ELSEVIER

Journal of Psychosomatic Research 51 (2001) 549–557

Journal of Psychosomatic Research

How many functional somatic syndromes?

Chaichana Nimnuan[a], Sophia Rabe-Hesketh[b], Simon Wessely[a], Matthew Hotopf[a,*]

[a]*Academic Department of Psychological Medicine, Guy's King's and St. Thomas' School of Medicine and the Institute of Psychiatry, 103 Denmark Hill, London SE5 8AZ, UK*

[b]*Department of Biostatistics, Guy's King's and St. Thomas' School of Medicine and the Institute of Psychiatry, 103 Denmark Hill, London SE5 8AZ, UK*

Received 11 October 2000; accepted 5 March 2001

Abstract

Objective: Patients with medically unexplained symptoms are given diagnoses dependent upon the particular medical specialty consulted — irritable bowel syndrome in gastroenterology, fibromyalgia in rheumatology and others. The purpose of this paper is to establish whether these 13 different syndromes are discrete entities. **Methods:** Consecutive new patients in seven outpatient clinics at two general hospitals were recruited. Patients completed questionnaires measuring symptoms and demographic data. Case notes were reviewed to ascertain whether the presenting symptoms were medically explained 3 months after the initial visit. **Results:** Complete data were available for 550 subjects. With 37 unexplained symptoms included in the model, 30% of the total variance could be explained by one factor using unrotated principal component analysis. When the 13 identified functional syndromes were included, it was evident that functional syndromes could not be assumed to be independent. A two-factor model was the best fit for the present data after rotation. **Conclusions:** This study suggests that the existence of distinct functional somatic syndromes (FSSynd) as defined clinically in medicine should be reconsidered.

Keywords: Functional somatic symptoms; Functional somatic syndromes; Overlapping syndromes

Introduction

Experiencing symptoms is part of normality [1,2]. Most of these symptoms are not associated with clear-cut biomedical diagnoses, and most do not lead to any use of medical services [3]. The symptoms are then referred to as "medically unexplained" or "functional," the latter term suggesting an alteration of function rather than of structure [4].

Functional somatic symptoms are an important problem in general medicine not only because of their prevalence but also on account of the high associated consumption of health service resources. In only 16% of one series of new outpatients attendees to the US internal medicine clinic was a definite biomedical cause identified for symptoms [5]. A study of inpatient admissions in Denmark shows that nearly 20% of high users of healthcare had no physical disorder to account for their admissions [6]. A survey of a Dutch medical outpatient clinic showed that 52% of new referrals remained medically unexplained [7].

When such symptoms are prominent, they may be elevated to the status of a syndrome to which a specific name is attached. These include irritable bowel syndrome and nonulcer dyspepsia in gastroenterology, premenstrual syndrome and chronic pelvic pain in gynaecology, fibromyalgia in rheumatology, and chronic fatigue syndrome in neurology. Each syndrome is claimed by some to be a unique diagnostic entity with its own characteristics, and for each, there is usually an operational definition.

Clinicians have long noted that patients with any particular functional syndrome often complain of symptoms *outside* the symptom complex of that particular syndrome. This leads to more difficulties in the prevalence study of functional somatic syndromes (FSSynd). Simply looking at the descriptive studies of any particular syndrome confirms this. For example, many gastroenterological researchers have drawn attention to nonalimentary symptoms of irritable bowel syndrome [8–11].

From that observation, it is a short step to look for the prevalence of functional syndromes, rather than symptoms,

* Corresponding author. Tel.: +44-207-848-0778; fax: +44-207-848-5129.

E-mail address: spjumhh@iop.kcl.ac.uk (M. Hotopf).

0022-3999/01/$ – see front matter
PII: S0022-3999(01)00224-0

among patients with any given syndrome. On the basis of a literature review, we concluded that considerable overlap is present even among the symptoms held to be characteristic of each disorder [12]. For example, several authors have commented on the comorbidity between fibromyalgia and chronic fatigue syndrome [13–16]. Other functional syndromes have also been reported in samples of CFS patients [17–19].

Recognizing this, some have proposed that certain subgroups exist — for example, irritable bowel syndrome, fibromyalgia, chronic tension headache, and primary dysmenorrhoea [13]. However, to date, there has been no study using a uniform method of data collection and analysis, permitting the diagnoses of all putative syndromes, and sampling from all the relevant medical specialities. In this study, we attempt to determine empirically whether or not these syndromes overlap by using a latent variable analysis.

Methods

This study was a part of the epidemiological study of medically unexplained somatic symptoms in the general hospital described in detail elsewhere [20].

Subjects and setting

Consecutive new patients are residents in southeast London referred by their general practitioners to outpatient clinics at King's College Hospital and Dulwich Hospital between 1995 and 1997. The clinics were gastroenterology, gynaecology, neurology, rheumatology, respiratory medicine, cardiology, and dentistry. Subjects were eligible for inclusion if they were aged between 16 and 65 years and were attending the above clinics. Subjects who could not read or speak English and those diagnosed as having psychotic or organic brain syndromes were excluded. Thirty-six medical and dental practitioners in the seven clinics were involved in helping recruit patients into this study.

Patients attending the above clinics were given a questionnaire with a return-stamped addressed envelope. Two postal and one telephone reminder were used to increase response rate. Case notes were reviewed to ascertain the final diagnosis approximately 3 months after the initial visit.

Case definition

For this study, *functional somatic symptoms* were defined as any current somatic complaint reported by a patient for whom no definite medical diagnosis could be found after physical examination and appropriate investigation. This judgement was made on the basis of investigation results and the physicians' opinions ascertained 3 months after the initial visit. The physicians' opinions were determined by the final diagnosis stated in the clinical case notes. If the physicians gave a diagnosis of "functional" or continued to defer the diagnosis because of no detected abnormality, we considered these as indicating that the symptoms were medically unexplained. We have shown elsewhere that this method has acceptable reliability [21].

We defined FSSynds as a group of *functional somatic symptoms*, which (1) consist of characteristic symptoms forming an operationally defined unexplained syndrome and (2) cause distress (defined by symptoms that cannot be ignored) or impairment. The definition of some syndromes also requires duration criteria (see Appendix A).

Measures

Symptom review questionnaire

We developed a new self-report questionnaire for detecting various FSSynds. The questionnaire consisted of 11 groups of symptoms, which correspond to 13 recognized FSSynds. Each group of symptoms provides a list of characteristic symptoms for each syndrome. We followed standard criteria for some FSSynds such as chronic fatigue syndrome [22] and irritable bowel syndrome [23]. However, there were some practical difficulties for the nonspecialist to diagnose some syndromes. For example, the diagnostic criteria of fibromyalgia proposed by the American College of Rheumatology require at least 11 tender points elicited from physical examination performed by trained specialists [24]. These criteria are impractical for a broad epidemiological survey. We therefore adjusted the criteria by adding associated symptoms described by Yunus [25] and Smythe and Moldofsky [26] but did not carry out clinical examination of tender points, which was impractical in the busy waiting clinics where the survey was conducted (see Appendix A). For others, we designed a symptom checklist from reviewing consensus articles describing the phenomenology of such FSSynds. The questionnaire also included 25 additional symptoms, including somatic symptoms, sleep, and psychological complaints. These symptoms were self-rated on symptom frequency (0–4) and degree of intrusion (0–4), which gave a combined severity score of 0–8.

Most criteria included a measure of severity. We rated this on three levels: mild ("symptoms can be ignored if the subject does not think about them"), moderate ("symptoms cannot be ignored but do not stop the subject from doing things"), and severe ("symptoms stop the subject from doing things"). Only moderate and severe levels were judged as significant in terms of distress and functional impairment.

We also recorded the duration of illness in order to fulfil the diagnostic criteria for some FSSynds, for example, 6 months for chronic fatigue syndrome, 3 months for irritable bowel syndrome, and 3 months for fibromyalgia. In practice, many FSSynds usually have a remitting and recurring

Table 1
Prevalence of subjects with any FSSynd ($N = 550$)

	Male		Female		Total	
Clinic	% Case (Number of subjects with complete data)	95% CI	% Case (Number of subjects with complete data)	95% CI	% Case (Number of subjects with complete data)	95%CI
Gastroenterology	55.0 (20)	31.5–76.9	62.5 (32)	43.7–78.9	59.6 (52)	45.1–73.0
Chest	51.9 (27)	32.0–71.3	65.6 (32)	46.8–81.4	59.3 (59)	45.7–71.9
Rheumatology	41.4 (29)	23.5–61.1	66.1 (62)	53.0–77.7	58.2 (91)	47.4–68.5
Cardiology	44.2 (43)	29.1–60.1	67.3 (49)	52.5–80.1	56.5 (92)	45.8–66.8
Neurology	50.0 (38)	33.4–66.6	58.5 (65)	45.6–70.6	55.3 (103)	45.2–65.1
Dental	50.0 (16)	24.7–75.3	49.1 (55)	35.4–62.9	49.3 (71)	37.2–61.4
Gynaecology	–	–	57.3 (82)	45.9–68.2	57.3 (82)	45.9–68.2
Total	48.0 (173)	40.3–55.7	60.2 (377)	55.1–65.2	56.4 (550)	52.1–60.6

course. As a result, we omitted the duration criteria for FSSynds with no existing standard criteria.

Analysis

The data on functional somatic symptoms were analysed using exploratory factor analysis. There were 37 functional symptoms included in the analysis. For symptoms that applied for women only (pelvic pain and premenstrual symptoms), the responses for men were treated as missing so that men did not contribute to the estimation of the factor loadings of these symptoms (using the pairwise missing option in SPSS version 7.5). Principle component analysis was used to extract the initial factors (components) and estimate the factor loadings. The initial solution was then simplified by varimax rotation and normalised.

The data on the presence or absence of each of 13 syndromes on 550 subjects were analyzed using factor analysis for binary variables. A logistic regression model was fitted whose linear predictor was given a linear combination of factor score and a constant. The factors were assumed to be normally distributed and uncorrelated (this is essentially a multiple-factor item–response model [27]). The likelihood was evaluated using a 10-point Gaussian quadrature and maximized using Stata's maximum likelihood function. The two syndromes that referred to women only (premenstrual syndrome and chronic pelvic pain) were treated as missing for men and all available data contributed to the maximum likelihood estimation, including data from subjects with missing data on some of the syndromes. The factor loadings were also rotated using varimax and normalized.

The overlap between any particular pair of syndromes was determined by Jaccard coefficient. The Jaccard coefficient was used as a descriptive measure of the degree of overlap between pairs of syndromes. For a given pair of syndromes, the Jaccard coefficient is defined as the ratio of the number of subjects with both syndromes divided by

Table 2
Prevalence of different FSSynds by clinic ($N = 550$)

	Gastro ($n = 52$)	Resp. med ($n = 59$)	Rheum ($n = 91$)	Cardio ($n = 92$)	Neuro ($n = 103$)	Dental ($n = 71$)	Gynae ($n = 82$)	Total ($n = 550$)
TH (%)	**15.4**	**10.2**	**23.1**	**19.6**	**21.4**	**12.7**	**18.3**	**18.0**
NCCP (%)	**13.5**	**39.0**	**14.3**	**27.2**	**16.5**	4.2	**9.8**	**17.5**
FMG (%)	**19.2**	**16.9**	**25.3**	7.6	**11.7**	7.0	**15.9**	**14.5**
IBS (%)	**25.0**	5.1	**11.0**	8.7	3.9	5.6	**19.5**	**10.5**
HV (%)	5.8	**15.3**	**9.9**	**12.0**	**9.7**	4.2	4.9	8.9
CFS (%)	**9.6**	6.8	**9.9**	4.3	**11.7**	4.2	**9.8**	8.2
NUD (%)	**11.5**	6.8	**9.9**	4.3	6.8	5.6	**9.8**	7.6
MCS (%)	**13.5**	3.4	5.5	7.6	1.9	7.0	3.7	5.6
GS (%)	7.7	6.8	2.2	6.5	6.8	0	3.7	4.7
AFP (%)	1.9	5.1	1.1	4.3	1.9	**14.1**	2.4	4.2
TMJ (%)	3.8	1.7	1.1	1.1	1.0	4.2	1.2	1.8
Female only	Gastro ($n = 32$)	Resp. med ($n = 32$)	Rheum ($n = 62$)	Cardio ($n = 49$)	Neuro ($n = 65$)	Dental ($n = 55$)	Gynae ($n = 82$)	Total ($n = 377$)
PMS (%)	**21.9**	**12.5**	**25.8**	**18.4**	27.7	**21.8**	**34.1**	**24.9**
CPP (%)	9.4	3.1	**12.9**	4.1	7.7	3.6	**15.9**	**9.0**

AFP = atypical facial pain, TMJ = temporomandibular dysfunction, FMG = fibromyalgic symptoms, CFS = chronic fatigue syndrome, IBS = irritable bowel syndrome, NUD = nonulcer dyspepsia, NCCP = noncardiac chest pain, MCS = multiple chemical sensitivity, GS = globus syndrome, HV = hyperventilation syndrome, TH = tension headache, PMS = premenstrual syndrome, CPP = chronic pelvic pain. Bold type shows 10% or more in each clinic.

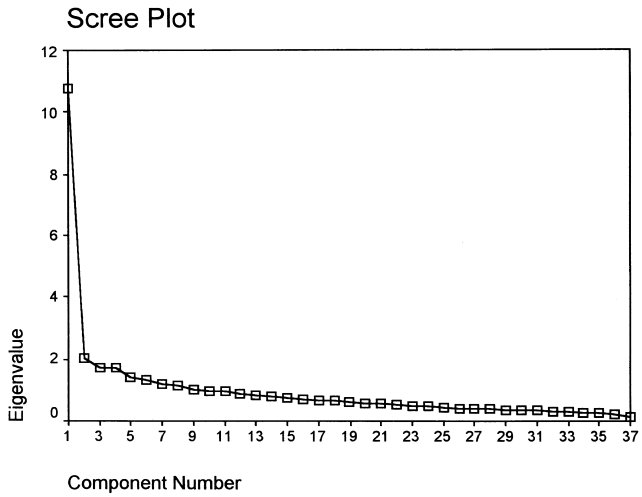

Fig. 1. Scree plot of total variance associated with each factor (component) based on unrotated principal components analysis.

the number of subjects with at least one of the two syndromes [28]. The Jaccard coefficient is therefore an estimate of the probability that a subject who has at least one of two particular syndromes has the other syndrome.

Results

Baseline characteristics

During the period of the study, 890 new patients attended the seven clinics. A total of 582 valid responses were obtained (65.4%). Of these, 32 case notes were missing, leaving 550 subjects to be included in the analysis. We found that the clinics differed in a number of demographic variables. Although there were no interclinic differences in marital status and social class, there were differences in gender, age, ethnicity, and work status (details reported elsewhere) [20].

More than half (56.4%, 95% CI = 52.1, 60.6) of new attenders to the clinics had at least one FSSynd and about half of these (53.6%) had more than one syndrome. The highest prevalence was found in the gastroenterology clinic (59.6%) and the lowest in the dental clinic (49.3%). For all clinics combined, the prevalence of FSSynds was significantly higher in females (difference = 12.2%, 95% CI = 3.3–21.2; Table 1).

The distribution of FSSynds is shown in Table 2. Some syndromes were considerably more common than others in particular clinics. Noncardiac chest pain and hyperventilation were the predominant syndromes in chest and cardiology clinics, irritable bowel syndrome in gastroenterology, and fibromyalgia in rheumatology. Tension headache and premenstrual syndrome were common in almost all clinics, as were noncardiac chest pain, fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome.

In the exploratory factor analysis of the symptoms using principle component method of extraction, nine factors with eigenvalues higher than 1 accounted for 60% of the variance in the functional somatic symptoms data. Approximately 30% of the variance were explained by the first factor. From the Scree plot (Fig. 1), it appeared that a one-factor model should be sufficient for the data. However, according to the Kaiser–Guttman rule for determining the number of factors (eigenvalue > 1.0), seven factors are required. The factor loadings of the seven factors after varimax rotation are shown in Table 3 where loadings less than .35 are not tabulated. The first five factors were labeled according to the group of symptoms.

Table 3
Factor loadings and factor structure of functional somatic symptoms with varimax rotation (normalized; $N = 550$)

	Factor								
	1	2	3	4	5	6	7	8	9
Trouble maintaining sleep	.83								
Early awakening	.77								
Too little sleep	.77								
Trouble falling asleep	.76								
Phonosensitivity		.74							
Photosensitivity		.59							
Palpitation		.56		.45					
Trembling		.53							
Dizziness		.47				.35	.36		
Mood swing		.43			.43		.40		
Disturbing dreams		.36							
Morning stiffness			.76						
Persistent pain			.75						
Low back pain			.64						
Felt pain all over			.63						
Numbness			.56						
Chest pain				.77					
Breathing difficulties				.63					
Heartburn				.61					
Discomfort in the throat				.45					
Abdominal pain				.39				.37	.36
Mental fatigue					.77				
Physical fatigue				.36	.62				
Daytime sleepiness	.38				.52				
Irritable		.43			.50				
Forgetfulness		.47			.50				
Dry mouth						.71			
Taste disturbance						.69			
Tinnitus						.49			
Menstrual symptoms							.79		
Nausea							.55	.38	
Pelvic pain							.55		
Chemical/food reactions								.65	
Vomiting								.59	
Itching								.52	
Facial pain									.69
Headache									.54
Eigenvalue	3.5	3.3	3.1	2.6	2.5	2.1	2.0	1.7	1.5
% Variance	9.4	8.9	8.3	7.0	6.8	5.8	5.5	4.5	4.1

Factor label: (1) sleep problems; (2) neurological mood; (3) general pain; (4) cardiorespiratory; (5) fatigue.

Table 4
The percentage of times that a subject having one of two syndromes also has the other syndrome (Jaccard coefficient) for all pairs of syndromes ($N = 550$)

	IBS	TMJ	AFP	NUD	CPP	TH	FMG	CFS	GH	MCS	HV	PMS	NCCP
IBS	100	10	14	28	19	22	21	17	9	17	14	13	11
TMJ		100	38	8	2	5	2	2	9	5	5	2	4
AFP			100	8	0	7	4	6	9	4	6	4	4
NUD				100	12	14	16	10	13	9	12	6	13
CPP					100	14	19	8	2	5	8	19	7
TH						100	23	18	12	7	17	18	14
FMG							100	15	12	9	17	14	13
CFS								100	3	4	15	9	9
GH									100	6	14	4	11
MCS										100	16	4	10
HV											100	6	23
PMS												100	8
NCCP													100

AFP = atypical facial pain, TMJ = temporomandibular dysfunction, FMG = fibromyalgic symptoms, CFS = chronic fatigue syndrome, IBS = irritable bowel syndrome, NUD = nonulcer dyspepsia, NCCP = noncardiac chest pain, MCS = multiple chemical sensitivity, GS = globus syndrome, HV = hyperventilation syndrome, TH = tension headache, PMS = premenstrual syndrome, CPP = chronic pelvic pain.

Table 6
Number of FSSynds by factor ($N = 550$)

Number of FSSynds	Factor 1 [*N* (%)]	Factor 2 [*N* (%)]
0	340 (61.8)	432 (78.6)
1	118 (21.5)	91 (16.6)
2	42 (7.6)	27 (4.9)
3	23 (4.2)	–
4	18 (3.3)	–
5	6 (1.1)	–
6	3 (0.6)	–

Table 4 shows, for each pair of syndromes, the chances that a subject who has at least one of the syndromes will also have the other syndrome. Irritable bowel syndrome, tension headache, fibromyalgia, nonulcer dyspepsia, hyperventilation, and noncardiac chest pain were likely to overlap with one another. In contrast, the likelihood of overlap between temporomandibular joint dysfunction and other syndromes, except atypical facial pain, was low.

Table 5 shows the two-factor model for FSSynds. The increase in log-likelihood between a zero-factor model and a one-factor model was 178.0 ($df = 13$) and the increase between one-factor and two-factor models was 471.1 ($df = 13$; results not shown). The two-factor model therefore provided a significantly better fit to the data than the one-factor solution ($P < .001$). The data were too sparse to estimate a three-factor model. It is clear that the syndromes cannot be assumed to be independent but more than a single factor is required to model the interdependencies. The matrix of factor loadings for two factors corresponds to factor variances of 2.5 and 4.7, respectively.

About 38% of subjects had at least one syndrome belonging to factor 1, and of these, 44% had two or more syndromes within the same factor (Table 6). About 21% of subjects had at least one syndrome belonging to factor 2. Of these, 23% had both noncardiac chest pain and hyperventilation.

Table 5
Factor loadings and factor structure for FSSynds with varimax rotation (normalized; $N = 550$)

Syndromes	Factor 1	Factor 2
Irritable bowel syndrome	**.6779**	.2014
Temporomandibular joint dysfunction	**.4816**	.0472
Atypical facial pain	**.2892**	.0122
Nonulcer dyspepsia	**.2609**	.1313
Chronic pelvic pain	**.1999**	.0744
Tension headache	**.1754**	.1005
Fibromyalgia	**.1685**	.0986
Chronic fatigue syndrome	**.1445**	.0773
Globus hystericus	.1069	.1334
Multiple chemical sensitivity	.1035	.1172
Hyperventilation	.0931	**.2043**
Premenstrual syndrome	.0772	.0517
Noncardiac chest pain	−.0121	**.9124**

Discussion

Our study asked patients to report any disturbing symptoms irrespective of their principal complaint or the clinic they attended. The descriptive study showed that FSSynds are indeed common and frequently occur in many bodily systems belonging to many specialties. Some syndromes are common across clinics (tension headache and premenstrual syndrome) but others tend to predominate in particular clinics, e.g., irritable bowel syndrome in gastroenterology, fibromyalgia in rheumatology, and so on. However, coexisting syndromes are also evident. For example, noncardiac chest pain and hyperventilation are likely to coexist. Likewise, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, and nonulcer dyspepsia all tend to occur together.

At the symptom level, a general predisposition towards functional somatic symptoms was empirically confirmed using a statistical model (factor analysis). The principal component analysis suggested that the first unrotated principle factor accounted for nearly 30% of the total variance, while the cumulative variance for all seven factors with eigenvalues greater than 1 accounted for 60% of the total variance. This suggests that a sizeable amount of variance can be explained by a single underlying factor. When the factor loadings for all functional symptoms were rotated, the first two factors with the highest amount of the variance also belonged to groups of symptoms that were generalized rather than specific to a named medical syndrome. However, some factors were consistent with precisely defined syndromes, for example, the third factor was consistent with fibromyalgia and the fifth factor with fatigue syndrome.

At the syndrome level, overlapping patterns were also empirically confirmed. Overlapping syndromes were then empirically confirmed using a statistical model (factor analysis of binary outcome variables). The model confirmed that each FSSynd does not exist independently but instead form clusters. Our findings suggest two such clusters. One is what we label as "fatigue pain" (i.e., chronic fatigue syndrome, fibromyalgia, etc.). This supports and unifies previous reports [13,15,16,29–36]. The other is what we label as "cardiorespiratory" (i.e., noncardiac chest pain and hyperventilation), which also supports previous studies [37–40].

Such suggestions are not new [12]. The concept of overlapping syndromes has also been supported by recent studies. One survey showed that almost two-thirds of medical outpatients were presented with multiple symptoms [41]. When Fink [42] looked at the illness histories of a population-based sample of somatizers, he found that as a group, the persistent somatizers had their admissions across a wide range of specialities and diagnoses. Thus, although 96% of the sample had been admitted with a gastrointestinal diagnosis, usually abdominal pain, they had accumulated a long list of other labels as well. The median number of separate diagnoses, nearly all medically unexplained, was eight.

Robbins et al. [43], however, studied FSSynds using a latent variable model and the results supported the discrete existence of irritable bowel syndrome, chronic fatigue syndrome, fibromyalgia, somatic anxiety, and somatic depression as discrete group of symptoms. This is in contrast to our findings. The differences may be due to the type of data collected and the technique of analyses used. Syndrome definitions in the Canadian study relied on the Diagnostic Interview Schedule (DIS) where the exclusion of medical diagnoses was based only on the subject's own report. Moreover, this report used exploratory factor analysis while the previous report [43] used confirmatory factor analysis, which was restricted by the model to be tested. These two approaches may lead to different findings.

We also wonder about the interpretation of the Canadian findings. When the data from Robbins et al.'s study [43] were reanalyzed, the variance previously attributed to five discrete syndromes was rather general and shared within a common source of variance [44]. Deary [44] suggested that the variance be better explained at the general dispositional level rather than attributed to the individual syndromes. In other words, five apparently distinctive syndromes may still be the presentation of an unobserved latent factor.

Aaron et al. [45] have recently presented new empirical evidence suggesting the overlapping syndromes. In a study of patients attending a tertiary care clinic specializing in the management of chronic fatigue syndrome, fibromyalgia, and temporomandibular joint dysfunction, they reported that patients were more likely to have other syndromes such as irritable bowel syndrome, multiple chemical sensitivity, and headache in their lifetime. Our sample is of consecutive new attenders to a more general range of medical outpatient clinics. We therefore confirm their findings and extend their generalizability from a specialist chronic fatigue syndrome clinic to the wide field of general medicine.

Our study has limitations. The definition of some FSSynds had to be compromised due to either lack of preexisting criteria or practical difficulties in assessment. For example, there are no operationally defined criteria for diagnosis of nonulcer dyspepsia, noncardiac chest pain, and chronic pelvic pain. We therefore had to construct our own based on the available literature. Performing tender point examinations (which is required for the diagnosis of fibromyalgia) was not possible within the constraints of this study. Further, the definitions for some syndromes were much less stringent than others; therefore, it may be misleading to give them all similar weights in the factor analysis of syndromes.

FSSynds are important in medicine. Our findings question the diagnostic validity of discrete FSSynds and suggest that attempts to classify syndromes into different categories on the grounds of a single main presenting symptoms may be misguided. Yet, in clinical practice, each specialist is familiar with some syndromes but not others. Physicians instinctively seek and treat only conditions they know well. As a result, coexisting conditions may be ignored. Patients may be seen in several clinics, which increase the risk of overinvestigation and iatrogenesis. We argue that such an approach is outdated. Instead, an appreciation of the fundamental unity of those syndromes may reduce the potential for iatrogenic harm whilst encouraging continuity of care.

Acknowledgments

Dr. Nimnuan is supported by the Thai government as a part of a Ph.D. programme. We are grateful to the following consultants who allow access to their clinics: Dr. W. Gardner, Dr. I. Forgacs, Dr. M. Blott, Dr. D. Scott, Prof. N. Johnson, Dr. C. Pankhurst, Dr. T. Britton, Dr. D. Jewitt, and Prof. J. Moxham. We thank all patients and medical staff who took part.

References

[1] Reidenberg M, Lowenthal D. Adverse non-drug reactions. N Engl J Med 1968;279:678–9.
[2] Verbrugge L, Asione S. Exploring the iceberg: common symptoms and how people care for them. Med Care 1987;25:539–63.
[3] Banks M, Beresford S, Morrell D, Watkins C, Waller J. Factors influencing demand for primary medical care in women aged 20–40 years: a preliminary report. Int J Epidemiol 1975;4:189–255.
[4] Trimble M. Functional disease. BMJ 1982;285:1768–70.
[5] Kroenke K, Mangelsdorff A. Common symptoms in ambulatory care: incidence, evaluation, therapy and outcome. Am J Med 1989;86:262–6.

[6] Fink P. The use of hospitalizations by persistent somatizing patients. Psychol Med 1992;22:173–80.
[7] Van Hemert A, Hengeveld M, Bolk J, Rooijmans H, Vanderbroucke J. Psychological disorders in relation to medical illness among patients of a general medical outpatient clinic. Psychol Med 1993;23:167–73.
[8] Watson W, Sullivan S, Corke M, Rush D. Globus and headache: common symptoms of the irritable bowel syndrome. Can Med Assoc J 1978;118:387–8.
[9] Whorwell P, McCallum M, Creed F, Roberts C. Noncolonic features of the irritable bowel syndrome. Gut 1986;27:37–40.
[10] Nyhlin H, Ford M, Eastwood J, Smith J, Nicol E, Elton R, Eastwood MA. Non-alimentary aspects of the irritable bowel syndrome. J Psychosom Res 1993;37:155–62.
[11] Maxton D, Morriss J, Whorwell P. Ranking of symptoms by patients with irritable bowel syndrome. BMJ 1989;299:1138.
[12] Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes — one or many. Lancet 1999;354:936–9.
[13] Yunus M, Masi A, Aldag J. A controlled study of primary fibromyalgia syndrome: clinical features and association with other functional syndromes. J Rheumatol 1989;16(Suppl 19):62–71.
[14] Wysenbeek A, Shapira Y, Leibovici L. Primary fibromyalgia and the chronic fatigue syndrome. Rheumatol Int 1991;10:227–9.
[15] Norregaard J, Bulow P, Prescott E, Jacobsen S, Danneskiold-Samsoe B. A four-year follow-up study in fibromyalgia: relationship to chronic fatigue syndrome. Scand J Rheumatol 1993;22:35–8.
[16] Prescott E, Jacobsen S, Kjoller M, Bulow P, Danneskiold-Samsoe B, Kamper-Jorgensen F. Fibromyalgia in the adult Danish population: II. A study of clinical features. Scand J Rheumatol 1993;22:238–42.
[17] Manu P, Matthews D, Lane T. Food intolerance in patients with chronic fatigue. Int J Eating Disord 1993;13:203–9.
[18] Fiedler N, Kipen HM, DeLuca J, Kelly-McNeil K, Natelson B. A controlled comparison of multiple chemical sensitivities and chronic fatigue syndrome. Psychosom Med 1996;58:38–49.
[19] Buchwald D, Garrity D. Comparison of patients with chronic fatigue syndrome, fibromyalgia and multiple chemical sensitivities. Arch Intern Med 1994;154:2049–53.
[20] Nimnuan C, Hotopf M, Wessely S. Medically unexplained symptoms: an epidemiological study in seven specialities. J Psychosom Res 2001;51:361–7
[21] Reid S, Crayford T, Richards S, Nimnuan C, Hotopf M. Recognition of medically unexplained symptoms — do doctors agree? J Psychosom Res 1999;47:483–5.
[22] Schluederberg A, Straus S, Peterson P, Blumenthal S, Komaroff A, Spring S, Landay A, Buchwald D. Chronic fatigue syndrome research: definition and medical outcome assessment. Ann Intern Med 1992; 117:325–31.
[23] Thompson W, Dotevall G, Drossman D, Heaton K, Kruis W. Irritable bowel syndrome: guidelines for the diagnosis. Gastroenterol Int 1989;2:92–5.
[24] Wolfe F, Smythe H, Yunus M, Bennett R, Bombardier C, Goldenberg D, Tugwell P, Campbell SM, Abeles M, Clark P. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: report of the multicenter criteria committee. Arthritis Rheum 1990;33:160–73.
[25] Yunus M. Fibromyalgia syndrome: new research on an old malady. BMJ 1989;298:474–5.
[26] Smythe HA, Moldofsky H. Two contributions to understanding of "fibrositis" syndrome. Bull Rheum Dis 1977;28:928–31.
[27] Bartholomew DJ. Latent variable models and factor analysis. New York: Oxford Univ. Press, 1987.
[28] Everitt BS. Cluster analysis. 3rd ed. London: Edward Arnold, 1993.
[29] Triadafilopoulos G, Simms R, Goldenberg D. Bowel dysfunction in fibromyalgia syndrome. Dig Dis Sci 1991;36:59–64.
[30] McCain G, Scudds R. The concept of primary fibromyalgia (fibrositis): clinical value, relation and significance to other chronic musculoskeletal conditions. Pain 1988;33:273–87.
[31] Blasberg B, Chalmers A. Temporomandibular pain and dysfunction syndrome associated with generalized musculoskeletal pain: a retrospective study. J Rheumatol 1989;19:87–90.
[32] Buchwald D, Goldenberg D, Sullivan J, Komaroff A. The "chronic active Epstein–Barr virus infection" syndrome and primary fibromyalgia. Arthritis Rheum 1987;30:1132–6.
[33] Eriksson P, Lindman R, Stal P, Bengtsson A. Symptoms and signs of mandibular dysfunction in primary fibromyalgia syndrome (PFS) patients. Swed Dent J 1988;12:141–9.
[34] Goldenberg D, Simms R, Geiger A, Komaroff A. High frequency of fibromyalgia in patients with chronic fatigue seen in a primary care practice. Arthritis Rheum 1990;33:381–7.
[35] Gomborone JE, Gorard DA, Dewsnap PA, Libby GW, Farthing MJG. Prevalence of irritable bowel syndrome in chronic fatigue. J R Coll Physicians London 1996;30:512–3.
[36] Kirmayer L, Robbins J. Functional somatic syndromes. In: Kirmayer L, Robbins J, editors. Current concepts of somatization: research and clinical perspectives. Washington, DC: American Psychiatric Press, 1991. pp. 79–106.
[37] Bass C, Cawley R, Wade C, Ryan KC, Gardner WN, Hutchison DCS, Jackson G. Unexplained breathlessness and psychiatric morbidity in patients with normal and abnormal coronary arteries. Lancet 1983;i: 605–9.
[38] Bass C, Chambers JB, Gardner WN. Hyperventilation provocation in patients with chest pain and a negative treadmill exercise test. J Psychosom Res 1991;35:83–9.
[39] Mayou R. Atypical chest pain. J Psychosom Res 1989;33:393–406.
[40] Mayou R, Bryant B, Forfar C, Clark D. Non-cardiac chest pain and benign palpitations in the cardiac clinic. Br Heart J 1994;72:548–53.
[41] Kroenke K, Arrington M, Mangelsdorff D. The prevalence of symptoms in medical outpatients and the adequacy of therapy. Arch Intern Med 1990;150:1685–9.
[42] Fink P. Physical complaints and symptoms of somatizing patients. J Psychosom Res 1992;36:125–36.
[43] Robbins JM, Kirmayer LJ, Hemami S. Latent variable models of functional somatic distress. J Nerv Ment Dis 1997;185:606–15.
[44] Deary IJ. A taxonomy of medically unexplained symptoms. J Psychosom Res 1999;47:51–9.
[45] Aaron LA, Burke MM, Buchwald D. Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder. Arch Intern Med 2000;160:221–7.

Appendix A. Operational definition of each FSSynd.

	FMG	TH	AFP	TMJ
Characteristic symptoms	1. Persistent aches and pains in several parts 2. Nonrestorative sleep 3. One or more of the following: felt pain all over; back pain; stiffness	1. Headache or neck pain 2. Pain is tight or pressing; aggravated by stress; getting worse as day progresses	1. Pain in the face, jaw, or mouth 2. Two or more of the following: teeth hurt; burning sensation in the tongue, gums, or lips; pain relieved by eating or drinking	1. Pain in the face, jaw, or mouth 2. Two or more of the following: having trouble opening the mouth; pain aggravated by moving or pressing jaw; pain coming with a clicking sound
Duration	> = 3 months	> = 6 months	> = 3 months	> = 3 months
Severity	Symptoms cannot be ignored or stop subjects from doing things			
Negative Ix	1. − ve Ix results 2. Final dx as functional; defer dx because no medical cause detectable			

	NCCP	NUD	IBS
Characteristic symptoms	1. Chest pain 2. Pain, which does not usually occur after exertion; occurs at rest; usually lasts longer than 20 min	1. Abdominal pain above the navel 2. Having pain aggravate food; absence of night pain	1. Abdominal pain below the navel 2. Pain related to the following: having more bowel movement; being relieved by a bowel movement; having looser stool; experiencing urgency; having strain; feeling incomplete after finishing a bowel movement 3. Bloating; having mucus in stool 4. Change in bowel habit or consistency of the stools
Duration		> = 3 months	> = 3 months
Severity	Symptoms cannot be ignored or stop subjects from doing things		
Negative Ix	1. − ve Ix results 2. Final dx as functional; defer dx because no medical cause detectable		

	CFS	HV	GH
Characteristic symptoms	1. Having physical fatigue 2. Having mental fatigue	1. Breathing more than normal 2. Two or more of the following: felt dizzy or faint; heart pounding; numbness or tingling; trembling	1. Discomfort in the throat 2. Swallowing all the time; symptoms relieved by swallowing food; symptoms aggravated by saliva or dry swallowing
Duration	> = 6 months		> = 3 months
Severity	Symptoms cannot be ignored or stop subjects from doing things		
Negative Ix	1. − ve Ix results 2. Final dx as functional; defer dx because no medical cause detectable		

(*continued on next page*)

Appendix A. (*continued*)

	MCS	PMS	CPP
Characteristic symptoms	1. Unpleasant reactions to particular substances of which two or more different substances can be defined 2. At least two different symptoms reported	1. Clearly defined symptom or symptoms 2. Symptom(s) disappear soon after the period	1. Pelvic pain does not get before a period
Duration		> = 2 cycles	> = 6 months
Severity	subject avoid those particular substance	Symptoms cannot be ignored or stop subjects from doing things	
Negative Ix		1. − ve Ix results 2. Final dx as functional; defer dx because no medical cause detectable	

Glossary: FMG = fibromyalgia, TH = tension headache, AFP = atypical facial pain, NCCP = noncardiac chest pain, NUD = nonulcer dyspepsia, IBS = irritable bowel syndrome, CFS = chronic fatigue syndrome, HV = hyperventilation syndrome, GH = globus hystericus, MCS = multiple chemical sensitivity, PMS = premenstrual syndrome, CPP = chronic pelvic pain, Ix = investigation, − ve = negative, dx = diagnosis, NPQ = new patient questionnaire.