



A comparative study of iatrogenesis, medication abuse, and psychiatric morbidity in chronic pain patients with and without medically explained symptoms

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Received 25 November 1997; received in revised form 18 February 1998; accepted 31 March 1998

Abstract

We report a case control study comparing patients attending a pain clinic whose symptoms were not considered medically explained (cases) with those whose symptoms were considered medically explained (controls). Principal comparisons were psychiatric morbidity, medication use, and iatrogenic factors assessed by interview, and questionnaire measures of anxiety, depression, functional impairment, coping strategies and pain beliefs. Medically unexplained symptoms were associated with the presence of psychiatric morbidity (odds ratio = 3.4, 95% C.I.: 1.4,8.2), and of possible iatrogenic factors. There were no significant differences with regards to medication abuse/dependence. © 1998 International Association for the Study of Pain. Published by Elsevier Science B.V.

Keywords: Chronic pain; Iatrogenic factors; Psychiatric morbidity; Drug abuse/dependence; Medically unexplained symptoms

1. Introduction

There is now consensus that physical, psychological and social factors all contribute to the development of chronic pain syndromes, and that the relative contribution made by each variable differs in individual patients. It is also accepted that those variables are not categorically, but dimensionally distributed.

We report a case control study in which we have elected to compare patients at two ends of the spectrum – those in which biomedical factors appear to play the predominant part in the aetiology of pain ('medically explained') and those in which they do not ('medically unexplained').

In previous papers we have reported the prevalence of iatrogenic factors and medication misuse/abuse in a pain clinic (Kouyanou et al., 1997a,b). In this paper we now compare two subpopulations within the pain clinic.

Chronic pain is a complicated, difficult to handle problem both for the patient and the health care system. Following

the initial work up of a pain problem continuing investigations to elicit a cause has not been shown to be of any help. Chronic pain is an intractable condition and very few treatments have been shown to be of significant benefit. By providing further unhelpful investigations and treatment the health care system reinforces unrealistic and passive beliefs which in turn impede the patient to develop coping skills.

Our hypotheses were that patients with medically unexplained pain will have a higher prevalence of iatrogenic factors, higher prevalence of psychiatric morbidity and medication abuse/dependence.

2. Methods

2.1. Subjects

Patients were recruited from the pain clinics of St. Thomas' Hospital (STH) and King's College Hospital (KCH). Both are large teaching hospitals in south London. Full

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details of the sample recruitment, demographics and clinics are provided elsewhere (Kouyanou et al., 1997a). The sample was characteristic of those attending specialist UK pain clinics, but with a bias towards more chronic subjects seen at STH.

Inclusion criteria were: (1) pain duration longer than 6 months, (2) age between 18 and 65 years, (3) new referrals to the pain clinics. Excluded were those with a diagnosis of cancer.

2.2. Instruments

(I) St. Thomas' Pain Management Center, Pain History Questionnaire. This is a self report measure covering how the pain started, its location and duration. It also summarizes the different kinds of treatment received for pain and the current medication regime.

(II) The patients' recollection of previous experiences with doctors and the advice received was assessed using a semi-structured checklist designed by the investigator. (A) Data were obtained on the range and type of investigations received. Predefined categories of over-investigation and over-treatment were created. Full details are provided elsewhere (Kouyanou et al., 1997a), but in brief over-investigation was defined as: (1) more than three hospital admissions for the pain, (2) more than one CT scan, MRI scan, bone scan, myelogram or endoscopy, (3) more than two types of scans. Over-treatment was defined as: (1) more than two operations for the pain, (2) more than two courses of the same type of injections (e.g. three epidurals), (3) more than two different types of injections (e.g. epidural, facet joint injection, nerve block), (4) more than four referrals for physiotherapy, (5) more than five types of treatment (e.g. medication, physiotherapy, acupuncture, osteopathic treatment, chiropractic treatment, surgery). (B) Patients' recollection of advice and information given about their pain problem. We specifically looked for: (1) advice regarding rest (e.g. suggestion that rest is helpful or prescriptions for bed rest at home or hospital), (2) direct or indirect suggestion that patients 'imagined' their pain, (3) any explanation given regarding the nature of patients' pain. We asked subjects whether or not their treating doctor(s) made an effort to give plausible explanations for the patient's pain. (C) Patients' satisfaction with how their pain problem was handled by their health care providers. (D) Patients' opinion as to whether their pain problem had been thoroughly investigated, and whether further investigations were needed.

(III) Data about medicine prescription and use were acquired via a semistructured checklist Patients were asked to provide information about: (A) type and dose of medicines prescribed and (B) instructions given by doctors regarding medication use. Inappropriate prescribing was defined as: (1) prescription of analgesics on pain contingent basis ('prn'), (2) prescribing without specific instructions, (3) prescription of tranquilizers on a long-term basis, (4)

prescription of two tranquilizers of the same class or of two antidepressants of the same class or of two or more analgesics of the same class.

(IV) All subjects were given a questionnaire booklet to complete at home. This included: (1) the hospital anxiety and depression scale (HAD) (Zigmond and Snaith, 1983), (2) the medical outcomes study (MOS) 36-item short form health survey (Ware and Sherbourne, 1992), (3) coping strategies questionnaire (CSQ) (Rosentiel and Keefe, 1983); this questionnaire assesses the extent to which subjects reported using each of six different cognitive coping strategies and one behavioural coping strategy in response to pain (diverting attention, reinterpreting pain sensations, coping self statements, ignoring pain sensations, praying or hoping, catastrophising, increasing activity level); at the end of the questionnaire, patients are asked to make two ratings of the overall effectiveness of whichever coping strategies they used, (4) pain beliefs and perceptions inventory (PBP1) (Williams and Thorn, 1989); PBP1 identifies the extent to which subjects reported endorsement of the following four belief factors: mystery, self-blame, pain permanence, and pain constancy.

(V) Each patient was interviewed using the National Institute of Mental Health Diagnostic Interview Schedule, Version III-Revised (DIS-R) (Robins et al., 1991). Only the following sections were completed (i.e. not psychosis): mood disorders, panic disorder, generalized anxiety disorder, post-traumatic stress disorder, obsessive compulsive disorder, somatisation disorder, alcohol abuse and dependence and substance use disorders. The DIS-R was used to assign current and lifetime DSM-III-R diagnoses. We made a prior decision to compare the groups on only five categories – lifetime prevalence of major depression, panic disorder, alcohol abuse, total psychiatric diagnoses and current episode of major depression.

Diagnosis of medication abuse/dependence for psychoactive substances (opioid analgesics, antidepressants, benzodiazepines) was based on the DSM-III-R in the light of information obtained from the medical record, and the results of the clinical evaluation performed by the consultant anaesthetist on the day of the interview. Similarly patients who often (but not systematically) used their medication above the recommended dose were also considered as cases of medication misuse. For the purposes of this study a substance use disorder was considered to be in remission if no pathological use or resulting impairment had occurred within the past year (Hoffmann et al., 1995).

2.3. Statistical analysis

Case control differences were investigated using the independent samples *t*-test to compare means and the chi-square statistic (Fisher's exact for small expected frequencies) to compare proportions. Although some variables were positively skewed, we had sufficient cases in both groups to use

parametric tests. Taking logarithms to decrease the positive skew of the variables: duration of pain, time off work, age and age left school, gave similar results. To test for an association between ordinal variables, we used the Mantel–Haenszel test. Because of the likely confounding effects of age and gender on variables such as lifetime prevalence and family history of psychiatric disorders, odds ratios were calculated using logistic regression to control for relevant cofounders. We used analysis of covariance to control duration of pain for age.

3. Results

3.1. Subjects

One hundred and ninety-three patients were approached to take part in the study; 125 (64%) gave informed consent and completed the study. Patients who did not agree to participate or did not complete the study did not differ in terms of gender and duration of pain. Patients were classified into three groups. Group I consisted of 58 patients (46.4%) whose symptoms did not have a clear biomedical basis, group II consisted of 45 patients (36%) with known organic pathology and group III consisted of 22 unclassified patients (17.6%) (patients that it was not possible to place definitely in one of these two groups) (see below for details). Comparisons were performed between group I and group II. This is similar to the methods used by Magni and Merskey (1987).

All patients had been thoroughly investigated, usually by at least three doctors (general practitioner, specialist consultant, pain specialist). The final decision was taken by the pain specialist after review of all the available data. The classification was made blind to the psychiatric interview results.

Diagnoses of patients with known organic pathology (group II) according to the International Association for the Study of Pain (IASP) classification system is presented in Table 1 (Merskey and Bogduk, 1994).

Demographic characteristics of the two groups are shown in Table 2. The controls were older than the cases ($t = -3.70$, $df = 84.69$, $P < 0.01$). The differences in duration of pain were no longer significant after controlling for age ($F_{1,100} = 0.942$, $P = 0.334$). There was also a significant gender difference. Women were more in the group of cases ($\chi^2 = 4.72$, $df = 1$, $P = 0.029$).

3.2. Psychiatric diagnoses and family history

As shown in Table 3, 32 out of 58 (55.2%) cases (medically unexplained) had a lifetime history of major depression compared with 11 out of 45 (24.4%) controls (medically explained) ($\chi^2 = 9.83$, $df = 1$, $P = 0.001$). Eight cases (13.8%) had a current diagnosis of major depression compared with three controls (6.7%) (Fisher's

exact test $P = 0.34$). Twelve cases (20.7%) had a lifetime history of panic disorder compared with two controls (4.4%) ($\chi^2 = 5.69$, $df = 1$, $P = 0.01$). A lifetime history of alcohol abuse was observed in eight cases (13.8%) and eight controls (17.8%). Table 3 shows the diagnoses we investigated as determined using the DIS-R. Lifetime history for any of those diagnoses was observed in 43 cases (74.1%) and in 19 controls (42.2%) ($\chi^2 = 10.7$, $df = 1$, $P = 0.001$).

Lifetime prevalence of statistically significant differences in psychiatric morbidity was adjusted for age and gender. Differences in family history of chronic pain and alcohol abuse were also adjusted for gender. These are shown in Table 4.

We also assessed the association between diagnoses of major depression and alcohol abuse and the later development of chronic pain. Sixteen cases (27.6%) and four controls (8.9%) had suffered from one or more major depressive episodes before the onset of their chronic pain. Seven cases (12.1%) and four controls (8.9%) had abused alcohol before the onset of chronic pain.

Table 1

Diagnoses of patients with organic pathology according to IASP classification (Merskey and Bogduk, 1994)

Diagnosis	Code	No. of patients
1 Lumbar discogenic pain	XXVI-11	10
Lumbar spinal pain due to failed spinal surgery	XXVI-10	
2 Lumbar discogenic pain	XXVI-11	7
3 Lumbar spinal pain due to osteoarthritis	XXVI-5.3	5
4 Osteoarthritis hip	XXXII-3	4
5 Osteoarthritis knee	XXXIII-2	2
6 Traumatic avulsion of brachial plexus	XI-3	2
7 Prolapsed intervertebral disc	XXVI-2.3	2
Lumbar spinal pain due to failed spinal surgery	XXVI-10	
8 Complex regional pain syndrome type 1	1.4	2
9 Spondylolysis	XXVI-22	1
Lumbar spinal pain due to failed spinal surgery	XXVI-10	1
10 Acceleration/deceleration injury of neck	IX-8	
Lumbar discogenic pain	XXVI-11	1
11 Cervical discogenic pain	IX-10	
Adhesive capsulitis	XI.10	1
12 Carpal tunnel syndrome	XI.16	1
13 Vascular disease of limbs	XII	1
14 Local leg pain	1-3.5	1
15 Thoracic zygoapophyseal joint pain	X-10	1
16 De Quervain's tenosynovitis	XI-13	1
17 Syringomyelia	I-7	1
18 Thoracic spinal pain due to fracture of vertebral body	X-1.1	1
19 Neuropathic pain chest wall		1

Table 2

Demographic characteristics

	Cases (<i>n</i> = 58)			Controls (<i>n</i> = 45)		
	Mean	SD	Median	Mean	SD	Median
Age (years)	36.7	9.7	34.0	44.7	11.7	42.0
Age left school (years)	16.1	1.0	16.0	15.7	1.2	16.0
Duration of pain (months)	75.2	46.9	61.0	102.4	76.5	96.0
Time off work (months)	52.4	40.8	37.0	48.6	44.1	36.5
		%			%	
Sex						
Male		24.0			44.0	
Marital status, living with a mate		57.0			69.0	
Work status, full or part-time employed		24.0			31.0	
Receiving disability income		72.0			62.0	
Current or past litigation/compensation		34.0			29.0	
Ethnic origin						
Caucasian		91.5			84.5	
Black		3.5			6.5	
Asian		5.0			4.5	
Other		0.0			4.5	
Site of pain						
Low back		44.0			57.5	
Upper back and neck		7.0			7.0	
Upper limbs		20.5			13.0	
Lower limbs		3.5			16.0	
Pelvis/abdomen		9.0			0.0	
Everywhere		12.0			2.0	
Other (thorax, face)		3.5			4.5	
Circumstances in which pain began						
At work		40.0			29.0	
Motor vehicle		7.0			11.0	
Non-work/non-motor vehicle		10.0			7.0	
Following surgery		5.0			7.0	
Following illness		2.0			0.0	
No reason		33.0			37.0	
Other		3.0			9.0	

Thirty cases (51.7%) and 12 controls (26.7%) had at least one first degree family member with chronic pain ($\chi^2 = 6.58$, $df = 1$, $P = 0.01$). 15 cases (25.9%) and two controls (4.4%) had at least one first degree relative with alcohol abuse ($\chi^2 = 8.43$, $df = 1$, $P = 0.003$).

3.3. Iatrogenic factors

Data was obtained from all subjects on over-investigation, over-treatment, information received, satisfaction with treatment, and advice on management. We also inquired if the patient had ever felt that their doctor regarded their pain as 'imagined' or 'all in the mind'. Results are shown on Tables 5 and 6.

3.4. Medication use, misuse and abuse or dependence is presented in Table 7

Although medication abuse/dependence was rare in both groups the proportion of patients with medication abuse/dependence both present and in remission was greater

amongst cases than controls (psychoactive medication abuse or dependence $P = 0.09$, psychoactive medication abuse or dependence in remission $P = 0.07$).

3.5. Assessment of: functional impairment, anxiety, depression, coping strategies and pain beliefs and perceptions (Table 8).

Self reported functioning and well-being assessed by the MOS 36-item shortform health survey (SF-36) revealed very low values for the eight health concepts. There were no significant differences between groups on any of the subscales. There were also no significant differences on HAD between the two groups.

The CSQ showed significantly higher scores for the catastrophising coping strategy for cases ($t = 2.30$, $df = 83.30$, $P = 0.02$). The rest of the parameters did not differ in the two groups.

Cases were found to exhibit significantly higher scores in the perception of pain as mysterious (mystery subscale) when assessed by the pain beliefs and perception inventory

Table 3

DSM-III-R diagnoses

	Cases (n = 58)		Controls (n = 45)	
	No.	%	No.	%
Atypical bipolar disorder (bipolar II)	1	1.7	0	0.0
Major depression	32	55.2	11	24.4
Past only	24	41.4	8	17.8
Current only	3	5.2	1	2.2
Current and past	5	8.6	2	4.4
Dysthymia	2	3.4	0	0.0
Somatisation disorder	7	12.1	0	0.0
Panic disorder	12	20.7	2	4.4
Current	7	12.1	2	4.4
In remission	5	8.6	0	0.0
Post-traumatic stress disorder	1	1.7	1	2.2
Alcohol abuse/dependence	8	13.8	8	17.8
Alcohol abuse				
Current	3	5.2	3	6.7
Past	5	8.6	3	6.7
Alcohol dependence				
Current	0	0.0	0	0.0
Past	0	0.0	2	4.4
Illegal substance abuse/dependence	1	1.7	1	2.2
Illegal substance abuse				
Current	0	0.0	0	0.0
Past	1	1.7	1	2.2
Illegal substance dependence	0	0.0	0	0.0
Obsessive compulsive disorder	0	0.0	0	0.0
Life time prevalence of any of the above	43	74.1	19	42.2

(PBPI) ($t = 3.25$, $df = 76.87$, $P = 0.002$). There were no other significant differences.

4. Discussion

To contribute to the understanding of chronic pain in specialist care we compared chronic pain patients with medically unexplained symptoms to those whose symptoms were considered to be medically explained.

4.1. Limitations

We are aware that this distinction may be criticized. Physical and non-physical factors contribute to the morbidity of all chronic pain patients. Nevertheless, the relative contributions do differ, and we think it is reasonable to compare the two ends of the spectrum, whilst acknowledging the limitations of the approach (Magni and Merskey, 1987; Kisely et al., 1997). We also accept that the decision to assign patients to either category is always a matter of judgement – but point out that doctors make these judgements everyday in clinical practice. Thus we believe that the two groups do correspond to current medical concepts of chronic pain. We also draw attention to the

number of patients who could not be meaningfully classified on this dimension.

4.2. Demographic factors

Patients with medically unexplained symptoms were younger than patients with medically explained symptoms and were more likely to be female. The latter is not surprising as chronic pain disorders are diagnosed twice as frequently in women than men (Kaplan and Sadock, 1995). The two groups did not differ in other demographic characteristics.

4.3. Iatrogenic factors

We have previously reported a high prevalence of iatrogenic factors in those attending pain clinics in two teaching hospitals in London. We had found a high prevalence of over-investigation, over or unhelpful treatment, inappropriate prescribing, and misdiagnosis as well as health care providers' unhelpful advice and attitude (Kouyanou et al., 1997a). We now suggest that iatrogenesis is more likely in those without adequate medical explanation. We observed that this group of patients reported a significantly higher frequency of direct disconfirmation of their pain by the doctors. We suggest that patients with medically unexplained symptoms are often exposed to attitudes that may paradoxically reinforce their determination to maintain the sick role, since to do otherwise would confirm the doctor's own view – that it was 'all in the mind' after all (Hadler, 1996). Patients without medical explanation were also more likely to say that they had not received adequate explanations of their pain. We also suspect that poor medical management of unexplained pain in turn leads to characteristic patient attitudes. Those who feel their doctors do not accept the legitimacy of their pain are more likely to desire further

Table 4

Age and gender adjusted odds ratios (logistic regression) for psychiatric morbidity

	Significance level	Odds ratio for cases/controls	95% C.I.
Lifetime prevalence of major depression	0.01	3.3	(1.3, 8.2)
Life-time prevalence of panic disorder	0.066	4.5	(0.9, 22.7)
Life-time prevalence of psychiatric disorder	0.008	3.4	(1.4, 8.2)
Family history ^a			
1st degree relative with alcohol abuse	0.012	7.2	(1.5, 33.9)
1st degree relative with chronic pain	0.019	2.8	(1.2, 6.5)

Separate logistic regression analyses each one controlling for gender and age (effects of gender and age are not reported).

^aControlled for gender only.

Table 5

Iatrogenic factors a

	Cases (n = 58)	%	Controls (n = 45) ^a	%	P	Odds ratio ^b	95% C.I.
Over investigation							
(a) More than three hospital admissions	7	12.1	1	2.2	0.13*	6.03	0.71, 51.00
(b) More than one CT, MRI, bone scan, myelogram, or endoscopy	12	20.7	12	26.7	0.47**	0.72	0.28, 1.79
(c) More than two types of scan	7	12.1	4	8.9	0.75*	1.40	0.38, 5.13
(d) Any of the above	19	32.8	15	33.3	0.95**	0.97	0.42, 2.22
Over treatment							
(a) More than two operations	3	5.2	4	8.9	0.69*	0.55	0.11, 2.63
(b) More than two courses of the same type of injections	7	12.1	5	11.1	0.88**	1.09	0.32, 3.71
(c) More than two different types of injections	6	10.3	6	13.3	0.64**	0.75	0.22, 2.50
(d) More than four referrals for physiotherapy	7	12.1	2	4.4	0.29**	2.95	0.58, 14.95
(e) More than five types of treatment	32	55.2	17	37.8	0.08**	2.02	0.91, 4.48
(f) Any of the above	35	60.3	20	44.4	0.11**	1.90	0.86, 4.18
Advice regarding rest							
(a) At least one type of rest c	43	74.1	27	60.0	0.12**	1.91	0.82, 4.41
(b) Bed rest at home or at hospital or both	30	51.7	22	48.9	0.77**	1.12	0.51, 2.44
Treating patients as if pain was 'imaginary'							
(a) Report of direct disconfirmation of pain	20	34.5	6	13.3	0.01**	3.42	1.23, 9.44
(b) Report of indirect disconfirmation of pain	28	48.3	15	33.3	0.12**	1.86	0.83, 4.17
	n = 46		n = 44				
Physicians' advice regarding medication use							
(a) No of patients on current medication	46	79.0	44	98.0			
(b) Medication prescribed on a time scheduled basis	11	23.9	15	34.1	0.28**	0.60	0.24, 1.52
(c) Medication prescribed on a 'prn' basis	6	13.0	6	13.6	0.93**	0.95	0.28, 3.20
(d) Medication prescribed both ways	5	10.9	3	6.8	0.71*	1.66	0.37, 7.43
(e) Medication prescribed without specific instructions	24	52.0	20	45.0	0.52**	1.30	0.57, 2.99
No. of patients prescribed							
(a) Long term benzodiazepine(s)	14	30.4	6	13.6	0.055**	2.77	0.95, 8.04
(b) Two or more analgesics of the same class	7	15.2	8	17.7	0.70**	0.80	0.26, 2.45
(c) Two sedatives of the same class	1	2.2	0	0.0			
(d) Two antidepressants of the same class	3	6.5	0	0.0			

^aControls.^bOdds ratio for cases/controls.^cAdvice to just rest, and/or bed rest at home, and/or bed rest at hospital.

*Fisher's exact test, **Chi-square test.

investigations thus setting in motion further iatrogenic cycles. In the remaining categories of iatrogenic factors presented in Tables 5 and 6 most categories were higher in patients with no organic pathology but these differences did not reach statistical significance.

4.4. Medication abuse/dependence

Medication use, misuse, and abuse or dependence has been previously reported in this chronic patient population (Kouyanou et al., 1997b). Patients with medically explained pain were more likely to use medication. No other significant difference or trend could be identified regarding medication use.

4.5. Psychiatric morbidity

The main findings of the present study regarding psychia-

tric morbidity are as follows. The current diagnosis of major depression in patients with unexplained symptoms was elevated, but not significantly, compared with patients with medically explained symptoms (13.8 versus 6.6%). Similarly, the measure of the severity of HAD in both chronic pain patient groups failed to identify any differences in the anxiety and depression subscales.

The lifetime prevalence of major depression in patients with medically unexplained symptoms was significantly higher than in patients with medically explained symptoms. There was also a trend for the former to have a higher frequency of panic disorder, just failing to reach statistical significance after adjusting for age and gender.

We observed that a substantial number of patients with medically unexplained pain had first-degree relatives with chronic pain and/or alcohol abuse. We detected a statistically significant difference in frequency of those parameters between cases and controls.

Table 6

Iatrogenic factors^b

	Cases (<i>n</i> = 58)		Controls (<i>n</i> = 45)	
	No.	%	No.	%
Information given to patients about chronic nature of their pain (<i>P</i> = 0.005)*				
Not informed	34	58.6	17	37.8
Some explanations	14	24.1	8	17.8
Well explained	10	17.2	20	44.4
Patients' satisfaction on how their GP handled the problem (<i>P</i> = 0.31)*				
Dissatisfied	22	37.9	11	24.4
Partially satisfied	4	6.9	7	15.6
Satisfied	32	55.2	27	60.0
Patients' opinion whether at least one doctor was aware of their case history (<i>P</i> = 0.95)*				
Not aware	20	34.5	15	33.3
Not sure	7	12.1	6	13.3
Aware	31	53.4	24	53.3
Patients' satisfaction with thoroughness of investigation (<i>P</i> = 0.04)*				
Dissatisfied	24	41.4	11	24.4
Not sure	7	12.1	4	8.9
Satisfied	27	46.6	30	66.7
Patients' opinion whether further investigation was needed (<i>P</i> = 0.01)*				
No need	13	22.4	21	46.7
Not sure	11	19	6	13.3
Necessary	34	58.6	18	40.0

GP, general practitioner.

*Mantel-Haenszel test for linear association.

The relationship between pain and depression continuous to be controversial. It has been argued that chronic pain is a variant of depression (Blumer and Heilborn, 1982) or a form of masked depression (Lesse, 1982). This hypothesis has been challenged by others as lacking empirical support, suggesting depression as secondary to pain (Hendler, 1984; Turk and Salovey, 1984; Romano and Turner, 1985; Brown, 1990). It has also been suggested that they share

some common pathogenetic mechanism but can remain distinct (Magni, 1987). Yet others have argued that depressive symptoms experienced by chronic pain patients might reflect aspects of abnormal illness behaviour, or somatic focusing (Pilowsky et al., 1977; Barsky, 1979; Dworkin et al., 1990). All have some empirical support – for example, depression is a risk factor for the development of chronic musculo-skeletal pain, but also vice versa (Leino and Magni, 1993; Magni et al., 1994). Rudy et al. (1988) have provided evidence that it is the cognitive appraisal variables of perceived interference and lack of self-control that mediate a pain-depression relationship. Our study is unable to untangle these various links. Instead, we have confirmed that chronic pain clinic patients have a higher rate of lifetime and current psychiatric diagnoses. We have extended this observation to show that this is commoner in those with medically unexplained pain, which in turn suggests that models based on the concept that depression is a reaction to the existence of pain per se are simplistic.

High rates of psychiatric morbidity have been previously reported in chronic pain patients with medically unexplained symptoms. In a study of 37 patients without lesions who suffered mainly from low back pain Katon et al. (1985) found a current prevalence of 32% for major depression. This is higher than the percentage of current diagnosis of major depression found in our group of patients with unexplained symptoms (13.8%) probably reflecting the inpatient, rather than outpatient setting. A higher percentage of depression compared with our findings has also been reported by Magni and Merskey (1987) in a study comparing patients with and without firm evidence of an organic disturbance to account for pain. The diagnostic system they used differed from the one used in the present study and their sample consisted of patients referred for psychiatric consultation.

Table 7

Medication use, misuse, and abuse or dependence

	Cases (<i>n</i> = 58)		Controls (<i>n</i> = 45)		
	No.	%	No.	%	
Patients taking medication at present	46	79.3	44	97.8	<i>P</i> = 0.005*
Analgesics					
Non opioid analgesics	26	56.5	24	54.5	<i>P</i> = 0.85*
Opioids	34	73.9	35	79.5	<i>P</i> = 0.52*
Psychoactive medication ^a					
Antidepressants	37	80.4	40	90.9	<i>P</i> = 0.15*
Benzodiazepines	13	28.3	13	29.5	<i>P</i> = 0.89*
Benzodiazepines	14	30.4	6	13.6	<i>P</i> = 0.055*
Medicine misuse ^b	10	21.7	6	13.6	<i>P</i> = 0.31*
	(<i>n</i> = 37)		(<i>n</i> = 40)		
Psychoactive medication abuse/dependence (DSM-III-R)	9	24.3	4	10.0	<i>P</i> = 0.09*
	(<i>n</i> = 58)		(<i>n</i> = 45)		
Psychoactive medication abuse or dependence in remission (DSM-III-R)	8	13.8	1	2.2	<i>P</i> = 0.07**

*Chi-square test.

^aOpioid analgesics, benzodiazepines, antidepressants.^bAny kind of analgesics, sedative, antidepressant.

**Fisher's exact test.

Table 8
Questionnaires

	Cases Mean (SD)	Controls Mean (SD)	<i>P</i>	
<i>CSQ</i>				
Diverting attention	2.00 (1.05)	1.93 (1.25)	<i>P</i> = 0.76*	
Reinterpreting pain sensations	1.02 (1.07)	1.15 (1.24)	<i>P</i> = 0.58*	
Coping-self statements	3.56 (1.05)	3.40 (1.19)	<i>P</i> = 0.48*	
Longing pain sensations	2.46 (1.14)	2.29 (1.32)	<i>P</i> = 0.48*	
Praying and hoping	2.06 (1.18)	2.46 (1.27)	<i>P</i> = 0.11*	
Catastrophising	2.95 (1.27)	2.28 (1.53)	<i>P</i> = 0.02*	
Increasing activity level	2.82 (0.87)	2.43 (1.14)	<i>P</i> = 0.057*	
Effectiveness ratings				
Control over pain	2.56 (1.19)	2.79 (1.50)	<i>P</i> = 0.39*	
Ability to decrease pain	2.12 (0.90)	2.02 (1.53)	<i>P</i> = 0.63*	
<i>PBPI</i>				
Mystery	0.75 (0.82)	0.08 (1.17)	<i>P</i> = 0.002*	
Self-blame	-1.54 (0.53)	-1.31 (0.85)	<i>P</i> = 0.10*	
Pain permanence	0.55 (0.85)	0.60 (1.04)	<i>P</i> = 0.78*	
Pain constancy	1.12 (0.86)	1.12 (0.93)	<i>P</i> = 0.96*	
<i>SF-36</i>				
Physical functioning	38.63 (24.42)	30.55 (24.31)	<i>P</i> = 0.10*	
Role-physical	10.45 (20.80)	20.00 (30.89)	<i>P</i> = 0.08*	
Bodily pain	32.09 (12.57)	30.48 (13.70)	<i>P</i> = 0.54*	
General health	43.87 (22.00)	45.40 (22.96)	<i>P</i> = 0.73*	
Vitality	26.63 (16.55)	29.22 (18.76)	<i>P</i> = 0.46*	
Social functioning	39.31 (23.74)	44.72 (24.49)	<i>P</i> = 0.26*	
Role-emotional	40.00 (41.77)	48.88 (39.94)	<i>P</i> = 0.28*	
Mental health	49.45 (16.26)	53.33 (19.39)	<i>P</i> = 0.27*	
	(<i>n</i> = 55) ^a	%	(<i>n</i> = 45)	%
<i>HAD</i>				
Anxiety subscale**				
Non-cases	12	21.8	12	26.7
Doubtful	20	36.4	12	26.7
Definite anxiety	23	41.8	21	46.7
Depression subscale***				
Non-cases	17	30.9	16	35.6
Doubtful	14	25.5	12	26.7
Definite depression	24	43.6	17	37.8

^aThree questionnaires not available.

t*- test, **Mantel–Haenszel test for linear association, *P* = 1.0, *Mantel–Haenszel test for linear association, *P* = 0.5.

Our finding of 55.2% life-time prevalence of major depression and of 20.7% panic disorder in patients with medically unexplained symptoms is comparable with Katon's report, Katon et al. (1985).

Out of 32 patients with medically unexplained symptoms and a lifetime history of major depression 16 had at least one major depressive episode before the onset of chronic pain. This finding strengthens the argument that a subgroup of chronic pain patients might have a causal relationship to depression.

It is unlikely that rates of psychiatric disorder were higher in those with unexplained symptoms as a result of greater functional impairment because we reported equal, and substantial, impairment in both groups.

The relationship between family history and chronic pain observed in the present study is in line with previous reports (Schaffer et al., 1980; Blumer and Heilborn, 1982; Violon

and Giurgea, 1984; Katon et al., 1985). This is further supported by the finding that somatisation disorder is often associated with a family history of alcoholism in male relatives (Bohman et al., 1984).

4.6. Cognitive factors

How the patients coped with their pain was measured by the CSQ. Ratings of coping strategies were comparable with the two groups with the exception of the catastrophising element which was significantly higher in those with medically unexplained symptoms. Patients' ratings for their ability to control and decrease pain were similar in both groups. The absolute ratings reported by the two groups are similar to a previous report on the use of coping strategies in chronic low back pain patients (Rosentiel and Keefe, 1983).

Previous reports have concluded that catastrophising as a

coping strategy is related to poorer emotional adjustment (Rosentiel and Keefe, 1983), and that success in dealing with pain is more a function of refraining from use of catastrophising rather than use of any particular coping strategy (Chaves and Brown, 1978; Spanos et al., 1979). A positive relationship between catastrophising/feeling unable to control pain and depression has also been reported (Rosentiel and Keefe, 1983; Turner and Clancy, 1986). The association between negative cognitions and depression in non-pain populations has been widely supported in the literature (Rush and Weissenburger, 1982).

Pain beliefs represent the patient's own conceptualization of what pain is and what pain means for them. They play a prominent role in pain perception, function and response to treatment (Williams et al., 1994). In the present study we observed that patients with medically unexplained pain significantly differed on the mystery scale but showed no differences in other scales. These results are in line with one previous study reporting that patients who believed their pain was enduring and mysterious were less likely to use cognitive coping strategies (e.g. reinterpretation of pain sensation), more likely to catastrophise, and less likely to rate their coping strategies as effective in controlling and decreasing pain than patients believing their pain to be understandable and of short duration (Williams and Keefe, 1991).

4.7. Conclusions

Our initial hypotheses were that patients with medically unexplained symptoms would exhibit higher frequency of psychiatric morbidity and iatrogenesis than patients with medically explained symptoms. These were confirmed. We did not confirm our expected differences in medication abuse/dependence between the two groups. We also confirmed a role for cognitive factors, finding, as predicted, that patients with medically unexplained pain were more likely to view their pain as mysterious, and more likely to react to pain in a catastrophic fashion. We therefore draw attention to the need for doctors to be very sensitive to the beliefs of patients when no immediate cause for chronic pain can be found. It is essential that the patient is not led to believe their pain is 'imaginary' thus potentially triggering a breakdown on the doctor–patient relationship, and a desire for further investigations 'to prove the doctor wrong'. Patients also require valid and understandable explanations for their symptoms, to reduce the tendency to view the process as not only mysterious but also beyond control.

Acknowledgements

We would like to thank Dr. S. Peat and her colleagues for allowing us to interview patients attending the pain clinic at King's College Hospital. K.K. is supported by a grant from the State Scholarships Foundation of Greece (S.S.F./I.K.Y.).

References

- Barsky, A.J., Patients who amplify bodily sensations, *Ann. Intern. Med.*, 91 (1979) 63–70.
- Blumer, D. and Heilborn, M., Chronic pain as a variant of depressive disease: the pain-prone disorder, *J. Nerv. Ment. Dis.*, 170 (1982) 381–406.
- Bohman, M., Cloninger, R., Von Knorring, A.L. and Sigvardsson, S., An adoption study of somatoform disorders. III Cross-fostering analysis and genetic relationship to alcoholism and criminality, *Arch. Gen. Psychiatry*, 41 (1984) 872–878.
- Brown, K.G., A causal analysis of chronic pain and depression, *J. Abnorm. Psychol.*, 99 (1990) 127–137.
- Chaves, J.F. and Brown, J., Self-generated strategies for control of pain and stress. In: S. Sanders (Chair), *Hypnosis and the Control of Pain*, Symposium presented at the meeting of the American Psychological Association, Toronto, 1978.
- Dworkin, S.F., Von Korff, M. and Le Resche, L., Multiple pains and psychiatric disturbance, *Arch. Gen. Psychiatry*, 47 (1990) 239–244.
- Hadler, N.M., If you have to prove you are ill, you can't get well. The object lesson of fibromyalgia, *Spine*, 21 (1996) 2397–2400.
- Hendler, N., Depression caused by chronic pain, *J. Clin. Psychiat.*, 43 (3) (1984) 30–36.
- Hoffmann, N.G., Olofsson, O., Salen, B. and Wickstrom, L., Prevalence of abuse and dependency in chronic pain patients, *Int. J. Addictions*, 30 (1995) 919–927.
- Kaplan, H.I. and Sadock, B.J., *Comprehensive Textbook of Psychiatry*, 5th Edition, Vol. I, Williams and Wilkins, Baltimore, MD, 1995, pp. 1264.
- Katon, W., Egan, K. and Miller, D., Chronic pain: lifetime psychiatric diagnoses and family history, *Am. J. Psychiatry*, 142 (1985) 1156–1160.
- Kisely, S., Goldberg, D. and Simon, G., A comparison between somatic symptoms with and without clear organic cause: results of an international study, *Psychol. Med.*, 27 (1997) 1011–1019.
- Kouyanou, K., Pither, C.E. and Wessely S., Iatrogenic factors and chronic pain, *Psychosom. Med.*, 59 (1997a) 597–604.
- Kouyanou, K., Pither, C.E. and Wessely, S., Medication misuse, abuse, and dependence in chronic pain patients, *J. Psychos. Res.*, 43 (1997b) 497–504.
- Leino, P. and Magni, G., Depressive and distress symptoms as predictors of low back pain, neck-shoulder pain, and other musculoskeletal morbidity: a 10-year follow-up of metal industry employees, *Pain*, 53 (1993) 89–94.
- Lesse, S., The masked depression syndrome: results of a seventeen year clinical study, *Am. J. Psychother.*, 37 (1982) 456–475.
- Magni, G. and Merskey, H., A simple examination of the relationships between pain, organic lesions and psychiatric illness, *Pain*, 29 (1987) 295–300.
- Magni, G., On the relationship between chronic pain and depression when there is no organic lesion, *Pain*, 31 (1987) 1–21.
- Magni, G., Moreschi, C., Rigatti-Luchini, S. and Merskey, H., Prospective study on the relationship between depressive symptoms and chronic musculoskeletal pain, *Pain*, 56 (1994) 289–297.
- Merskey, H. and Bogduk, N., *International Association for the Study of Pain (IASP) Classification of Chronic Pain*, IASP Press, 1994.
- Pilowsky, I., Chapman, C.R. and Bonica, J.J., Pain, depression and illness behaviour in a pain clinic population, *Pain*, 4 (1977) 183–192.
- Robins, L., Cottler, L. and Keating, S., *National Institute of Mental Health Diagnostic Interview Schedule, Version III-Revised*, Washington University School of Medicine, St. Louis, MO, 1991.
- Romano, J.M. and Turner, J.A., Chronic pain and depression: does the evidence support the relationship? *Psychol. Bull.*, 97 (1985) 18–34.
- Rosentiel, A. and Keefe, F., The use of coping strategies in low back pain patients: relationship to patient characteristics and current adjustment, *Pain*, 17 (1983) 33–44.
- Rudy, T., Kerns, R. and Turk, D., Chronic pain and depression: toward a cognitive mediation model, *Pain*, 35 (1988) 129–140.

- Rush, J. and Weissenburger, J., Depression and suicide. In: R. Grieger and I.Z. Grieger (Eds.), *Cognition and Emotional Disturbance*, Human Sciences Press, New York, 1982, pp. 76–109.
- Schaffer, C.B., Donlon, P.T. and Bittle, R.M., Chronic pain and depression: a clinical and family history survey, *Am. J. Psychiatry*, 137 (1980) 118–120.
- Spanos, N.P., Radtke-Botorik, H.L., Ferguson, J.D. and Jones, B., The effects of hypnotic susceptibility, suggestions for analgesia, and the utilization of cognitive strategies on the reduction of pain, *J. Abnorm. Psychol.*, 88 (1979) 282–292.
- Turk, C.D. and Salovey, P., 'Chronic pain as a variant of depressive disease': a critical reappraisal, *J. Nerv. Ment. Dis.*, 172 (1984) 398–404.
- Turner, J.A. and Clancy, S., Strategies for coping with low back pain: relationship to pain and disability, *Pain*, 24 (1986) 355–364.
- Violon, A. and Giurgea, D., Familial models for chronic pain, *Pain*, 18 (1984) 199–203.
- Ware, J. and Sherbourne, C.D., The MOS 36-item short-form health survey(SF-36) I. conceptual framework and item selection, *Med. Care*, 30 (1992) 473–481.
- Williams, D. and Thorn, B., An empirical assessment of pain beliefs, *Pain*, 36 (1989) 351–358.
- Williams, D.A. and Keefe, F.J., Pain beliefs and the use of cognitive-behavioral coping strategies, *Pain*, 46 (1991) 185–190.
- Williams, D.A., Robinson, M.E. and Geisser, M.E., Pain beliefs assessment and utility, *Pain*, 59 (1994) 71–78.
- Zigmond, A. and Snaith, R., The hospital anxiety and depression scale, *Acta Psychiatr. Scand.*, 67 (1983) 361–370.