

Functional disorders – new proposals for definition, classifications, etiology and therapies

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Summary

Functional disorders (FD) are common medical problems both in primary and in secondary health care. The mechanisms that cause symptoms such as primary pain, fatigue, and dizziness are still unknown. Various classifications, including ICD-10 and DSM-5, describe these conditions differently, and new proposals are being developed, e.g., in ICD-11, RDoC. Many controversies are evoked by a lack of unequivocal explanatory theory. The early psychoanalytical concept has been modified by other explanations, such as immunological abnormalities, dysfunction of the vegetative system and HPA axis, central sensitization, diverted processes of perception or predictive processes within cognitive homeostasis dysregulation. Insufficient scientific evidence makes therapies unsuccessful and justifies further study. Psychotherapy, pharmacotherapy and complementary medicine are supplemented by new experimental methods of treatment connected with progress in neuroscience. The recently developed non-invasive transcranial direct current stimulation (tDCS), transcranial magnetic stimulation (TMS) and EEG neurofeedback (EEG-NF), based on EEG registration, are undergoing tests. Applying complex mathematical algorithms to localized bioelectrical signal sources makes it possible to modulate and reshape connections of neuronal networks within specific cortex areas. This article presents the current state of knowledge concerning functional disorders, highlighting the ways in which different definitions of FD have an impact on approaches to treatment.

Key words: functional disorders, psychosomatics, somatization

Introduction

Functional disorders (FD), also referred to as psychosomatic disorders, are frequent clinical problems in general practice. Studies show that nearly 30% of all patient visits in primary or in secondary care are caused by FD [1, 2]. The symptoms originate mainly from cardiovascular, digestive, musculoskeletal and connective tissues. Non-specific pain, fatigue, tachycardia, and tinnitus are the most common complaints [3].

The most distinctive conditions are irritable bowel syndrome (IBS) and fibromyalgia (FM). Many studies with suggestions of nomenclature changes, classification corrections and proposals for new therapies have been published in recent years. The lack of scientific consensus concerning these disorders and multiple taxonomy proposals cause communication problems among clinicians. Another term – medically unexplained symptoms (MUS) – often used in primary care, may have a negative effect on the patient-clinician relations and does not fulfill the patients' expectations [4]. The new proposal of the EURONET-SOMA (European Network to Improve Diagnostic, Treatment and Health Care for Patients with Persistent Somatic Symptoms) concerning corrections to the ICD-11 version is an important voice in the debate regarding the unification of the nomenclature of these disorders. Burton et al. [5] propose to add to ICD-11 a new label, Functional Somatic Disorders (FSD). This name is supposed to offer a neutral alternative to the historical opposition between physical and mental symptoms defined as functional disorders. The proposal has its basis in new scientific evidence that indicates a complex interaction between the brain and the rest of the human body, and deserves to be considered.

Aim

This article presents a current review of functional disorders, their definitions, suggested corrections for ICD-11 and proposals for new therapies.

Method

The review of recent literature concerning functional disorders was conducted using PubMed, Google Scholar and Scopus. The main dimensions of analysis involved: definitions, current and proposed classifications, etiology and innovative approaches.

Characteristics of functional disorders

Functional symptoms are described either as somatic (pain, palpitations) or as mental (fatigue, dizziness). In clinical practice it is difficult to isolate the two, because they often coexist, overlap and constitute one disease entity, but are still coded separately in different sections [6], as is the case for irritable bowel syndrome (IBS) or fibromyalgia (FM). Their symptoms range from abdominal and muscle pain to fatigue and weakness. The conditions are coded twice; they have “dual parentage”. On the one hand, they are coded as separate digestive or musculoskeletal diseases and on the other, as single, non-specific “unexplained” symptoms. Such a difficult situation evokes problems and generates tension between clinicians and patients. The final diagnosis is often established after long-term observation and excluding an organic cause. Additional medical tests are often performed which generate financial costs. The diagnosis is also a compromise and constitutes the acceptance of non-specific factors as the cause of the disorder. Therefore, it seems to be justified to assign such disorders as IBS and FM to this aforementioned group of dual parentage.

Some functional symptoms are coded as pertaining to one organ system, while others are assigned to “Symptoms, signs and abnormal clinical and laboratory findings” [7]. For clinicians this makes it difficult to establish the main reason for consultation and increases the risk of an erroneous diagnosis. Referring patients to other health professionals to request additional consultations is also a tendency.

The current and proposed classifications and other categories for FD

In none of the current coding models is there no separate chapter comprising FD. The two main taxonomies represent the FD in different ways.

The first, International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) describes the symptoms in Chapter V “Mental and behavioral disorders” (F00-F99) in section “Neurotic, stress-related and somatoform disorders” (F40-F48). Category F45 details subgroups in the form of somatization disorder (F45.0), hypochondriacal disorders (F45.2), somatoform autonomic dysfunction (F45.3), and persistent somatoform pain disorders (F45.4). The single symptoms and syndromes are included in Chapter XVIII “Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified” (R00-R99). They include: “Symptoms and signs involving the circulatory and respiratory systems” (R00-R09), “Symptoms and signs involving the digestive system and abdomen” (R10-R19), “Symptoms and signs involving the skin and subcutaneous tissue” (R20-R23), “Symptoms and signs involving cognition, perception, emotional state and behavior” (R40 – R46), “Symptoms and signs involving speech and voice” (R47-R49), and “General symptoms and signs” (R50-R69).

The single disorders are included within the parts that concern individual organs, such as “Irritable bowel syndrome” (K58) in Chapter XI “Diseases of the digestive system” (K00 – K93) or “Fibromyalgia” (M79.7) in Chapter XIII “Diseases of musculoskeletal system and connective tissue” (M00-M99). The ICD-11 is to be released in the near future, containing a new category of functional symptoms. A wide spectrum of somatoform disorders from the ICD-10 are collected together as “Disorders of bodily distress or bodily experience” – (6C20–6C2Z) [8]. It is quite a new definition of conditions which does not exist within the ICD-10 [9, 10]. Two separate categories include “Bodily distress disorder” (6C20) [11] and “Body integrity dysphoria” (6C21). The first concept constitutes the equivalent of the somatic symptoms called “somatoforms” (F45) in ICD-10 [12, 13]. Burton et al. [5] from the EURONET-SOMA group have made additional proposals to reframe the classification of functional disorders. They propose to consider such new conditions as e.g., catastrophization. The authors also suggest including primary chronic pain in the category of FD. According to the International Association for the Study of Pain, this condition, which has to last at least three months, does not have organic causes [14].

The second classification, containing psychiatric conditions, DSM-5 (Diagnostic and Statistical Manual for Mental Disorders, fifth edition), defines the FD categories in the chapter “Somatic Symptom Disorder” – SSD (300.81). This group of symptoms includes at least one somatic condition, which is persistent for at least six months and

disrupts everyday life significantly. It is also accompanied by persistent and excessive thoughts about the seriousness of one's symptoms, which absorb time and energy and evoke undue anxiety concerning health [15].

An additional division of psychosomatic disorders is proposed by Flava et al. [16], which is an important element for the explanation of the somatization process. The authors, based on a structured interview, distinguished between several different syndromes in extracted subgroups. The criteria of inclusion for each category were described in the form of Psychological Factors Affecting Medical Conditions. The authors also proposed tools with which these indicators can be measured (Diagnostic Criteria for Psychosomatic Research – DCPR).

Another proposal of new research concerning the somatization process and wide spectrum of perception of somatosensory systems has been initiated by the National Institute of Mental Health (NIMH) in the USA. It is called Research Domain Criteria (RDoC). It constitutes a systematic explanation of symptoms on all levels – from genetics to behavior. There are six consecutive functional areas responsible for brain activity: (1) negative valence (fear, anxiety, frustration), (2) positive valence (reward, motivation), (3) cognitive systems (visual, auditory perception, sense), (4) systems for social processes (communication), (5) arousal/regulatory systems (circadian rhythms), and (6) sensorimotor systems (action planning) [17].

The concept of etiological mechanisms

The connections between mental and somatic states have been the subject of many studies. Psychoanalysis associated somatization with conversive (S. Freud) and dissociative (P. Janet) disorders. The theories presented by H.E. Dunbar and F. Alexander connected psychosomatic disorders with the personality profile and category of stress. Similar descriptions referred to dysfunctional behavioral patterns type A, C and D [18, 19]. Current scientific methods involving scientific observation and modern technologies facilitate recognizing other mechanisms causing functional disorders. These mechanisms can be better observed and understood thanks to the analysis of fMRI and EEG data concerning brain processes and symptoms reported by patients.

Among all the contemporary proposals explaining the etiology of functional disorders – seven deserve to be singled out. The first, immunological, connects chronic fatigue symptoms with hepatitis C virus (HCV) infection. Russel et al. [20] proved an interaction between treatment using interferon-alpha (IFN- α) of HCV infected patients and chronic fatigue syndrome (CFS). The second concept – described by Rizzi et al. [21] – underlines the role of the dysfunctional vegetative nervous system in fibromyalgia (FM). It concerns the hyperactivity of the sympathetic system in chronic pain. The third theory, published by Nijs et al. [22], highlights the connection between the dysfunction of the hypothalamic-pituitary-adrenal gland axis and CFS. The authors emphasize the importance of central sensitization, the negative impact of excessive stress factors on patients and complicity of infection in the hyperalgesia phenomenon. In the next concept of Tomas and Newton [23], new studies were analyzed. They found

that abnormal immunological regulations, mitochondrial abnormalities, may play a role as biomarkers in patients suffering from FSD.

The importance of the central sensitization phenomenon, as one of the main mechanisms explaining functional symptoms, is also found in a study of Bourke et al. [24]. Its authors describe a close similarity between brain processes in functional disorders in the studies of what was formerly classified as psychogenic pain. These bring the classification of FD closer to the definition of chronic primary pain (CPP), which is described in detail by Nicholas et al. [25] and is separately coded in ICD-11 as well. Other theories concerning FD are linked to the dysfunction of activation of systems that connect distant areas of perception within brain networks and subnetworks, explaining such symptoms as tinnitus and dizziness [26].

The last two concepts concern the significance of cognitive structures, interpretations of sensorimotor impulses and merging of cognitive processes. The abnormal psychological adaptation and the representations of particular conditions within the imagination system in the patients' brains have been analyzed multidimensionally by McAndrew et al. [27]. The authors described the psychological categories that could have impact on intensification or mitigation of functional disorders. They investigated mental representations and defined a self-regulating, common-sense model of interpretation of one's suspected disorder. The patients who were convinced that the symptoms are formed in their mind perceived their symptoms as more severe and their coping was less effective. Such variables as "illness representations", "self-management/coping strategy" and "health outcomes" were correlated. The conclusion drawn from the study was that the experienced symptoms depended significantly on the way the illness was perceived, the psychological distress experienced and the quality of life. McAndrew et al. [27] concluded that better understanding by patients of the processes of perception and interpretation of their illness and familiarity with strategies of emotional regulation are significant factors reducing the severity of functional disorders.

The last, seventh etiological concept explains the formation of functional symptoms as a result of complex psychological mechanisms concerning predictive processes within cognitive homeostasis dysregulation of the human brain. In theoretical scientific work by Henningsen et al. [28, 29], the dominant view is that FD patients suffer from an imbalance between the input of significant, specific, peripheral sensorimotor signals and their assessment at the central level. This means that there are mechanisms of processing data from extero – and interoceptors that occur in the brain. These data are analyzed with respect to their potential as a threat to health. The autonomic nervous system plays an important role. In the cases of disturbed analytical processes, the input impulses are interpreted as supposedly harmful and unfavorable. The somatosensory analyzing system interprets the incorrect information as pathological symptoms, such as pain, tinnitus, dizziness. Henningsen et al. [28, 29] defined the organization of brain processes as a predictive model with minimal bias of prediction.

Another explanation of predictive processes, concerning also medical aspects, as a free energy flow within the human brain has been presented by Friston [30]. According to his concept, the brain constitutes a predictive structure perceiving afferent sensorimotor impulses. It also has a tendency to minimize predictive error, which

means reducing the difference between external sensorimotor impulse and internally generated model of interpretation. Each change in adaptative processes of the brain, like perception processes, tends to reduce energy expenditure and lasts milliseconds. In another article, Friston and Kiebel [31] claim that the brain, interpreting the afferent stimuli reaching its cognitive systems, influences the neuroplasticity and neuromodulation at the synaptic level. According to the authors, this phenomenon is one of the evolutionary developmental mechanisms in the human brain.

The above-mentioned mechanisms can affect the formation of incorrect representations in the brain cortex and generation of inappropriate sensations by patients. The free energy flow principle in brain processes has been documented in terms of mathematics in the works of Friston and Kiebel [31] and Clark [32].

The proposed therapies

The etiological concepts listed above comprise therapeutic suggestions; however, there are no effective methods for treatment of functional disorders. Nevertheless, the appearance of modern technologies facilitating visualization of the brain and neuropsychological analyses create new possibilities for neuromodulation techniques. Traditional treatment approaches concern various forms of psychotherapy, especially cognitive-behavioral therapy, social support, pharmacology and other methods in the field of alternative and complementary medicine. Therapies should privilege nonpharmacological strategies, avoiding side effects of drugs and encouraging modulation of the cognitive processes. Henningsen et al. [33], based on a literature review from the last ten years, suggest five potential areas for therapeutic interventions.

The first strategy is pharmacological, using medication affecting peripheral receptors. This covers such diseases as irritable bowel syndrome [34], disorders coexisting with inflammatory processes [35] and also accompanied by nociceptive pain [36]. The second strategy concerns central nervous system pharmacology, especially with disturbed perception processes [37], data transformation and in combination with affective disorders [38]. The next method includes intervention in terms of behavioral processes. The end goal is to change interpersonal behaviors, the way patients interpret the sensorimotor stimuli and their model of perception. In order to modify these mechanisms, exercises changing sensorimotor processes [39] and different types of psychotherapies are recommended. An integrated therapeutic team consisting of medical professionals is also indicated [40]. The fourth approach concerns passive interventions in the form of physical methods [41], including surgical procedures [42] and other treatment procedures involving skin tissue [43]. The fifth category encompasses therapeutic strategies from so-called complementary and alternative medicine. These are methods preferred both by some patients and by some clinicians depending on their competences and personal experience. They include herbal medicine and acupuncture [44].

New experimental methods of treatment are still being developed. Transcranial direct current stimulation (tDCS), transcranial magnetic stimulation (TMS) and EEG-neurofeedback (EEG-NF) are undergoing tests. The last method, EEG-NF, has been

applied with tentative success in patients suffering from chronic primary pain [45] and somatization (somatoforms) [46]. The mechanism is based on feedback between sensorimotor stimuli and the brain's electrical activity. Multiple, systematic training sessions in patients support the process of autoregulation of bioelectrical brain function. The basic function is connected with an instrumental conditioning mechanism. The person trained receives constant reciprocal information about their own brain activity in the form of understandable visual or auditory information. Studies show that the modulation of activity of the extensive neuronal networks and analysis of brain microstates could be the basis for a successful therapeutic intervention. It facilitates a better understanding of the processes involved in functional disorders. The usefulness of the EEG-NF method was reported in children diagnosed with ADHD [47], in chronic primary pain patients [48], and in depression [49]. Within new versions of neurofeedback, multichannel EEG-NF is used, which consists in placing multiple electrodes over the head of the patient to register the activity of their brain waves. Applying mathematical algorithms to localized bioelectrical signal sources makes it possible to modulate specific cortex areas, subcortical structures and remote connections of neuronal networks [50].

Recapitulation

Functional (psychosomatic) disorders are frequently encountered problems in clinical practice, both in primary and secondary health care. These disorders usually present in the form of nonspecific pain, fatigue, dizziness and tinnitus. Due to their nonspecific nature and a lack of effective treatment methods, FD constitute significant clinical problems. In addition, there is a lack of unequivocal classification and clinical divisions. Patients with symptoms of FD often display frustration because of the ineffective course of treatment and negate the influence of the mental sphere on the present symptoms. Clinicians treat these individuals as difficult patients. The classification systems cause communication difficulties between therapists and patients. The currently used classification systems include ICD-10 and DSM-5. Other ones – DCPR-SSI, RDoC – are undergoing intensive research.

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