and the rheumatoid arthritis groups in terms of the duration of their pain problems. The average pain duration for the fibromyalgia patients was 7.79 years with a standard deviation of 5.12 years. The rheumatoid arthritis group had a pain duration of 7.97 years with a standard deviation of 5.98 years.

All subjects were requested not to take any analgesics or non-steroidal anti-inflammatory medications for a minimum period of 12 h before testing. Testing of all subjects occurred in the Rheumatic Diseases Unit out-patient clinic at University Hospital.

Materials

Pressure dolorimeter

A Fischer variable pressure dolorimeter was used to apply pressure to a point ~2 inches above the wrist. This point is not considered to be a fibromyalgia tender point. The subject's arm was pronated and supported. The dolorimeter is a spring-loaded gauge with a range of 0–17 kg, tipped with a protective rubber stopper that has a diameter of 1.0 cm. Pressure was applied by the experimenter at the rate of ~1 kg/sec. Pressure was applied first to the non-dominant arm and then to the dominant arm. Subjects were asked to indicate verbally when pain threshold (the point at which the stimulus is first perceived to be painful) and pain tolerance (the point where the subject indicates the maximum degree of pain he/she is willing to endure) were reached. Pressure was discontinued when tolerance was indicated by the subject or when the maximum pressure of 17 kg was reached.

Noise generator

A noise generator (Maico Electronic Company) was used to produce continuous white noise. Noise was presented through a headset that was controlled by an attenuator. The noise level was increased in 5 dB increments. Subjects were exposed to each noise level step for ~3 sec and were asked to indicate when noise tolerance was reached. This task was repeated three times so that the consistency of the ratings

could be examined. The presentation of the noise stimulus was discontinued when tolerance was indicated by the subject or when the maximum of 105 dB was reached.

Visual analogue scale

A 10 cm sliding rule visual analogue scale (VAS) with word delimiters at opposite ends (i.e. 'no pain' and 'worst pain ever') was used to obtain measures of pain intensity. Subjects were asked to rate their present pain intensity and to rate their average pain intensity for the previous month. All subjects completed the VAS ratings at the beginning of the testing session.

Psychological questionnaires to measure hypervigilance

Three questionnaires were selected to measure hypervigilance (i.e. sensitivity to sensory stimuli). Each is discussed below.

Noise Sensitivity Scale (NSS)

This scale consists of 21 questions designed to assess an individual's sensitivity to noise. It emphasizes affective reactions and avoids general inquiries about noise as an environmental problem. Subjects are asked to rate each question on a 6-point scale (1 = 'agree strongly' and 6 = 'disagree strongly'). Kuder-Richardson reliability of the scale has been reported to range from 0.84 to 0.87. Adequate validity has been reported (Weinstein 1978).

Kohn Reactivity Scale (KRS)

This scale consists of 24 items that assess an individual's level of reactivity or nervous system arousability. This measure has been shown to correlate negatively with pain tolerance and pain perception (Dubreuil and Kohn 1986). Subjects are asked to indicate the extent to which they agree with each item on a 5-point scale (1 = 'disagree strongly' and 5 = 'agree strongly'). Alpha reliabilities have been reported to range from 0.73 to 0.83 (Kohn 1985). Convergent validity has been demonstrated. The KRS is correlated negatively with instruments that are related conceptually but keyed in the opposite direction (e.g. the extraversion subscale of the Eysenck Personality Inventory, the reducing subscale on Vando's Reducer-Augmenter Scale, and the strength of excitation scale from the Strelau Temperament Inventory). In addition, the KRS has been shown to possess discriminant validity. For example, the KRS has non-significant correlations with the Desire for Novelty Scale, a conceptually unrelated scale that measures boredom and a desire for change.

Pennebaker Inventory for Limbic Languidness (PILL)

The PILL is a checklist that assesses the frequency of occurrence of 54 common physical symptoms and sensations. Subjects are asked to indicate on a 5-point scale how often they experience each symptom from 1 = 'have never or almost never experienced the symptom' to 5 = 'more than once every week'. The PILL has high internal consistency, with a Cronbach alpha of 0.88. In addition, the PILL has been shown to possess adequate test-retest reliability (e.g. 0.70 for a 2 month period) (Pennebaker 1982).

Several other questionnaires assessing coping strategies were completed by subjects. These findings will not be discussed in this report.

Procedure

Subjects were tested individually. The total testing time for each subject was ~75 min. First, subjects read a letter of information that explained the study in detail. Subjects were given an opportunity to have any questions or concerns addressed. When the questions had been answered, participants read and signed an informed consent form.

Fibromyalgia patients were the initial group to be tested because the rheumatoid arthritis and normal control groups had to be age and sex-matched to the fibromyalgia group.

All subjects were presented first with the visual analogue scale and were asked to make two ratings: present pain intensity and average pain intensity for the previous month.

Subjects in each of the three groups were assigned randomly to one of two orders. Half the subjects completed the psychological questionnaires first and then received the experimental measures. The remainder of the subjects received the experimental measures first, followed by the psychological questionnaires. Questionnaires were presented in one of two randomly determined orders, so that half of the subjects in each of the three groups received each order.

Results

Subject characteristics

As stated previously, the groups were matched for age and sex. There were 19 females and 1 male in each group. The results of univariate analyses of variance (ANOVAs) indicated that the groups did not differ significantly in terms of age ($F(2,57) = 0.95$, $P > 0.05$) or in the length of time from the onset of reported pain ($F(1,38) = 0.012$, $P > 0.05$).

Also, separate ANOVAs were performed to determine if there were order effects for the presentation of questionnaires or for the testing procedure (i.e. the order in which subjects received experimental measures and questionnaires). Both ANOVAs were non-significant.

Perception measures

A multivariate analysis of variance (MANOVA) was performed on the perception measures which consisted of the following: the VAS present pain intensity rating, the VAS pain intensity rating for the past 30 days, the average pain threshold (dominant and non-dominant arms), average pain tolerance (dominant and non-dominant arms), and the average noise tolerance rating (average of the three noise tolerance measures).

Pillais' statistic was chosen as the multivariate test of significance because it is one of the most robust in that it is not affected by minor violations of assumptions (Olson 1976). If the MANOVA results indicated that there was a significant multivariate effect, one-way ANOVAs were computed for each dependent variable. For any statistically significant ANOVA, Scheffé's post-hoc test of multiple comparisons (evaluated at the 0.05 level of significance) was used to determine which groups differed significantly.

A significant multivariate effect was obtained for the perception measures (Pillais = 0.93217, approximate $F(10,108) = 9.43$, $P < 0.0001$). Separate univariate ANOVAs were conducted on the dependent variables.

Visual Analogue Scale (VAS) Ratings

As stated previously, subjects made ratings on a VAS sliding scale with word delimiters 'no pain' and 'worst pain ever' at opposite ends. On a 10-point scale, 'no pain' was equivalent to a rating of 0, whereas 'worst pain ever' corresponded with a rating of 10. The univariate ANOVA for present pain intensity was statistically significant ($F(2,57) = 34.88$, $P < 0.0001$). Scheffé's post-hoc test indicated that fibromyalgia patients rated their pain as being significantly more intense (mean = 4.30, SD = 2.27) than the RA patients

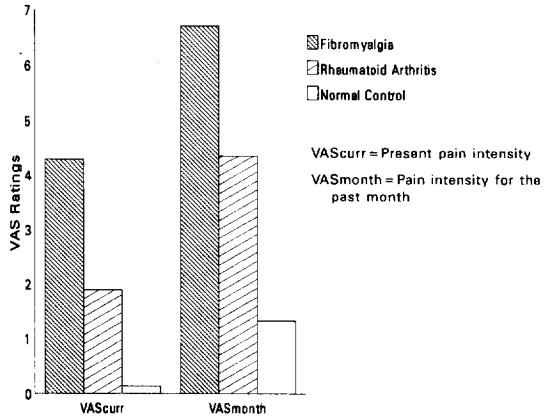

Fig. 1. Mean Visual Analogue scale (VAS) pain intensity ratings for the three groups. For both VAS ratings, the Fibromyalgia group differed significantly from the Rheumatoid Arthritis and Normal Control groups. The Rheumatoid Arthritis group differed significantly from the Normal Control group.

(mean = 1.89, SD = 1.49) and normal control subjects (mean = 0.14, SD = 0.34). In addition, the ratings of the RA group were significantly greater than those of the normal control group.

Similarly, the univariate ANOVA for average pain intensity over the past 30 days was statistically significant ($F(2,57) = 34.90$, $P < 0.0001$), with post-hoc tests revealing that fibromyalgia patients (mean = 6.72, SD = 1.90) rated their pain as significantly more intense than the RA (mean = 4.37, SD = 2.28) and normal control subjects (mean = 1.33, SD = 1.95). As well, the RA group had significantly higher values than the normal control subjects. Fig. 1 illustrates the VAS pain intensity findings.

Pain threshold and tolerance values

Pain threshold and tolerance were measured on the dominant and non-dominant arm of each subject. Separate *t*-tests were calculated for the dominant and non-dominant values for each group to determine if any differences existed. The results of *t*-tests for all groups were non-significant (all $P > 0.05$). Thus, the dominant and non-dominant values for each group were combined to give average pain threshold and tolerance values. The average values were analyzed.

The ANOVA performed on average dolorimeter pressure pain threshold indicated that there were significant group differences ($F(2,57) = 68.17$, $P < 0.0001$). As predicted, post-hoc tests revealed that the fibromyalgia patients had significantly lower pain thresholds (mean = 1.51 kg, SD = 0.72) than the RA group (mean = 2.89 kg, SD = 0.66) and the normal control group (mean = 5.50 kg, SD = 1.63). The RA group had significantly lower pain thresholds than the normal control group.

Similar findings were reported when average pain tolerance values were analyzed. The ANOVA indicated that there were statistically significant group differences ($F(2,57) = 53.83$, $P < 0.001$), with post-hoc tests revealing that the fibromyalgia patients had significantly lower pain tolerance (mean = 2.78 kg, SD = 1.28) when compared with the RA group (mean = 4.59 kg, SD = 1.57) and the normal control group (mean = 8.05 kg, SD = 1.97). Again, the RA group reported significantly lower pain tolerance values than the normal control group. Fig. 2 illustrates the pain threshold and pain tolerance values for each of the groups.

Noise tolerance values

As stated previously, subjects were asked to provide three noise tolerance determinations. Separate *t*-tests were calculated for each of the three groups to determine if significant differences existed among the three noise blocks. The *t*-test results indicated that no differences existed (all $P > 0.05$). Thus, the three values were combined to create an average noise tolerance value. These were analyzed using a one-way ANOVA. The results indicated that the groups differed significantly ($F(2,57) = 64.18$, $P < 0.001$). Post-hoc tests showed that the fibromyalgia patients had significantly lower noise tolerance values (mean = 66.17 dB, SD = 9.15) when compared with the RA group (mean = 75.98 dB, SD = 12.35) and the normal control group (mean = 100.48 dB, SD = 7.47). In addition, the RA subjects reported significantly lower values than the normal control group. Fig. 3 depicts the noise tolerance values for each of the groups.

These findings provide support for the generalized hypervigilance hypothesis. The pain threshold, pain tolerance, and noise tolerance levels were each in the predicted direction, with the fibromyalgia and RA groups having lower values than the normal control group, and the fibromyalgia patients having lower

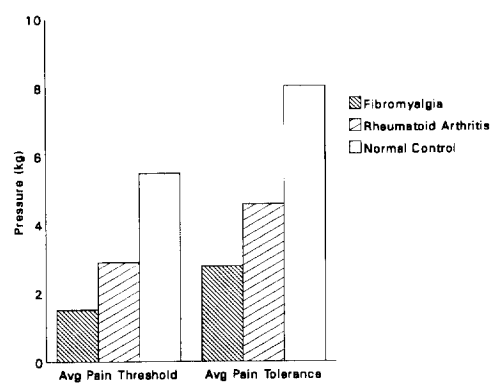

Fig. 2. Average pain threshold and tolerance for the three groups. The Fibromyalgia group differed significantly from the Rheumatoid Arthritis and Normal Control groups. The Rheumatoid Arthritis group differed significantly from the Normal Control group.

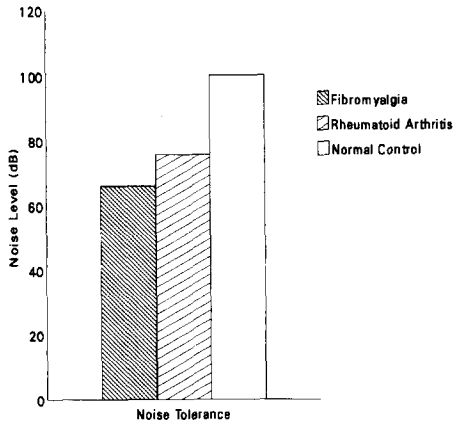

Fig. 3. Average noise tolerance for the three groups. The Fibromyalgia group differed significantly from the Rheumatoid Arthritis and Normal Control groups. The Rheumatoid Arthritis group differed significantly from the Normal Control group.

values than the RA group. These differences remained significant when the effects of present and average pain intensity were controlled for statistically.

Psychological measures

A MANOVA was performed to test for the significance of the NSS, KRS, and PILL measures. A statistically significant multivariate effect was obtained (Pillais = 0.64894, approximate $F(6,112) = 8.97$, $P < 0.0001$). The results of the univariate ANOVAs are discussed below.

Noise Sensitivity Scale (NSS)

A univariate ANOVA was used to analyze the NSS scores. The results indicated that significant group differences existed on this measure ($F(2,57) = 6.70$, $P < 0.01$). Post-hoc tests revealed that the fibromyalgia patients (mean = 96.35, SD = 13.18) were significantly more noise sensitive than the normal control subjects (mean = 79.90, SD = 13.14). No significant differences were found to exist between the patient groups (for the RA patients, mean = 85.55, SD = 16.72).

Kohn Reactivity Scale (KRS)

The results of a one-way ANOVA revealed significant group differences ($F(2,57) = 9.81$, $P < 0.001$) for this measure. Post-hoc tests indicated that the fibromyalgia patients (mean = 88.70, SD = 14.10) and the RA patients (mean = 87.00, SD = 10.32) were significantly more reactive than the normal controls (mean = 73.95, SD = 9.64). The fibromyalgia and RA patients did not differ significantly from each other.

Pennebaker Inventory of Limbic Languidness (PILL)

The procedure used for calculating total scores for this measure was modified slightly. Typically, the total score consists of the sum of the 54 items. For the purpose of the present study, 6 items related to swollen and stiff joints, stiff and sore muscles, and back pain were omitted for it was assumed that including these items would artificially inflate the scores of the fibromyalgia and RA patients. Thus, 48 items were summed to create the total scores for the three groups of subjects.

The results of the one-way ANOVA indicated that there were significant group differences on this measure ($F(2,57) = 30.16$, $P < 0.0001$). As predicted, post-hoc tests revealed that the fibromyalgia patients reported experiencing symptoms (mean = 133.85, SD = 29.55) significantly more frequently than the RA patients (mean = 99.90, SD = 24.13) and the normal control subjects (mean = 76.80, SD = 13.52). In addition, the RA patients reported experiencing symptoms significantly more frequently than the normal control group. Fig. 4 illustrates the findings of the PILL.

Discriminant function analyses

An a priori prediction was made that significant differences would be found among the groups on the following measures related to hypervigilance: average pain threshold, average pain tolerance, average noise tolerance, and the total scores on the Noise Sensitivity Scale (NSS), the Kohn Reactivity Scale (KRS) and the Pennebaker Inventory of Limbic Languidness (PILL). Using these 6 variables as predictors of group membership, a discriminant function analysis was performed. The purpose of this analysis was two-fold: to interpret the dimension(s) along which the groups differed, and to determine what proportion of subjects was classified correctly.

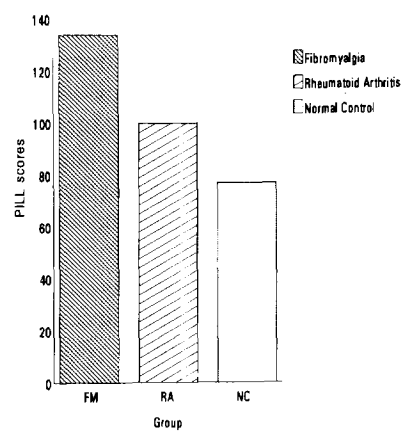

Fig. 4. Mean scores for the Pennebaker Inventory of Limbic Languidness (PILL) for the three groups. The Fibromyalgia group differed significantly from the Rheumatoid Arthritis and Normal Control groups. The Rheumatoid Arthritis group differed significantly from the Normal Control group.

Each variable was entered directly into the analysis as no a priori assumption had been made regarding the relative importance of the variables. When a direct analysis is performed, all predictors enter the equation at once and each predictor is assigned only the unique association it has with the groups. Shared variance among the predictors contributes to the total relationship, but not to any one predictor (Tabachnick and Fidell 1989).

Two discriminant functions were derived, with a combined $\chi^2(12) = 108.93$, $P < 0.00001$. After the first function was removed, the association between the groups and the predictors was $\chi^2(5) = 10.08$, $P > 0.05$, implying that the second discriminant function was not statistically significant. The eigenvalues associated with the discriminant functions indicated that 96.2% of the between-group variability was accounted for by the first discriminant function and 3.8% of the variability was accounted for by the second function. To observe how the discriminant functions separated the groups, the centroids (the mean discriminant scores for each group on a function) were plotted, with the first discriminant function on the x axis and the second function on the y axis (see Fig. 5). Since only the first discriminant function was found to be statistically significant, it is the one that will be interpreted.

As can be seen from Fig. 5, the fibromyalgia and RA groups fall at one end of the first discriminant function while the normal control group is located at the opposite end. Interpreting the meaning of a discriminant function is inferred by the pattern of correlations between the variables and the discriminant function. These correlations are referred to as structure coefficients (see Table I).

As shown in Table I, the variables that correlate most strongly with the first discriminant function (values greater in magnitude than 0.30 are considered of interest when defining a discriminant function) are average pressure pain threshold, average noise tolerance, average pressure pain tolerance, and the total score for the PILL. The threshold and tolerance measures correlate positively with the discriminant function while the PILL variable correlates negatively with the function. The pattern of correlations between these four variables and the discriminant function suggests that this is a 'non-hypervigilance' dimension.

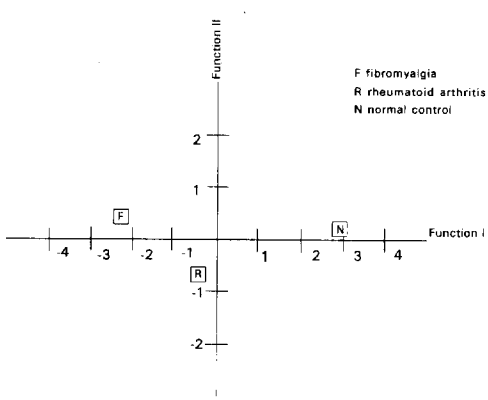

Fig. 5. Plot of the group centroids for Fibromyalgia, Rheumatoid Arthritis, and Normal Control groups on the two discriminant functions. Only the first function is statistically significant.

TABLE I
CORRELATIONS BETWEEN DISCRIMINATING VARIABLES AND THE CANONICAL DISCRIMINANT FUNCTION FOR THE FIBROMYALGIA, RA, AND CONTROL SUBJECTS

	Discriminant function I
Painthresh[a]	0.68255
Noisetol[b]	0.66115
Paintol[c]	0.60655
PILL[d]	−0.43488
KRS[e]	−0.25178
NSS[f]	−0.20015

[a]Average pain threshold.
[b]Average noise tolerance.
[c]Average pain tolerance.
[d]Pennebaker Inventory of Limbic Languidness.
[e]Kohn Reactivity Scale.
[f]Noise Sensitivity Scale.

Scheffé's test was used to determine if the three group centroids for the first discriminant function differed significantly from each other. When univariate tests are applied to multivariate data, it is recommended that a conservative test such as Scheffé's be used and should be evaluated at a conservative alpha level (e.g. 0.01) (Gardner 1992). These recommendations were followed. The results of Scheffé's tests indicated that each group centroid differed significantly from the other two group centroids (evaluated at $F(2,17)$, all $P < 0.01$). For example, as illustrated in Fig. 5, the normal control group had significantly higher scores on the first discriminant function than either the RA or the fibromyalgia groups, indicating that the normal control group was significantly less hypervigilant than either of the pain groups. In addition, the fibromyalgia and RA groups differed significantly from each other, with the RA group having significantly higher scores on the function than the fibromyalgia group. This suggests that the RA group is significantly less hypervigilant than the fibromyalgia group.

The second purpose of the discriminant function analysis was to determine the degree of accuracy with which the groups were classified. As stated above, a highly significant separation into 3 groups was achieved using the six variables ($\chi^2(12) = 108.93$, $P < 0.00001$). Table II presents both the actual group membership and the

TABLE II
DISCRIMINANT FUNCTION CLASSIFICATION FOR FIBROMYALGIA, RA, AND NORMAL CONTROL GROUPS

Actual Group	*N*	Predicted group membership		
		FM	RA	NC
FM[a]	20	15 (75%)	5 (25%)	0 (0%)
RA[b]	20	3 (15%)	16 (80%)	1 (5%)
NC[c]	20	0 (0%)	0 (0%)	20 (100%)

Percent of cases classified correctly: 85.0%.
[a]Fibromyalgia patients.
[b]Rheumatoid Arthritis patients.
[c]Normal Control subjects.

group membership assigned by the discriminant function.

Of all the cases, 85% were classified correctly, compared with a chance distribution of 33.33%. The fibromyalgia group was classified with 75% accuracy, with 25% of these patients being classified incorrectly as members of the RA group. The members of the RA group were classified with 80% accuracy, with 15% being misclassified as belonging to the fibromyalgia group and 5% as members of the normal control group. Finally, the normal control group was classified with 100% accuracy.

Although the classification rates are impressive, results obtained from discriminant function analyses should be interpreted with caution. They tend to be an overestimation because they capitalize on chance. Cross-validation procedures are recommended so that the utility of the coefficients can be tested on another sample (Tabachnick and Fidell 1989).

Discussion

The results of the present study indicate that fibromyalgia patients, rheumatoid arthritis patients, and healthy control subjects differ in their perception of noxious stimuli and their assessment of bodily sensations.

Perceptual measures

The fibromyalgia and RA patients responded to the pain and auditory stimuli in a hypervigilant manner, with fibromyalgia patients being significantly more vigilant to pressure and to noise than the RA subjects. These findings are of considerable interest in considering theories concerning the pathogenesis of fibromyalgia.

There have been proposals that fibromyalgia is due to dysfunctions at an early stage of somatosensory processing. For example, Neeck and Riedel (1994) stated, 'it seems logical to place the origin of the disorder in the muscle'. Ursin et al. (1993) declared, 'muscle pain must originate in muscles'. Lindman et al. (1995) proposed that fibromyalgia might be caused by a disturbance in muscle microcirculation, a finding supported by the discovery of decreased high energy phosphate levels in the skeletal muscles of fibromyalgia patients (Bengtsson et al. 1986) and abnormalities in peripheral red blood cells (Russell and Vipraio 1993). In contrast, Goldenberg (1995) concluded that studies involving nuclear magnetic resonance spectroscopy (e.g. Jacobsen et al. 1992; Jubrias et al. 1994; Simms et al. 1994) have 'convincingly demonstrated that muscle is not the primary pathologic factor in fibromyalgia'.

Others have considered abnormalities at a more central level. Russell et al. (1994) found a 3-fold elevation in cerebrospinal fluid levels of substance P in fibromyalgia patients. Russell et al. (1992b), having determined that blood serum serotonin concentration was lower in fibromyalgia patients than controls (Russell et al. 1992a), discovered lower than normal levels of serotonin, norepinephrine, and dopamine metabolites in the cerebrospinal fluid of fibromyalgia patients. Bennett (1993) suggested a disruption in the neuroendocrine axis controlling growth hormone production and Zimmermann (1991) raised the possibility of neuronal hyperexcitability and disturbed axonal transport. Jara et al. (1991) pointed to the possibility of dysfunctions in immunoregulation.

Griep et al. (1993) proposed that fibromyalgia is a neuroendocrine disorder, characterized by hyperreactive pituitary ACTH release and adrenal insufficiency, while van Denderen et al. (1992) suggested, as well, a disturbance of sympathetic activity. Russell (1993) reviewed more than 160 papers concerning neurotransmitters, hormones, metabolites, cytokines, and structural proteins and concluded, 'a central abnormality in the function of serotonin could explain many, if not all of the clinical manifestations of fibromyalgia syndrome'. More recently, PET scans revealed that fibromyalgia patients have bilateral abnormalities in regional cerebral blood flow in both the thalamus and the head of the caudate nucleus (Mountz et al. 1995), leading the authors to suggest that fibromyalgia may result from a functional abnormality in the central nervous system.

It seems highly improbable that fibromyalgia arises when a constellation of neural, hormonal, immunological, and neurochemical mechanisms involving peripheral, spinal, brainstem, midbrain, and cortical structures dysfunction independently. While some of these factors may be of primary importance in the pathophysiology of the disease, most must be secondary influences and thus should be viewed as correlates rather than causes of the disorder. Henriksson (1994) cautioned, 'it should not be forgotten that chronic pain is a

stressor and that neuroendocrinological aberrations could be a consequence of chronic pain'. He noted that we are unable to say whether changes in serotonin metabolism are primarily a central event, a consequence of long-standing bombardment of the central nervous system by primary nociceptive neurons, an aftermath of decreased central pain inhibition, or an effect due to sleep disturbance. Likewise, increased substance P levels in the cerebrospinal fluid may follow from hyperactivity in primary nociceptors and, eventually, lead to alterations in central nervous system structures.

Any models which seek to account for the biological factors responsible for initiating and maintaining fibromyalgia must broaden their scope to address why patients show hypervigilance for other stimuli such as noise. The pattern of complaints and perceptual performance associated with fibromyalgia requires a central mechanism which extends beyond the somatosensory system. While peripheral factors may play a decisive role in the early phases of fibromyalgia, it seems that emphasis should be placed upon such considerations as 'an aberration of normal central mechanisms' with 'amplification of pain' (Yunus 1992a), 'altered central nociception' (Arroyo and Cohen 1993), or a 'perceptual style in which aversive events are amplified or in which the usual cognitive filtering mechanisms are not fully engaged' (Rollman and Lautenbacher, 1993).

It has been suggested that fibromyalgia patients may have a dysfunctional central nervous system mechanism that does not adequately minimize pain perception (Yunus 1992b) or that amplifies relatively moderate pain resulting from muscular hypertonia or hyperactivity (Graber 1991). Bohr (1995) has gone so far as to propose that a designation such as 'pain amplification syndrome' (Barsky 1979; Hart 1988) or 'hypervigilance syndrome' (Rollman and Lautenbacher 1993) should be substituted for 'fibromyalgia', suggesting that these terms are 'more neutral and consistent with psychophysiologic formulations that encompass both soma and psyche'.

Bennett (1993) considered that 'somatic distress and functional disability may result from a true enhancement of pain through a reduction in the descending inhibitory pathways of pain'. He hypothesized that sleep disturbances and consequent hormonal imbalances, coupled with a genetic predisposition, may lead to muscle microtraumas and subsequent pain but that central factors maintain and enhance the symptoms. As Bennett and Jacobsen (1994) noted, 'most likely the initiation of this condition is multifactorial and the combination of peripheral and central factors that constitute a vicious circle may perpetuate the condition into a chronic state'.

One is left with a puzzling 'chicken and egg' issue in assessing the role of hypervigilance in disorders such as fibromyalgia. It is plausible to suggest that the hyperresponsiveness to sensory stimuli seen here might be a consequence of the symptoms associated with pain, since both patient groups are hypervigilant when compared to controls. Possibly, stress, anxiety, sleep disturbance, and psychosocial factors may lead to a 'central modulation change' and pattern of amplification (Granges and Littlejohn 1993a) or an 'aberration of central pain mechanisms' related to a 'dysfunctional spectrum syndrome' (Yunus 1994). If so, parallel changes in perceptual behavior should be seen generally in pain conditions, since they also lead to stress, anxiety, and other emotional and physical reactions, but that is not the case. For many pain disorders, patients are not hypervigilant to noxious stimuli. Rather, their pain threshold and tolerance are significantly higher than those of controls (Naliboff and Cohen 1989), favoring the adaptation level model, a comparison process between endogenous and exogenous pain proposed by Rollman (1979, 1983).

In each of the perceptual tests conducted in this study, the fibromyalgia patients were significantly more hypervigilant than the RA patients. We suggest that a perceptual pattern of hypervigilance is one of a number of predisposing factors in the onset of fibromyalgia. Hypervigilance, when accompanied by yet to be specified muscular, metabolic, or neural dysfunctions, may give rise to the fibromyalgia syndrome. Hypervigilance, when accompanied by different pathophysiology should give rise to other symptom patterns and, thus, other syndromes. If so, the hyperresponsiveness to auditory stimulation shown in this study should not be limited to fibromyalgia and should be present in a number of pain complaints including, for example, generalized nonarticular rheumatism (Quimby et al. 1988). If so, individuals with multiple tender points who have not sought treatment (Bradley et al. 1995; Wolfe et al. 1995b) should evidence considerably less hypervigilance than those who have brought their complaints to a physician. If so, as well, normal individuals who show evidence of hypervigilance to sensory stimuli or demonstrate pain intolerance in laboratory settings (Chen et al. 1989; Geisser et al. 1992) (or, perhaps, even pain anxiety (Rollman 1995)) should be at greater risk for later establishing the symptoms of fibromyalgia or several other pain disorders.

The hypervigilant pattern of perceiving which contributes to the onset of fibromyalgia and other painful conditions may also contribute to the maintenance of the disorders. Moreover, impairments in central regulatory processes which normally function to modulate pain may lead to amplification of this perceptual process, leading to enhancements of both the sensory component of the patients' pain and the associated affective and cognitive elements.

Psychological questionnaires

The results of the Kohn Reactivity Scale (KRS) indicated that the fibromyalgia and RA patients were significantly more reactive than the normal control sub-

jects. When the Noise Sensitivity Scale (NSS) was examined, the results revealed that the fibromyalgia patients were significantly more noise sensitive than the normal control subjects. There were no significant differences between the pain groups on either measure.

The results of the Pennebaker Inventory of Limbic Languidness (PILL) (with the items related to muscle and joint complaints omitted) indicated that the fibromyalgia patients reported experiencing common physical symptoms significantly more frequently than the RA and normal control subjects. In addition, the RA group had significantly higher scores on this measure than the normal control subjects. These results suggest that various types of pain patients may have an exaggerated focus on bodily functioning, with fibromyalgia patients being particularly preoccupied with their physical experiences.

Moreover, the findings from the PILL appear to be consistent with the suggestion that fibromyalgia patients may experience musculoskeletal sensations as being more noxious, intense, and disabling because they have an unusually elevated awareness of bodily sensations or an 'amplifying perceptual style' (Robbins et al. 1990). This corresponds with experimental studies that suggest that body awareness may increase the probability that an individual will perceive internal experiences as being noxious, resulting in increased symptom reporting (Pennebaker and Lightner 1980).

Summary

While the notion of generalized hypervigilance provides a framework for conceptualizing the behavior of fibromyalgia patients, it is still in its developmental stages. For example, it does not explain why individuals respond to sensory stimuli in an exaggerated manner. Nor does it indicate whether this pattern of perceptual response is related to cognitive coping strategies (e.g. Bradley et al. 1991; Harris and Rollman 1985). The underlying mechanisms that may be responsible for generalized hypervigilance need to be explored.

Factors that may contribute to fibromyalgia patients' exaggerated response to noxious stimuli were discussed earlier. However, few attempts have been made at moving beyond the pain domain, and trying to identify factors that may account for the more generalized perceptual amplification of sensory experiences observed in some fibromyalgia patients.

One wonders what role the nature of the pathophysiology has on hypervigilant behavior. Is a pattern of generalized hypervigilance unique to disorders, like fibromyalgia, that do not have an identified organic etiology or is generalized hypervigilance also seen in disorders with an established organic basis? The data reported here for the RA patients suggest that hypervigilance can be seen, to a lesser degree, in some such conditions, but the elevated pain and tolerance thresholds and diminished rating of noxious stimuli associated with the adaptation level model (Rollman 1979, 1983) predominate in other organic disorders (Boureau et al. 1991; Naliboff and Cohen 1989).

The present study has provided support for the hypothesis that fibromyalgia patients have an altered perceptual style. The next step is to elucidate the mechanisms that contribute to this type of hypervigilant presentation and to determine whether this pattern of responding is typical in patients who present with disorders of uncertain etiology. The answers to these questions will be helpful in understanding the pathophysiology of painful disorders and in selecting appropriate treatment modalities.

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References

Arroyo, J.F. and Cohen, M.L., Abnormal responses to electrocutaneous stimulation in fibromyalgia, J. Rheumatol., 20 (1993) 1925–1931.

Barsky, A.J., Patients who amplify body sensations, Ann. Intern. Med., 91 (1979) 63–70.

Bengtsson, A., Henriksson, K.G. and Larsson, J., Reduced high energy phosphate levels in the painful muscles of patients with primary fibromyalgia, Arthritis Rheum., 29 (1986) 817–821.

Bennett, R.M., Fibromyalgia and the facts. Sense or nonsense, Rheum. Dis. Clin. North Am., 19 (1993) 45–59.

Bennett, R.M. and Jacobsen, S., Muscle function and origin of pain in fibromyalgia, Bailliere's Clin. Rheumatol., 8 (1994) 721–746.

Block, S.R., Fibromyalgia and the rheumatisms. Common sense and sensibility, Rheum. Dis. Clin. North Am., 19 (1993) 61–78.

Bohr, T.W., Fibromyalgia syndrome and myofascial pain syndrome. Do they exist? Neurologic Clinics, 13 (1995) 365–384.

Boureau, F., Luu, M. and Doubrere, J.F., Study of experimental pain measures and nociceptive reflex in chronic pain patients and normal subjects, Pain, 44 (1991) 131–138.

Bradley, L.A., Alarcón, G.S., Alexander, R.W., Alexander, M.T., Aaron, L.A., Alberts, K.R. and Martin, M.Y., Abnormal central processing of dolorimeter stimuli in patients and community residents with fibromyalgia (FM): One year reliability, Proceedings of the 14th Annual Scientific Meeting of the American Pain Society, 1995, A-137.

Bradley, L.A., Scarinci, I.C. and Richter, J.E., Pain threshold levels and coping strategies among patients who have chest pain and normal coronary arteries, Med. Clin. North Am., 75 (1991) 1189–1202.

Chapman, C.R., Pain: The perception of noxious events. In: R.A. Sternbach (Ed.), The Psychology of Pain, Raven Press, New York, 1978, pp. 169–202.

Chen, A.C., Dworkin, S.F., Haug, J. and Gehrig, J., Human pain

responsivity in a tonic pain model: psychological determinants, Pain, 37 (1989) 143–160.

Drummond, P.D. and Woodhouse, A., Painful stimulation of the forehead increases photphobia in migraine sufferers, Cephalgia, 13 (1993) 321–324.

Dubreuil, D.L. and Kohn, P.M., Reactivity and response to pain, Pers. Individ. Differ., 7 (1986) 907–909.

Gardner, R.C., Fundamentals of multivariate analysis of variance, Unpublished manuscript, Department of Psychology, University of Western Ontario, London, Canada, 1992.

Geisser, M.E., Robinson, M.E. and Pickren, W.E., Differences in cognitive coping strategies among pain-sensitive and pain-tolerant individuals on the cold-pressor test, Behav. Ther., 23 (1992) 31–41.

Gerster, J.C. and Hadj-Djilani, A., Hearing and vestibular abnormalities in primary fibrositis syndrome, J. Rheumatol., 11 (1984) 678–680.

Goldenberg, D.L., Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome, Curr. Opin. Rheumatol., 7 (1995) 127–135.

Graber, G., Epidemiological research on the etiological factors behind dysfunctional diseases of the motor apparatus: the stomatognate system as an example. In: W. Muller (Ed.), Generalisierte Tendomyopathie (Fibromyalgie), Steinkopff Verlag, Darmstadt, 1991, pp. 221–229.

Granges, G., Gibson, S.J., Littlejohn, G. and Helme, R.D., Cerebral event related potentials and heat pain thresholds in fibromyalgia syndrome, J. Musculoskel. Pain, 1 (1993) 177–184.

Granges, G. and Littlejohn, G., Postural and mechanical factors in localized and generalized fibromyalgia/fibrositis syndrome. In: H. Vaerøy and H. Merskey (Eds.), Progress in Fibromyalgia and Myofascial Pain, Elsevier, Amsterdam, 1993a, pp. 329–348.

Granges, G. and Littlejohn, G., Pressure pain threshold in pain-free subjects, in patients with chronic regional pain syndromes, and in patients with fibromyalgia syndrome, Arthritis Rheum., 36 (1993b) 642–646.

Griep, E.N., Boersma, J.W. and de Kloet, E.R., Altered reactivity of the hypothalamic-pituitary-adrenal axis in the primary fibromyalgia syndrome, J. Rheumatol., 20 (1993) 469–474.

Hadj-Djilani, A. and Gerster, J.C., Meniere's disease and fibrositis (psychogenic rheumatism): relationships in audiometric and nystagmographic results, Acta Otolaryngol., 406 (1984) 67–71.

Harris, G. and Rollman, G.B., Cognitive techniques for controlling pain: generality and individual differences. In: H.L. Fields, R. Dubner and F. Cervero (Eds.), Advances in pain research and therapy, Vol. 9, Raven Press, New York, 1985, pp. 847–851.

Hart, F.D., Fibrositis (fibromyalgia). A common non-entity? Drugs, 35 (1988) 320–327.

Henriksson, K.G., Chronic muscular pain: aetiology and pathogenesis, Bailliere's Clin. Rheumatol., 8 (1994) 703–719.

Jacobsen S., Jensen K.E., Thomsen C., Danneskiold-Samsoe B. and Henriksen O., ^{31}P magnetic resonance spectroscopy of skeletal muscle in patients with fibromyalgia, J. Rheumatol., 19 (1992) 1600–1603.

Jara, L.J., Lavalle, C., Fraga, A., Gomez-Sanchez, C., Silveira, L.H., Martinez-Osuna, P., Germain, B.F. and Espinoza, L.R., Prolactin, immunoregulation, and autoimmune diseases, Arthritis Rheum., 20 (1991) 273–284.

Jubrias S.A., Bennett R.M. and Klug G.A., Increased incidence of a resonance in the phosphodiester region of ^{31}P nuclear magnetic resonance spectra in the skeletal muscle of fibromyalgia patients, Arthritis Rheum., 37 (1994) 801–807.

Kohn, P.M., Sensation-seeking, augmenting-reducing, and strength of the nervous system. In: J.T. Spence and C.E. Izard (Eds.), Motivation, Emotion, and Personality, Elsevier, Amsterdam, 1985, pp. 167–173.

Lautenbacher, S., Rollman, G.B. and McCain, G.A., Multi-method assessment of experimental and clinical pain in patients with fibromyalgia, Pain, 59 (1994) 45–53.

Lautenschläger, J., Segalias, J., Brückle, W. and Müller, W., Comparisons of spontaneous pain and tenderness in patients with primary fibromyalgia, Clin. Rheumatol., 10 (1991) 168–174.

Leavitt, F., Katz, R.S., Golden, H.E., Glickman, P.B. and Layfer, L.F., Comparison of pain properties in fibromyalgia patients and rheumatoid arthritis patients. Arthritis Rheum., 29 (1986) 775–781.

Lindman, R., Hagberg, M., Bengtsson, A., Henriksson, K.G., Thornell, L-E., Capillary structure and mitochondrial volume density in the trapezius muscle of chronic trapezius myalgia, fibromyalgia and healthy subjects, J. Musculoskel. Pain, 3 (1995) 5–22.

McCain, G.A. and Scudds, R.A., The concept of primary fibromyalgia (fibrositis): clinical value, relation and significance to other chronic musculoskeletal pain syndromes, Pain, 33 (1988) 273–287.

Mountz, J.M., Bradley, L.A., Modell, J.G., Alexander, R.W., Triana-Alexander, M., Aaron, L.A., Stewart, K.E., Alarcon, G.S. and Mountz, J.D., Fibromyalgia in women. Abnormalities of regional cerebral blood flow in the thalamus and the caudate nucleus are associated with low pain threshold levels, Arthritis Rheum., 38 (1995) 926–938.

Naliboff, B.D. and Cohen, M.J., Psychophysical laboratory methods applied to clinical pain patients. In: C.R. Chapman and J.D. Loesser (Eds.), Issues in Pain Measurement: Advances in Pain Research and Therapy, Vol. 12, Raven Press, New York, 1989, pp. 365–386.

Neeck, G. and Riedel, W., Neuromediator and hormonal perturbations in fibromyalgia syndrome: results of chronic stress? Bailliere's Clin. Rheumatol., 8 (1994) 763–775.

Olson, C.L., On choosing a test statistic in MANOVA, Psychol. Bull., 83 (1976) 579–586.

Pennebaker, J.W., The Psychology of Physical Symptoms, Springer-Verlag Inc., New York, 1982.

Pennebaker, J.W. and Lightner, J.M., Competition of internal and external information in an exercise setting, J. Pers. Soc. Psychol., 39 (1980) 165–174.

Perry, F., Heller, P.H. and Levine, J.D., Differing correlations between pain measures in syndromes with or without explicable organic pathology, Pain, 34 (1988) 185–189.

Pilowsky, I., Dimensions of hypochondriasis, Br. J. Psychiatr., 113 (1967) 89–93.

Quimby, L.G., Block, S.R. and Gratwick, G.M., Fibromyalgia: generalized pain intolerance and manifold symptom reporting, J. Rheumatol., 15 (1988) 1264–1270.

Robbins, J.M., Kirmayer, L.J. and Kapusta, M.A., Illness worry and disability in fibromyalgia syndrome, Int. J. Psychiatr. Med., 20 (1990) 49–63.

Rollman, G.B., Signal detection theory pain measures: empirical validation studies and adaptation level effects, Pain, 6 (1979) 9–21.

Rollman, G.B., Measurement of experimental pain in chronic pain patients: methodological and individual factors. In: R. Melzack (Ed.), Pain Measurement and Assessment, Raven Press, New York, 1983, pp. 251–258.

Rollman, G.B., Measurement of pain in fibromyalgia in the clinic and laboratory, J. Rheumatol., 16 (Suppl. 19) (1989) 113–119.

Rollman, G.B., Gender differences in pain: the role of anxiety, Pain Forum, 4 (1995) 331–334.

Rollman, G.B. and Lautenbacher, S., Hypervigilance effects in fibromyalgia: pain experience and pain perception. In: H. Værøy and H. Merskey (Eds.), Progress in Fibromyalgia and Myofascial Pain, Elsevier, Amsterdam, 1993, pp. 149–159.

Russell, I.J., A metabolic basis for fibromyalgia syndrome. In: H. Værøy and H. Merskey (Eds.), Progress in Fibromyalgia and Myofascial Pain, Elsevier, Amsterdam, 1993, pp. 283–309.

Russell, I.J., Michalek, J.E., Vipraio, G.A., Fletcher, E.M., Javors, M.A. and Bowden, C.A., Platelet [^{3}H]imipramine uptake receptor density and serum serotonin levels in patients with fibromyalgia/fibrositis syndrome, J. Rheumatol., 19 (1992a) 104–109.

Russell, I.J., Værøy, H., Javors, M. and Nyberg, F., Cerebrospinal fluid biogenic amine metabolites in fibromyalgia/fibrositis syndrome and rheumatoid arthritis, Arthritis Rheum., 35 (1992b) 550–556.

Russell, I.J., Orr, M.D., Littmann, B., Vipraio, G.A., Alboukrek, D., Michalek, J.E., Lopez, Y. and MacKillip, F., Elevated cerebrospinal fluid levels of substance P in patients with the fibromyalgia syndrome, Arthritis Rheum., 37 (1994) 1593–1601.

Russell, I.J. and Vipraio, G.A., Red cell nucleotide abnormalities in fibromyalgia syndrome, Arthritis Rheum., 36 (1993) S223.

Scudds, R.A., Rollman, G.B., Harth, M. and McCain, G.A., Pain perception and personality measures as discriminators in the classification of fibrositis, J. Rheumatol., 14 (1987) 563–569.

Simms, R.W., Roy, S.H., Hrovat, M., Anderson, J.J., Skrinar, G., LePoole, S.R., Zerbini, C.A., de Luca, C. and Jolesz, F., Lack of association between fibromyalgia syndrome and abnormalities in muscle energy metabolism, Arthritis Rheum., 37 (1994) 794–800.

Smythe, H.A., Tender points: evolution of concepts of the fibrositis/fibromyalgia syndrome, Am. J. Med., 81 (1986) 2–5.

Tabachnick, B.G. and Fidell, L.S., Using Multivariate Statistics, Harper Collins, New York, 1989.

Tunks, E., Crook, J., Norman, G. and Kalaher, S., Tender points in fibromyalgia, Pain, 34 (1988) 11–19.

Ursin, H., Endresen, I.M., Håland, E.M. and Mjellem, N., Sensititization: a neurobiological theory for muscle pain. In: H. Værøy and H. Merskey (Eds.), Progress in Fibromyalgia and Myofascial Pain, Elsevier, Amsterdam, 1993, pp. 413–427.

van Denderen, J.C., Boersma, J.W., Zeinstra, P., Hollander, A.P. and van Neerbos, B.R., Physiological effects of exhaustive physical exercise in primary fibromyalgia syndrome (PFS): is PFS a disorder of neuroendocrine reactivity? Scand. J. Rheumatol., 21 (1992) 35–37.

Waylonis, G.W. and Heck, W. Fibromyalgia syndrome. New associations, Am. J. Phys. Med. Rehabil., 71 (1992) 343–348.

Weinstein, N.D., Individual differences in reaction to noise: a longitudinal study in a college dormitory, J. Appl. Psychol., 63 (1978) 458–466.

Wolfe, F., Ross, K., Anderson, J. and Russell, I.J., Aspects of fibromyalgia in the general population: sex, pain threshold, and fibromyalgia symptoms, J. Rheumatol., 22 (1995a) 151–156.

Wolfe, F., Ross, K., Anderson, J., Russell, I.J. and Hebert, L., The prevalence and characteristics of fibromyalgia in the general population, Arthritis Rheum., 38 (1995b) 19–28.

Wolfe, F., Smythe, H.A., Yunus, M.B., Bennett, R.M., Bombardier, C., Goldenberg, D.L., Tugwell, P., Campbell, S.M., Abeles, M., Clark, P., Fam, A.G., Farber, S.J., Fiechtner, J.J., Franklin, C.M., Gatter, R.A., Hamaty, D., Lessard, J., Lichtbroun, A.S., Masi, A.T., McCain, G., Reynolds, W.J., Romano, T.J., Russell, I.J. and Sheon, R.P., The American College of Rheumatology 1990 criteria for the classification of fibromyalgia, Arthritis Rheum., 33 (1990) 160–172.

Woodhouse, A. and Drummond, P.D., Mechanisms of increased sensitivity to noise and light in migraine headache, Cephalgia, 13 (1993) 417–421.

Yunus, M.B., Towards a model of pathophysiology of fibromyalgia: aberrant central pain mechanisms with peripheral modulation, J. Rheum., 19 (1992a) 846–850.

Yunus, M.B., Fibromyalgia: a dysfunctional syndrome with chronic pain. In: F. Sicuteri, L. Terenius, L. Vecchiet and C.A. Maggi (Eds.), Pain versus Man: Advances in Pain Research and Therapy, Vol. 20, Raven Press, New York, 1992b, pp. 131–140.

Yunus, M.B., Psychological aspects of fibromyalgia syndrome: a component of the dysfunctional spectrum syndrome, Bailliere's Clin. Rheumatol., 8 (1994) 811–837.

Yunus, M.B., Ahles, T.A., Aldag, J.C. and Masi, A.T., Relationship of clinical features with psychological status in primary fibromyalgia, Arthritis Rheum., 34 (1991) 15–21.

Yunus, M.B., Masi, A. and Aldag, J.C., A controlled study of primary fibromyalgia syndrome: clinical features and associations with other functional syndromes, J. Rheumatol., 16 (Suppl. 19) (1989) 62–71.

Zimmermann, M., Pathophysiological mechanisms of fibromyalgia, Clin. J. Pain, 7 (Suppl. 1) (1991) S8–S15.