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Resistant somatoform symptoms: Try CBT and antidepressants

Preferred strategy for ‘mismatched’ category of illnesses

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Treatment-resistant somatoform disorders are chronic (duration >1 year), can cause significant functional impairment, and respond poorly to routine care.

In the somatoform category, DSM-IV-TR includes diverse diagnoses such as conversion disorder, hypochondriasis, pain disorder, and body dysmorphic disorder. But like mismatched shoes, these disorders do not fit together well—one reason they are often misdiagnosed and ineffectively treated. This article describes:

- debate about how to categorize somatoform disorders—as psychological or physiologic
- evidence supporting psychotherapy and antidepressants to help patients with treatment-resistant somatoform disorders.
Somatoform disorders

Box 1

Somatoform disorders: Interacting psychiatric and biologic processes

Psychobiologic causes of somatoform disorders are poorly understood. In a recent review, Rief and Barsky emphasized that somatoform symptoms such as abdominal pain, headaches, or dizziness “are not strictly mental events, but are associated with a diversity of biological processes.” They propose that the following factors might contribute to somatoform disorders.

**Autonomic physiologic arousal** may lead patients to misperceive the meaning of normal bodily symptoms, but most studies have found an equivalent or correlate closely with changes in the cardiovascular system. For example, patients with somatoform spectrum disorders who performed mentally distressing tasks did not have the same decrease in heart rate after completing the task as normal controls did, suggesting a deficit in autonomic reactivity.

**Hypothalamic-pituitary-adrenal (HPA) axis** studies also have been equivocal. Some have found low cortisol in patients with somatoform disorders—suggesting commonalities with conditions such as posttraumatic stress disorder—but other studies have found normal or even elevated cortisol. Although a relationship between the HPA axis and somatoform disorders is likely, its nature remains unclear or may be indirect.

**Serotonin** is known to alter pain perception in major depressive disorder, so this neurotransmitter also probably plays a role in somatoform disorders. Low serotonin—mediated in part by alterations in branched-chain amino acid concentration—may be linked to increased pain perception.

**Perception and filtering of body signals.** A signal-filtering model of somatoform symptoms proposes that physical sensations enter consciousness influenced by numerous factors. These signals are then sent to a filter system, which itself is subject to factors that may decrease its activity. Cortical perception of distress may occur and symptoms begin to manifest if enough factors come into play.

**WHICH CATEGORY?**

Somatoform disorders are common in primary care. A medical utilization survey of 1,500 primary care patients found somatization symptoms in >20%.

Controlling for comorbid psychiatric or medical illness did not change the study’s findings, which suggests that somatization is a distinct entity and not a symptom of another underlying disorder.

Little is known about somatoform disorders’ pathophysiology (Box 1), but their unifying theme is that psychological factors contribute to, amplify, or alter the presentation of physical illness. Not only do these disorders not form a coherent DSM category, but—as described by Mayou et al—the lack of clearly defined thresholds between normal and pathologic behaviors is one of numerous problems that complicate diagnosis and treatment (Box 2, page 107).

**Psychosomatic diad.** Despite DSM-IV’s claims to etiologic neutrality, the origin of somatoform disorders’ physical symptoms clearly is meant to be psychological. As Lipowski said, somatization is “a tendency to experience and express somatic distress and symptoms unaccounted for by pathological findings, to attribute them to physical illness, and to seek medical help for them. It is often assumed that somatization becomes manifest in response to psychosocial stress brought about by life events that are personally stressful to the individual.”

Kroenke and others, however, have pointed out 2 shortcomings of this definition:

- the difficulty in knowing when a physical
symptom truly is unexplained, especially in patients with comorbid medical illness. The instability of somatoform diagnoses (in a cohort examined with the same questionnaire 12 months apart, 43% of “lifetime somatic symptoms” patients reported at the first screening were not reported at the second). Kroenke suggests using “physical symptom disorder” as an etiologic-neutral descriptor of unexplained physical symptoms. He would place this category on Axis III and shift the causal emphasis from psychological to unexplained. This category would replace somatization disorder, undifferentiated somatoform disorder, and pain disorder in DSM.

Similarly, Mayou et al contend that because most patients with somatoform disorders are treated by primary care physicians, having their disorders understood as psychiatric does not serve them well.

**Psychiatric component.** Conversely, patients with somatization disorder often have psychological symptoms, and many have personality disorders. The number of somatic symptoms with unexplained cause may be a normally distributed trait, with somatization disorders at the extreme end of the spectrum. Thus:

- Hypochondriasis could be reconsidered as health anxiety disorder because it features anxiety about potential illness.
- Conversion disorders might be regrouped with other disorders focused on dissociation.
- Body dysmorphic disorder might be regrouped with obsessive-compulsive disorder.

These changes would shift focus away from the disorders’ physiologic presentations, emphasize the psychiatric disorders to which they likely are related, and provide insight into treatments and clinical investigations.

Pain disorder could be removed from DSM because of persistent concerns about the validity of this diagnostic category. Tyrer reviewed his clinical experience and reported shifting from a view that people with excessive pain had a psychiatric disorder to the view that living with chronic pain produces a profile similar to that of a person with a psychiatric disorder.

**Physiologic component.** Others recommend caution before radically altering DSM’s categorizations. Rather than shift symptoms to Axis III—as Kroenke suggests—Starcevic would use unexplained physical symptoms as an organizing principle and group disorders with common features, such as somatization disorder, conversion disorder, pain disorder, and undifferentiated somatoform
disorder. Body dysmorphic disorder and hypochondriasis—focusing on dysfunctional appraisal of physical symptoms—would likely move elsewhere. Hiller and Rief—those who advocate strongly for keeping somatoform disorders in DSM—suggest 4 categories: monosymptomatic, polysymptomatic, hypochondriasis, and body dysmorphic disorder. They believe grouping diagnoses in this way would improve and refine existing nosology.

NEW TREATMENT APPROACHES
As the categorization debate continues, a treatment approach is developing that includes cognitive-behavioral therapy (CBT) and antidepressants to address the psychological and physiologic effects of resistant somatoform disorders (Box 3).

Consultation letters. Sending a consultation letter to the patient’s primary care physician is considered the standard of care (Box 4, page 114). In the study that introduced the consultation letter, patients with somatization disorder were randomly assigned to treatment (a consultation letter) or control (treatment as usual). Health care utilization costs declined approximately 50%—largely because of decreased hospitalization—when patients’ physicians received consultation letters, compared with no change for usual treatment.

Consultation letters may reduce health care spending but are less effective in improving symptoms. Evidence is changing treatment as psychotherapies have been found to help patients with somatoform disorders.

Group psychotherapy. In a controlled trial, primary care patients with somatization disorder received short-term group CBT or treatment as usual, with follow-up 6 months later. Those in the CBT group—who had received patient education and relaxation training—showed moderate but significant improvement in physical illness and somatic preoccupation, hypochondriasis, and medication use. Usual-care patients did not improve.

CBT vs relaxation. A group of 191 inpatients described as “highly impaired” by somatization syndrome—28 DSM-IV somatoform symptoms—was evaluated for psychopathology, subjective health status, and life satisfaction. They then were randomly assigned to somatization-focused CBT (“soma”) or relaxation training and compared with 34 control patients. At 1-year follow-up, doctor visits had declined significantly in patients who received CBT (“soma”), and their somatoform symptoms were reduced compared with controls.

Psychotherapy vs listening. In a randomized, controlled trial, 102 patients with chronic refractory irritable bowel syndrome were assigned to receive exploratory psychotherapy or supportive listening. After 12 weeks, psychotherapy was more effective in improving physical and psychological symptoms,
Dose Dependency of Adverse Events in Short-Term, Placebo-Controlled Trials—Extrapyramidal Symptoms—In an acute-phase controlled clinical trial in schizophrenia, there was no significant difference in ratings scales incidence between any dose of oral olanzapine (2.5, 5.0, 10, 15, and 20 mg/dL) and placebo for parkinsonism (Simpson-ANGUS Scale total score >3) or akathisia (Barnes Akathisia Global score >2). In the same trial, only akathisia events (spontaneously reported) were significantly associated with terms akathisia and hyperkinesia showed a statistically significantly greater adverse events incidence with 2 higher doses of olanzapine than with placebo. The incidence of significant extrapyramidal events was significantly greater than placebo only with the highest dose of oral olanzapine (30 mg/dL). In controlled clinical trials of intramuscular olanzapine for injection, there were no statistically significant differences from placebo in occurrence of any treatment-emergent extrapyramidal symptoms, assessed by either rating scales incidence or spontaneously reported adverse events.

Other Adverse Events—Dose-related adverse events was assessed using data from a clinical trial involving 3 fixed oral dose ranges compared with placebo. The following treatment-emergent events showed a statistically significant trend: asthenia, dry mouth, nausea, somnolence, tremor.

Statistical Changes—Oral olanzapine was associated with orthostatic hypotension and tachycardia in clinical trials. Intramuscular olanzapine for injection was associated with bradycardia, hypotension, and tachycardia in clinical trials (see PRECAUTIONS).

Weight Gain—In placebo-controlled 6-month schizophrenia studies, weight gain was reported in 5.6% of the olanzapine patients (average 2.6 kg gain) compared to 0.4% of placebo patients (average 0.4 kg loss); 29% of olanzapine patients gained >7% of their baseline weight, compared to 3% of placebo patients. During continuation therapy (238 median days of exposure), 36% of patients met the criterion for having gained >7% of their baseline weight. Average gain was 2.6 kg during long-term therapy (3–1.4 kg).

Laboratory Changes—Olanzapine is associated with asymptomatic increases in SGPT, SGOT, and bilirubin. and increases in serum prolactin and CPK (see PRECAUTIONS). Asymptomatic elevation of eosinophil was reported in 0.3% of olanzapine patients in premarketing trials. There was no indication of adverse clinical events related to eosinophilia.

In clinical trials among olanzapine-treated patients with baseline random triglyceride levels of <150 mg/dL, 46 of 602 patients had an increase in triglyceride levels of >200 mg/dL, while during the trials more than placebo-treated patients (N=602; 3.6% vs 2.2% respectively). In placebo-controlled trials, triglyceride levels increased in 15/100 patients. Infrequent events occurred in 11/100 to 1000 patients: rare events occurred in <1/1000 patients. Body as a Whole—Frequent: abdominal pain increased, headache, dry mouth, nausea, vomiting, palpitations, tremor, dizziness, decreased appetite; Common: decreased weight, skin rash, sweating, fatigue, myalgia, back pain, diarrhea, flatulence, increased salivation, thirst.

Cardiovascular—Frequent: cardiovascular disorder, syncope, hypotension, palpitations, orthostatic hypotension, atrial fibrillation, bradycardia, cerebrovascular accident, congestive heart failure, heart arrest, hemorrhage, migraine, palpitations, vasodilatation, ventricular extrasystoles; Rare: arrhythmia, heart failure, pulmonary embolism. Digestive—Frequent: Flatulence, increased salivation, thirst, dysphagia, esophagitis, fecal impaction, fecal incontinence, gastritis, gastrointestinal, gnawing, hepatitis, hepatitis, jaundice, nausea, vomiting, oral ulceration, periodontal disease, rectal hemorrhage, stomatitis, tongue edema, tooth loss; Rare: aphthous stomatitis, orthostatic hypotension, dysphagia, esophagitis, esophageal ulcer, external oblique, intestinal obstruction, liver fatty degeneration, tongue discoloration. Endocrine—Frequent: diabetes mellitus; Rare: diabetic acidosis, gout, Hemic and Lymphatic—Frequent: adenopathy; Rare: lymphadenopathy.

Hematologic—Frequent: leukopenia, lymphopenia, lymphocytosis, thrombocytopenia. Rare: normocytic anemia, anemia, thrombocytopenia. Metabolic—Frequent: hyperglycemia, hypoglycemia, hyperlipidemia, hyperlipoproteinemia, hyperuricemia, hyperkalemia, hypokalemia, hypernatremia, hyperuricemia, hyperthyroidism, hypothyroidism, hypoglycemia, hyperglycemia, hypertension, hypotension, hypothermia, ileus, ketosis, water intoxication. Musculoskeletal—Frequent: joint stiffness, twitching. Infrequent: arthritis, arthralgia, leg cramps, myalgia, bone pain. Rare: joint pain, muscle spasm, osteoporosis, myopathies, arthritis. Nervous System—Frequent: abnormal dreams, amnesia, delusions, emotional lability, euphoria, manic reaction, paraphasia, schizophrenic reaction; infrequent: akathisia, alcohol misuse, anxiety reaction, ataxia, axial muscle atrophy, dysphoria, dizziness, dementia, depersonalization, depersonalization dysphoria, facial paralysis, hypnolalia, hypokinesia, hypotonia, incarceration, libido decreased, libido increased, obsessive-compulsive disorder, palpitations, palpitations, paresthesia, salivation, sleep disturbance, tinnitus, vertigo, withdrawal syndrome; Rare: circumoral paresthesia, coma, esotropia, myoclonus, obturation, psychomotor retardation; Infrequent: axial muscle atrophy, hyperreflexia, somnolence, tachycardia, tremor.

Somatoform disorders

Box 4
Consultation letter for somatization: Discourage saying 'it's in your head'

Describe somatoform disorder, its relapsing course, and low morbidity and mortality rates
Encourage the primary care physician to:
- serve as the patient’s primary doctor and avoid fragmented care from numerous sources
- schedule regular appointments with the patient
- perform physical exams at each visit
- eliminate unnecessary tests or hospitalizations
- avoid statements such as “it’s all in your head” when medical tests are negative

Source: Reference 13

Extended-release venlafaxine. A pilot study enrolled 112 adult primary care patients with multisomatoform disorder (≥3 medically unexplained, bothersome physical symptoms plus ≥2-year history of somatization) and comorbid major depressive disorder, generalized anxiety disorder, or social anxiety disorder. Patients were randomly assigned to double-blind treatment with venlafaxine ER, ≤225 mg/d (n=55), or placebo (n=57).

Primary outcome was change in the 15-item Patient Health Questionnaire (PHQ-15) somatic symptom severity score. After 12 weeks, PHQ-15 scores declined significantly (P <0.0001) in both groups but did not improve significantly more with venlafaxine ER than with placebo (-8.3 vs -6.6, respectively, P=0.097). Among secondary measures, venlafaxine ER was more effective than placebo in improving bodily pain (P=0.03), physical symptoms (P=0.02), and anxiety (P=0.02).17

Citalopram. In an 8-week trial, investigators compared the efficacy of a selective serotonin reuptake inhibitor (SSRI) and a selective noradrenaline reuptake inhibitor (SNRI) on pain symptoms in 35 patients with somatoform pain disorder. Patients were randomly assigned to double-blind treatment with the SSRI citalopram, 40 mg/d (n=17), or the SNRI reboxetine, 8 mg/d (n=18).

In patients receiving citalopram, scores decreased significantly from baseline on the Present Pain Intensity scale (3.5 vs 2.8, P=0.045) and Total Pain Rating Index of the McGill Pain Questionnaire (41.9 vs 30, P=0.004), but these scores did not change significantly in patients receiving reboxetine. Depression symptoms, as measured by the Zung Self-Rating Depression Scale, did not change significantly in either group.

The authors concluded that citalopram was moderately effective for somatoform pain disorder in this small trial. Although antidepressants’ efficacy for somatoform symptoms may be mediated through changes in comorbid mood and anxiety disorders, these authors observed that citalopram’s analgesic effect appeared to be independent of how patients rated their depressive symptoms.18

TREATMENT RECOMMENDATIONS
Based on the evidence and our experience, we recommend offering CBT to patients with recent symptom onset and insight into their comorbid
mood and anxiety disorders. If the patient does not improve after 8 to 12 sessions, consider adding an antidepressant such as:

- citalopram, 20 to 60 mg/d
- venlafaxine XR, 150 to 375 mg/d.

For patients with chronic somatization, start with combined pharmacotherapy and CBT. **Side effects** are a frequent concern in this patient population, so titrate dosages slowly. Aim for the target antidepressant dosages used to treat major depression, and avoid declaring a treatment failure without first completing adequate trials. Once the patient is stable on medication, continue for a least 1 somatization-free year.

**Allow patients** to discuss their physical concerns, and attempt to support them in their suffering. At the same time, help them focus on attaining realistic goals for occupational and social functioning. **Work closely** with the primary care provider in treatment planning to avoid sending the patient mixed messages. Communicating in the spirit of respect and collaboration with primary care colleagues can help prevent "splitting," in which the patient may come to idealize one practitioner and devalue the other.

Remember that patients with somatization can become medically ill. Remind their primary care providers to perform expected evaluations as dictated by objective findings.

**References**