Psychiatric Aspects of Chronic Fatigue Syndrome and Fibromyalgia

Boudewijn Van Houdenhove · Stefan Kempke · Patrick Luyten

Published online: 30 March 2010
© Springer Science+Business Media, LLC 2010

Abstract Chronic fatigue syndrome and/or fibromyalgia (CFS/FM) consists of highly overlapping, medically unexplained symptoms, including long-lasting fatigue, effort intolerance, cognitive dysfunction, and widespread pain and tenderness. CFS/FM often seems to be triggered by infections and physical trauma, but depression, sleep disturbances, and personality may also be involved. Moreover, dysregulation of the stress system, the immune system, and central pain mechanisms may determine the pathophysiology of the illness, leading to a loss of capacity to adapt to all kind of stressors. CFS/FM patients can be best helped by a pragmatic and individualized approach aimed at adjusting lifestyle and optimizing self-care, which in the long run may contribute to a restoration of physical and mental adaptability. Future psychiatric research into CFS/FM should focus on the complex interrelationships among pain/fatigue, stress/depression, and personality, as well as on processes of therapeutic change and the advantages of customized treatment.

Keywords Etiology · Chronic fatigue syndrome · Diagnosis · Fibromyalgia · Pathogenesis · Psychiatry · Treatment

Introduction

Syndromes characterized by chronic, medically unexplained fatigue; effort intolerance; cognitive dysfunction; and widespread musculoskeletal pain and tenderness are highly prevalent in medicine; cause a great deal of individual and familial suffering; and often lead to serious physical, mental, and socio-professional disability.

Operational criteria have been formulated defining these symptom clusters as chronic fatigue syndrome (CFS) [1] and fibromyalgia (FM) [2], respectively (Table 1). However, pain and fatigue not only frequently co-occur [3], but the two syndromes largely overlap, making a common, integrative approach highly preferable [4].

The purpose of this article is to present an update on the psychological/psychiatric literature on CFS and FM by reviewing selected recently published articles against the background of our own clinical experience. Although the CFS and FM literature generally follows distinct pathways, we consider both syndromes as one overarching symptom cluster and abbreviate it as CFS/FM.

Diagnostic Issues

Definition

Both CFS and FM are still ill defined and the subject of controversy. As for CFS, some clinicians, researchers, and patients use alternative diagnostic terms (eg, myalgic
Table 1 Operational diagnostic criteria of chronic fatigue syndrome and fibromyalgia

<table>
<thead>
<tr>
<th>Chronic fatigue syndrome</th>
<th>Fibromyalgia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medically unexplained fatigue</td>
<td>Medically unexplained, widespread pain</td>
</tr>
<tr>
<td>At least 6 months’ duration</td>
<td>At least 3 months’ duration</td>
</tr>
<tr>
<td>At least 4 additional symptoms among the following:</td>
<td>At least 11 positive “tender points”</td>
</tr>
<tr>
<td>Muscle/joint pain</td>
<td></td>
</tr>
<tr>
<td>Concentration/memory disturbances</td>
<td></td>
</tr>
<tr>
<td>Nonrefreshing sleep</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Sore throat and tender lymph nodes</td>
<td></td>
</tr>
<tr>
<td>Postexertional malaise</td>
<td></td>
</tr>
</tbody>
</table>

encephalomyelitis (ME) and chronic fatigue and immune dysfunction syndrome (CFIDS), and different case definitions also have been proposed [5]. Furthermore, the Centers for Disease Control and Prevention criteria for CFS that are currently used most often [1] are often criticized as too inclusive and putting insufficient emphasis on neurocognitive dysfunction, abnormal fatigability, and postexertional malaise [5].

As for FM, “tender point” count (registration of specific painful places on the body when applying a standard amount of pressure, suggesting abnormal pain processing) has been defined as a major diagnostic criterion by the American College of Rheumatology [2]. However, as this criterion has been found to be flawed by empiric research during the past two decades [6], many clinicians now base the FM diagnosis primarily on the patient’s report of widespread musculoskeletal pain and tenderness in the absence of an alternative somatic diagnosis [7].

Subgroups

It is highly probable that patients diagnosed with CFS/FM are heterogeneous. Different subgroups have been proposed (eg, dependent on mode of onset, severity of symptoms, presence or absence of psychiatric comorbidity, or ways of coping) [8]. Recent studies even suggest that in medically unexplained chronic fatigue and CFS, discrete endophenotypes may be delineated [9].

Likewise, some authors and patient support groups have argued that ME should be defined as a unique “neurological” disease to be distinguished from psychiatric chronic fatigue [10]. However, this assertion has up to now not been supported by empiric research. For example, in a Belgian study comparing two groups of patients attending a psychosocially oriented CFS center and a biologically oriented CFS/ME center, respectively, no major differences in psychopathology could be detected [11].

CFS/FM and Psychiatric Comorbidity

Depression

Although it leaves no doubt that CFS/FM and major depressive disorder (MDD) are distinct entities [12], the two syndromes partially overlap [13, 14]; this is particularly the case for atypical forms of depression [15]. Of note, a considerable proportion of MDD patients show painful symptoms [16] that may be based on common neurobiological underpinnings in pain and depression [17]. Moreover, CFS/FM patients have frequent depressive comorbidity and a high lifetime prevalence of MDD [18, 19].

Nonetheless, little is known about the specific relationship between CFS/FM and MDD. Some speculate that both conditions may be part of a spectrum of stress-related disorders with a possible common familial-genetic basis [20]. Furthermore, early-life stress seems to be a risk marker for MDD and CFS/FM [21]. From a neurobiological point of view, however, most MDD patients show hyperreactivity of the hypothalamic-pituitary-adrenal (HPA) axis, whereas in CFS/FM patients, hyporeactivity has mostly been found—particularly in those with a traumatic history [22, 23]—although the opposite also has been reported [24].

Sleep Disorders

CFS/FM patients generally awake nonrefreshed, but clinical experience shows that they are quite heterogeneous with regard to sleep. Some patients present with severe nightly sleep loss (often associated with a sleep–wake cycle reversal), whereas others show normal or even exaggerated sleep duration.

Despite repeated findings that CFS/FM patients may overestimate their subjective sleep problems [25], recent studies have reported subtle disruptions in sleep architecture that may at least partially explain the overwhelming fatigue and pain in these patients [26]. Similarly, electroencephalographic measures have shown disturbed sleep homeostasis [27] as well as increased heart rate and low heart rate variability during sleep, pointing to continuous nightly arousal that may be due to an abnormal sympathovagal balance [28, 29].
An Integrative Etiopathogenetic Hypothesis

Loss of Adaptability?

From an etiologic point of view, clinical experience and empiric research suggest that the onset of CFS/FM mostly follows an accumulation of psychosocial and/or physical stressors [30-32]. In this respect, not only person-independent stress (eg, losing a loved one) may play a role, but also self-generated, person-dependent stress (eg, by repeatedly exceeding physical or mental limits or creating interpersonal conflicts), which may be fostered by personality features such as maladaptive perfectionism [33], tendency for persistence [34, 35], and a highly “action-prone” lifestyle [36, 37].

Other potentially relevant predisposing personality factors in CFS/FM may include negative affectivity or neuroticism [38] and alexithymia [39, 40], although findings concerning the latter characteristic remain inconclusive. Also, the association between CFS/FM and personality disorders, as defined by the DSM-IV Axis II, remains equivocal [41•, 42].

The pathophysiologic mechanisms underlying CFS/FM are still poorly understood but most probably include complex and interrelated disturbances of the neurobiological stress system (ie, the HPA axis, sympathetic nervous system, and different brain neurotransmitters), which operate in intimate connection with the immune system and central pain processing mechanisms. More specifically, CFS/FM symptoms may refer to a fundamental and persistent loss of adaptability of this system, which may be formulated in terms of a failure of allostasis [29••, 43, 44]. Vulnerability to this dysregulation may be genetically based in interaction with early-life experiences and particularly [45, 46], at least in subgroup of patients, with childhood trauma [21••, 22].

Following this line of thinking, we and others have hypothesized that the pathophysiologic basis of CFS/FM may involve a “switch” of the stress system from a state of “overdrive” to “underdrive,” leading to an inadequate response to future physical or mental stressors [43]. This switch usually follows a chronic or intense period of overburdening—to which the person typically reacts with persistent, (over)active coping—and is eventually triggered by an additional physical and/or emotional event (eg, an infection, a painful whiplash trauma, or increasing professional responsibilities).

HPA axis hypofunction may promote abnormal inflammatory activity and be responsible for the “sickness behavior” that is often observed in CFS/FM patients, particularly when they exceed their limits: under these circumstances, proinflammatory cytokines (and other inflammatory mediators) may influence the brain and induce physiologic symptoms such as light fever, as well as a characteristic fatigue/pain symptom pattern that patients often describe as flu-like (ie, profound lethargy, increased fatigability, concentration loss, generalized pain, and hypersensitivity to all kinds of physical and mental load [emotions, mental pressure, loud noise, bright light]), leading to an overwhelming wish to withdraw from the environment and sleep [43].

It should be noted that with respect to pain symptoms, other central nervous system and psychological mechanisms may play a role in sensitizing central pain mechanisms and lowering pain threshold. Indeed, in both FM and CFS, evidence has been found for inadequate descending pain control; neuroplastic changes in the spinal cord and brain; and for reinforcing cognitive, emotional, and behavioral factors (eg, pain-related negative affect, catastrophizing, and poor sleep) [47, 48].

Perpetuating Factors

Once ill, many CFS/FM patients get stuck in multiple negative spirals that reinforce and maintain symptoms, illness behavior, and disability, eventually making recovery less probable [49•]. Somatic factors such as physical deconditioning, persistent sleep disturbances, chronic hyperventilation, and possibly opportunistic infections may lead to further deterioration of the illness in some patients.

In many patients, a whole range of psychosocial factors may also play a perpetuating role. Notably, perceptual-cognitive factors (somatic hypervigilance and preoccupation, rigid somatic attribution, excessive worrying and catastrophizing about the illness, and low self-efficacy), as well as affective factors (comorbidity depression, anxiety disorders, and kinesiophobia), personality factors (perfectionism/dependency, introversion, problematic affect regulation, and alexithymia), behavioral factors (lack of acceptance and periodic overactivity), social factors (lack of understanding from the environment, membership in a patient support group and secondary gain) and finally iatrogenic factors have been found to potentially perpetuate the illness [49•].

Psychiatric Aspects of Treatment

Treatment Goals

According to some authors, the therapeutic goal in CFS/FM should be full recovery. To that aim, patients should be encouraged to correct unhelpful thoughts and attitudes and gradually increase activities in accordance with their personal objectives. Moreover, once recovered, patients
should “normalize” perceptions of their own health (including periodic occurrence of fatigue), thus leaving the CFS label definitively behind [50].

Other authors assert that optimizing coping with the illness and adaptation to functional limitations is a more realistic goal [51]. Within the latter view, patients are advised to carefully and consistently pace activities, adjust lifestyle, and prioritize life objectives, which may improve their functioning and quality of life and in the long run facilitate a “natural” restoration of their stress system. This view also implies that even after regaining physical and mental adaptability, vulnerability may remain, and relapse is not improbable [49•, 51].

Illness Management

Because a short-term cure for CFS/FM is not available, patients should first be helped to accept their ailment and its functional consequences and be provided with a plausible and acceptable illness theory that may be a starting point for a realistic and pragmatic therapeutic approach [49•].

Second, meta-analyses have demonstrated that current evidence-based treatments for CFS/FM consist of cognitive-behavioral therapy (CBT) and graded exercise therapy (GET), which are often combined [52•, 53•]. Both strategies may assist patients in correcting faulty cognitions, improving physical condition, optimizing sleep hygiene and healthy diet, and—perhaps most importantly—balancing lifestyle and activity by avoiding a typical “boom-and-bust” activity pattern. Although CBT is not a panacea and should be applied flexibly and with the patient’s full consent [49•, 51], this therapeutic approach has proven valuable for many patients and—contrary to some critical assertions [54]—to have no detrimental effects on the illness [55]. Moreover, as for GET, guidelines have been formulated that take into account the fluctuating nature of the symptoms and prevent too-vigorous effort, which is likely to provoke symptom exacerbations and immunologically induced, postexertional pain and malaise [56•].

Third, psychopharmacologic treatment, although it is not curative, may contribute substantially to symptom amelioration by controlling pain and emotional distress, correcting sleep disorders, and treating psychiatric comorbidity, as well as indirectly facilitate functioning and improve quality of life. However, medication should always be used in the context of self-care, and clinicians should be aware of polypharmacy and related iatrogenic effects and drug interactions as a possible problem in CFS/FM [57, 58].

Fourth, in recent years, increasing attention has been paid to customizing treatment to the heterogeneity of the illness by targeting perpetuating factors that are individually important [49•, 59]. For example, when responses from significant others clearly reinforce the patient’s illness behavior, operant-behavioral interventions strategies may be useful [60]. However, in other CFS/FM patients, cognitive approaches, insight-oriented therapy, family interventions, and/or relaxation or meditation strategies may be most suited to assist patients in finding a “new equilibrium” in their lives [49•, 51].

Finally, for the small subgroup of CFS/FM patients who are severely physically invalidated (and often also show a traumatic history and psychiatric comorbidity such as borderline personality disorder), a multimodal inpatient rehabilitation program may be considered.

Psychiatric Research Perspectives

Personality Research

Current studies concerning the role of personality in CFS/FM are scarce, largely cross-sectional, and predominantly based on self-report [41•]. Clearly, more personality research is needed, but future studies should adopt a more dynamic, multi-informant, and multilevel approach. This implies that personality-related processes should be investigated as they unfold in controlled or naturalistic situations (eg, during interactions with significant others), using different informants (eg, by self-report and partner report), and focusing on not only subjective but also physiologic, neuroendocrine, and neural aspects. In this way, the complex mechanisms involved in these processes could be uncovered, and their role in the etiology of CFS/FM as predisposing, precipitating, and/or perpetuating factors could become more clear. Currently, the technology and methodological know-how for such studies are widely available and have already yielded an increase in our knowledge in this domain [61].

Finally, research on developmental issues in CFS/FM, including gene–environment interactions underlying the links among early-life stress, attachment style, and personality, could throw an interesting new light on a possible specific vulnerability for the illness.

Psychotherapeutic Research

Despite the proven efficacy of CBT and exercise therapy for CFS/FM, many questions remain regarding the mediating and moderating processes underlying mechanisms of therapeutic change [49•, 62], as well as the usefulness of these treatments for more complex cases encountered in the clinical setting [51]. Thus, future research should investigate therapeutic processes in much detail and also test the effectiveness of various treatment strategies in routine clinical practice.

Furthermore—in line with the tendency to customize treatment in CFS/FM—future studies should try to answer...
the question of “What works for whom?” For example, it could be investigated whether some patients may need specific psychotherapeutic strategies that target personality-related mechanisms such as perfectionism to help them reach a “new equilibrium” [63]. More generally, subgroups of CFS/FM patients could be empirically validated to determine who may benefit most from psychotherapeutic, physiotherapeutic, or pharmacotherapeutic approaches, or a combination of all three.

Pharmacotherapy Research

Due to the recent discovery of an infectious retrovirus in the blood cells of at least a subgroup of CFS/FM patients [64, 65], the search for immune therapies that may correct (parts of) the pathophysiology of the illness will presumably be boosted during the coming years.

Nonetheless, future pharmacotherapy studies should not neglect other important aspects of CFS/FM, such as further unraveling common neurobiological underpinnings of chronic pain/fatigue, stress, and depression [14•, 43], including the search for specific psychopharmacologic agents [57, 58].

Conclusions

The chronic fatigue and pain symptom cluster, labeled as CFS/FM, remains a great challenge for modern medicine from a diagnostic, etiopathogenetic, and therapeutic point of view. Recent literature shows that an integrated biopsychosocial approach is best suited to not only understand causal determinants and mechanisms of the illness but also to provide realistic, pragmatic, and individualized therapeutic help. In future research, psychological and psychiatric aspects of CFS/FM should continue to be thoroughly investigated.

Disclosure  No potential conflicts of interest relevant to this article were reported.

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
• Of major importance

a landmark article reviewing current evidence from animal and human studies for the neurobiological determination of vulnerability for depression and depression-like syndromes (eg, CFS/FM) by early-life trauma and adversities.


29. Staud R: Heart rate variability as a biomarker of fibromyalgia syndrome. Fut Rheumatol 2008, 3:475–483. This interesting review summarizes current knowledge about autonomous nervous system disturbances in FM and gives a new perspective on the use of biomarkers related to stress system functioning (eg, heart rate variability) for diagnosis and outcome of clinical trials.


37. Harvey SB, Wadsworth M, Wessely S, Hotopf M: Etiology of chronic fatigue syndrome: testing popular hypotheses using a national birth cohort study. Psychosom Med 2008, 70:488–495. This was a prospective study showing that individuals who exercise frequently are more likely to report a diagnosis of CFS in later life, which may be due to the direct effects of this behavior or associated personality factors. The authors also found that remaining active despite increasing fatigue may be a crucial step in the development of CFS. This study supports common clinical observations about CFS patients’ premorbid “overactive” lifestyle and preoccupation with achievement.


41. Van Geelen SM, Sinnema G, Hermans HJ, Kuis W: Personality and chronic fatigue syndrome: methodological and conceptual issues. Clin Psychol Rev 2007, 27:885–903. This article rightly underscores the current lack of knowledge of the role played by personality factors in determining vulnerability in CFS. The authors also discuss several methodological difficulties that hamper studies in this domain.


49. Van Houdenhove B, Luyten P: Customizing treatment in chronic fatigue syndrome/fibromyalgia: the role of perpetuating factors. Psychosomatics 2008, 49:470–477. This is a literature review on the biopathogenesis of CFS/FM with a focus on different perpetuating factors, and a pragmatic perspective on customizing treatment based on identifying these factors in individual patients.


52. Reid SF, Chalder T, Cleare A, et al.: Chronic fatigue syndrome. Clin Evid (Online). 2008, pii:1101. This prestigious database, which is updated regularly, discusses various evidence-based and other treatment strategies in CFS.

53. Häuser W, Bernardy K, Arnold B, et al.: Efficacy of multidisciplinary treatment in fibromyalgia syndrome: a meta-analysis of randomized controlled clinical trials. Arthritis Rheum 2009, 61:216–224. This is an impressive meta-analysis on treatments combining various strategies in FM. The authors found strong evidence for reduction of pain, fatigue, depressive symptoms, and limitations to health-related quality of life, and improvement of self-efficacy, pain, and physical fitness after treatment. However, most of these benefits were not maintained in the long run.

54. Twisk FH, Maes M: A review on cognitive behavioral therapy (CBT) and graded exercise therapy (GET) in myalgic encephalomyelitis (ME) / chronic fatigue syndrome (CFS): CBT/GET is not
only ineffective and not evidence-based, but also potentially harmful for many patients with ME/CFS. Neuro Endocrinol Lett 2009, 30:284–299.


