Insomnia and Depression: If it Looks and Walks Like a Duck…


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WHILE A NUMBER OF PSYCHIATRISTS WITH AN INTEREST IN INSOMNIA AND MOOD DISORDERS HAVE LINKED THE TWO,1,2 MY READING OF THE LITERATURE has given me the sense that psychiatric sleep specialists have been reluctant to use the “C” word, (ie, the “cause” word). One can find many statements in the literature along the lines that: “major depressive disorder is associated with sleep disturbance…” or “…sleep is biologically linked to mood disorders…” However, even though it is recognized that episodes of depression are often preceded by many weeks of poor sleep,3,4 few investigators have used the “C” word and state, “Insomnia causes depression.” In her recent excellent review of sleep disorders and mood disorders,1 Ruth Benca raises the important, unanswered question, “…does the abnormal sleep pattern specifically lead to an increased susceptibility to depression, as suggested by some of the longitudinal and family studies?” Benca makes a convincing case that all individuals with sleep complaints should be examined for possible mood disorders in view of the strong association between sleep disturbance and mood disorders. David Kupfer has also noted that the effective management of insomnia in depressed patients can markedly improve their depression.3 However, let me go one step further and throw down a gauntlet and state, “Insomnia causes major depression—and possibly other mood disorders.” Of course, not all insomniacs will become depressed, and not all major depression is caused by insomnia. However, if insomnia is a primary cause of at least some significant percentage of depression, then treating insomnia should perhaps be considered as a frontline therapeutic intervention for depression.

A paper in this issue of SLEEP by Taylor and colleagues reaffirms the close relationship of insomnia and depression (as well as anxiety), using empirically validated diagnostic criteria for insomnia.5 The study found that people with insomnia were 9.82 times more likely to have “clinically significant” depression than noninsomniacs, and increased insomnia frequency and increased number of awakenings were related to increased depression. While numerous previous studies have found significant relationships between insomnia and depression, the Taylor et al study is the first to exclude individuals with an organic sleep disorder and to control for possible confounding variables for other possible explanations of the relationship. The link is clear even if the cause is not.

It has been estimated that more than 90% of patients suffering from major depression also have sleep disturbances,6 a truly huge correlation linking these 2 biomedical disorders. Of course, such correlations and the strong associations between depression and insomnia do not provide any information on causality. However, as Benca has noted, it has historically been “assumed” (my quotes) that mood disorders “cause” changes in sleep patterns.1 While this may be a historical truth, is it any more or less likely to hypothesize or assume that disturbed sleep patterns cause mood disorders? The middle ground here is to hypothesize that common neural substrates that underlie both mood and the sleep-wake cycle, when altered, can lead to disruption in both mood and sleep. Indeed, animal studies support the hypothesis that common neural substrates may underlie disturbed sleep and mental health. In 2 animal models for depression, the Wistar-Kyoto rat and the Flinders Sensitive Line rat, alterations in the sleep-wake cycle that are similar to those observed in depressed patients have been observed.7,8 Although it has been difficult to create validated and high-fidelity animal models for insomnia, the creation of such models could lead to new insights into the causative effects of insomnia for depression. Given the considerable neuroanatomic and pharmacologic data linking the regulation of the sleep-wake cycle and mood, this duality-of-effect hypothesis has considerable merit.9,10

However, it is difficult to evoke the common-cause hypothesis when disturbed sleep can predate depression by many weeks. Strong support for disturbed sleep as a cause of depression comes from recent longitudinal studies, indicating that insomnia can precede episodes of depression by about 5 weeks.11 The hypothesis here is not only that disordered sleep can bring on an episode of depression, but also that treating the insomnia may prevent or shorten the period of depression. Evidence of insomnia being a causal factor comes from Perlis and colleagues, who reported a strong link between insomnia and the maintenance of depression at the 2005 meeting of the Associated Professional Sleep Societies.12 After following 1801 men and women over the age of 65 diagnosed with depression, they found that individuals suffering from insomnia were 4.7 and 10.8 times more likely to be depressed 6 and 12 months later, respectively, than noninsomniacs.12 A variety of symptoms are associated with insomnia, including, fatigue, difficulty in concentration, irritability and the loss of interest in social activities,1 events that could lead to a smooth transition from insomnia to depression.

An approach that holds great promise of going from the bench to the bedside for gaining new insights into the cause-and-effect relationships between insomnia and depression involves genetics. To date, it has not been possible to identify depression genes in humans, presumably due to the multigene basis of mood disor-
ders. It may be difficult to use animal models for elucidating the underlying genetics basis for depression, given the difficulty in defining and equating depression in rodents with that of humans (although, see Ohl et al13 and Holmes et al14 for promising new genetic models of depression). However, a few laboratories are using both forward and reverse genetic approaches in rodents (and flies) to identify the genes involved in the regulation of the sleep-wake cycle.15-17 Identifying how specific genetic changes impact the sleep-wake cycle in animal models, and how such changes affect symptoms of depression in these models, may provide a better understanding of the interrelationships between the control of sleep and mood. Indeed, it may well be that some of the elusive “depressive genes” are also “sleep genes.”

In a relatively small, and limited in design, study out of Australia,18 it was reported that 70% of depressed insomniac subjects (N = 49), who improved their sleep through a nonpharmacologic approach, showed a reduction or elimination of their depression. In contrast, all 7 subjects not sleeping better showed no improvement. Such preliminary data, along with an extensive “suggestive” literature, call for comprehensive clinical trials to (1) determine if early treatment of insomnia can prevent and/or attenuate subsequent episodes of depression and (2) whether treating the insomnia of a depressed patient is itself an antidepressant therapy.

Interestingly, a recent study, again reported at this year’s Associated Professional Sleep Societies meeting in Denver, indicates that taking a hypnotic in combination with Prozac on a long-term basis had a greater effect in reducing or eliminating depression than did the use of Prozac alone.19 Perhaps it is time for head-to-head clinical trials comparing insomnia treatment with Paxil, Zoloft, Prozac, or other antidepressants for the treatment of depression. The recent availability of hypnotics that have been approved for clinical trials examining the effectiveness of hypnotics (or nonpharmacologic approaches for the treatment of insomnia) in the treatment of depression associated with insomnias.

In the absence of clinical trials examining the effectiveness of treating insomnia for either preventing depression and/or as an effective treatment for depression, one can only note the “strong association” between depression and insomnia, and the finding that insomnia often precedes the onset of depression by many weeks, as indicators that there is a causal effect of insomnia leading to depression. However, when taken in total, the data indicate that “it looks like a duck, walks like a duck, talks like a duck,” but is it a duck?

REFERENCES