

Functional somatic syndromes are defined as physical syndromes without an organic disease explanation, demonstrable structural changes or established biochemical abnormalities. The reality of these disorders has been accepted by clinicians and intensive scientific inquiry continues to reveal their multiple biological aspects. This book reviews the state of scientific and clinical understanding of the nine most common functional somatic syndromes, conditions which disable patients and often frustrate clinicians through the absence of consistently effective therapeutic interventions.

For each syndrome, expert authors provide a brief historical perspective, a current definition, a case presentation, confirmatory and contradictory research findings, a discussion of the leading pathogenetic hypotheses, and guidelines for diagnosis and treatment. Advice is given for the determination of disability of patients with these medically unexplained disorders, and both medical and psychiatric interventions are described.

Stressing the importance of a sound therapeutic relationship as a basis for treatment, this is a sympathetic, innovative and scientifically sophisticated account of a range of conditions that are as perplexing to clinicians as they are distressing to affected patients. For professionals in primary care and many other disciplines, this book will enlighten, inform and encourage good practice.

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# Functional Somatic Syndromes: Etiology, Diagnosis and Treatment

EDITED BY

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# Preface

This book describes the clinical characteristics and the available treatments for a group of nine conditions often seen in primary care practice. The entities are chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, premenstrual syndrome, temporomandibular joint pain and dysfunction syndrome, interstitial cystitis, nonischemic chest pain syndrome, repetitive strain injuries and multiple chemical sensitivities. Their common denominators are the presence of multiple somatic symptoms, the lack of defining structural defects or laboratory abnormalities, the frequent association with psychiatric disorders, the absence of proven pathophysiological mechanisms and the paucity of effective therapeutic interventions.

The book is addressed to primary care physicians, because they are seeing patients with these vexing, puzzling and disabling conditions every day in the office and clinic; to physicians practicing psychiatry, neurology and physical rehabilitation, to whom these patients are often referred for consultation and treatment; to the postgraduate trainees in the above-mentioned fields; and to the relatively large number of patients with one or more of these syndromes who perceive the need to educate themselves and their families.

In selecting the format for the presentation of the state of the science we have been guided by the principles of evidence-based medicine and combined in-depth review of the best available publications with the rich clinical experience of our group of expert collaborators. We start with the definition of functional symptoms, syndromes and illnesses and the evaluation of the way in which paradigmatic shifts of the past decade have influenced perception and practice. Data regarding the individual syndromes are then presented according to a common descriptive sequence which includes a brief history, the standard definition, a clinical case presentation, prevalence, economic costs, research confirmations (i.e., similar findings obtained by at least two

independent groups of investigators), research contradictions (i.e., unequivocally opposite findings in independent studies with comparable methodologies), a discussion of the leading pathogenetic hypotheses, diagnostic and treatment approaches, and a summary of the clinically relevant facts. As much of the available treatment modalities focus on the associated psychiatric symptomatology, we offer separate chapters on the psychopharmacology and psychotherapy of functional somatic syndromes. A distinct contribution analyzes the difficult process of assessing the occupational disability claimed by patients with these diagnoses. Finally, we examine the extent to which research data have identified common denominators of these syndromes.

This project brought together a group of academic physicians who selflessly gave their time despite the unceasing demands of their heavy clinical workload. I acknowledge with gratitude the efforts of my collaborators for their lucid appraisals and their help in obtaining a degree of homogeneity for data of such diversity. I am also indebted to Richard Barling of Cambridge University Press for his tenacity, patience and kindness in assisting my attempts to clarify the objectives and to shape the content of this book. Thanks are also extended to Glenn Affleck, Javier Escobar, Victor Hesselbrock, Hank Kranzler, Howard Tennen and Simon Wessely, mentors, colleagues and friends during my struggle to begin to understand some of the complexities of the interfaces between psychology, psychiatry and medicine.

Peter Manu

# 1

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## Definition and Etiological Theories

PETER MANU

### Definitions

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Functional somatic syndromes are physical illnesses without an organic disease explanation and devoid of demonstrable structural lesion or established biochemical change (Lipkin, 1969; Smith, 1991; Sharpe et al., 1995). Alternative modern descriptors are somatoform disorders and medically unexplained symptoms; other terms which implied occult disease (hysteria), imagined illness ((hypochondriasis), or psychogenesis (psychosomatic syndrome, somatization and abnormal illness behavior) are only rarely used (Sharpe et al., 1995).

The term functional is often misinterpreted to mean that the illness is not very significant, that the suffering is not real, that the treatment will be difficult, time-consuming and likely to fail, and that the patients are unhappy and dull (Lipkin, 1969). In contrast to these misperceptions stands a vast body of recent research that has accepted the reality of functional disorders and has accorded them equal status as targets for serious scientific inquiry into their multiple biological dimensions. A search of the literature published from 1990 to 1996 identified nine syndromes which were intensely studied by numerous and prolific researchers; there were 1051 publications on chronic fatigue syndrome, 728 on fibromyalgia, 656 on irritable bowel syndrome, 609 on premenstrual syndrome, 598 on temporomandibular pain and dysfunction syndrome, 263 on interstitial cystitis, 133 on atypical (noncardiac) chest pain, 112 on multiple chemical sensitivities and 48 on repetitive strain injury. The analysis of the yearly scientific output indicated a steady rate of publications, undoubtedly reflecting continuous interest and the availability of funding.

The degree to which these syndromes have been characterized as unique entities is variable. On one end of the spectrum one can find fibromyalgia, a condition defined exclusively in objective terms. The

diagnosis is made only if the subject has muscle pain at 11 of 18 specified anatomical locations; the amount of digital or instrumental pressure to be applied is defined and the technique of measuring pain responses carefully described to ensure reproducibility. As described by Abeles (Chapter 3), this definition has been the result of a prospective clinical study conducted by a group of experts with documented nationwide recognition and has been endorsed by the American College of Rheumatology (Wolfe et al., 1990). At the other end of the spectrum is the syndrome of multiple chemical sensitivities, a condition said to consist of multiple symptoms produced by exposure to multiple chemicals at levels below those known to cause morbid effects in the general population. This completely subjective construct is popular with patients and some health care practitioners but, as Abba Terr indicates in his contribution to this volume (Chapter 10), major professional associations and the World Health Organization have not endorsed the definition and have not legitimized the syndrome (UNEP-ILO-WHO, 1996). Somewhere in the middle of the spectrum is the definition of premenstrual syndrome, which requires an assessment of severity of a specified type of affective disturbance that is restricted to the luteal phase of the menstrual cycle. Although the clinical description is based on subjective data, the aggregation during the luteal phase offers a degree of objectivity. As indicated by Pearlstein's contribution (Chapter 5), the definition has been extensively used in research studies and has been included among the diagnostic standards of the American Psychiatric Association (American Psychiatric Association, 1994). An unusual case is the repetitive strain injury syndrome which includes conditions with demonstrable pathology (and therefore not functional) such as carpal tunnel syndrome, but also ill-defined muscle weakness, cramping and tenderness. In his contribution, Tyrer (Chapter 9) points out that this heterogeneity might be due to workmen's compensation and social security disability systems that have focused on the relationship between complaints and job-related activities rather than on the association between complaints and objective clinical findings (Bammer & Bignault, 1988).

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## Etiological theories

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A number of paradigmatic theoretical approaches have been formulated during the past decade and anchored by three major postulates: that functional somatic syndromes represent atypical forms of established psychiatric disorders, that they represent expressions of psychoemotional distress in a somatic language influenced by sociological trends, or that they are distinct disorders with specific dysfunctions and individualized genetic and biological abnormalities.

Functional somatic syndromes as forms of affective spectrum disorder with a common biological causation

In 1989 two Harvard Medical School researchers published an analysis of the association between fibromyalgia and psychopathology (Hudson & Pope, 1989). This association was documented, according to the authors, by work belonging to six distinct lines of evidence:

- (1) symptoms of depression, anxiety, irritability, poor concentration, loss of interest and difficulty with concentration;
- (2) results of psychological testing or rating scales consistently similar to those usually observed in patients with affective, anxiety and somatoform disorders;
- (3) elevated rates of specific psychiatric disorders, significantly higher than those found among patients with the disabling painful condition of rheumatoid arthritis;
- (4) high lifetime rates of major depressive disorder in the relatives of patients with fibromyalgia;
- (5) encouraging response of fibromyalgia symptoms to treatment with antidepressant drugs;
- (6) high rates of psychiatric disorders, predominantly from the mood disorder category, among patients with chronic fatigue syndrome, a disorder displaying features similar to those of fibromyalgia.

Hudson and Pope then formulated the three explanatory hypotheses for the association between fibromyalgia and psychopathology: fibromyalgia is the cause of psychopathology; fibromyalgia is the effect of psychopathology; fibromyalgia and psychopathology are the result of a common underlying morbid process. The first hypothesis was rejected by the authors' findings that the onset of the psychiatric disorder had preceded the onset of fibromyalgia syndrome in a majority of patients and that many of these patients' relatives had a history of major depressive disorder. The second hypothesis was ruled out by the fact that a substantial number of patients with fibromyalgia did not satisfy criteria for any psychiatric diagnosis at any time during their illness; the possibility that fibromyalgia is a factitious or hysterical disorder was dismissed, given fibromyalgia's display of stable, stereotyped symptom pattern. The outcome of this analysis was to strengthen the third hypothesis, which postulated that fibromyalgia is a member of a cluster of associated and overlapping disorders that included chronic fatigue syndrome and irritable bowel syndrome and that the entities of this cluster are all caused by a common pathophysiological process.

In addition to the three functional somatic syndromes mentioned, the cluster identified by Hudson and Pope comprised migraine

headache and the psychiatric disorders major depression, bulimia, cataplexy, panic disorder, obsessive compulsive disorder and attention deficit disorder with hyperactivity. The cluster was named 'affective spectrum disorder'. The common features of its component syndromes were high comorbidity with each other; high rates of major depression or another component syndrome in first-degree relatives; and therapeutic response to antidepressant agents belonging to three or more pharmacological classes (Hudson & Pope, 1989). The antidepressant classes considered were tricyclic agents, monoamine oxidase inhibitors, serotonin uptake inhibitors and atypical agents and the treatment-response model implied that these patients had a disordered neurotransmission (Hudson & Pope, 1990). Sleep abnormalities and hypercortisolism were mentioned as possible common biological markers, but the precise nature of the underlying pathophysiological process was not defined (Hudson & Pope, 1989).

#### Functional somatic syndromes as expressions of somatization with a common psychosocial causation

In 1990, a University of Toronto clinical scientist reported her observations on 50 patients who carried the diagnosis of 'environmental sensitivity', one of the names of the functional somatic syndrome described in this book as multiple chemical sensitivities (Stewart, 1990). The hypothesis tested in the study postulated that the patients with multiple chemical sensitivities are 'chronic somatizers' who tend to have many nonspecific and vague symptoms such as fatigue, headache, muscle and joint pains, digestive complaints, dizziness, irritability and difficulty with concentration. It was also hypothesized that these patients adopt newly described diseases (or 'diseases of fashion') as the explanation for their long-standing ailments.

The median age of the group was 39 years and 74% of the patients had a college education. Forty-two (88%) of the study patients were women. All patients had stopped working and most were receiving long-term disability payments through their previous employers. The patients provided their past medical histories and had their medical records reviewed. The results indicated that 64% of patients had also been diagnosed with chronic fatigue syndrome (often named postinfectious neuromyasthenia or chronic Epstein-Barr virus infection), 50% with severe premenstrual syndrome, 18% with fibromyalgia and 12% with temporomandibular joint syndrome. Besides, many patients carried the diagnoses of food allergy causing psychological symptoms (76%), candidiasis hypersensitivity syndrome (58%), idiopathic hypoglycemia (46%) and vitamin or mineral deficiency (24%). Only 10% of the patients had had none of these other conditions diagnosed at some time during the ten years prior to the diagnosis of multiple chemical

sensitivities. Over the three years of the study, the patients' own diagnostic attribution showed common trends; in 1985 a majority thought that their symptoms were allergic responses to food or environmental agents, in 1986 the cause was considered by many to be *Candida albicans* and in 1987 many patients believed that their suffering was the result of reactivated Epstein–Barr virus infection. Only 20% of the patients had been diagnosed by a physician. The majority (62%) of patients first considered the diagnosis of multiple chemical sensitivities themselves based on information obtained from popular books for the layperson or through the broadcast or print media. The remaining patients (18%) had been 'diagnosed' by a relative, friend or nonphysician health care provider.

These findings were interpreted to confirm the fact that patients with one functional somatic syndrome, multiple chemical sensitivities, have a tendency to endorse other disorders with uncertain etiology and multiple symptoms. They seek explanations in the lay literature and actively incorporate poorly substantiated theories such as immune dysfunction, environmental allergies, overgrowth of *Candida albicans* and reactivation of dormant Epstein–Barr virus as the cause of their illness. Other characteristics of this population include the over-representation of 'well-educated women at the end of their child-bearing years who have unhappy personal and marital relationships', the high prevalence of psychiatric disorders pre-dating their functional somatic syndrome by many years, and the increased utilization of health care services for symptoms of somatization. A biological explanation for these features appeared unlikely; instead, these patients were considered to be suggestible and 'at high risk for acquiring diagnoses that are popularized by the media'.

#### Functional somatic syndromes as distinct entities with variable biological and psychosocial causations

This construct was published in 1994 by the late Robert Kellner, a University of New Mexico psychiatrist who had devoted decades of clinical research to the understanding of psychosomatic processes (Kellner, 1994). His approach consisted in a careful analysis of the published data and an attempt to define the major contributing factors to the causation of these syndromes. For fibromyalgia, he suggested that physical disease, psychopathology and low serotonin concentration cause abnormalities in nonrapid eye movement sleep. The sleep abnormality decreases the pain threshold and thus produces the main clinical features of the syndrome. He understood chronic fatigue syndrome as having multiple causations. For some patients, he postulated an immunological complication of a viral infection; others seemed to have acquired their illness because they had experienced postviral

fatigue, avoided physical activity and ended up with impaired fitness and exercise intolerance; for yet another group of chronic fatigue patients, the main cause was a depressive disorder. For irritable bowel syndrome, he believed that the biological factor consisted in an increased sensitivity to gas and feces, with consequent pain and enhanced bowel motility. The psychiatric symptoms, like the majority of all the noncolonic complaints, were considered to be related to patterns of seeking medical help rather than as necessary factors for the development or maintenance of the irritable bowel. On the other hand he suggested that the causation of the noncardiac chest pain was closely related to one or more psychiatric disorders, those frequently represented being panic disorder, major depression and hyperventilation.

Kellner also addressed the tendency for clustering of functional somatic syndromes, a prominent feature of the work of Hudson & Pope (1989) and Stewart (1990). The operational concept was the relationship between the number and severity of symptoms and the severity of both emotional disturbance and psychopathology. Clustering was, understood to reflect the process of somatization (i.e. an individual tendency to express emotional distress as physical symptoms and to seek medical attention for them), as well as the clinical expression of stress-induced physiological changes in multiple organs and systems.

Kellner's work has been continued and expanded in the latest contribution to the evolution of ideas regarding the etiology of these syndromes (Mayou et al., 1995). This group of clinician-investigators from the Warneford Hospital and John Radcliffe Hospital, Oxford avoided a unifying causal construct; instead, they attempted to structure the problem by highlighting the predisposing, precipitating and perpetuating factors that are believed to contribute to the clinical presentation and outcome of these syndromes. Prominent predisposing factors include abnormal personality traits (such as excessive health consciousness), illness beliefs, personal or family history of major physical illness and genetic predispositions. Among the precipitating factors the authors included physiological variability in arousal, muscle tension, quality of sleep, physical performance, respiratory rate, and the effect of diet, alcohol and drugs; anatomical changes, such as benign tissue lumps and inconsistencies; minor physical illnesses; psychiatric disorders; stressful events and chronic difficulties; and the lack of social support and problems in coping. Important perpetuating factors are primary or secondary psychiatric disorders; perceived functional disability and its relationship with litigation and long-term disability benefits; the side-effects of inappropriate therapeutic interventions, such as avoidance of physical activities or restricted diets; and the realization that suffering is not taken seriously by relatives, friends and health care providers.



In the following chapters we allow the scientific evidence to demonstrate biological and psychological abnormalities in patients with functional somatic syndromes. This approach is dictated by clinical realities, as we need to provide the knowledge base for the understanding of these disorders and their logical treatment rather than solutions to the unknown of their causes.

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