

Psychosomatic Assessment

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Key Words

Psychosomatic medicine • Depressive disorders • Anxiety disorders • Somatization • Clinimetrics • Stress, psychological • Macroanalysis • Quality of life • Psychological well-being • Diagnostic Criteria for Psychosomatic Research

Abstract

The primary goal of psychosomatic medicine is the incorporation of its operational strategies into clinical practice. The traditional attitude toward disease and the functional/organic dichotomy were criticized by George Engel in the early sixties. Only recently, however, there has been increasing awareness of the limitations of disease as the primary focus of medical care. It is not that certain disorders lack an organic explanation; it is our assessment that is inadequate in most clinical encounters. The research evidence which has accumulated in psychosomatic medicine offers unprecedented opportunities for the identification and treatment of medical problems. Taking full advantage of clinimetric methods (such as the use of Emmelkamp's two levels of functional analysis and the Diagnostic Criteria for Psychosomatic Research) may greatly improve the clinical process, including shared decision making and self-management. Endorsement of the psychosomatic perspective may better clarify

the pathophysiological links and mechanisms underlying symptom presentation. Pointing to individually targeted methods may improve final outcomes and quality of life.

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A considerable body of evidence has accumulated in psychosomatic medicine related to concepts such as quality of life, stressful life events, somatization, illness behavior and personality, but it has not resulted in operational tools whereby psychosocial aspects of medical disease could be routinely assessed. This paper is concerned with the psychosomatic assessment, a crucial step toward effective patient management.

Inadequacy of the Concept of Disease

In 1960, George Engel [1] sharply criticized the concept of disease: 'The traditional attitude toward disease tends in practice to restrict what it categorized as disease to what can be understood or recognized by the physician and/or what he notes can be helped by his intervention. This attitude has plagued medicine throughout its history and still stands in the way of physicians' fully appreciating disease as a natural phenomenon.' Further, 'many

kinds of processes or experiences may be thought of in terms of disease or related to disease even though they are not currently so regarded. For example, the experience of grief as ordinarily follows the loss of a loved person, a valued possession, or an ideal, fulfils all the requirements of a disease process as we have defined it' (pp. 471–472). Engel [2] elaborated this example and his observations have not lost their validity [3, 4]. His unified concept of health and disease was subsequently elaborated within the biopsychosocial model [5–7]. The introduction of structured methods of data collection and control groups has allowed to substantiate the link between life events and a number of medical disorders, encompassing endocrine, cardiovascular, respiratory, gastrointestinal, autoimmune, cutaneous and neoplastic disease [6, 8–13].

Not surprisingly, Engel was very critical of the disease concept of functional medical disorder or medically unexplained symptoms. For instance, he regarded the view that irritable bowel syndrome is caused by psychological influences as an oversimplification [14]. The concept of functional medical disorder indeed comprises a spectrum of disturbances ranging from mild transitory illness to chronic disorders with severe disability [15].

The Concept of Functional Medical Disorder

In the late eighties, our research group became concerned with the psychosomatic aspects of cardiac neurosis (neurocirculatory asthenia). The starting assumption was that disturbances were mainly the expression of an underlying affective disorder. In a preliminary investigation [16], we attempted to apply DSM-III-R criteria to a sample of patients who fulfilled the criteria of Kannel et al. [17] for neurocirculatory asthenia. We chose these criteria because they had been validated in the Framingham study, were above a certain threshold of severity, and were more precise than definitions of atypical chest pain. We were impressed by the fact that associated psychopathology departed from the classical descriptions, and had a limited power in explaining cardiac symptomatology. The classification of somatoform disorders was of little or no help.

Lipowski [18] had defined somatization as the tendency to experience and communicate psychological distress in the form of physical symptoms and to seek medical help for them. In those years we were also interested in subclinical symptoms of mood and anxiety disorders, with special reference to their longitudinal development (prodromal, acute, residual phases) and their staging [19,

20]. We thus thought that the process of somatization could be disclosed by more sensitive methods of assessment and attention to the longitudinal course of disturbances. In a study we designed, DSM-III-R criteria were supplemented by the use of rating scales which had been found to be particularly sensitive in research on subclinical symptoms of mood and anxiety disorders [19], including Paykel's Clinical Interview for Depression [21], Kellner's Symptom Questionnaire [22], and Kellner's Illness Attitude Scales [23]. In more than half of the patients who fulfilled the criteria of Kannel et al. [17], a psychiatric diagnosis (mainly an anxiety disorder) antedated the onset of neurocirculatory asthenia, which was defined as secondary, particularly since cardiorespiratory symptoms were part of the mental symptomatology [24]. In doing so, we were influenced by Robins and Guze's [25] primary/secondary dichotomy, which was based on chronology and course of follow-up. The anxiety disturbances were, however, mostly atypical and with close links to various manifestations of health anxiety [26]. In about 40% of patients, neurocirculatory asthenia was the primary disorder [24]. These patients did not significantly differ from healthy control subjects in all the dimensional variables that were selected, except for observer-rated depression [21]. At 1 year of follow-up, patients with primary neurocirculatory asthenia had a much better prognosis than those with secondary neurocirculatory asthenia [24]. In a subsequent investigation [27], a sample of patients meeting the criteria of Kannel et al. [17] for neurocirculatory asthenia and a control group of healthy subjects were studied as to the occurrence of recent life events with a very sensitive and accurate method, i.e. Paykel's Interview for Recent Life Events [28]. The results suggested a strong relationship between life stress and neurocirculatory asthenia, irrespective of the primary/secondary distinction.

Emergence of New Models

The term 'psychosomatic disorder' was strongly criticized by several psychosomatic researchers, notably Engel and Lipowski [29]. Engel [30] wrote that the term 'psychosomatic disorder' was misleading, since it implied a special class of disorders of psychogenic etiology and, by inference, the absence of a psychosomatic interface in other diseases. On the other hand, he viewed reductionism, which neglected the impact of nonbiological circumstances upon biological processes, as a major cause of mistreatment [5]. Lipowski [18] criticized the concept of

psychosomatic disorder since it tended to perpetuate the obsolete notion of psychogenesis, which is incompatible with the doctrine of multicausality, a core postulate of current psychosomatic medicine. Kissen [31] clarified that the relative weight of psychosocial factors may vary from one individual to another within the same illness and underscored the basic conceptual flaw of considering diseases as homogeneous entities.

It took many years to translate Engel’s unified concept of health and disease into clinical perspectives. In 2004, Tinetti and Fried [32] suggested that time has come to abandon disease as the primary focus of medical care. When disease became the focus of medicine in the past two centuries, the average life expectation was 47 years and most clinical encounters were for acute illness. Today the life expectancy in Western countries is much higher and most of clinical activities are concentrated on chronic disease or non-disease-specific complaints. ‘The changed spectrum of health conditions, the complex interplay of biological and nonbiological factors, the aging population, and the interindividual variability in health priorities render medical care that is centred primarily on the diagnosis and treatment of individual diseases at best out of date and at worst harmful. A primary focus on disease, given the changed health needs of patients, inadvertently leads to undertreatment, overtreatment, or mistreatment’ [32, p. 179]. Disease-specific guidelines provide very limited indicators for patients with multiple conditions [33]. Tinetti and Fried [32] suggest that the goal of treatment should be the attainment of individual goals, and the identification and treatment of all modifiable biological and nonbiological factors, according to Engel’s biopsychosocial model [5].

In the same year of Tinetti and Fried’s paper [32], psychometric theory, the basis for developing assessment instruments in psychiatric and most medical research, was regarded as an obstacle to the progress of clinical research [34, 35]. Clinimetrics, a term introduced by Alvan R. Feinstein to indicate a domain concerned with indices, rating scales and other expressions that are used to describe or measure symptoms, physical signs and other distinctly clinical phenomena in medicine [36], was regarded as the conceptual ground for a substantial revision of assessment tools and for linking co-occurring syndromes [34, 35]. Important innovations were Emmelkamp’s two levels of functional analysis in psychological assessment [37]: macroanalysis (establishing links among coexisting syndromes or symptoms to determine which problem should be treated first, taking into account the patient’s priorities) and microanalysis (a care-

Table 1. Psychosocial variables affecting illness vulnerability

Presence of physical and/or sexual abuse at some point in life
Life events
Grief reactions
Perception of an environment as exceeding personal resources (allostatic load)
Interpersonal relationships providing a buffering role for stress
Psychological assets and well-being

Table 2. Psychosocial correlates of medical disease

Psychiatric disturbances
Psychological symptoms
Illness behavior
Quality of life

ful analysis of symptoms, with all the details). This approach was found to be particularly helpful in the sequential treatment of depression, where residual symptoms and impairment after pharmacotherapy alone were the primary targets of treatment, even though they could not be ascribed to discrete diseases [38]. Further, the purpose of the science of clinimetrics is to provide a home for a number of clinical phenomena which do not find room in customary clinical taxonomy, such as type, severity and sequence of symptoms, rate of progression of illness (staging), well-being and distress [36]. In recent years, there have been several exemplifications of this approach in research on mood and anxiety disorders [38–44].

Psychosocial Foundations of Clinical Assessment

A fundamental characteristic of clinical medicine is the sensitive and systematic collection of information from patients in various settings [45], and the medical interview is most important in this process [46]. Goldberg and Novack [47] developed a psychosocial review of systems, which were grouped as follows: smoking/alcohol/drugs; stress; expectations/fears/meanings; living situation/social support; sexual life; marital status; work/finances/education; psychiatric history/mood/cognition; functional status. Fava and Sonino [8] suggested the need for specific evaluations in medical assessment (tables 1, 2) that may be performed by psychosomatic specialists. Table 2 displays the main psychosocial correlates of med-

ical disease. They include comorbid psychiatric disturbances, psychological symptoms, illness behavior (the ways in which individuals experience, perceive and respond to their health status) and quality of life (the functional status of the individual and his/her appraisal of health) [48–52]. This information may be crucial in managing patients with unexplained medical symptoms, difficult patient-doctor relationships, partial response to treatment, suspected psychiatric complications of medical illness, and abnormal illness behavior [53]. It may require expert interviewing, self-rating inventories, and/or techniques of self-observation (self-monitoring of daily activities and recording of the observed findings in a diary) [8].

Disturbances are generally translated into diagnostic endpoints, where the clinical process stops. This does not necessarily explain the mechanisms by which the symptom is produced [54, 55]. Not surprisingly, psychological factors are often advocated as an exclusion resource when symptoms cannot be explained by standard medical procedures, a diagnostic oversimplification which both Engel [14] and Lipowski [56] refused. Macroanalysis [34, 37] may allow to identify modifiable factors and their interactions. Two examples show how clinical assessment and management follow similar patterns in case the disorder is either functional or organic. The case which is illustrated in Appendix 1 exemplifies the use of macroanalysis in the setting of a functional bowel disorder. Recurrent headaches together with additional symptoms of autonomic arousal and exaggerated side effects from medical therapy, signs of low sensation threshold and high suggestibility indicated a syndrome of persistent somatization [48–50]. This category identifies patients in whom psychophysiological symptoms tend to cluster [57], as is frequently the case in patients with irritable bowel syndrome [58]. The clinical psychologist approached the psychological problems sequentially [38], starting from lifestyle modification [8], proceeding to explanatory therapy [59] and then to exposure, cognitive restructuring and well-being therapy [60]. The treatment team was multidisciplinary and involved the collaboration of a primary care physician who referred the patient to a psychiatrist, a gastroenterologist, a clinical psychologist and a nutritionist.

The case depicted in Appendix 2 is that of an apparently straightforward hypothyroidism on replacement therapy. The endocrinologists the patient had previously consulted only looked at her thyroid hormone levels; they did not understand what was wrong, since thyroid function parameters were satisfactory, and what they could do

for her. As the patient was pointing out, quality of life may be compromised even though the patient is apparently doing fine according to a hormonal viewpoint. In fact, in clinical endocrinology, there is often the tendency to rely exclusively on ‘hard data’, preferably expressed in the dimensional numbers of laboratory measurements, excluding ‘soft information’, such as disability and well-being [61–63]. Soft information, however, can now be assessed.

The issue is to take full advantage of clinimetric tools in the clinical process. It is not that certain disorders lack an organic explanation; it is our assessment that is inadequate in most clinical encounters and this particularly strikes when ‘hard data’ are missing. As Feinstein [55] remarks, ‘even when the morphologic evidence shows the actual lesion that produces the symptoms of a functional disorder, a mere citation of the lesion does not explain the functional process by which the symptom is produced (...). Thus, the clinician may make an accurate diagnosis of gallstones, but if the diagnosed gallstones do not account for the abdominal pain, a cholecystectomy will not solve the patient’s problem’ (p. 270). Alvan Feinstein [64] was also the one who warned against the destruction of the pathophysiological bridges from bench to bedside.

Expanding the Spectrum of Psychosocial Assessment

Replication attempts in psychosomatic studies are often disappointing, as one would expect from characteristics of modest sensitivity and low specificity in heterogeneous medical entities. A different strategy was thus attempted: to translate psychosocial characteristics observed in various medical diseases in Diagnostic Criteria for Psychosomatic Research (DCPR) [65]. The DCPR have now undergone extensive validation and these studies have been summarized in a monograph [48]. They have been found to be more suitable than DSM criteria in describing psychological distress in a variety of medical settings [49].

Fava and Wise [50] have suggested to modify the DSM-IV category concerned with psychological factors affecting medical conditions, that is a poorly defined diagnosis with virtually no impact on clinical practice. They suggested a new section which consists of the 6 most frequent DCPR syndromes [49]. The clinical specifiers, listed in table 3, include the DSM diagnosis of hypochondriasis and its prevalent variant, disease phobia [49]. Both the DSM somatization disorder and undifferentiated so-

matoform disorder are replaced by the DCPR persistent somatization, conceptualized as a clustering of functional symptoms involving different organ systems [57]. Conversion may be redefined according to Engel's stringent criteria [66], involving features such as ambivalence, histrionic personality, and precipitation of symptoms by psychological stress of which the patients is unaware. DCPR illness denial, demoralization, and irritable mood offer further specifiers. Persistent denial of having a medical disorder and needing treatment (e.g. lack of compliance, delay in seeking of medical attention) frequently occurs in the medical setting [67]. Demoralization connotes the patient's consciousness of having failed to meet his or her own expectations (or those of others) with feelings of helplessness, hopelessness, or giving up [68]. It can be found in almost a third of medical patients and can be differentiated from depressive illness [69]. Irritable mood, that may be experienced as brief episodes or be prolonged and generalized, has also been associated with the course of several medical disorders, carrying important clinical implications [70]. Other DCPR constructs involve functional somatic symptoms secondary to a psychiatric disorder, type A behavior, alexithymia, health anxiety and thanatophobia [48, 65].

The advantage of this classification is that it departs from the organic/functional dichotomy and from the misleading and dangerous assumption that if organic factors cannot be identified, there should be psychiatric reasons which may be able to fully explain the somatic symptomatology. The psychosomatic literature provides an endless series of examples where psychological factors could only account for part of the unexplained medical disorders [8, 56]. Similarly, the presence of a nonfunctional medical disorder does not exclude, but indeed increases the likelihood of psychological distress and abnormal illness behavior [56, 71]. McKegey [72] found a coexisting organic disease in about half of patients with conversion symptoms referred for psychiatric consultations from the medical and surgical wards. Orchard [73] has drawn attention to the occurrence of atypical chest pain in about 50% of patients who had suffered from myocardial infarction. Lishman [74] outlined the range of problems which may be associated with silent or mild cerebrovascular disorders (including hypochondriasis and bodily preoccupations) and may be prodromal to cognitive deterioration. Indeed, depression, anxiety, irritability and somatic symptoms are often prodromes of a medical disorder [74, 75]. Not surprisingly, psychological assessment with DCPR was found to be more suitable than DSM-IV criteria in identifying somatization in pa-

Table 3. New proposed classification for psychological factors affecting either identified or feared medical conditions [20]

Hypochondriasis (DSM)
Disease phobia (DCPR)
Persistent somatization (DCPR)
Conversion symptoms (DCPR)
Illness denial (DCPR)
Demoralization (DCPR)
Irritable mood (DCPR)

tients with functional gastrointestinal disturbances or cardiac disease [76]. Further, the use of DCPR has disclosed that not all coronary artery disease patients display type A behavior, and, vice versa, that type A behavior is present in other settings including dermatology, gastroenterology, cancer patients and frequent attenders of primary care [48, 77, 78].

Expanding the spectrum of psychological classification by the introduction of psychosomatic constructs has allowed a more specific designation of problems in clinical medicine.

Finding Pathophysiological Links

Feinstein [64] remarks that, when making a diagnosis, thoughtful clinicians seldom leap from a clinical manifestation to a diagnostic endpoint. The clinical reasoning goes through a series of 'transfer stations' [54, 55], where potential connections between presenting symptoms and pathophysiological processes are drawn. The lack of a psychosocial perspective, as is generally the case in current medicine, deprives the clinical process of a number of important links.

(a) McEwen [9] proposed a formulation of the relationship between stress and disease onset based on the concept of allostasis, the ability of the organism to achieve stability through change. The concept of allostatic load refers to the wear and tear that results from either too much stress or from insufficient coping, such as not shutting off response when it is no longer needed. Biological parameters of allostatic load, such as glycosylated proteins, coagulation/fibrinolysis and hormonal markers, have been linked to cognitive and physical functioning and mortality [9, 79, 80].

(b) Prospective population studies have substantiated the role of social support in relation to mortality, psychiatric and physical morbidity, and adjustment to and re-

covery from chronic disease [8]. An area that is now called 'social neuroscience' is beginning to address the effects of the social environment on the brain and the physiology it regulates [9].

(c) Lipowski [56] remarks that 'once the symptoms of a somatic disease are perceived by the person, or he has been told by a doctor that he is ill even if symptoms are absent, then this disease-related information gives rise to psychological responses which influence the patient's experience and behavior as well as the course, therapeutic response and outcome of a given illness episode' (p. 483). Recent advances in psychoneuroimmunology offer links between endogenous danger signals and the brain cytokine system that organizes the sickness response in its subjective, behavioral and metabolic components [81]. The neurobiology of illness behavior, including the placebo effect [82], is beginning to unravel a number of clinical phenomena [81–83].

(d) The autonomic system has been a traditional target for exploration of psychosomatic research. Autonomic imbalance, such as a state of low heart rate variability, may be associated with a wide range of psychological and medical dysfunctions [84] and may affect response to medical treatments [85].

(e) Mood and anxiety disorders have been associated with a variety of medical conditions [51]. The neurotransmitter imbalances which are underlying, such as reinforcement-reward dysregulation, central pain and psychomotor functioning, may provide pathophysiological bridges for a number of clinical phenomena [86]. Similar considerations apply to the neurobiology of anger and irritability [61, 87–89].

(f) Positive health is often regarded as the absence of illness, despite the fact that, half a century ago, the World Health Organization defined health as a 'state of complete physical, mental and social well-being and not merely the absence of disease or infirmity' [90]. Research on psychological well-being has indicated that it derives from the interaction of several related dimensions [91, 92]. A large body of evidence suggests that psychological well-being plays a buffering role in coping with stress and has a favorable impact on disease course [93, 94]. Research on the neurobiologic correlates of resilience and well-being [79, 95] has disclosed how different circuits may involve the same brain structures, and particularly the amygdala, the nucleus accumbens, and the medial prefrontal cortex.

The neurobiology of personality features, such as reward dependence and novelty seeking [96], alexithymia [97–99] and type A behavior [100], provides other valu-

able pathophysiological insights into the tendency to develop symptoms and abnormal illness behavior in the setting of medical disease.

Conclusions

Psychosomatic medicine may be defined as a comprehensive, interdisciplinary framework [8, 18] for the assessment of psychosocial factors affecting individual vulnerability, course and outcome of any type of disease; holistic consideration of patient care; integration of psychological therapies in the prevention, treatment and rehabilitation of medical conditions. Its primary goal is its incorporation into clinical practice [101]. The interdisciplinary dimension, that includes the psychosocial domain, characterizes many rehabilitation units and pain clinics and is an operational translation of psychosomatic models [62, 102, 103].

Psychosomatic assessment may be pursued both at the level of the individual practicing physician and of health specialists in multidisciplinary settings. The interest in health promotion rather than disease prevention, and the consideration of patients as partners in managing their own disease are new emerging concepts to be further developed. In particular, the partnership paradigm includes collaborative care (a patient-physician relationship in which physicians and patients make health decisions together) [104] and self-management (a plan that provides patients with problem-solving skills to enhance their self-efficacy) [105]. An interesting holistic method is currently exemplified by functional medicine [106]. It refers to a comprehensive analysis of the manner in which all components of the human biological system interact functionally with the environment over time, with particular emphasis on pathophysiological process. So far therapeutic efforts have been concerned with diseases as homogeneous entities, comparing one or more psychosocial ingredients with treatment as usual, for all patients sharing the same diagnosis.

At present, the challenge of psychosomatic research is to demonstrate, in randomized controlled trials, that an individually targeted method may improve clinical outcomes and quality of life, as was found to be the case with rehabilitation research [107, 108].

Appendix 1. Macroanalysis of a case of irritable bowel syndrome

Ms. X is a 24-year-old woman who was diagnosed with *irritable bowel syndrome* (abdominal pain, diarrhea) on the basis of her symptomatology, after extensive negative medical workup. She was in a situation of chronic stress and suffered from recurrent headache (muscle tension type). Symptomatic medications that were prescribed yielded very limited relief. She was then referred for psychiatric consultation. Interviewing did not identify a specific psychiatric disorder, but disclosed the presence of a considerable *allostatic load* (she felt overwhelmed by her job demands as a journalist), a tendency to *perfectionism*, and also *phobic avoidance* (as to certain types of food she thought could worsen her symptoms) and *lack of assertiveness* (both at work and within her family). No psychotropic drugs were prescribed. She was referred to a clinical psychologist who found *persistent somatization* and first introduced some lifestyle modifications as to her allostatic load. The psychologist then addressed abnormal illness behavior with explanatory therapy for correcting hypochondriacal fears and beliefs, phobic food avoidance with exposure and with the help of a nutritionist, perfectionism with cognitive restructuring, and lack of assertiveness with well-being therapy. After a few months there was a remarkable general improvement, which was maintained at a 2-year follow-up.

The various elements of macroanalysis are highlighted in italics.

Appendix 2. Macroanalysis of a case of hypothyroidism

Mrs. Y is a 54-year-old woman who was diagnosed with *hypothyroidism*. She was prescribed replacement therapy which restored thyroid hormone levels within the normal range, but kept feeling miserable, with a very bothersome *globus in the throat*. She consulted several endocrinologists, who all stated that her thyroid replacement was fine and there was nothing wrong with her, which made her angry and dissatisfied. She was then referred by her primary care physician to a Psychoneuroendocrinology Service. Careful interviewing in this setting disclosed the presence of *agoraphobia* (fear of public spaces and going out alone) with sporadic panic attacks and that she attributed the globus sensation and panic to the thyroid. She was adjusting by herself thyroid replacement in relation to her current feelings. She also reported *marital problems*. The psychosomatic assessment and physical examination led to diagnosing *persistent somatization* and explaining that agoraphobia is a psychological disorder, her globus sensation was related to it, not to the thyroid, and that changing herself thyroid replacement could only make things worse. A brief course of cognitive treatment by a psychologist did improve her agoraphobia and marital problems greatly, with disappearance of panic attacks and only sporadic symptoms of globus sensation related to anxiety.

The various elements of macroanalysis are highlighted in italics.

References

- Engel GL: A unified concept of health and disease. *Perspect Biol Med* 1960;3:459–485.
- Engel GL: Is grief a disease? A challenge for medical research. *Psychosom Med* 1961;23:18–22.
- Maj M: Are we able to differentiate between true mental disorders and homeostatic reactions to life events? *Psychother Psychosom* 2007;76:257–259.
- Buchi S, Mörgeli H, Schnyder U, Jenewein J, Hepp U, Jina E, Neuhaus R, Fauchère JC, Bucher HU, Sensky T: Grief and post-traumatic growth in parents 2–6 years after the death of their extremely premature baby. *Psychother Psychosom* 2007;76:106–114.
- Engel GL: The need for a new medical model: a challenge for biomedicine. *Science* 1977;196:129–136.
- Novack DH, Cameron O, Epel E, Ader R, Waldstein SR, Levenstein S, Antoni MH, Wainer AR: Psychosomatic medicine: the scientific foundation of the biopsychosocial model. *Acad Psychiatry* 2007;31:388–401.
- Fava GA, Sonino N: The biopsychosocial model thirty years later. *Psychother Psychosom* 2008;77:1–2.
- Fava GA, Sonino N: The clinical domains of psychosomatics medicine. *J Clin Psychiatry* 2005;66:849–858.
- McEwen BS: Physiology and neurobiology of stress and adaptation: central role of the brain. *Physiol Rev* 2007;87:873–904.
- Rozanski A, Blumenthal JA, Kaplan J: Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation* 1999;99:2192–2217.
- Sonino N, Tomba E, Fava GA: Psychosocial approach to endocrine disease. *Adv Psychosom Med* 2007;28:21–33.
- Wright RJ, Rodriguez M, Cohen S: Review of psychosocial stress and asthma. *Thorax* 1998;53:1066–1074.
- Faravelli C, Catena M, Scarpato A, Ricca V: Epidemiology of life events. *Psychother Psychosom* 2007;76:361–368.
- Engel GL: Psychological aspects of gastrointestinal disorders; in Reiser MF (ed): *American Handbook of Psychiatry*. New York, Basic Books, 1975, vol 4, pp 653–692.
- Rosendal M, Olesen F, Fink P: Management of medically unexplained symptoms. *BMJ* 2005;30:4–5.
- Conti S, Savron G, Bartolucci G, Grandi S, Magelli C, Semprini F, Saviotti FM, Trombini G, Fava GA, Magnani B: Cardiac neurosis and psychopathology. *Psychother Psychosom* 1989;52:88–91.
- Kannel WB, Dawber TR, Cohen ME: The electrocardiogram in neurocirculatory asthenia (anxiety neurosis or neuroasthenia). *Ann Intern Med* 1958;49:1351–1360.
- Lipowski ZJ: Psychosomatic medicine: past and present. 2. Current state. *Can J Psychiatry* 1986;31:8–13.
- Fava GA, Kellner R: Prodromal symptoms in affective disorders. *Am J Psychiatry* 1991;148:823–830.
- Fava GA, Kellner R: Staging. A neglected dimension in psychiatric classifications. *Acta Psychiatr Scand* 1993;87:225–230.
- Paykel ES: The clinical interview for depression. *J Affect Disord* 1985;9:85–96.
- Kellner R: A symptom questionnaire. *J Clin Psychiatry* 1987;48:269–274.

- 23 Sirri L, Grandi S, Fava GA: The illness attitude scales. *Psychother Psychosom* 2008;77:337–350.
- 24 Fava GA, Magelli C, Savron G, Conti S, Bartolucci G, Grandi S, Semprini F, Saviotti FM, Belluardo P, Magnani B: Neurocirculatory asthenia: a reassessment using modern psychosomatic criteria. *Acta Psychiatr Scand* 1994;89:314–319.
- 25 Robins E, Guze SB: Classification of affective disorders: the primary-secondary, the endogenous-reactive, and the neurotic-psychotic concepts; in Williams TA, Katz MM, Shield JA (eds): *Recent Advances in the Psychobiology of the Depressive Illness*. Washington, Government Printing Office, 1972, pp 283–293.
- 26 Fava GA, Grandi S: Differential diagnosis of hypochondriacal fears and beliefs. *Psychother Psychosom* 1991;55:114–119.
- 27 Sonino N, Fava GA, Boscaro M, Fallo F: Life events and neurocirculatory asthenia. *J Intern Med* 1998;244:523–528.
- 28 Paykel ES: The interview for recent life events. *Psychol Med* 1997;27:301–310.
- 29 Fava GA: The concept of psychosomatic disorder. *Psychother Psychosom* 1992;58:1–12.
- 30 Engel GL: The concept of psychosomatic disorder. *J Psychosom Res* 1967;11:3–9.
- 31 Kissen DM: The significance of syndrome shift and late syndrome association in psychosomatic medicine. *J Nerv Ment Dis* 1963;136:34–42.
- 32 Tinetti ME, Fried T: The end of the disease era. *Am J Med* 2004;116:179–185.
- 33 Tinetti ME, Bogardus ST, Agostini JV: Potential pitfalls of disease-specific guidelines for patients with multiple conditions. *N Engl J Med* 2004;351:2870–2874.
- 34 Fava GA, Ruini C, Rafanelli C: Psychometric theory is an obstacle to the progress of clinical research. *Psychother Psychosom* 2004;73:145–148.
- 35 Bech P: Modern psychometrics in clinimetrics. *Psychother Psychosom* 2004;73:134–138.
- 36 Feinstein AR: *Clinimetrics*. New Haven, Yale University Press, 1987.
- 37 Emmelkamp PMG: The additional value of clinimetrics needs to be established rather than assumed. *Psychother Psychosom* 2004;73:142–144.
- 38 Fava GA, Tomba E, Grandi S: The road to recovery from depression. *Psychother Psychosom* 2007;76:260–265.
- 39 Benazzi F: Is there continuity between bipolar and depressive disorders? *Psychother Psychosom* 2007;76:70–76.
- 40 Stangier U, Ukrow U, Schermelleh-Engel K, Grabe M, Lauterbach W: Intrapersonal conflict in goals and values in patients with unipolar depression. *Psychother Psychosom* 2007;76:162–170.
- 41 Hetrick SE, Parker AG, Hickie IB, Purcell R, Yung AR, McGorry PD: Early identification and intervention in depressive disorders: towards a clinical staging model. *Psychother Psychosom* 2008;77:263–270.
- 42 Fava GA, Rafanelli C, Tossani E, Grandi S: Agoraphobia is a disease. *Psychother Psychosom* 2008;77:133–138.
- 43 Dobkin PL, Filipski M, Looper K, Schieir O, Baron M: Identifying target areas of treatment for depressed early inflammatory arthritis patients. *Psychother Psychosom* 2008;77:298–305.
- 44 Van HL, Dekker J, Peen J, van Aalst G, Schoevers RA: Identifying patients at risk of complete non-response in the outpatient treatment of depression. *Psychother Psychosom* 2008;77:358–364.
- 45 Lipkin M, Quill TE, Napodano RJ: The medical interview. *Ann Intern Med* 1984;100:277–284.
- 46 Hampton JR, Harrison MJG, Mitchell JRA, Prichard JS, Seymour C: Relative contributions of history-taking, physical examination, and laboratory investigation to diagnosis and management of medical outpatients. *BMJ* 1975;2:486–489.
- 47 Goldberg RJ, Novack DH: The psychosocial review of systems. *Soc Sci Med* 1992;35:261–269.
- 48 Porcelli P, Sonino N (eds): *Psychological Factors Affecting Medical Conditions. A New Classification for DSM-V*. Basel, Karger, 2007.
- 49 Fava GA, Fabbri S, Sirri L, Wise TN: Psychological factors affecting medical condition: a new proposal for DSM-V. *Psychosomatics* 2007;48:103–111.
- 50 Fava GA, Wise TN: Psychological factors affecting either identified or feared medical conditions: a solution for somatoform disorders. *Am J Psychiatry* 2007;164:1002–1003.
- 51 Prince M, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, Rahman A: No health without mental health. *Lancet* 2007;370:859–877.
- 52 Leplège A, Hunt S: The problem of quality of life in medicine. *JAMA* 1997;278:47–50.
- 53 Sonino N, Peruzzi P: A psychoneuroendocrinology service. *Psychother Psychosom* 2009;78:346–351.
- 54 Feinstein AR: An analysis of diagnostic reasoning. 1. The domains and disorders of clinical macrobiology. *Yale J Biol Med* 1973;46:212–232.
- 55 Feinstein AR: An analysis of diagnostic reasoning. 2. The strategy of intermediate decisions. *Yale J Biol Med* 1973;46:264–283.
- 56 Lipowski ZJ: Physical illness and psychopathology. *Int J Psychiatry Med* 1974;5:483–497.
- 57 Kellner R: Psychosomatic syndromes, somatization and somatoform disorders. *Psychother Psychosom* 1994;61:4–24.
- 58 Aaron LA, Buchwald D: A review of the evidence for overlap among unexplained clinical conditions. *Ann Intern Med* 2001;134(9 Pt 2, suppl):868–881.
- 59 Fava GA, Grandi S, Rafanelli C, Fabbri S, Cazzaro M: Exploratory therapy of hypochondriasis. *J Clin Psychiatry* 2000;61:317–322.
- 60 Fava GA: Well-being therapy. *Psychother Psychosom* 1999;68:171–178.
- 61 Sonino N, Fava GA: Psychosocial aspects of endocrine disease. *Clin Endocrinol* 1998;49:1–7.
- 62 Sonino N, Fava GA: Rehabilitation in endocrine patients. A novel psychosomatic approach. *Psychother Psychosom* 2007;76:319–324.
- 63 Balercia G, Boscaro M, Lombardo F, Carosa E, Lenzi A, Jannini EA: Sexual symptoms in endocrine diseases. *Psychother Psychosom* 2007;76:134–140.
- 64 Feinstein AR: Basic biomedical science and the destruction of the pathophysiological bridge from bench to bedside. *Am J Med* 1999;107:461–467.
- 65 Fava GA, Freyberger HJ, Bech P, Christodoulou G, Sensky T, Theorell T, Wise TN: Diagnostic criteria for use in psychosomatic research. *Psychother Psychosom* 1995;63:1–8.
- 66 Engel GL: Conversion symptoms; in MacBryde CM, Blacklow RS (eds): *Signs and Symptoms*. Philadelphia, Lippincott, 1970, pp 650–699.
- 67 Goldbeck R: Denial in physical illness. *J Psychosom Res* 1997;43:575–593.
- 68 de Figueredo JM: Demoralization and psychotherapy. *Psychother Psychosom* 2007;76:129–133.
- 69 Mangelli L, Fava GA, Grandi S, Grassi L, Ottolini F, Porcelli P, Rafanelli C, Rigatelli M, Sonino N: Assessing demoralization and depression in the setting of medical disease. *J Clin Psychiatry* 2005;66:391–394.
- 70 Mangelli L, Fava GA, Grassi L, Ottolini F, Paolini S, Porcelli P, Rafanelli C, Rigatelli M, Sonino N: Irritable mood in Italian patients with medical disease. *J Nerv Ment Dis* 2006;194:226–228.
- 71 Härter M, Baumeister H, Reuter K, Jacobi F, Höfler M, Bengel J, Wittchen HU: Increased 12-month prevalence rates of mental disorders in patients with chronic somatic diseases. *Psychother Psychosom* 2007;76:354–360.
- 72 McKegney PF: The incidence and characteristics of patients with conversion reactions. *Am J Psychiatry* 1967;124:542–545.
- 73 Orchard WH: Anxiety in patients with coronary disease. *Aust N Z J Psychiatry* 1969;3:316–320.
- 74 Lishman WA: *Organic Psychiatry*, ed 3. Oxford, Blackwell, 1998, pp 384–385.
- 75 Fava GA, Morphy MA, Sonino N: Affective prodromes of medical illness. *Psychother Psychosom* 1994;62:141–144.

- 76 Mangelli L, Bravi A, Fava GA, Ottolini F, Porcelli P, Rafanelli C, Rigatelli M, Sonino N: Assessing somatization with various diagnostic criteria. *Psychosomatics* 2009;50:38–41.
- 77 Beresnevaite M, Taylor GJ, Bagby RM: Assessing alexithymia and type A behavior in coronary heart disease patients. *Psychother Psychosom* 2007;76:186–192.
- 78 Ferrari S, Galeazzi GM, Mackinnon A, Rigatelli M: Frequent attenders in primary care. *Psychother Psychosom* 2008;77:306–314.
- 79 Ryff CD, Dienberg Love G, Urry HL, Muller D, Rosenkranz MA, Friedman EM, Davidson RJ, Singer B: Psychological well-being and ill-being. *Psychother Psychosom* 2006;75:85–95.
- 80 Schubert C: Psychological well-being and ill-being and their biological correlates. *Psychother Psychosom* 2007;76:252–253.
- 81 Dantzer R: Somatization: a psychoneuroimmune perspective. *Psychoneuroendocrinology* 2005;30:947–952.
- 82 Price DD, Finniss DG, Benedetti F: A comprehensive review of the placebo effect. *Annu Rev Psychol* 2008;59:565–590.
- 83 Walach H, Bosch H, Lewith G, Naumann J, Schwarzer B, Falk S, Kohls N, Haraldsson E, Wiesendanger H, Nordmann A, Tomasson H, Prescott P, Bucher HC: Effectiveness of distant healing for patients with chronic fatigue syndrome. *Psychother Psychosom* 2008;77:158–166.
- 84 Thayer JF, Brosschot JF: Psychosomatics and psychopathology. *Psychoneuroendocrinology* 2005;30:1050–1058.
- 85 Zachariae R, Paulsen K, Mehlsen M, Jensen AB, Johansson A, von der Maase H: Chemotherapy-induced nausea, vomiting and fatigue. *Psychother Psychosom* 2007;76:376–384.
- 86 Carroll BJ: Brain mechanisms in manic depression. *Clin Chem* 1994;40:303–308.
- 87 Fava GA: Irritable mood and physical illness. *Stress Med* 1987;3:293–299.
- 88 Abbate-Daga G, Fassino S, Lo Giudice R, Rainero I, Gramaglia C, Marech L, Amianto F, Gentile S, Pinessi L: Anger, depression and personality dimensions in patients with migraine without aura. *Psychother Psychosom* 2007;76:122–128.
- 89 Kamarck TW, Haskett RF, Muldoon M, Flory JD, Anderson B, Bies R, Pollock B, Manuck SB: Citalopram intervention for hostility. *J Consult Clin Psychol* 2009;77:174–188.
- 90 World Health Organization: World Health Organization Constitution. Geneva, World Health Organization, 1948, p 28.
- 91 Ryff CD, Singer B: Psychological well-being. *Psychother Psychosom* 1996;65:14–23.
- 92 Fava GA, Tomba E: Increasing psychological well-being and resilience by psychotherapeutic methods. *J Pers*, in press.
- 93 Pressman SD, Cohen S: Does positive affect influence health? *Psychol Bull* 2005;131:925–971.
- 94 Chida Y, Steptoe A: Positive psychological well-being and mortality. *Psychosom Med* 2008;70:741–756.
- 95 Charney DS: Psychobiological mechanisms of resilience and vulnerability. *Am J Psychiatry* 2004;161:195–216.
- 96 Cloninger CR: Systematic method for clinical description and classification of personality. *Arch Gen Psychiatry* 1987;44:573–588.
- 97 Tabibnia G, Zaidel E: Alexithymia, interhemispheric transfer, and right hemispheric specialization. *Psychother Psychosom* 2005;75:81–92.
- 98 Romei V, De Gennaro L, Fratello F, Curcio G, Ferrara M, Pascual-Leone A, Bertini M: Interhemispheric transfer deficit in alexithymia. *Psychother Psychosom* 2008;77:175–181.
- 99 Galderisi S, Mancuso F, Mucci A, Garra-mone S, Zamboli R, Maj M: Alexithymia and cognitive dysfunction in patients with panic disorder. *Psychother Psychosom* 2008;77:182–188.
- 100 Fava M, Littman A, Halperin P: Neuroendocrine correlates of the type A behavior pattern. *Int J Psychiatry Med* 1987;17:289–307.
- 101 Engel GL: How much longer must medicine's science be bound by a seventeenth century world view? *Psychother Psychosom* 1992;57:3–16.
- 102 Dafoe W, Husten P: Current trends in cardiac rehabilitation. *CMAJ* 1997;156:527–532.
- 103 Nieuwenhuijsen ER, Zemper E, Miner KR, Epstein M: Health behavior change models and theories. *Disabil Rehabil* 2006;28:245–256.
- 104 Joosten EA, DeFuentes-Merillas L, de Weert GH, Sensky T, van der Staak CP, de Jong CA: Systematic review of the effects of shared decision-making on patient satisfaction, treatment adherence and health status. *Psychother Psychosom* 2008;77:219–226.
- 105 Bodenheimer T, Lorig K, Holman H, Grumbach K: Patient self-management of chronic disease in primary care. *JAMA* 2002;288:2469–2475.
- 106 Jones DS: Textbook of Functional Medicine. Gig Harbor, Institute for Functional Medicine, 2005.
- 107 Lolak S, Connors GL, Sheridan MJ, Wise TN: Effects of progressive muscle relaxation training on anxiety and depression in patients enrolled in an outpatients pulmonary rehabilitation program. *Psychother Psychosom* 2008;77:119–125.
- 108 Korstjens I, May AM, von Woert E, Mesters I, Tan F, Ros WJ, Hoekstra-Weebers JE, van der Schans CP, van den Borne B: Quality of life after self-management cancer rehabilitation. *Psychosom Med* 2008;70:422–429.