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Research on Somatization and Somatic Symptom Disorders: *Ars longa, vita brevis*

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Abstract

The new Diagnostic and Statistical Manual of Mental Disorders (DSM5) defines Somatic Symptom and Related Disorders (SSRD) as longstanding somatic symptoms that are associated with disproportionate thoughts, feelings, and behaviors, irrespective of whether or not a medical cause for these symptoms can be determined. In this Special Section of *Psychosomatic Medicine,* several articles address diagnostic issues and the central nervous system correlates of SSRD and document new developments in its treatment.

Keywords

somatic symptom disorders; somatization; replication; clinical trials

Writing the DSM5 was a long dialectical process accompanied by spirited debate about virtually every clause in the book. The Somatic Symptom and Related Disorders (SSRD) section was particularly controversial because it proposed major changes by de-emphasizing the centrality of medically unexplained symptoms. In making a diagnosis of Somatic Symptom and Related Disorders, DSM5 considers instead longstanding somatic symptoms that are associated with disproportionate thoughts, feelings, and behaviors[1]. This decision was made for a number of reasons. Medically unexplained symptoms are all too often dismissed as not authentic even though the relationship between structural severity of illness and subjective symptom report is notoriously weak throughout medicine[2]. Similarly, while today's symptom may be regarded as "unexplained," it could just as well be "not yet recognized."

How somatic symptoms are experienced and communicated is at the marrow of psychosomatic medicine, whether the symptom pathophysiology is crystal clear or opaque. The journal has continued to publish groundbreaking research in this area (see for example the editorial perspective by Barsky[3] and the work by Maunder et al[4]). This history shows that understanding somatization is a lifelong challenge with burdens and obstacles and slow progress. As is evident from the papers published in this special section of *Psychosomatic Medicine*, progress *is* made and new technologies and improved research designs will continue to move this field forward.

Disorders such as somatic symptom disorder and illness anxiety disorder are distressing to patients, their families, and their physicians. They are also common and have porous borders with anxiety and depression. Participants in the work group that designed the somatic

symptom disorder criteria laid out a series of research challenges that the diagnosis would need to address in the future[56]. The current issue of *Psychosomatic Medicine* features six articles that address some of these research challenges necessary for improved understanding and treatment of these troubling disorders. It is striking to observe that these papers were written by investigators from Korea, Japan, Belgium, Germany, Denmark, Norway, the Netherlands, and the United Kingdom. In a time when isolationism is on the uptick, psychosomatic medicine reminds us that humanity shares disorders, regardless of geographical borders.

A good study should be replicable; it should provide a clear enough "recipe" so that others could duplicate its design. The authors of these articles did indeed describe their recipes, and the papers employed subtly different criteria for diagnosis. That is not necessarily a scientific sin. We do not need to genuflect in front of DSM5 criteria (or for that matter ICD criteria), but we always need to be clear about what is being studied. This is a challenge for all of medicine, but it is compounded when we lack structural findings or diagnostic laboratory tests.

The DSM5 criteria for SSRD differ substantially from prior formulations. Nonetheless, questionnaires that were originally developed to identify somatoform disorders may still be useful for the diagnosis of SSRD. Laferton and colleagues[7] evaluated the PHQ-15, the Whiteley Index, and the Scale for Assessing Illness Behavior and found reasonably good diagnostic accuracy for these questionnaires as compared to clinical interviews as the gold standard. More recent questionnaires, such as the SSD-12 [8], have been specifically designed to evaluate the B criteria for SSRD (cognitive, affective and behavioral components) and may prove to be even more clinically useful.

Ahn et al. searched for a physiological marker that might differentiate between patients with somatic symptom disorders, patients with major depressive disorder and a healthy comparison group [9]. Using quantitative electroencephalography, they examined resting-state functional connectivity in various parts of the brain. There were differences in the synchrony of the brain, not just in patients versus healthy controls but also in patients with somatic symptom disorder and patients with depression. One of the advantages of this study is that it employed a technology that is reasonably easy to adopt elsewhere. Will this approach eventually translate into a clinically useful laboratory test? If future studies replicate the findings, we may indeed have both a mechanistic insight as well as a laboratory test. The fact that quantitative electroencephalography is less costly than many brain imaging techniques makes such tests more likely to be implemented across a wide range of clinical settings.

The importance of replication (and its cost) is highlighted by the interesting study by Kano et al[10]. Increasingly, studies use functional magnetic resonance imaging (fMRI) to probe the brain's response. The problem with fMRI is that each scan is costly to perform and generates so many separate regions of interest in the brain that it poses statistical problems unless relatively large sample sizes are obtained[11]. These two issues make replication crucially important and, regrettably, all too rare. Kano et al's design was clever. They specifically examined the brain's response to stimuli in the vulnerable organ system and then

they manipulated how the individual construed the stimulus. How do we process uncomfortable somatic signals? How does a lifetime of facing intermittent, uncertain stimuli affect the response to new stimuli? One worries that few research centers will have the expertise and funds to attempt to replicate these findings, but this is a powerful approach.

Similar to Kano et al, the study by van den Houte et al. induces somatic symptoms by manipulating emotional states[12]. Healthy controls reported similar somatic symptoms whether they viewed positive, neutral, or negative images. In contrast, patients with fibromyalgia and/or chronic fatigue syndrome reported more somatic symptoms when they viewed negative images. These observations in patients appear to have been mediated by patients' difficulties in identifying feelings, which is one of the components of alexithymia. It is interesting to note that the DSM5 workgroup was relatively mum about the role of alexithymia in somatic symptom disorder. Van den Houte et al's observations may argue for a reconsideration of this construct in future diagnostic approaches. The experimental design of this study is a potentially productive approach to evaluate in other patient samples.

Rief et al. offer a deceptively-simple approach with important consequences[13]. Once we identify the disorder and once we start to compare treatments for these disorders, what should be measured in clinical trials? How do we define "success"? One of the advantages of the clinical trials perspective is that it encourages us to pre-specify study outcomes. Rief et al. remind us that clinical trials need to go beyond merely specifying classification and outcome. It is not enough to specify a diagnosis; studies also need to provide information on issues like duration and intensity of the symptoms as well as their impact on the patient's functioning. In terms of outcomes, one should consider domains such as quality of life, health care utilization and treatment satisfaction. This paper offers a shrewd assessment of such design considerations for assessing future clinical trials.

Finally, this special section of the journal includes a clinical trial. Löwe et al examined the effectiveness of a stepped care intervention for patients with somatoform disorders [14]. Many previous clinical trials have demonstrated beneficial interventions in psychosomatic medicine[15], but because the DSM5 is still new, few clinical trials have employed these new criteria. The Löwe et al study was successful in getting patients into treatment (no mean accomplishment) but failed to improve their clinical outcomes. It is incumbent upon the field to scrutinize this study carefully. Why was it negative? Was there a peculiarity about the patient sample? Was it an ineffective intervention? Was the dose of the intervention adequate? Was it properly powered? Were the wrong outcomes measured? These are the sorts of questions one needs to ask when a trial yields an unexpected result. The paper is a model of clarity to the field as we continue to sort out what "works," "where," and "how."

This section of papers focused on somatic symptom disorder mechanisms and issues in clinical trials design. What's missing? One can't squeeze everything into one special section in one issue of *Psychosomatic Medicine.* But we do need more research in certain areas that are chronically under-studied. One looks forward to future studies of genetic factors, neurobehavioral and psychoneuroimmunological processes and of life course exposures in patients with somatic symptom disorder. More than enough to do for future researchers!

Twenty-four hundred years ago, Hippocrates memorably reminded us of the challenges of "the Art [of medicine]." (Figure 1)

> "Life is short, the Art long, opportunity fleeting, experiment treacherous, judgment difficult."
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> Hippocrates, Aphorisms, First Section I

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FIGURE 1.

Ars Longa, Vita brevis, Interior of Altes Rathaus, Göttingen, Photograph by Hans A. Rosbach. Available at https://commons.wikimedia.org/w/index.php?curid=16501267 under a CC BY-SA 3.0 license.