Does Depression Hurt?

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Issue: *Depression, a disorder of mood, is also associated with painful physical symptoms that are often not emphasized.*

Is Depression in Your Mind or in Your Body?

Depression is primarily characterized as an illness with emotional symptoms, such as anxiety, and vegetative symptoms, such as sleep disturbance, so it is not surprising that a great deal of emphasis is placed on the recognition and treatment of depressed mood and these commonly associated symptoms. On the other hand, depression is also an illness that frequently presents with a large number of unexplained physical symptoms. Such symptoms are often not emphasized and are even excluded as components of the formal DSM-IV diagnostic criteria for major depressive disorder. In fact, 8 of the 9 formal diagnostic criteria for a major depressive episode list various emotional and vegetative symptoms with only 1 criterion for the physical symptom of fatigue or loss of energy and no mention of painful physical symptoms.[1]

Does Depression Hurt?

In primary care practices, up to 80% of depressed patients present exclusively with physical symptoms that can include headache, abdominal pain, and musculoskeletal pains in the lower back, joints, and neck.[2] If such painful physical symptoms are so common in depression, and may even be the only presenting symptoms in significant numbers of patients, why aren't they emphasized more in the recognition of depression? One possible reason is that such complaints, especially in primary care practices, may be interpreted as symptoms of a somatic illness and lead only to a workup for medical illness. While most physicians respond to psychological and emotional complaints with a high index of suspicion for anxiety or depression, many physicians may be misled into an exhaustive search for somatic causes without considering depression in patients who complain of fatigue, low energy, and painful physical ailments but not emotional or vegetative symptoms. To attain a complete remission of depression, it is now the recognized standard of care in managing depressed patients that all symptoms—emotional, vegetative, and painful—must be eliminated.[3]

"Look out, Descartes! We're crossing the mind-body divide!"

For many years, it has been widely hypothesized that the monoamine neurotransmitters serotonin and norepinephrine are involved in the pathophysiology of depression.[4] Both the serotonin and norepinephrine systems have their most important cell bodies in small areas of the brainstem that serve as headquarters for sending axonal projections throughout the brain in specific pathways that mediate specific functions. Multiple serotonergic and noradrenergic pathways may be dysfunctional in depression, generating many different symptoms.

What has been relatively neglected until recently is that the headquarters for the monoamine cell bodies also send axonal projections down the spinal cord where they act as key homeostatic regulators by determining whether one should be vigilant either to external threats or to sensations coming from the internal milieu of the body.[5] Normally, the sensations associated with routine functioning of the body, such as autonomic input from the stomach during digestion as well as somatic input from the musculoskeletal system, are suppressed from consciousness so that attention can be paid to more important events outside of the body. These regulators may be at work, for example, when a person is shot and yet feels no pain until the attackers have been outrun or when a person who is jogging begins to have a stomachache that disappears as soon as the jogger must run from a feral dog. Descending serotonergic and noradrenergic pathways normally help to

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suppress such routine body input even when it causes minor discomfort. It now seems possible, however, that a malfunctioning of these descending serotonergic and noradrenergic pathways could allow routine sensory input to be interpreted as uncomfortable or even painful physical symptoms.[5] Thus, many depressed patients complain of headache, abdominal pain, or musculoskeletal pain in the lower back, joints, and neck as well as fatigue and loss of energy. Instead of being suppressed, these sensations escape up the spinal cord and into the brain where they are interpreted as pain. This malfunction may be the reason no pathologic explanations for multiple physical symptoms turn up during medical evaluation of depressed patients.

Treating Depression in Your Body as Well as Pain in Your Brain

Response in depression has long been defined as at least a 50% reduction in emotional and vegetative symptoms, which can be attributed to drugs that boost serotonin, norepinephrine, or both. A 100% reduction in symptoms of depression would be possible if we raised the bar for treatment and also eliminated the painful symptoms. Now that we better understand the psychopharmacology of depression, we have the ability to go for the gold and eliminate all symptoms, including painful ones, not just reduce some of them. Any antidepressant can result in remission of all symptoms in some patients, but chances of remission are significantly enhanced if a dual-action antidepressant, acting to inhibit the reuptake of both serotonin and norepinephrine, is given.[6] Agents with these pharmacologic properties are listed in Table 1, including some new agents in clinical trials[7] or available in Europe and Japan.

Take-Home Points

- Although the diagnostic criteria emphasize emotional and vegetative symptoms, depression is also frequently associated with painful physical symptoms, such as headache, backache, stomachache, and joint and muscle aches.
- The neurotransmitters serotonin and norepinephrine may regulate not only the emotional and vegetative symptoms of depression but also the painful physical symptoms of depression.
- Antidepressants that block reuptake of both serotonin and norepinephrine may have a greater chance of eliminating painful physical symptoms and lead to remission of depression.

Table 1. Dual-Action Reuptake Inhibitors

Most tricyclic antidepressants
Venlafaxine
Milnacipran (approved in Europe and Japan; testing for fibromyalgia in the U.S.)
Duloxetine (in late clinical development)

The importance of removing physical symptoms of depression can not be overemphasized[8]—the return of normal energy, motivation, and interest and the loss of the sense of fatigue and listlessness as well as the elimination of painful physical symptoms are required before a patient has complete remission from major depressive disorder. Neglecting the treatment of fatigue, low energy, and painful physical symptoms in depressed patients can lead to unsatisfactory outcomes, characterized by a failure of depressed patients to return to normal social and occupational functioning. On the other hand, targeting monoamine pathways for both serotonin and norepinephrine in not only the brain but also the spinal cord with antidepressants may prove to be the best strategy to achieve remission of symptoms and the most favorable outcomes from depression.

Summary

Depression is an illness that causes symptoms in both the body and the brain, i.e., painful physical as well as emotional and vegetative symptoms. Ascending serotonergic and noradrenergic pathways may mediate the emotional and vegetative symptoms of depression and can potentially be targets of serotonin and norepinephrine reuptake inhibitors to obtain relief of these symptoms. Descending serotonergic and noradrenergic pathways may regulate the painful physical symptoms of depression, and when targeted by serotonin and norepinephrine reuptake inhibitors, relieve these symptoms as well. Selective serotonin reuptake inhibitors have a remission rate of 35%, and dual-action reuptake inhibitors have a 45% remission rate.[6] Despite these results, the best treatment of depression currently recognizes the 3 types of symptoms and targets them all for complete remission no matter which drug is used. ◆

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