

## Review Article

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# The Conundrum of Medically Unexplained Symptoms: Questions to Consider

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**Background:** *The classification and etiology of medically unexplained symptoms remain a clinical challenge. Recent proposals to improve systems of classification include ending the tradition of separating symptoms into medical or psychiatric groups. Method:* *Several research questions are proposed to resolve some of the divergent opinions about the nature of these difficulties. Conclusion:* *Unitary models of somatic symptom causation should not be presumed. Examination of the causes and nature of somatic distress in those with and without psychiatric disorders requires separate investigation for each, and these should not be presumed to be similar. Psychophysiological models of somatic symptoms are required that can be studied in research protocols.*

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The classification and clinical management of widespread musculoskeletal pain and related nonspecific somatic distress are some of the most vexing conceptual challenges facing clinicians, whether they be physicians or mental health professionals.<sup>1</sup> The magnitude of this clinical problem is considerable, given that approximately one-quarter to one-half of all presentations to primary and secondary care are a consequence of somatic symptoms not well characterized by medical conditions.<sup>1</sup> One of the major difficulties in creating a uniform approach to these patients has been that somatic symptoms are often picked up by various subspecialties of medicine, which creates idiosyncratic and overlapping approaches that lack consensus.<sup>2</sup> Consequently, many of the specific diagnostic labels that have been coined, such as chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity, have considerable overlap of their symptoms. In essence, two competing systems of classification have arisen: the somatoform disorders, in psychiatry, and functional disorders, in medicine, with little cross-reference to each other.<sup>3</sup>

Against the background of the deficiencies of the current systems of classification, alternative strategies for

DSM-V have been proposed to resolve many of the current conundrums. The multiple overlapping and competing frames of references that exist for the diagnosis of these patients is one of the main problems requiring clarification.

Any new system of classification ultimately will have its validity tested through the creation of a framework of testable clinical hypotheses that include the domains of phenomenology, epidemiology, and etiology. This article outlines issues emerging from existing research that should be systematically addressed by any proposed future system of classification. In this context, we have proposed a strategy to assist in clarifying the etiology of these syndromes and the associated challenge of developing a diagnostic system to assist rational clinical management.

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### CLASSIFICATION: THE PRESENT AND FUTURE PROPOSALS

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Patients who present with somatic symptoms for which there is no readily-identified physical etiology pose a considerable diagnostic conundrum for medical practitioners. The "Somatoform Disorders" classification in the DSM-IV (including Somatization Disorder, Pain Disorder, and Hypochondriasis) provides one system of phenomenological classification. Four sources of imprecision in this approach<sup>3</sup> include the following: 1) the variable interpretation of the thresholds of severity required for these disorders; 2) the substantial error in doctors' rating of "Medically Unexplained Symptoms" (MUS); 3) the requirement that symptoms are not better explain by some other psychiatric disorder, such as depression or anxiety; and 4) the lack of stated direction about how to deal with the considerable overlap between somatoform disorders and functional medical syndromes.

Furthermore, a recent systematic review of the research literature concluded that there was poor discriminatory validity of the somatoform disorders from other Axis I and II disorders in DSM-IV.<sup>3</sup> The paucity of the literature around somatoform disorders was contrasted with the much greater body of research examining the "functional" medical syndromes. An alternative formulation postulated that somatoform disorders are interface disorders between mental and organic disorders and, as a consequence, should be incorporated into Axis III, which is for medical conditions.<sup>4</sup>

In light of a number of such conceptual issues, Kroenke et al.<sup>1</sup> have highlighted the idea that there are some areas of consensus but also important areas of divergence that require further clarification. Sharpe and Mayou,<sup>5</sup> in considering these conundrums, have suggested that there are three matters that should be addressed in a new approach to MUS: 1) The symptoms in their own right require attention, and classifying them as either medical or psychiatric should not be done in such a way as to obscure the importance of understanding a particular symptom because it is subsumed by diagnosis. 2) Any system should allow for the possibility of multiple etiological factors and, in so doing, not conceptualize symptoms as solely an expression of bodily pathology or psychopathology. 3) The dichotomization of patients into medical or psychiatric categories should be avoided because this tends to discourage the development of effective treatment for the actual symptoms.

Sharpe and Mayou<sup>5</sup> and Mayou et al.<sup>6</sup> have challenged

the convention in psychiatry for dealing with somatic symptoms and have made specific suggestions for a new approach in DSM-V. They suggest that psychiatry has too readily accepted the role of classifying and implicitly presuming to understand patients presenting with unexplained somatic symptoms, particularly given that patients have difficulty accepting a psychiatric explanation for their symptoms. This divergence often creates a communication gulf between patient and doctor, impeding effective intervention.<sup>4</sup>

Second, Sharpe and Mayou<sup>5</sup> suggest that attributing a psychiatric diagnosis can convey the ambiguous message that the cause is purely psychogenic, when there are some possible biological underpinnings. Third, somatoform disorders are not a coherent group, and they have a range of possible presentations. Furthermore, they have highlighted that somatoform disorders are, in fact, rare in epidemiological studies.<sup>7-11</sup> Mayou et al.<sup>6</sup> suggest that the matter should be resolved by creating a new third axis in DSM-V, which would incorporate somatic syndromes and symptoms. Under this system, the somatic manifestations of depression and anxiety would be included under Axis I, and hypochondriasis would be renamed as health-anxiety disorder. The patients who do not readily fit into these groups should be included in the third axis category.

In summary, these proposals are contrary to the existing system of classification, and they represent a major reformulation. They suggest that many bodily symptoms do not have a simple causal relationship with psychopathology.<sup>5</sup> Their approach is supported by more general criticisms of the categorical diagnostic systems in DSM-IV and the need for research into the dimensional nature of psychopathology and its neurobiological underpinnings.<sup>12</sup> This premise is an important foundation for research into the nature of MUS. Further clarification of the utility of this approach and its validity will be examined in the context of a series of research issues derived from the current literature. The very large body of work in this domain and its multiple conceptual frameworks do not allow a systematic review;<sup>3</sup> rather, we will characterize the general themes.

#### Research Issues to Help Clarify the Nature of Medically Unexplained Symptoms

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*1. Are somatic symptoms distinct from anxiety and depression?* A longstanding question exists as to whether somatic distress is a distinct psychological dimension, as contrasted with anxiety and depression.<sup>13</sup> This argument goes

back to the origins of neurasthenia and the question of whether it was an independent psychiatric disorder. One approach to the resolution of this dilemma is to examine the level of correlation between somatic distress, anxiety, and depression.

Goldberg<sup>14</sup> found that somatic symptoms were only moderately correlated with anxiety ( $r=0.53$ ) and depression ( $r=0.48$ ), in contrast to the correlation found between anxiety and depression ( $r=0.68$ ). This lack of strong correlation underpinned the rationale for the structure of many questionnaires, such as the General Health Questionnaire (GHQ) and the SPHERE depression questionnaire. Studies of Persian Gulf War veterans<sup>15,16</sup> support this argument that symptoms of anxiety and depression fall on a distinct axis, separate from factors characterizing patterns of somatic distress. In these veterans, only approximately half of those who satisfied the diagnostic criteria for chronic fatigue syndrome incurred a psychiatric diagnosis, as is the case with a number of other studies.<sup>17</sup>

Such findings argue for the need to characterize separate axes of somatic and psychological distress and to explore these relationship in a range of populations, including medically ill patients, those with psychiatric disorders, and a combination of physical and psychological disorders. Any system of classification should have equal utility in all settings. An important question is to explore whether these are distinct subpopulations characterized by variations in the degree of interrelationship between these two axes of distress and the intervening role of psychiatric disorders.

*2. Are distinct somatic syndromes valid entities?* There are a number of well-recognized “functional” syndromes that are built up on a subset of symptoms of nonspecific distress, for example, chronic fatigue, fibromyalgia, and multiple chemical sensitivity syndromes. One of the important conceptual challenges is to determine whether there are core symptoms shared by these syndromes, which are simply being reclassified because of some immediate proximal event or exposure to an etiological agent. The symptoms of fatigue, muscle pain, headaches, dizziness, unrefreshing sleep, impaired memory, and problems with concentration and executive function are some of the “nonpsychological” problems that are shared by a number of syndromes.

The problem is that the proximal cause of these symptoms is often defined according to the experience and ideological stance of the relevant researcher or clinician from a particular specialty, who then attempts to establish a spe-

cific phenomenology, etiology, and treatment based on their standpoint. What is lost in this pattern of description is establishing the commonality and the similarities with other conditions. The question equally remains as to whether there are subgroups of patients who will present with the same nonspecific symptom upon exposure to a particular agent. If this is the case, it remains that there may be multiple etiologies for these nonspecific symptoms, or, alternatively, that such symptoms could be indicative of nonspecific distress within the individual.

One future strategy that could assist in the unraveling of this conundrum is the removal of any of the symptoms that are shared by more than three of these syndromes. Inevitably, the specificity of such shared symptoms will lack any utility, and their value as an indicator of disorder would not survive psychometric scrutiny. Aggregations of “typical” symptoms that are developed should be tested in field trials to ascertain what impact the changes in the diagnostic criteria have on specificity and sensitivity of particular symptoms. Kroenke *et al.*<sup>1</sup> have emphasized, for example, that, for pain disorder, “positive” behavioral indices should be defined. Ultimately, the separation of diagnoses can only be justified if separation is achieved by the specific symptom criteria. Populations that have sustained physical injury are likely to provide valuable insights into the clustering and separation of syndromes.

*3. Is there a specific psychophysiological basis for specific somatic symptoms?* A further challenge in grouping and classifying nonspecific symptoms is the lack of knowledge about the underlying origin of many such symptoms. For example, despite the importance of fatigue as a symptom of illness, the underlying mechanisms remain poorly understood. The attribution of significance to the symptom, by doctor and patient alike, is critical to the impact of the symptom on an individual’s perceived well-being. In this way, the treating doctor is in a position to influence the patient’s expectations of recovery or improvement.

Many symptoms are indicative of patterns of particular psychophysiological arousal. For example, the complexity of the nerve plexus of the bowel means that the link between autonomic activity and bowel symptoms is often a part of human symptomatology.<sup>18</sup> There has been a long-standing body of research linking psychiatric disorders with irritable bowel, and a range of psychological treatments benefit the symptoms of irritable bowel syndrome.<sup>19</sup> This is one example of the inevitable conundrum of attempting to separately characterize psychological and

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physical disease and their relationship to psychophysiological modulation.

Against this background, the characterization of the relationships between subjective symptom-clusters and patterns of particular psychophysiological arousal should be a research priority. The psychophysiological measurement needs to consider how psychological and physical environmental demands both affect an individual's state. "Stress" creates a particular fascination in terms of its relation to health and disease because of its capacity to drive dysregulation of physiological homeostasis. However, stress, as a concept, requires precise definition and measurement.

A research goal should be to better characterize a stimulus response that is no longer within the normal physiological range or when a pattern of psychophysiological reactivity becomes autonomously driven by endogenous processes. Such research will better characterize the concepts of allostasis<sup>20</sup> and sensitization,<sup>21</sup> which are critical to understanding the vulnerability of the body's homeostatic systems to dysregulation. It may be the case that looking at a continuum of functioning and the interrelationship between different regulatory systems may be critical to defining individuals who are in a transition between health and a disease state that is characterized by a range of nonspecific somatic symptoms.

### 4. What influences thresholds for reporting symptoms?

Patients' patterns of cognitive appraisal of symptoms affect thresholds of recognition and complaint.<sup>22</sup> "Normalizers" have a propensity to dismiss their distress and symptoms, making the diagnosis of physical and psychological disorders difficult, in contrast to patients who are "psychologizers" or "somatizers," whose pattern of complaint is more easily detected in general-medical settings. Parker and Parker<sup>22</sup> highlight the question of whether standard screening instruments, using a unitary threshold, are able to pick up the levels of distress of the normalizing group because of their tendency not to complain.

This interaction between reported symptoms and style of health-attribution is a critical issue because the existence of MUS may primarily indicate the existence of a lower threshold for reporting distress, rather than actual physiological dysregulation. Hence, the aggregation of reported symptoms may not simply be indicative of their existence but, rather, it may indicate a particular type of scanning or self-monitoring that leads to somatic preoccupation. For example, Barsky et al.<sup>23</sup> found that the ECG recording of palpitations had very little correlation with patients' self-

report. This finding highlights the limitations of self-report as an adequate detector of the underlying physiological parameters of distress.

Effective sensory gating is also critical to managing the many somatic inputs that are central to consciousness.<sup>24</sup> Patients with a strong tendency to somatize their distress are less able to distinguish between relevant and irrelevant somatosensory stimuli,<sup>25,26</sup> and hence ignore many somatic inputs. Similarly, panic disorder and generalized anxiety disorder patients are more sensitive to bodily changes than are nonanxious individuals.<sup>27</sup> On objective measurements, however, there were few differences in physiological arousal between the control subjects and the anxious patients. Hence, it appears that the anxiety disorders are associated with a less accurate perception of bodily status.

From a research perspective, further investigations should both characterize the threshold of symptom-detection and its relationship to cognitive style, peripheral psychophysiology, and central gating of sensory inputs. To date, this matter has not been addressed in the classification or etiology of somatization syndromes.

### 5. Do source-monitoring deficits determine illness beliefs?

The striking characteristic of some individuals with undiagnosed patterns of somatic distress is their elaborate and strongly held beliefs about the cause of their condition. Barsky and Borus<sup>28</sup> found that, increasingly, doctors from a range of specialties have to deal with patients who commence a consultation having already arrived at a particular diagnosis for their disorder. These patients might have a range of somatic symptoms that cannot be explained by a specific diagnosis, but remain substantially disabled. Showalter<sup>29</sup> has highlighted the propensity of these patients to be dismissive and derogatory of both medical opinion and evidence from various domains that does not support their illness-beliefs. Subsumed under this attribution is a series of other beliefs; for example, the individuals see themselves as being ill and have particular expectations about how they may or may not respond to treatments and other interventions.

This characteristic raises the question as to whether the pathology is of the personality or coping style that underpin such powerful attributions about sickness and symptom-amplification.<sup>30</sup> Focusing solely on the symptoms of physical distress may be to ignore the possibility that the primary abnormality is one of belief, akin to a delusional or compulsive disorder. In psychotic disorders, such as schizophrenia, patients are known to show a deficit in the source-monitoring function, which refers to the set of pro-

cesses involved in the attribution of an origin to memories or beliefs. Particular underlying patterns of neuropsychological performance relate to different subcomponents of source-monitoring function in schizophrenia.<sup>31</sup>

An important area for future investigation is to characterize the patterns of source-monitoring in patients with unexplained medical symptoms.

*6. What role does traumatic stress play in somatic symptoms?* Andreski *et al.*<sup>32</sup> have determined that, of all the psychiatric disorders, posttraumatic stress disorder (PTSD) is the one that has the strongest relationship with somatization and, particularly, medically unexplained pain. Although there is substantial literature relating somatization to PTSD,<sup>33–38</sup> this body of knowledge is seldom referred to in the broader literature about somatization, which has largely focused on the role of depression and anxiety. Particularly in the light of more recent epidemiological studies, which suggest the previous underestimation of prevalence of traumatic events and PTSD in many settings,<sup>39</sup> there is a greater need to focus on the possible role of trauma in populations with MUS.

There has also been a significant interest in the relationship that traumatic stress has played in the unusual manifestations of somatic conditions,<sup>33–38</sup> independent of psychiatric disorders. McLean *et al.*<sup>40</sup> have highlighted the importance of a model for explaining the transition from acute traumatic injury to chronic pain via the role of fear-avoidance. Although they focus particularly on a multivariate model of chronic pain pathogenesis,<sup>41,42</sup> pain-related fear and avoidance has a central role in creating a trajectory to chronic pain, and shares some phenomena with PTSD. This coping style, which shapes a pattern of behavioral adaptation, leads to the amplification of peripheral sensations. The model further links this psychological process to an underlying complex cascade of the neurohormonal stress systems of the CNS. A substantial body of research has now been conducted in PTSD that has documented a series of domains of change in the stress-response systems.<sup>43,44</sup>

There is a need for a systematic research agenda that explores the relationship of traumatic memories and somatization from a series of perspectives. First, pain can be one aspect of a traumatic memory, where the experience of pain remains part of the somatosensory imprint of the traumatic memory that is reexperienced in a range of sensory domains.<sup>45</sup> Also, traumatic stress, via the process of sensitization, can modify the underlying mechanism of working memory and attention, leading to difficulties in

accurate processing and interpretation of environmental information.<sup>46</sup> Future studies of somatic distress should carefully document the history of trauma exposure and the related psychopathology, in light of the emerging epidemiological data about the prevalence of these exposures.

*7. Is it being ill that makes patients psychologically distressed?* Henningson *et al.*<sup>47</sup> conducted a metaanalysis of the literature, looking at the aggregation of somatic and psychological symptoms, by comparing the rates of depression and anxiety in four functional somatic syndromes and somatization disorder with rates in healthy controls in 243 studies with a total of 18,690 participants. They utilized an interesting approach, where they compared populations with particular manifestations of nonspecific symptoms with an equivalent disease of known organic pathology. For example, they compared the rates of depression in irritable bowel syndrome with those in known inflammatory bowel disease and compared fibromyalgia with rheumatoid arthritis. The second dimension they examined was the extent to which depression and anxiety differentiated those with MUS who did and did not seek medical assistance.

In general, they found those patients diagnosed with one of four functional syndromes (irritable bowel, non-ulcer dyspepsia, fibromyalgia, chronic fatigue) had significantly higher rates of current major depression or any current anxiety disorder when compared with healthy controls or patients with known organic pathology who showed similar physical phenomena. In general, the effect sizes were highly significant. In contrast, there were no significant differences in the rate of depression or the degrees of symptomatic distress in these patients compared with mixed groups of patients with psychiatric disorders. Depression did not characterize those who presented with gastrointestinal functional syndromes, whereas anxiety symptoms did. They concluded that the higher rates of depression and anxiety in patients with MUS than patients with medical disorders of known etiology weighs against the possible explanation that the psychological symptoms in these disorders are simply a consequence of the experience of pain and physical symptoms.<sup>48</sup>

Second, Henningson *et al.*<sup>47</sup> found that MUS often do arise in the absence of a specific depressive or anxiety disorder. The moderate size of the relationship between depression and anxiety in these somatic symptoms supports the view that somatic symptoms cannot simply be seen as

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the bodily expression of depression or anxiety or their psychophysiological consequences.

The substantive point that needs to be addressed in future research is that MUS are not simply mental disorders, and there is no primacy of mental over physical symptoms. Smith et al.<sup>49</sup> further highlighted the idea that the current formulation of somatoform disorders is less effective at characterizing the psychiatric pathology in these patients than the role accounted for by anxiety and depression. There is a need for careful measurement of somatic symptoms, depression, anxiety, and PTSD as distinct axes of distress in future studies.

### PRINCIPLES FOR RESEARCH TO IMPROVE CLASSIFICATION

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The proposals of Mayou et al.<sup>6</sup> and Kroenke et al.<sup>1</sup> about the future classification of MUS create a framework for a research agenda that should be considered. In summarizing a number of the salient research questions, we suggest that there are several principles that could inform future examination of these proposed systems of classification:

#### 1. No "One Size Fits All:" Different Causations Within Populations of Interest

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There are multiple reasons why individuals in an epidemiological sample may present predominantly with patterns of somatic distress. In general, however, populations are looked at from a unitary perspective. This is perhaps best demonstrated in studies of Persian Gulf War veterans,<sup>15,16</sup> which examined patterns of nonspecific distress in veterans, as contrasted with control groups. The lack of any difference in patterns of complaint led to the conclusion that the patterns of distress did not argue for a unique etiology; rather, that the population had greater levels of psychological morbidity, which was confirmed by the relevant diagnostic interviews. However, such a methodology does not address the possibility that there were small subgroups who did have high exposures to some identified agent that left them with an unusual pattern of physical ill health.

Methodological and analytic strategies need to consider the existence of different pathologies from within the broader pool of nonspecific MUS and need to examine the hypothesis that both physical and psychological mechanisms are contributing to the documented symptoms. Specific symptoms, rather than diagnoses, should be studied, using the approach of recruiting patients from groups of

various, rather than single, medical or psychiatric disorders.

#### 2. Definition of Subgroups of Interest: Somatizers With a Psychological Disorder Versus Those Without a Psychological Disorder

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Sharpe and Mayou<sup>5</sup> suggest that patients should not be dichotomized to "medical" or "psychiatric" categories. However, in order to better understand patterns of somatic distress, there is a need to separate those individuals who do have a psychiatric disorder that may explain their pattern of somatic distress in contrast to those who do not, independent of whether some secondary factor is playing a significant role. This strategy would assist in investigating the different etiologies in those with and without psychiatric disorders that can lead to common endpoint symptoms.

It is important to explore these relationships in populations who have not been recruited through medical clinics, because that selection process immediately creates a bias toward individuals who perceive themselves as ill. However, it remains the case that a causal factor in nonspecific symptoms of physical distress might have a separate effect in disrupting cognitive functioning and influencing the risk of psychiatric disorder.

#### 3. The Need for Pathophysiological Models of Symptoms

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Until a clear etiology is established, the convention advocated by DSM-III should be adopted; this excludes any presumed cause from the diagnostic category title. Against this background, testable etiological hypotheses should be proposed for each of the symptoms that fall under the rubric of MUS, as suggest by Sharpe and Mayou.<sup>5</sup> These models include the possibilities that:

1. There maybe some abnormality of neurotransmission in the peripheral nervous system and the spinal cord (i.e., neuropathic pain), when the patient continues to report the sensation of pain in the absence of pathology in the region of the nociceptor. There is also the potential for a combination of both peripheral and neurogenic causes of symptoms, if the symptoms emerge in the aftermath of a triggering injury or illness.

2. A further possibility is that there is an abnormality of central processing, similar to the abnormalities of working memory in PTSD.<sup>50</sup> Although the issue of the processing of somatic stimuli has not been studied in PTSD, it has demonstrated that these patients have an inability to differentiate targets. Specific studies of patients with so-

matization disorders have found similar information-processing abnormalities,<sup>51,52</sup> suggesting that some somatizing patients have difficulty attending to relevant and ignoring irrelevant somatic sensations. This process is at the core of self-awareness and consciousness.<sup>24</sup> It is not surprising that if this highly complex process of automatic scanning and integration of somatic self-representations becomes disrupted, the individual becomes preoccupied with somatic sensations that would normally be ignored.

3. There has been an increasing recognition of a shared pattern of etiology between whiplash, fibromyalgia, chronic fatigue, irritable bowel syndrome, and PTSD. Specifically, disorders of the HPA axis have been identified in these disorders.<sup>53–55</sup> These can be characterized by enhanced negative feedback. Such stress-induced changes have been associated with major impacts on neurogenesis and brain functioning;<sup>56,57</sup> these changes can also play an important role in the onset of chronic widespread musculoskeletal pain, as shown in a general-population sample.<sup>58</sup> We may better characterize the underpinnings of the origin of somatic symptoms by noting shared hypotheses in the existing literature and clarifying these mutual ideas; these include the role of allostasis in stress-induced alterations of hippocampal neurogenesis, and various forms of gene expression.<sup>59</sup> Another potentially promising area of investigation in the onset of pain syndromes and psychiatric disorders such as depression and PTSD is the associated role of neural sensitization as a central process resulting from exposure to stressful life events.<sup>60</sup> The amygdala plays a central role in kindling of the fear response in PTSD,<sup>61</sup> and these central processes are similar to the neural networks associated with the phenomena of wind-up of C-fiber-evoked pain<sup>62</sup> in fibromyalgia and chronic fatigue syndrome.<sup>63,64</sup> The interaction between fear-avoidance and sensitization has broad relevance to understanding individuals' reporting of subjective health complaints<sup>65</sup> and modified pain sensitivity in irritable bowel syndrome.<sup>66,67</sup>

4. Apart from the underlying neurobiology of symptoms, the cognitive style of appraisal requires systematic assessment as a separate axis of etiology. Fear-avoidance is a central aspect of the response of individuals to traumatic events and injury, leading to patients' attempting to control and manage their distress by avoiding sensory, environmental, and behavioral triggers of their symptoms.

This process can drive the misinterpretation of peripheral stimuli that have registered. For example, an individual who was exposed to DDT (an insecticide that is now banned in many countries) may become unusually preoccupied with any minor symptoms of ill health, fearing that he had been poisoned. Thus, the meaning of peripheral symptoms can be modified by a fear of illness or contamination. Such fears can arise from realistic and unrealistic perceptions of internal and external threats.

## CONCLUSION

The symptoms of nonspecific somatic distress and psychiatric disorder may be easily confounded.<sup>1</sup> There is no unitary model that best explains the relationships between somatoform disorders, anxiety, depression, and functional syndromes, and there are many disagreements about how to best resolve the problem.<sup>1</sup> Against this background, various strategies for better classifying somatic disorders have been proposed for DSM–V, which include treating somatic symptoms as a separate axis and independent of presumed medical or psychiatric origin. A better understanding of the nature of MUS and effective treatments will only be developed when the different axes that contribute to such distress are clearly articulated and better understood through systematic research.

In our view, the recent proposals<sup>5,6</sup> for novel approaches to classification in DSM–V will go forward if research strategies address the etiological underpinnings of MUS and are thus directed by a series of precise research questions. As suggested by Sharpe and Mayou,<sup>5</sup> the nature of MUS will only be unraveled by focusing on the multiple etiological factors that can lead to the subjective complaint of somatic distress. These factors include the psychophysiological underpinnings of symptoms, the determinants of the thresholds of symptom-reporting, and the effects of traumatic stress. There is a need to separately investigate the nature of MUS in patients with and without psychiatric disorders, with a unitary approach to classification, independent of the patterns of comorbidity.

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