

Antidepressants and Somatic Symptoms: Therapeutic Actions Are Expanding Beyond Affective Spectrum Disorders to Functional Somatic Syndromes

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Issue: *Having expanded their original role as primary treatment for depression to preferred treatment for anxiety disorders, antidepressants are now emerging as potential therapeutic agents for many other disorders characterized by distressing or even painful somatic symptoms.*

Antidepressant Uses: The Emerging Frontier

The expanded use of antidepressants beyond the treatment of major depressive disorder (MDD) to numerous additional affective and anxiety disorders is one of the remarkable therapeutic advances in psychiatry of the past decade. Thus, numerous antidepressants now have proven efficacy in premenstrual dysphoric disorder, bulimia, panic disorder, generalized anxiety disorder, social anxiety disorder, posttraumatic stress disorder, and obsessive-compulsive disorder (Table 1). This expansion appears not yet to be complete, and another remarkable therapeutic advance in psychiatry may be in the offing for the coming decade.

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Numerous conditions that have high comorbidity with depression but are themselves characterized by prominent somatic symptoms may also be treated effectively with antidepressants. The frontier for yet further therapeutic uses of antidepressants has thus shifted from depression and anxiety to illnesses considered either to be components of an affective spectrum disorder (Table 1)^{1,2} or to be members of a category known as “functional somatic syndromes” (Table 2).^{3,4} Prominent conditions with encouraging new findings suggesting efficacy of antidepressants include not only fibromyalgia⁵ and irritable bowel syndrome,⁶ but also a variety of chronic pain conditions.^{3,4}

Do Conditions That Respond to the Same Drugs Have the Same Pathophysiology?

It is plausible that conditions that respond to numerous classes of antidepressants may share a common causal factor.¹ This does not necessarily mean that depression causes these conditions (listed in Tables 1 and 2), but it does imply that boosting serotonergic neurotransmission, noradrenergic neurotransmission, or both with an antidepressant may compensate for

a common causal factor in each of these conditions. That factor might be abnormally functioning neuronal circuits that are regulated by serotonin (5-HT) and/or norepinephrine (NE). Circuits in one part of the CNS may mediate symptoms of sadness and depressed mood,⁷ and in another, anxiety and fear,⁸ and in still other areas, diffuse and often painful somatic complaints.⁹ Boosting 5-HT and/or NE neurotransmission in one circuit may reduce sadness, and in another circuit, somatic symptoms.⁷

In MDD, some patients may experience improvement of their sadness and depressed mood, but not their somatic symptoms, while taking an antidepressant. These individuals are not in full remission. Increasing attention is being paid to recognizing and treating those with depression who experience less than full remission of symptoms, which has led recently to a much-enhanced appreciation of just how common yet frequently neglected somatic symptoms are in mood and anxiety disorders.⁹⁻¹⁴ Targeting both 5-HT and NE in neuronal circuits that mediate somatic symptoms is the therapeutic strategy most widely employed to reduce these somatic

Table 1. Affective Spectrum Disorder

Mood disorders
Major depressive disorder
Dysthymic disorder
Premenstrual dysphoric disorder
Anxiety disorders
Generalized anxiety disorder
Panic disorder
Obsessive-compulsive disorder
Posttraumatic stress disorder
Social phobia/social anxiety disorder
Painful somatic disorders
Fibromyalgia
Irritable bowel syndrome
Migraine
Others
Attention-deficit/hyperactivity disorder
Bulimia nervosa
Cataplexy

symptoms in depression and thus result in more remission.⁷

Treating Somatic Symptoms When the Patient Is Not Depressed

Although the actions of antidepressants on somatic symptoms in MDD are becoming widely recognized,⁷ it is only now becoming apparent that conditions with somatic symptoms but without sadness or depressed mood (Table 2) may also be treated by these same agents, especially those with dual 5-HT/NE actions.

If the brain circuits that mediate somatic symptoms in these conditions overlap with those that mediate somatic symptoms in MDD yet are independent of the brain circuits that mediate sadness and depressed mood, it would not be necessary for sadness to be present in order for antidepressants to be therapeutic for such somatic symptoms. Although many conditions characterized as functional somatic syndromes have a high degree of comorbidity with depression, a considerable body of evolving yet still preliminary data suggests that antidepressants may be useful in reducing somatic symptom

Take-Home Points

- ◆ All known antidepressants act upon monoamine neurotransmitter systems, usually by inhibiting a presynaptic transporter often called a reuptake pump. This psychopharmacologic action has resulted not only in effective antidepressants but also broadly useful anxiolytics across a spectrum of affective and anxiety disorders.
- ◆ Patients who suffer primarily from an affective or anxiety disorder commonly experience somatic symptoms that are distressing or even painful and which must be eliminated by antidepressant treatment for full remission of the affective or anxiety disorder to occur.
- ◆ A very high number of patients suffer from distressing or even painful somatic symptoms that are not recognized as part of an affective or anxiety disorder but are increasingly being shown nevertheless to respond to treatment with antidepressants. This treatment response represents a potential opportunity to expand the vistas of antidepressant therapy to a wider range of functional somatic syndromes.

burden in functional somatic syndromes.^{5,6} Validating the usefulness of antidepressants in functional somatic syndromes could lead to fulfilling a significant unmet need for disorders that are very common yet have no currently approved treatments and would usher in an entirely new era for therapeutic applications of antidepressants. ◆

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Table 2. Functional Somatic Syndrome

Conditions with prominent painful somatic symptoms
Fibromyalgia
Chronic cervical or lumbar back pain
Irritable bowel syndrome
Temporomandibular joint syndrome
Interstitial cystitis/female urethral syndrome/vulvodynia
Primary dysmenorrhea
Regional musculoskeletal pain/myofascial pain syndrome
Chronic tension headache
Non-cardiac chest pain
Burning mouth syndrome
Conditions with distressful and often vague somatic symptoms
Chronic fatigue syndrome
Somatoform disorder
Multiple chemical sensitivity
Exposure syndromes (Gulf War illnesses; "sick-building syndrome")

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