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Multi-method assessment of experimental and clinical pain in patients with fibromyalgia

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Summary Experimental measures of responsiveness to painful and non-painful stimuli as well as measures of typical and present clinical pain were assessed in 26 female patients with fibromyalgia and in an equal number of age-matched healthy women. Pressure pain thresholds, determined by means of a dolorimeter, were lower in the patients compared to the control subjects both at a tender point (trapezius) and at a non-tender control point (inner forearm). The same was true for the heat pain thresholds, measured using a contact thermode. In contrast, the pain thresholds for electrocutaneous stimuli were decreased only at the tender point. The detection thresholds for non-painful stimuli (warmth, cold and electrical stimuli) seemed to be less affected in the fibromyalgia patients, with only the detection threshold for cold being lower at both sites. Tender points were more sensitive than control points for mechanical pressure. The reverse was found for the other modalities which were tested. Although the 3 experimental pain thresholds showed patterns of either generalized or site-specific pain hyperresponsiveness, the between-methods correlations were not very high. While the correlations between the experimental pain thresholds and the various measures of clinical pain (Localized Pain Rating, McGill Pain Questionnaire) in the patients were generally low, there were significant negative correlations between pressure pain thresholds at the two sites and the level of present pain assessed by the Localized Pain Rating. We conclude that a pattern of pain hyperresponsiveness, generalized across the site of noxious stimulation and across the physical nature of the stressor, is associated with fibromyalgia. The pattern of hyperresponsiveness appears to involve both peripheral factors (e.g., sensitization of muscle nociceptors) and central ones (e.g., hypervigilance or a lack of nociceptive inhibition).

Key words: Fibromyalgia; Heat pain; Pressure pain; Electrical pain; Tender point; Pain hyperresponsiveness

Introduction

The chronic pain syndrome, fibromyalgia, is characterized by diffuse, widespread pain and the presence of multiple tender points at characteristic sites. Diagnostic accuracy is minimally diminished when only tender point testing is used (Lautenschläger et al. 1989; Wolfe et al. 1990). Hence, a disturbance of pressure pain sensitivity is an integral part of the symptomatology in fibromyalgia.

Although some contradictory findings exist (Campbell et al. 1983; Simms et al. 1988), considerable evidence has been amassed to indicate that patients with fibromyalgia are exceedingly responsive to noxious pressure, not only at the designated tender points but also at various other body sites (Scudds et al. 1987; Lautenschläger et al. 1988; Quimby et al. 1988; Tunks et al. 1988; Mau and Raspe 1990; Wolfe et al. 1990; Mikkelsson et al. 1992; Smythe et al. 1992; Granges et al. 1993; Granges and Littlejohn 1993b). Furthermore, in some of these studies, even healthy persons have shown an increased responsiveness to pressure pain at the 'tender point' sites of fibromyalgia compared to control sites. Consequently, the relatively enhanced tenderness at tender points does not seem to be spe-

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cific for fibromyalgia. This suggests that the tender points of fibromyalgia patients are only the most pain-sensitive sites in generally pain-sensitive individuals (see also, Block 1993).

Some theoretical proposals have been developed to account for this pattern of generally increased responsiveness to pain. Rollman and Lautenbacher (1993) applied the 'hypervigilance' model to fibromyalgia. According to this concept, a perceptual style or tendency, characterized by augmentation of stimuli with an aversive character, predisposes certain individuals to present with fibromyalgia. Granges and Littlejohn (1993a) proposed an extended model of fibromyalgia in which a variety of factors, including stress and anxiety, contribute, through a change in central modulation, to amplification of local tenderness and muscle pain. Yunus (1992) suggested that the central-nervous component of pain transmission in fibromyalgia is affected by serotonergic dysregulations, leading to a lack of nociceptive inhibition or an accentuation of nociceptive facilitation. Værøy and Merskey (1993) summarize a review of the literature by noting that fibromyalgia researchers from vastly different disciplines "seem to converge on the common factor of a central contribution to the pain disorder".

Data relating to these hypotheses are limited since hyperalgesia has typically been demonstrated only by means of variable pressure dolorimeters (e.g., the type described by Fischer (1987)). There are very few studies of pain responsiveness in which other stimulation methods were employed.

Scudds et al. (1987) applied electrical current and constant pressure to non-tender control points at the upper extremities in order to measure pain and tolerance thresholds. As well, a variable pressure dolorimeter test (Fischer 1987) was used. With the latter method, patients with fibromyalgia had significantly lower pain and tolerance levels than healthy controls. When compared with rheumatoid arthritis patients, fibromyalgia patients differed significantly only for dolorimeter tolerance. There were no significant differences between groups for electrical current or constant pressure. However, the fibromyalgia patients showed non-significant trends toward lower threshold values for these stressors. Hence, the findings provided only weak evidence that the hyperalgesia in fibromyalgia is generalized with respect to the nature of the noxious stimulus.

Rollman (1989) indicated the need for replications with various forms of pain induction, specifically including thermal pain. Heat pain and pressure pain are signalled by different sets of nociceptive afferents. Since strong thermal stimuli primarily engage polymodal and mechano-thermal nociceptors serving the skin, they activate fibers other than the muscle nociceptors which some (e.g., Henriksson and Bengtsson 1991) believe may be sensitized in fibromyalgia. Hence, one aim of the present study was to investigate the pain responsiveness of fibromyalgia patients by means of both thermal and mechanical stimuli. Similarities in response patterns across these forms of pain induction would suggest the action of central rather than peripheral processes.

The study by Scudds et al. (1987) was guided by the concept of generalized hyperalgesia. Consequently, testing of tender points was not included. However, it is possible that there are localized forms of hyperalgesia at the tender points in addition to an overall enhancement of pain responsiveness. Therefore, in this study, both tender and non-tender points were investigated. As well, since Vecchiet et al. (1991) demonstrated that electrical pain stimulation is effective in investigating myofascial trigger points (i.e., localized forms of muscle hyperalgesia), we chose to again include this form of excitation.

Findings, such as those obtained by Scudds et al. (1987), might be the consequence of hyperaesthesia rather than hyperalgesia. That is, the response to all somatosensory stimuli, not only aversive ones, may be modified in patients suffering from fibromyalgia. Tests with non-painful somatosensory stimulation are needed for clarification. Such tests were conducted in the present study, using non-painful intensities of temperature and electrical current.

It is tempting to assume that widespread clinical pain and hyperresponsiveness to experimental pain are two manifestations of the same pathological process. However, the correlations between the two variables have been found to be weak (Scudds et al. 1989; Lautenschläger et al. 1991). We believe that there are at least two possible explanations, aside from the assumption of no relationship.

First, clinical pain and hyperresponsiveness to acute or induced pain may mutually influence each other at the early stages of fibromyalgia, become increasingly independent from each other later, and appear only weakly related at the stage of a full-blown syndrome, when patients display all of the obligatory criteria for the disorder and a considerable portion of the associated ones. At this point, clinical pain and hyperresponsiveness to induced pain may both be high and maintained by third factors. In the studies cited above, patients with severe forms of fibromyalgia were investigated.

Second, the measures used for the assessment of clinical pain and pain responsiveness may have differed in the time frame upon which they were based. If, for example, laboratory pain measures reflect a short-term state while clinical measures reflect the average pain level experienced over a much longer span, weak correlations could be due to disparity in the period used for evaluation. The present study tried to control for this possibility by assessing the clinical pain both in its

typical form (in the recent past) and in its present form (at the time of investigation).

Methods

Subjects

Twenty-six female patients, diagnosed as having fibromyalgia according to the criteria of the American College of Rheumatology (Wolfe et al. 1990) took part in the study. They were out-patients of the Rheumatic Disease Unit, University Hospital, London (Canada). Only women were investigated because the majority (approximately 70–90%) of fibromyalgia patients are female (Boissevain and McCain 1991). Since all patients were having serious complaints due to their disorder (see Results), medication could not be withdrawn for study purposes. An age-comparable group of pain-free women was recruited by advertisement and personal contact (see Table I).

All subjects were paid for participation. The study protocol was approved by the Ethics Committee of the University.

Apparatus and procedure

At the beginning of the session, each subject filled out a series of questionnaires. The McGill Pain Questionnaire (MPQ) (Melzack 1975) was given to the patients. They had to select adjectives from a list of 78, divided into 20 categories, which were most suitable to describe their pain. The only limitation was that not more than 1 adjective per category could be chosen. Subjects were told to refer to the typical pain in their recent past. The Pain Rating Index (PRI) was computed according to the weighted-rank method (Melzack et al. 1985) for the whole questionnaire (PRI-T) and for the categories measuring the sensory pain dimension (PRI-S), the affective pain dimension (PRI-A), the evaluative pain dimension (PRI-E) and miscellaneous pain aspects (PRI-M). The 6-point scale for assessment of the Present Pain Intensity (PPI) was then used to describe the pain which the subject had 'just now'.

Next, the Localized Pain Rating (LPR), devised by Lautenschläger et al. (1991), was presented. Two body maps (front and back view) depicted 21 typical pain areas in fibromyalgia. The pain intensity was rated for each area separately on a 6-point scale. A sum score was computed by adding up all single ratings. Therefore, the maximum score was 126. Subjects were instructed to refer once to typical pain in the recent past (LPR-T, this version was given only to the patients) and once to present pain (LPR-P).

With a third questionnaire, the duration and the frequency of fibromyalgia pain, the presence of some of the most frequent complaints associated with fibromyalgia, medication usage, body size measures and age were assessed.

Although tenderness in fibromyalgia is normally symmetrically distributed, a preponderance on one body side is possible. The tenderness of a typical tender point at the shoulder was assessed bilaterally (see below for procedure) and the more tender body side was chosen for further investigation. This turned out to be the right body side in 18 patients and 17 controls and the left body side in 8 patients and 9 controls.

The experimental tests of responsiveness began at a designated non-tender point, called a control point (CP) in the following. The point was located on the volar forearm, just between the proximal crease of the wrist and the transverse crease of the elbow. After all tests had been conducted at the CP, the designated tender point (TP) was investigated. We chose as TP the upper edge of the trapezius muscle, halfway between the shoulder-joint and the base of the neck.

First, responsiveness tests using thermal stimuli were carried out at each site. The stimulator was a temperature-controlled contact thermode with a stimulation surface of 1.6×3.6 cm^2. Contact pressure could be regulated and was held at 0.4 N/cm^2. This was accomplished by mounting the thermode on a swivel arm device consisting of dual spring bearings, an indicator for the applied pressure and an adjusting screw which permitted the pressure to be maintained at a constant level for any spatial orientation of the stimulator (Galfe et al. 1990). The thermode was attached so that the CP or the TP were just below the midpoint of the thermode surface. The apparatus (PATH Tester MPI 100; for complete details see Galfe et al. 1990) also included a thermode controller with a microprocessor for regulating thermal stimulation and an IBM-compatible computer for controlling the procedures.

Detection thresholds of warmth and cold were first assessed. Starting at a temperature of 32°C, 7 warm stimuli and then 7 cold stimuli were administered. The rate of temperature change was 0.7°C/sec. Subjects had to press a button as soon as they noticed a change in temperature. Thereupon, the temperature returned to the base value (1.5°C/sec). The mean differences between the base temperature and the peak temperature in the 2 sets of 7 trials were taken as measures of the warmth and cold thresholds. The intertrial interval lasted 10 sec. The stimuli were delayed between 1 and 3 sec (pseudo-randomized intervals) after visual and acoustic warning signals for the start of a trial.

The heat pain threshold was measured next. Beginning at a temperature of 38°C, 8 heat stimuli were applied with a rate of temperature change of 0.7°C/sec. The subjects were instructed to press a button as soon as they felt pain. Each time they pressed the button, the temperature returned to the base value at a cooling rate of 1.5°C/sec. An upper limit was set at 52°C for safety reasons. The start of each trial was announced visually and acoustically, but the stimulus was presented with a pseudo-randomized delay of between 1 and 3 sec. The intertrial interval lasted 10 sec. The pain threshold was calculated as the mean of the peak temperatures of the last 5 trials.

The responsiveness tests using electrocutaneous stimuli followed. After skin preparation (cleaning and abrading), 2 Dantec 1-way electrodes (13L20) with a surface of 0.3 cm^2 were attached 5 cm from each other, slightly proximal and slightly distal to the CP or the TP (cathode proximal, anode distal). The stimuli were delivered by a constant-current stimulator (CCS-1, Frederic Haer and Company) and consisted of 15 4-msec monophasic square-wave pulses with a stimulus onset asynchrony of 10 msec (100 Hz). These parameters

TABLE I

MEANS (±SD) OF AGE, HEIGHT, WEIGHT AND OF SCORES ON THE LPR-P AS WELL AS THE PREVALENCE OF FUNCTIONAL COMPLAINTS IN PATIENTS WITH FIBROMYALGIA AND HEALTHY CONTROLS (n = 26 in both groups)

	Fibromyalgia patients	Healthy controls
Age (years)	44.0 ± 11.6	42.7 ± 8.2
Height (cm)	162.1 ± 7.5	161.4 ± 7.3
Weight (kg) [a,**]	70.1 ± 12.5	60.6 ± 15.1
LPR-P [a,***]	31.8 ± 16.9	2.5 ± 3.5
Morning stiffness [b,***]	92.3%	26.9%
Fatigue [b,***]	92.3%	42.3%
Headache [b,**]	92.3%	53.8%
Sleep disturbance [b,***]	84.6%	30.8%
Irritable bowel [b,***]	69.2%	11.5%
Subjective finger swelling [b,***]	65.4%	11.5%
Depressive mood	57.7%	30.8%

[a] t test (1-tailed).
[b] Chi-square test.
** $P < 0.01$; *** $P < 0.001$.

resulted in a duration of 144 msec per stimulus. The start of each stimulus was signaled by a light.

Detection and pain thresholds were measured in 3 ascending series with discrete steps of 0.075 mA. An upper limit was set at 7.5 mA for safety reasons. The average in the 3 series was taken as the corresponding threshold value.

Last, pressure pain thresholds were assessed. A variable pressure dolorimeter (Fischer 1987) with a footplate surface of 0.8 cm^2 and a scale range from 0 to 17 kg was used. The footplate was positioned at the center of each point on the first trial and then moved slightly proximally or distally on the other trials in order to minimize local sensitization. The investigator was trained to increase the pressure at a constant rate of 1 kg/sec. Pressure was raised until the subject signalled that she felt pain. There were 3 ascending trials. The mean of these trials was used as a threshold measure.

Evaluation

A 2-way analysis of variance (ANOVA) with a group factor (Fibromyalgia vs. Control) and a repeated-measurement factor for site comparisons (Control Point vs. Tender Point) was computed for each threshold measure. For simple group comparisons, *t* tests were used in the case of continuous variables and chi-square tests in the case of categorical variables. Pearson correlation coefficients described the relationships between 2 variables. One-tailed significance testing was used throughout because directed hypotheses were available, i.e., 'more clinical pain and associated dysfunctions and lower responsiveness thresholds in fibromyalgia patients than in control subjects' and 'positive relationships among experimental pain measures as well as between experimental and clinical pain measures'. Alpha was set at 0.05.

Results

Characteristics of fibromyalgia pain

The mean duration of pain complaints was 9.9 years (SD = 7.8 years; range: 1–30 years). Twenty-four of the 26 patients had pain every day, 1 at least once a week and 1 at least once a month.

The scores of the MPQ for typical pain in the recent past were: PRI-T, 32.5 ± 10.9; PRI-S, 17.5 ± 5.3; PRI-A, 6.2 ± 4.9; PRI-E, 2.7 ± 1.5; and PRI-M, 6.0 ± 2.5. With respect to the total score (PRI-T), our values were clearly above those reported by Perry et al. (1988) and Gaston-Johansson et al. (1985), which were around 25, and below those reported by Nolli et al. (1988) and Ferraccioli et al. (1990), which were around 37. It is uncertain whether actual differences in pain severity or differences in the type of pain rated (e.g., present, typical, maximum) account for the dissimilar findings. Words that were chosen by more than 50% of the patients were 'aching' (69%), 'throbbing' (65%), 'tender' (54%) and 'exhausting' (54%). The mean value of the Present Pain Index (PPI) was 2.3 (SD = 0.8), slightly above the 2.1 reported by Perry et al. (1988). Accordingly, most of our patients were experiencing 'mild' or 'discomforting' fibromyalgia pain.

The patients had a mean score of 48.2 (SD = 15.8) on the LPR for typical pain in the recent past (LPR-T). Lautenschläger et al. (1991) reported a mean value of 45.5 for fibromyalgia patients, without giving the time frame of measurement (present pain, typical pain in the recent past). The mean ratings for present pain (LPR-P) in this study were lower (31.8) but, nevertheless, very significantly different from those of the control group (2.5) (see Table I). Similar differences between usual pain and present pain in fibromyalgia patients were also reported by McDermid and Rollman, who used visual analog scales (unpublished data). The very low values for present pain in the control subjects suggest that this group was essentially pain

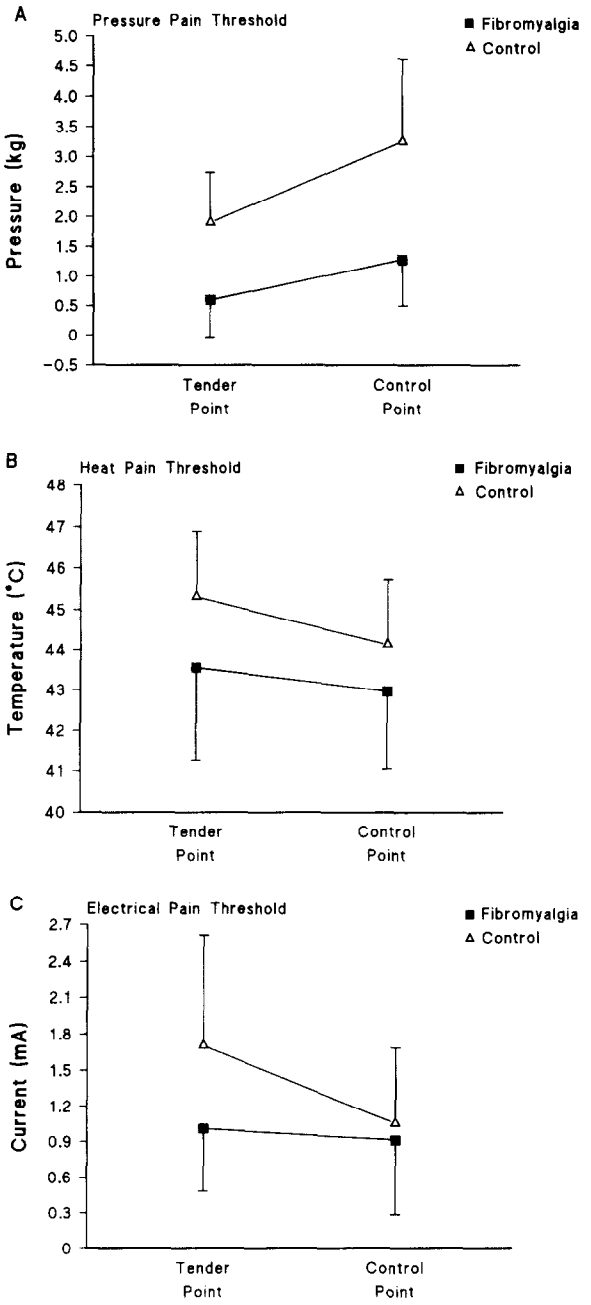

Fig. 1. Mean and 1 SD of the pressure pain threshold in kg (A), the heat pain threshold in °C (B) and the electrical pain threshold in mA (C) of fibromyalgia patients and healthy control subjects at a tender point and at a control point (n = 26 in both groups).

free, with the exception of a few subjects who had minor aches.

The functional and psychovegetative complaints which are typically associated with fibromyalgia (Wolfe et al. 1990) were also very common in our sample of patients (see Table I). With the exception of depressive mood, all complaints were significantly more frequent in the patients than in the controls. Since a considerable portion of the controls reported at least some of the complaints, i.e., headache, fatigue, sleep disturbances, depressive mood, it seems that these complaints are also common in non-clinical samples of women of this age group. Alternatively, the manner of assessment, using a yes/no rating for the presence of the complaints, might have resulted in an overestimation of prevalence.

In summary, the fibromyalgia patients of our sample had a long history of pain, moderate to high levels of continuous pain both in the recent past and at present and frequent functional and psychovegetative complaints. This conforms to the usual depiction of a full-blown syndrome in fibromyalgia.

Experimental responsiveness to painful and non-painful stimuli

The pressure pain thresholds of the fibromyalgia patients and the healthy controls are shown in Fig. 1A.

TABLE II

RESULTS OF THE ANOVA WITH THE FACTORS OF GROUP (Fibromyalgia vs. Control) AND SITE (Tender Point vs. Control Point) AND THE CORRESPONDING INTERACTION FOR THE THRESHOLDS OF RESPONSIVENESS TO PAINFUL AND NON-PAINFUL STIMULATION (*P* values of 1-tailed tests)

	df	*F*	*P*
Pressure pain			
Group	1,50	53.61	< 0.001
Site	1,50	54.76	< 0.001
G×S	1,50	5.89	0.010
Heat pain			
Group	1,50	9.10	0.002
Site	1,50	20.91	< 0.001
G×S	1,50	2.28	0.066
Electrical pain			
Group	1,50	5.85	0.010
Site	1,50	20.78	< 0.001
G×S	1,50	11.51	< 0.001
Warmth			
Group	1,50	2.18	0.073
Site	1,50	68.92	< 0.001
G×S	1,50	0.46	0.351
Cold			
Group	1,50	4.22	0.023
Site	1,50	21.88	< 0.001
G×S	1,50	0.73	0.199
Electrical detection			
Group	1,50	1.77	0.095
Site	1,50	39.60	< 0.001
G×S	1,50	1.75	0.096

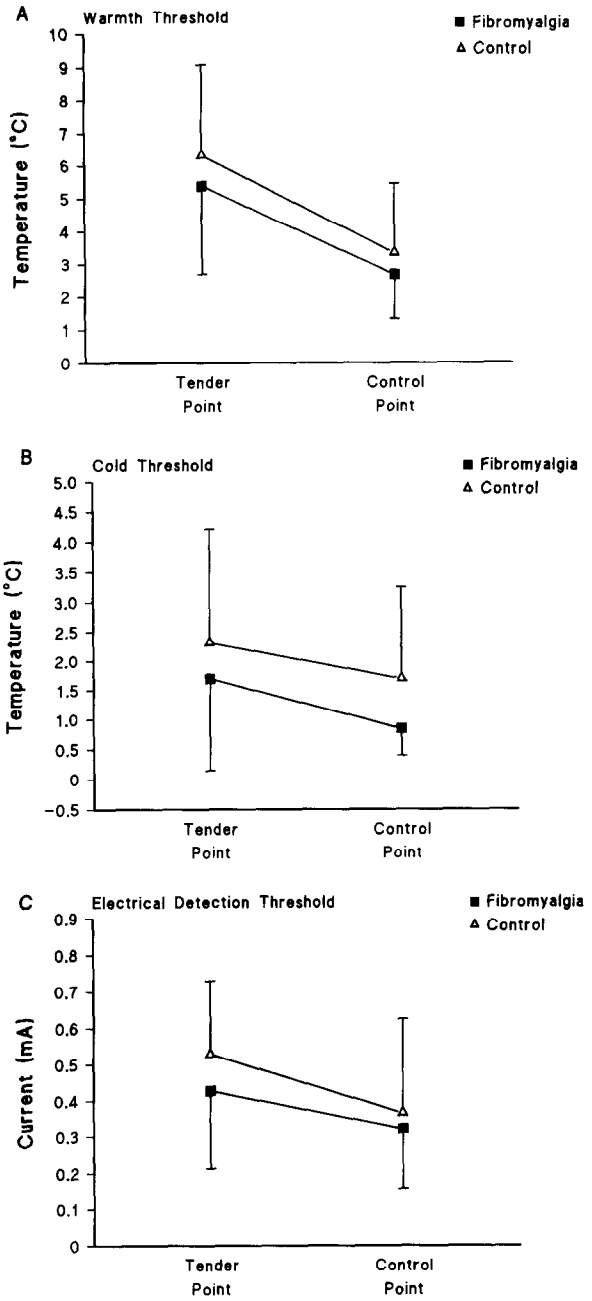

Fig. 2. Mean and 1 SD of the warmth (A) and cold (B) thresholds in °C and the electrical detection threshold in mA (C) of fibromyalgia patients and healthy control subjects at a tender point and at a control point (n = 26 in both groups).

The corresponding results of the analysis of variance are presented in Table II. The group factor and the site factor were both highly significant, with lower values for the fibromyalgia patients and for the tender points (TP). The Group × Site interaction was also significant, reflecting a greater difference between the 2 groups at the control point (CP) than at the TP. However, comparisons between the 2 groups for each site separately, using *t* tests, did not indicate great importance for this interaction (TP: $t = 40.4$, $P < 0.001$; CP: $t = 40.7$, $P < 0.001$).

TABLE III

PEARSON CORRELATIONS (1-tailed testing) BETWEEN THE 3 PAIN THRESHOLDS (P = pressure, H = heat, E = electrical current) ASSESSED AT THE TENDER POINT AND AT THE CONTROL POINT IN THE GROUPS OF FIBROMYALGIA PATIENTS AND CONTROL SUBJECTS (n = 26 in both groups)

	Fibromyalgia patients	Healthy controls
Tender point		
P×H	0.422 *	0.423 *
P×E	0.346 *	0.305
H×E	0.316	0.465 **
Control point		
P×H	0.323	0.318
P×E	0.132	0.028
H×E	0.231	0.450 *

* $P < 0.05$; ** $P < 0.01$.

The analysis of the heat pain thresholds provided similar results with respect to the group factor (see Fig. 1B and Table II). The fibromyalgia patients again had the lower thresholds. Although the site factor was significant, as was the case with the pressure pain threshold, the direction of the site difference was opposite. There were higher heat pain thresholds at the TP than at the CP. However, the non-significant Group × Site interaction suggested that the lower heat pain thresholds in the fibromyalgia group were not site-specific.

With the electrical pain threshold, the group factor was significant while the site factor and the Group × Site interaction were highly significant (see Fig. 1C and Table II). This pattern of results was due to the clearly lower pain thresholds of the fibromyalgia patients, compared to the controls, at the TP. The t tests showed a highly significant group difference for the TP ($t = 11.4$, $P < 0.001$) but no significant difference at the CP ($t = 0.6$, $P = 0.212$). The TP again appeared to be less pain sensitive, on average, than the CP.

Considering the sensitivity for non-painful stimulation (detection thresholds of warmth, cold and electrical current), the group factor was significant only once, i.e., for the detection threshold of cold (see Figs. 2A–C and Table II). This threshold was lower in the fibromyalgia patients than in the control subjects. The site factor was highly significant for all 3 measures, with the TP always having higher threshold values than the CP. No Group × Site interaction was significant.

Given the pattern of generally lower pain thresholds in the fibromyalgia group, it seemed appropriate to examine whether the three types of pain threshold (pressure, heat, electrical current) reflect a common process of pain amplification. Correlations between the experimental pain measures are presented in Table III. Four of the 6 correlations determined for the tender point were significant, contrasted to only 1 of 6 at the control site. However, they were not high enough to lend strong support to the notion that a single mechanism was tapped by the different forms of pain induction.

Correlations between experimental pain and clinical pain (patients only)

The assumption that increased responsiveness to experimental pain is directly associated with strong clinical pain in fibromyalgia can be probed by looking at the correlations between the 2 sets of variables. The coefficients are presented in Table IV. Out of 48 correlations (36 for typical pain and 12 for present pain), only 4 were significant, including the 2 for the LPR-P and pressure pain. The significant relationships were of modest size and might be chance findings. Nonetheless, the correlations which were significant were consistent, across tender and control points, and were all in the expected negative direction.

TABLE IV

PEARSON CORRELATIONS (1-tailed testing) BETWEEN THE 3 PAIN THRESHOLDS (pressure, heat, electrical current) ASSESSED AT THE TENDER POINT AND AT THE CONTROL POINT AND THE MEASURES OF CLINICAL PAIN IN THE GROUP OF FIBROMYALGIA PATIENTS (n = 26)

	PRI-S	PRI-A	PRI-E	PRI-M	PRI-T	LPR-T	PPI	LPR-P
Tender point								
Pressure pain	−0.053	0.047	0.068	−0.199	−0.041	−0.113	−0.162	−0.372 *
Heat pain	0.009	0.126	0.128	−0.255	0.019	−0.140	0.053	−0.180
Electrical pain	0.001	−0.050	0.316	−0.340 *	−0.059	−0.325	−0.208	0.127
Control point								
Pressure pain	−0.129	−0.026	0.079	−0.250	−0.122	−0.165	−0.266	−0.403 *
Heat pain	0.066	0.033	< 0.001	−0.138	0.015	−0.024	−0.008	−0.153
Electrical pain	0.158	−0.084	0.095	−0.428 *	−0.047	−0.173	−0.137	0.048

MPQ: PRI (PRIs were assessed for the typical pain in the recent past), S = sensory, A = affective, E = evaluative, M = miscellaneous, T = total, $P < 0.05$. PPI. LPR: T = typical pain in the recent past and P = present pain.

Discussion

The data from the present study demonstrate increased pain responsiveness in fibromyalgia patients, not only for pressure but also for heat and electrical current. Hence, fibromyalgia is not solely a condition with enhanced sensitivity to noxious mechanical stimulation. Rather, the hypothesis of a generalized pain hyperresponsiveness in fibromyalgia (Rollman and Lautenbacher 1993) gains support.

There is considerable evidence that pressure pain responsiveness is increased in fibromyalgia at loci additional to the traditional tender points (Scudds et al. 1987; Lautenschläger et al. 1988; Tunks et al. 1988; Quimby et al. 1988; Mau and Raspe 1990; Wolfe et al. 1990; Mikkelsson et al. 1992; Smythe et al. 1992; Granges and Littlejohn 1993b). The present study confirmed this. Moreover, this study demonstrated a generalization of the effect to further forms of experimental pain induction. Hyperresponsiveness, whether at tender or control points, is not limited to pressure applied to the muscles.

Some qualifications need to be considered. There were interesting distinctions between the results obtained by assessment of the heat pain thresholds and the electrical pain thresholds. The heat pain thresholds were lower for the patients irrespective of the site tested (tender point or control point). Similar findings occurred with the pressure pain thresholds. In contrast, the lowering of the electrical pain threshold was restricted to the tender point. Scudds et al. (1987), who measured electrocutaneous pain thresholds only at a control point, also found no significant differences for this stressor between fibromyalgia patients and healthy controls. Arroyo and Cohen (1993), testing electrocutaneous pain thresholds at control points on the arm and neck, did find that fibromyalgia patients were more responsive than controls. Either electrical pain stimulation is less sensitive than pressure or heat in demonstrating generalized pain hyperresponsiveness in fibromyalgia or else stimulus parameters, sites, or electrode diameters selectively engage peripheral and central mechanisms.

Interestingly, electrical pain threshold was the only response measure that uniquely differentiated the tender point from the control point. Fibromyalgia patients differed from healthy subjects at both tender points and control points for pressure and for heat pain. They differed only at tender points for electrically induced pain.

Vecchiet et al. (1991) described studies in which electrical current was used in the evaluation of myofascial trigger points. Electrical pain thresholds were lower at the sites of active trigger points and at the sites of referred pain for patients compared to controls. Since others have noted that the distinction between tender points in fibromyalgia and trigger points in myofascial pain syndrome is sometimes ambiguous (e.g., Wolfe et al. 1992), our findings and those of Vecchiet et al. suggest that the assessment of electrical pain thresholds may be useful in studying localized forms of hyperirritability.

While the fibromyalgia patients had almost uniformly lower pain thresholds than the healthy controls, the correlations between the three types of pain thresholds (pressure, heat, electrical current) were not strikingly high in either patients or in controls. This holds for measurements at both the tender point and at the control point, although the correlations were higher at the former site. The proportion of common variance ranged from 2 to 18% in the patients and from 0 to 22% in the controls. Hence, the similar pattern of group differences for the 3 pain thresholds does not simply signify that the thresholds reflect a unitary perceptual process.

One interpretation might be that the 3 thresholds are indicative of distinct aspects of pain perception and that all 3 aspects are altered by fibromyalgia. This is probably not a full account, since stronger relationships between pain thresholds assessed by diverse types of stimulation were found in previous studies (Harris and Rollman 1983; Lautenbacher and Rollman 1993). The subjects in the earlier studies were undergraduate students of both genders. Such observers may be more proficient than our subjects in using a response criterion which remains consistent across the different perceptual qualities evoked by unlike noxious stressors.

The discovery of both generalized and localized forms of hyperalgesia suggests an interaction of central and peripheral dysfunctions. A similar proposal was recently advanced by Bennett (1993). A number of conceptual models have been advanced to explain the pattern of hyperresponsiveness. Yunus (1992) considered the central element to be a lack of inhibition or an augmented facilitation in the processing of pain stimuli. Granges and Littlejohn (1993a) proposed that psychological factors amplify muscle pain. Rollman and Lautenbacher (1993) postulated a pattern of perceptual hypervigilance to aversive events. Ursin et al. (1993) put forward a neurobiological model of muscle pain which incorporates both peripheral and central sensitization coupled with psychological interpretation and attribution mechanisms. Henriksson and Bengtsson (1991) have also suggested that the peripheral disturbance of nociception in fibromyalgia is mainly due to sensitized muscle nociceptors.

Heat pain thresholds are determined by activity in skin nociceptors rather than muscle nociceptors. Consequently, one would not expect a peripheral basis for group differences. The dissimilarity in heat pain thresholds between the fibromyalgia patients and the controls appear to be caused by central factors. Similar

conclusions come from the finding by Granges et al. (1993) that fibromyalgia patients have a lower pain threshold than controls for stimulation of the hand by means of a CO_2 laser, coupled with an increase in the peak-to-peak amplitude of the nociceptive evoked response. The hyperresponsiveness to pressure pain, on the other hand, may reflect both peripheral pathology, i.e., sensitization of muscle nociceptors, and disturbed central mechanisms, i.e., mechanisms which also affect heat pain thresholds.

A group difference for the electrically induced pain threshold occurred only at the tender point, likely reflecting the influence of peripheral factors. It appears that our small electrodes, parameters or stimulation sites picked up a localized disturbance in fibromyalgia, but not the generalized effect. Arroyo and Cohen (1993), using other conditions, did find that the patients' tolerance threshold at control points was lower.

Since our responsiveness measures for non-painful stimulation (detection thresholds of warmth, cold and electrical current) did not show clear differences between the fibromyalgia patients and the healthy controls, the hyperalgesic responses of the patients were not likely due to a general hyperaesthesia. The perceptual changes in fibromyalgia were largely specific to pain. The only significant group difference at non-noxious levels was found for the detection threshold of cold. Cold is one of the major aggravating factors of fibromyalgia pain (Campbell et al. 1983; Gaston-Johansson et al. 1985; Brückle and Müller 1991); fibromyalgia patients may be particularly disposed to detect early signs of these factors.

As regards the concept of tender points, it was somewhat surprising to find that the tender point was less instead of more sensitive than the control point for 5 of the 6 threshold measures (detection and pain). Even heat pain and electrical pain thresholds were higher at the tender point than at the control point. Thus, the increased tenderness implied by the term 'tender point' (whether one is considering patients or controls) only means a locally increased responsiveness to pressure pain; it does not apply to other types of painful and non-painful stimulation.

The weak relationship between the experimental pain thresholds and the measures of clinical pain did not indicate that increased pain responsiveness and widespread clinical pains are two signs of the same pathological process in fibromyalgia. We assessed both typical pain in the recent past and present pain in order to avoid ambiguity due to a poorly defined time frame for clinical pain judgments. Only 2 of 36 correlations between the 'typical pain' measure and the pain thresholds were significant.

The situation was somewhat more favorable with the measures of present pain. Here, 2 of 12 correlations were significant. Moreover, these 2 significant negative correlations (the LPR and the pressure pain thresholds assessed at the tender point and at the control point) parallel the findings of other investigators. Lautenschläger et al. (1991) discovered similar correlations between the 2 measures taken after acupuncture therapy, but not before, suggesting that such relationships may be dependent upon the severity of the syndrome. Scudds et al. (1989) also reported a significant negative correlation between pressure tolerance and present pain. As well, some therapy studies have shown that the amelioration of clinical pain was paralleled by an increase in pressure pain threshold (McCain 1986; Scudds et al. 1989; Værøy et al. 1989; Lautenschläger et al. 1991).

These considerations suggest that a linkage may exist between responsiveness to noxious pressure and the present pain state in fibromyalgia. Individuals whose clinical level of pain is high seem inclined to report that increasing mechanical pressure, at both tender and control points, becomes painful sooner than those experiencing less ongoing discomfort. Furthermore, the therapeutic studies cited above indicate that changes in clinical pain level are accompanied by changes in responsiveness to noxious pressure. However, other components of pain hyperresponsiveness (e.g., reaction to strong heat and electrical pulses) and of clinical pain (e.g., history) are not directly related. Hence, in the full-blown fibromyalgia syndrome, which has received most attention, pain hyperresponsiveness and clinical pain are, to a considerable degree, distinct features. There may well be stronger relationships, with one factor provoking the other, in the early stages of the disease. Subjects who are hyperresponsive to pain but who do not present with a clinical pain disorder may still be at risk for fibromyalgia. Longitudinal studies are required to test this assumption.

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