Review

Functional somatic syndromes: one or many?

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We review the concept and importance of functional somatic symptoms and syndromes such as irritable bowel syndrome and chronic fatigue syndrome. On the basis of a literature review, we conclude that a substantial overlap exists between the individual syndromes and that the similarities between them outweigh the differences. Similarities are apparent in case definition, reported symptoms, and in non-symptom association such as patients' sex, outlook, and response to treatment. We conclude that the existing definitions of these syndromes in terms of specific symptoms is of limited value; instead we believe a dimensional classification is likely to be more productive.

Patients seek help from doctors for symptoms and doctors diagnose diseases to explain them. Symptoms are the patient's subjective experience of changes in his or her body. Diseases are objectively observable abnormalities in the body. Difficulties arise when the doctor can find no objective changes to explain the patient's subjective experience. The symptoms are then referred to as medically unexplained or functional.[1] Many different functional syndromes have been described. In fact, each medical specialty seems to have at least one: for rheumatologists, prominent muscle pain and tenderness is fibromyalgia; for gastroenterologists, abdominal pain with altered bowel habit is irritable bowel syndrome; and for infectious-disease specialists, chronic fatigue and myalgia is a postviral or chronic fatigue syndrome (panel).

We postulate that the existence of specific somatic syndromes is largely an artefact of medical specialisation. That is to say that the differentiation of specific functional syndromes reflects the tendency of specialists to focus on only those symptoms pertinent to their specialty, rather than any real differences between patients. To explore this hypothesis, we reviewed the research literature with regard to three questions. (1) Do the published diagnostic criteria for each of the specific functional syndromes overlap in their constituent symptoms? (2) Do patients identified as having one functional somatic syndrome also meet symptom criteria for others? (3) Are there similarities across syndromes in the non-symptom characteristics of sex, coexisting emotional disorder, proposed aetiology, prognosis, and response to treatment?

Various names have been given to medically unexplained symptoms. These include somatisation, somatoform disorders, medically unexplained symptoms, and functional somatic symptoms. In this review, we use the term functional somatic symptoms.[1] We define a functional somatic symptom as one that, after appropriate medical assessment, cannot be explained in terms of a conventionally defined medical disease.

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Functional somatic syndromes by speciality

Gastroenterology	Irritable bowel syndrome, non-ulcer dyspepsia
Gynaecology	Premenstrual syndrome, chronic pelvic pain
Rheumatology	Fibromyalgia
Cardiology	Atypical or non-cardiac chest pain
Respiratory medicine	Hyperventilation syndrome
Infectious diseases	Chronic (postviral) fatigue syndrome
Neurology	Tension headache
Dentistry	Temporomandibular joint dysfunction, atypical facial pain
Ear, nose, and throat	Globus syndrome
Allergy	Multiple chemical sensitivity

Functional somatic symptoms and syndromes pose a major challenge to medicine. These symptoms are common, frequently persistent, and are associated with significant distress, disability, and unnecessary expenditure of medical resources. In UK primary care, somatic symptoms and syndromes account for 20% of consultations.[2] Among medical outpatients, somatic complaints accounted for 25% of new referrals in a Dutch study[3] and for 35% in a UK study.[4] Even among medical inpatients, a substantial proportion have complaints that are found to be functional.[5]

Functional somatic symptoms are not only common, they are also clinically important. The prevalence of emotional distress and disorder in patients who attend hospital with functional syndromes (such as irritable bowel syndrome) is higher than in patients with comparable medical conditions (such as inflammatory bowel disease).[6] Furthermore, far from merely representing the "worried well", many such patients are severely disabled. For example, chronic fatigue syndrome is associated with worse disability than conditions such as heart failure.[7]

Conventional medical therapy is fairly ineffective for these patients. The result is frustrated physicians and disabled and dissatisfied patients with chronic symptoms. In a follow-up study of patients with non-cardiac chest pain, Potts and Bass[8] found that three quarters of patients had symptoms more than 10 years after presentation.[8] The resulting costs to patients and to the health system are substantial, especially if patients undergo repeated investigation and treatment in hospital. Thus, functional somatic complaints constitute a large, clinically important,

and costly health-care issue that urgently requires better understanding and improved management. But does the current classification of such complaints into distinct functional somatic syndromes aid or hinder this process?

Are there specific functional somatic syndromes?

Each medical specialty has defined its own syndrome or syndromes in terms of symptoms that relate to their organ of interest. In addition, other more controversial syndromes such as multiple chemical sensitivity and repetitive strain injury have been proposed but less widely accepted. Each syndrome tends to be regarded as a unique diagnostic entity with its own special characteristics. Furthermore, many of these syndromes are dignified by their own formal case definition and body of research that focuses solely on those patients identified as having the syndrome. We question this orthodoxy and ask whether these syndromes represent specific diagnostic entities, or are they rather more like the elephant to the blind man—simply different parts of a larger animal?

Hypothesis 1: overlap in case definitions of specific syndromes

We compared the case definitions of those functional syndromes for which a published definition was available. We found that even the so-called core or diagnostic features of these syndromes overlap. For example, bloating or a feeling of abdominal distention is reported in eight of 12 published case definitions for somatic syndromes, and abdominal pain features in six. Headache is mentioned in eight and fatigue in six (data available from authors). Our hypothesis that there is substantial overlap in the case definitions of specific functional somatic syndromes is therefore supported by our review of published case definitions.

Hypothesis 2: patients with one functional syndrome frequently meet diagnostic criteria for other syndromes

Clinicians frequently observe that patients who meet the criteria for specific functional syndromes report symptoms other than those included in the case definition. A review of the clinical research literature confirms this observation. For example, many studies confirm that if patients who meet the criteria for irritable bowel syndrome or non-ulcer dyspepsia are asked about non-alimentary symptoms (which they are usually not) they report them. Furthermore, these other symptoms commonly include ones that define different syndromes. Thus, patients with irritable bowel syndrome may also have symptoms indicative of atypical facial pain, chronic fatigue syndrome, non-cardiac chest pain, food allergy, and chronic hyperventilation (references available from authors). To find out the extent to which this overlap occurs with all the above syndromes, we carried out a series of cross-referenced MEDLINE searches to look for papers that sought to determine whether patients who had received a diagnosis of one functional somatic syndrome also reported symptoms of others. We found 13 references for chronic fatigue syndrome that described symptoms which overlapped with fibromyalgia, tension headache, multiple chemical sensitivity, food allergy, premenstrual syndrome, and irritable bowel syndrome. Conversely, irritable bowel syndrome was linked with hyperventilation syndromes, fibromyalgia, chronic fatigue syndrome, tension headache, aytpical facial pain, non-cardiac chest pain, chronic pelvic pain, non-ulcer dyspepsia, and premenstrual syndrome (data available from authors). These findings lend support to the hypothesis that patients with one functional syndrome frequently meet criteria for others.

Hypothesis 3: patients with different functional syndromes share non-symptom characteristics

Sex—Almost all functional somatic symptoms are more common in women than in men. In the large US Epidemiological Catchment Area study,[9] 20 of 22 non-menstrual somatic complaints were more common in women than in men—the exceptions were chest pain and difficulties with walking. Other investigations have reported similar findings, even after the exclusion of gynaecological disorders.[10,11] This predominance of women also applies to samples of patients selected on the basis of those who met criteria for specific functional somatic syndromes. Clinical studies of patients with chronic fatigue syndrome, irritable bowel syndrome, temporomandibular joint dysfunction, atypical facial pain, globus syndrome, and tension headache have all shown that such symptoms predominant among women. Even in community studies, women predominate among patients with globus syndrome, irritable bowel syndrome, chronic fatigue syndrome, non-ulcer dyspepsia, fibromyalgia, and irritable bowel syndrome.

Emotional disorder—There is a strong association between the range of functional somatic symptoms and psychological distress. Russo and Colleagues[12] showed that the number of functional complaints was significantly and positively related to the number of current and past episodes of anxiety and depression. The findings of community[13] and primary-care studies[14,15] also support a close and linear relation between the number of somatic symptoms and measures of emotional distress. Most studies of emotional distress and disorder in patients who attend hospital with a specific functional somatic syndrome show a substantially increased rate of such disorders, irrespective of whether the diagnosis is chronic fatigue syndrome, multiple chemical sensitivity, or irritable bowel syndrome. We are aware of only a handful of exceptions (references available from authors). Patients who are identified in non-specialist settings as having functional somatic syndromes are also likely to have an increased rate of current and lifetime emotional distress and disorder, but the association is usually weaker.

Physiology—Although there has been limited research into the physiological mechanisms associated with functional somatic symptoms, Sharpe and Bass[16] report findings that lend support to several identifiable mechanisms. These findings serve to remind us that such complaints are not to be regarded as "all in the mind",[17] and also suggest further overlap between these syndromes. In the most general sense, there is empirical evidence of a link between functional somatic syndromes and altered functioning of the central nervous system, which has gradually replaced suggested abnormalities in specific organ systems. For example, although muscle dysfunction was originally suggested as the basis of chronic fatigue syndrome, fibromyalgia, or both, this explanation has been largely replaced by an appreciation of the role of central and neuroendocrine mechanisms. Indirect evidence of abnormalities in serotonergic central-nervous-system pathways has also been presented for several disorders,

including non-nuclear dyspepsia, irritable bowel syndrome, chronic fatigue syndrome, and premenstrual syndrome (references available from authors).

History of childhood maltreatment and abuse—Childhood physical, and especially sexual, abuse is more common in women with functional pelvic pain than in comparison groups. This association does not seem to be specific, however, and has also been reported in patients with irritable bowel syndrome, premenstrual syndrome, tension headache, fibromyalgia, and chronic fatigue syndrome.

Difficulties in doctor-patient relationship—Commonalties can also be observed across functional syndromes in the interpersonal context, particularly in the doctor-patient relationship that is frequently unsatisfactory for both parties. Sharpe and colleagues[18] reported that patients with functional somatic symptoms were one of the three most common types of "difficult to help" patients. Numerous studies of individual syndromes, such as headache, non-cardiac chest pain, fibromyalgia, and chronic fatigue syndrome all reveal that dissatisfaction with medical care is common.

Summary—The hypothesis that patients with different functional syndromes also share non-symptom characteristics is therefore largely supported, although the available data are inadequate to answer this question definitively.

Hypothesis 4: all functional syndromes respond to the same therapies

General approaches to management—Numerous guides for the management of different functional somatic syndromes provide remarkably similar advice. Although subjected to only limited systematic evaluation, there are many themes in common, such as the need to pay attention to engagement, to explain the physiological nature of symptoms, to limit investigations, and to emphasise rehabilitation at the expense of cure.

Antidepressant drug treatment—Although there have been too few studies to allow definitive statements about the relative responsiveness of the various functional syndromes to antidepressants, certain similarities, differences, and uncertainties can be highlighted. For example, whereas large well-conducted studies have established the effectiveness of antidepressant drugs in premenstrual syndrome, atypical facial pain, and non-cardiac chest pain, their role in chronic fatigue syndrome and fibromyalgia is less clear, particularly with regard to the selective serotonin-reuptake inhibitors (references available from authors). The explanation for these differences is unclear and may simply reflect the small number of trials.

Psychological therapies—Broadly defined psychological treatment has been advocated for almost all the functional somatic syndromes and has been shown to be effective in many. Cognitive behavioural therapy is superior to minimum care for most of the syndromes in which this approach has been assessed, such as chronic fatigue syndrome, premenstrual syndrome, irritable bowel syndrome, and nearly all the various pain syndromes (references available from authors).

Summary—There is a similarity in the treatments recommended for patients with various functional somatic syndromes. There is also much evidence of similarity in response to treatment, although the existing evidence also points to some differences. For example, low-dose hydrocortisone therapy is helpful in the management of chronic fatigue syndrome,[19] exercise is beneficial in fibromyalgia[20] and mitral-valve prolapse,[21] and mebeverine is of value in irritable bowel syndrome.[22] However, whether or not these treatments truly are specific to certain syndromes (which goes against our hypothesis), or are simply used only in only specific clinical settings remains unclear. At present, the hypothesis that all functional syndromes respond to the same therapies seems to be partly supported.

Implications of the overlap in functional somatic syndromes

If we accept that the specific functional somatic syndromes as conventionally defined have much in common, what are the implications?

Classification—The main implication for classification is that the current practice of regarding patients with diagnoses of different functional somatic syndromes as having clinically significant differences is questionable. Rather, such patients may have similar conditions or variants of a general functional somatic syndrome. Do we have a more meaningful way to subclassify patients? Four approaches may be considered.

The first approach is based on apparent clustering in the existing case definitions. For example, chronic fatigue syndrome, fibromyalgia, and irritable bowel might form one cluster and non-cardiac chest pain and hyperventilation another (panel).

The second approach is based on epidemiological data. An empirical approach based on a mathemetical (latent variable) analysis of the functional somatic symptoms of primary-care patients in Montreal identified five distinct factors: irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, anxiety, and depression.[23] However, these factors were also highly correlated which suggests similarities between them.[24]

The third approach is to use one of the existing psychiatric classifications that subclassify most functional somatic syndromes into depressive, anxiety, and somatoform syndromes; the latter category being further subdivided into somatisation disorder and other syndromes. This approach has some value in so far as it encourages the identification of psychological and somatic symptoms and the diagnosis of potentially treatable symptoms. It also allows the identification of those patients who have longstanding multiple complaints, so-called somatisation disorder, with a poor prognosis. We suggest, however, that whatever system is chosen, a classification based purely on symptoms is of limited value and offers little clinically useful information about the patients.

The fourth alternative to the diagnostic suggestions outlined above is a multiaxial approach.[25] We suggest such a scheme may be of greater value to clinicians and researchers because it provides a fuller description of the patients and provides useful information for treatment. The relevant axes should include number of symptoms and their duration, associated mood disturbance, the patients' attributions for the symptoms, and identifiable physiological processes.[25]

Treatment—Most research on treatment selects patients on the basis of whether they meet criteria for a specific functional syndrome. This practice has limited the number of patients entered into trials and added a spurious complexity to our understanding of treatment. If we accept

that functional somatic syndromes are considered together, we open the way to more general strategies and services for their management.

Conclusion

Functional somatic symptoms and syndromes are a major health issue. They are common and may be persistent, disabling, and costly. Most of the current literature pertains to specific syndromes defined by medical subspecialties. We have put forward the hypothesis that the acceptance of distinct syndromes as defined in the medical literature should be challenged. We contend that the patients so defined actually have much in common. A review of the published evidence largely supports our suggestion. This hypothesis is open to further testing, and we are currently attempting to do just that in a study across medical specialties.

We do not wish to suggest that the care of patients with functional somatic syndromes should be transferred from medicine to psychiatry—that would simply be replacing one monolithic view with another. A more appropriate position is to call for the return of a "general physician" with a broad-based approach, perhaps aided by liaison with psychiatrists or psychologists. We propose an end to the belief that each "different" syndrome requires its own particular subspecialist adopting an idiosyncratic approach in apparent isolation from work elsewhere.

Our thesis is not new. A previous generation of physicians noted overlaps between what were then deemed "psychosomatic syndromes", and also recognised the alternation or sequence of different syndromes in the same individual. Among these were Ryle's multiple visceral neuroses,[26] Halliday's concept of psychosomatic affections,[27,28] and Kissen's theory of syndrome shift.[29] Unfortunately, none of these general theories were accompanied by empirical support, and consequently all have disappeared from our current thinking on the subject. We argue that their reinstatement is overdue.

A full list of citations for this paper, including the text and tables, is available from the authors, on request, or on *The Lancet*'s website (http://www.thelancet.com).

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