Insomnia, Psychiatric Disorders, and the Transdiagnostic Perspective

Allison G. Harvey

University of California, Berkeley

ABSTRACT—*Insomnia commonly occurs along with other psychiatric disorders. I aim to address two issues that arise from this observation. First, insomnia is commonly assumed to be epiphenomenal to the so-called "primary" psychiatric disorder. On the basis of new evidence, I argue instead that insomnia may be an important but under-recognized mechanism in the multifactorial cause and maintenance of psychiatric disorders. Second, insomnia may be a* transdiagnostic *process—a process that is common across psychiatric disorders. The move to identify and study transdiagnostic processes contrasts with the standard "disorder focused" approach in which classification systems and research programs specialize in a single disorder. The latter approach can neglect the intriguing and potentially important similarities across disorders. If it were feasible to develop transdiagnostic treatments, the public health implications would be startling. Research on the role of sleep in psychiatric disorders and tests of the validity and utility of a transdiagnostic approach provide rich opportunities for improving our understanding of, and the treatment of, psychiatric disorders.*

KEYWORDS—*sleep; insomnia; transdiagnostic approach; psychiatric disorders*

The best bridge between despair and hope is a good night's sleep.

E. Joseph Cossman

Sleep disturbance commonly accompanies psychiatric disorders. Its manifestations in different patient groups are numerous and include insomnia, hypersomnia, delayed sleep phase, circadian dysregulation, nightmares, and nocturnal panic attacks. Analyses of sleep architecture have observed abnormalities in rapid-eye-movement sleep and slow-wave sleep in certain disorders (Benca, Obermeyer, Thisted, & Gillin, 1992). Moreover, several puzzling sleep-related findings have emerged. For example, a rapid improvement in mood is observed in 40 to 60% of depressed unipolar and bipolar patients following total or partial sleep deprivation (Barbini et al., 1998). However, the symptoms of depression quickly return when the patient sleeps.

There is a paucity of data to solve many of the puzzles raised by the published sleep-related observations, with one exception: A burgeoning evidence base has been developing on insomnia. Insomnia is ongoing difficulty initiating or maintaining sleep, waking up too early, or experiencing chronically nonrestorative sleep. Table 1 highlights the range and number of psychiatric disorders for which insomnia is explicitly listed as a symptom. Moreover, it is a known common feature of a range of other psychiatric disorders that do not list it as a formal symptom—including social phobia, panic disorder, autism, chronic pain, and the eating disorders. Rates of comorbidity (co-occurrence) between insomnia and other psychiatric disorders among those presenting to a health facility average 53% and among community samples average 41.7% (Harvey, 2001). The rates are even higher when clinically significant insomnia that doesn't quite fulfill all diagnostic criteria is recognized. The goal of this paper is to address two questions that arise from recognizing the comorbidity between insomnia and psychiatric disorders.

QUESTION 1: IS INSOMNIA AN EPIPHENOMENON OR A MECHANISM?

A widely held assumption is that insomnia is secondary to, or an epiphenomenon of, the so-called "primary" psychiatric disorder. Consequently, complaints of insomnia have tended to be dismissed or regarded as trivial by both patients and their caregivers, or they are seen, at most, as a byproduct of the coexisting disorder. This is not a trivial issue. If insomnia is found to be epiphenomenal to the "other" disorder, then research effort and clinical intervention will

Address correspondence to Allison G. Harvey, Psychology Department, Sleep and Psychological Disorders Lab, University of California, 3210 Tolman Hall #1650, Berkeley, CA 94720-1650; e-mail: aharvey@berkeley.edu.

TABLE 1

DSM-IV-TR Diagnoses Listing Sleep Disturbance as a Criterion (Excluding the Sleep Disorders Section; American Psychiatric Association, 2000)

Diagnosis	DSM-IV-TR criteria
Separation anxiety disorder	Persistent reluctance or refusal to go to sleep without being near a major attachment figure or to sleep away from home*
	Repeated nightmares involving the theme of separation**
Alcohol withdrawal	Insomnia**
Amphetamine withdrawal	Insomnia or hypersomnia**
Caffeine intoxication	Insomnia**
Cocaine withdrawal	Insomnia or hypersomnia**
Nicotine withdrawal	Insomnia**
Opioid withdrawal	Insomnia**
Sedative, hypnotic, or anxiolytic withdrawal	Insomnia**
Major depressive disorder	Insomnia or hypersomnia nearly every day**
Dysthymic disorder	Insomnia or hypersomnia**
Bipolar disorder	Manic or hypomanic episode = decreased need for sleep**
	Depressive episode = insomnia or hypersomnia**
Posttraumatic stress disorder	Recurrent distressing dreams of the event**
	Difficulty falling or staying asleep**
Acute stress disorder	Reexperiencing of the traumatic event in dreams**
	Difficulty sleeping**
Generalized anxiety disorder	Sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)**
Diagnoses listed in the DSM-IV-TR as warranting further study	
Postconcussional disorder	Disordered sleep**
Premenstrual dysphoric disorder	Hypersomnia or insomnia**
Minor depressive disorder	Insomnia or hypersomnia nearly every day**
Mixed anxiety-depressive disorder	Sleep disturbance (difficulty falling } asleep or restless unsatisfying sleep)**

Note. *= symptom *must* be present, **= symptom is one of a *choice* of symptoms that must be present.

be most productive if focused on the other disorder. Conversely, if insomnia is found to be a clinical entity in its own right, research effort and clinical intervention must be focused on the insomnia (Harvey, 2001; Smith, Huang, & Manber, 2005).

Four lines of evidence suggest that insomnia is not necessarily epiphenomenal.

Importance of Sleep in Psychiatric Disorders

First, insomnia appears to be a risk factor for, and can contribute to the development and/or maintenance of, psychiatric disorders.

A robust finding is that insomnia is a significant risk factor for both a first episode of depression and for recurrent depressive episodes (e.g., Perlis et al., 2006). Moreover, insomnia and fatigue are the most common residual symptoms after the treatment of depression. The latter finding prompted a comparison between treating the depression only versus treating both the depression (with Escitalopram, an antidepressant) and the insomnia (with cognitive behavior therapy for insomnia). The combined approach was superior for both depression and insomnia outcomes (Manber et al., 2008).

The case for insomnia contributing to mood disturbance in bipolar patients is also compelling: Sleep loss is highly correlated with daily manic symptoms; among patients with bipolar disorder, insomnia is the most common preliminary symptom of mania and is a common preliminary symptom of depression; and induced sleep deprivation triggers hypomania or mania in a proportion of patients (Harvey, Mullin, & Hinshaw, 2006).

Persistent insomnia is associated with an increased risk of developing an anxiety disorder (Breslau, Roth, Rosenthal, & Andreski, 1996). Moreover, insomnia predicts the subsequent development of posttraumatic stress disorder (PTSD), and treating insomnia that is comorbid with PTSD improves the sleep problem and the PTSD symptoms (Krakow et al., 2001).

Parents of children with attention-deficit hyperactivity disorder (ADHD) report a two- to threefold higher rate of sleep disturbance in their children, compared to controls. Given that sleep deprivation increases irritability and aggression in both human and animal studies, it is more than tempting to speculate that the insomnia experienced by children with ADHD is not just a correlate but contributes to maintaining the disorder (Dahl & Harvey, 2007).

Importance of Sleep for Quality of Life

There is substantial evidence that insomnia (in the absence of another comorbid psychiatric disorder) impairs quality of life and incurs great personal costs due to economic and social disability. Consequences of insomnia include functional impairment, work absenteeism, impaired concentration and memory, and increased use of medical services (Roth & Ancoli-Israel, 1999). These consequences of poor sleep seem highly likely to contribute to the functional impairment experienced by patients with psychiatric disorders.

Importance of Sleep for Mood Regulation

Evidence from the sleep-deprivation literature suggests that one of the strongest adverse effects of sleep deprivation is increased negative mood. For example, Dinges et al. (1997) restricted the sleep of healthy nonpatient participants to 5 hours per night for one week. Mood disturbance progressively increased as sleep deprivation accumulated throughout the week. Bolstering this evidence are findings from functional imaging studies. For example, healthy participants who were sleep deprived for

35 hours or who had slept normally completed a task in which they viewed 100 images varying in emotional intensity while undergoing functional magnetic resonance imaging (fMRI; Yoo, Gujar, Hu, Jolesz, & Walker, 2007). Both groups exhibited amygdala activation to negative picture stimuli. This was expected, given that the amygdala is involved in the generation of emotions and the development of emotional memories. However, relative to those who slept normally, those who were sleep deprived exhibited more than 60% greater amygdala activity, and this large increase was associated with a loss of activity in the medial-prefrontal cortex (MPFC). The MPFC exerts top-down control on the limbic area (including the amygdala) and functions to modulate emotional responses so they are appropriate for the context. In other words, sleep contributes to maintaining connectivity between the MPFC and amygdala, which is critical for responding appropriately to emotional challenges the next day.

Importance of Sleep for Cognitive Functioning

A number of studies have shown adverse effects of sleep deprivation on cognitive functioning. For example, a study of young adults whose sleep was restricted for 4, 6, or 8 hours a night over 14 nights showed a dose-response decrement in performance on a psychomotor vigilance task, a working-memory task, and a serial addition/subtraction task (Van Dongen, Maislin, Mullington, & Dinges, 2003). A recent report by Walker and Stickgold (2006) demonstrates a critical role for sleep during the encoding and consolidation of memories. Participants were assigned to either 36 hours of sleep deprivation or were allowed to sleep normally. They then performed an incidental memory encoding task comprised of emotionally neutral, negative, and positive words. Relative to the normal sleepers, those who were sleep deprived exhibited a 40% decrement in memory retention across all word types. The most profound decrement was evident for positive words. The potential implications for patients with psychiatric disorders are provocative; one pathway by which insomnia may contribute to maintenance of symptoms and impairment may be poorer memory for the positive domains or events in their lives.

INTEGRATION: A BIDIRECTIONAL VICIOUS CYCLE?

How might insomnia and psychiatric disorders co-occur? Drawing on existing theories (Dahl, 1996; Wehr, 1990) and the convergent evidence presented, I suggest the following simple model can be valuable as an initial organizing structure for the existing and future research.

I suggest that there is a bidirectional relationship between sleep dysfunction and daytime symptoms and processes of psychiatric disorders, such that an escalating vicious cycle of disturbance in mood and symptoms during the day interferes with nighttime sleep and the effects of sleep deprivation contribute to mood-regulation difficulty and symptoms on the subsequent day. There is preliminary evidence for this simple model.

Evidence that daytime symptoms and processes of psychiatric disorders disturb sleep includes the findings that presleep mood and stress delay sleep onset and influence the content of dreaming, the emotion within a dream, the latency to rapid eye movement (REM) sleep, and REM density (number of eye movements; e.g., Nielsen, 2004). As articulated by Dahl (1996), these effects likely reflect that emotion or mood states and sleep are opponent processes. Going to sleep requires us to turn off our awareness and drop our vigilance to potential threats in the external world. Hence, sleep is naturally restricted to safe times and places (e.g., animals and birds tend to sleep in safe burrows, nests, or niches that minimize dangers). Hence, individuals experiencing presleep emotional and mood states often have difficulty getting to sleep. This system has adaptive advantages (inhibiting sleep when we are in danger) but clearly also has costs (Dahl, 1996).

QUESTION 2: IS INSOMNIA TRANSDIAGNOSTIC?

Revisiting themes from the early behavior therapists, there has been a resurgence of interest in explicitly identifying and studying "transdiagnostic" processes, those that are common across psychiatric disorders (Fairburn, Cooper, & Shafran, 2003). This is in contrast to the common "disorder focused" approach, in which classification systems and research programs specialize in a single disorder, seeking to systematically illuminate that disorder's cause, maintenance, and treatment. The transdiagnostic perspective argues that a disorder-focused research strategy can neglect the interesting and marked similarities across disorders.

It has been suggested that transdiagnostic processes may operate at various levels of explanation. At the biological level, it is possible that there may be abnormalities in brain structures (amygdala), circuitry (dopaminergic and serotonergic pathways), and genes (e.g., serotonin transporter gene, COMT) that are transdiagnostic. Recognition of transdiagnostic processes may also be relevant to personality (e.g., neuroticism), social factors (e.g., the role of the family), emotional processes (e.g., amplitude of the emotional response and regulation), and contextual factors (e.g., poverty). Considerable evidence suggesting that certain cognitive and behavioral processes are common across psychiatric disorders has accrued (see Harvey, Watkins, Mansell, & Shafran, 2004, for review).

I propose that consideration be given to insomnia as a transdiagnostic process on the basis of (a) the high rates of co-occurrence between insomnia and psychiatric disorders; (b) the evidence across a range of disorders that the insomnia is not an epiphenomenon but contributes to onset, relapse, and maintenance; and (c) the transdiagnostic applicability of the bidirectional sleep-and-mood model just presented. As with

other transdiagnostic processes, the advantages of explicitly recognizing insomnia as a transdiagnotic process are threefold (Harvey et al., 2004).

First, the results of the National Comorbidity Survey make a strong case for the relative rarity of "pure" cases (i.e., a single mental illness occurring by itself). The vast majority of the lifetime disorders are comorbid disorders. A transdiagnostic perspective argues that perhaps disorders co-occur because they share common mechanisms (e.g., insomnia).

Second, if some psychiatric disorders are similar with respect to the processes that maintain them, then advances made in the context of one disorder will be more rapidly tested for their application to other disorders. This already happens to some extent, but transfer is often alarmingly slow. The transdiagnostic perspective should lead to more rapid transfer of advances to a broader range of disorders.

Third, a transdiagnostic approach might lead to the specification of a single treatment or treatment components that are effective across a wide range of disorders. For example, a fascinating possibility with massive public health implications is the potential for developing and testing a transdiagnostic sleep intervention, a possibility to which I will return below.

It is emphasized that a transdiagnostic perspective recognizes that some processes are specific to certain disorders or certain groups of disorders. It may be that such "unique" processes contribute to the apparent differences between disorders. Future research will need to determine if insomnia is universally transdiagnostic or is a process that is common across a range of disorders but not occurring in every disorder (Harvey et al., 2004).

FUTURE RESEARCH

Future research to explore the potentially wide-reaching public health implications of this approach is needed. First, is it possible to develop one treatment protocol—a transdiagnostic treatment—that effectively treats insomnia in all psychiatric disorders? Or will disorder-specific adaptations be required? Unlike disorder-specific treatment protocols, a transdiagnostic treatment would have the great advantage of easy dissemination, reducing the heavy burden on clinicians, who must already learn multiple treatment protocols that often share many common theoretical underpinnings and interventions. Second, given the association between poor sleep and impaired quality of life, does improving sleep improve the functioning of individuals with a range of psychiatric disorders? Finally, if insomnia and the symptoms and processes of psychiatric disorders are mutually maintaining, then does a transdiagnostic treatment also reduce symptoms and processes associated with the comorbid psychiatric disorder?

As highlighted at the outset, there are other sleep disturbances exhibited by patients with psychiatric disorders. The prevalence and significance of these other sleep phenomena are yet to be determined. It will also be important to distinguish between evidence that implicates sleep disturbance as a trigger or precipitant of psychiatric disorders and sleep disturbance that perpetuates another, comorbid psychiatric disorder.

Insomnia and circadian-rhythm disturbance have both been implicated across psychiatric disorders. However, they are not identical processes. Although there is an interaction between them, the amount and patterning of sleep depends on many factors (e.g., life stress), of which the circadian rhythm is only one. Future research to parse out the independent contribution of sleep versus circadian influences in psychiatric disorders is needed.

A particularly important goal for future research will be to grapple with the distinction between insomnia, which is a *subjective perception* of a sleep deficit, and *sleep deprivation*, which is an objectively measured decrement in sleep. It is possible that the two may coincide in the majority of cases. In adults with insomnia, subjectively reported sleep complaints are more highly prevalent and objective evidence of sleep abnormalities can be more elusive. Studies including high-quality assessments of both subjectively perceived and objectively measured sleep across psychiatric disorders are needed.

Finally, a simple bidirectional model has been presented as an initial organizing structure for existing and future research. Next steps include determining the role of REM sleep and the associated neural mechanisms, including associations between the circadian, serotonin, and dopamine systems.

Recommended Reading

Harvey, A.G., Watkins, E., Mansell, W., & Shafran, R. (2004). (See References). A comprehensive review of the potential value and validity of a transdiagnostic approach to psychiatric disorders, with a focus on cognitive and behavioral processes.

Smith, M.T., Huang, M.I., & Manber, R. (2005). (See References). A clearly written paper that presents evidence that insomnia is an important mechanism across a broad range of psychiatric and medical disorders.

Van Dongen, H.P., Maislin, G., Mullington, J.M., & Dinges, D.F. (2003). (See References). A nicely designed study that addresses the impact of sleep deprivation on cognitive functioning.

Yoo, S., Gujar, N., Hu, P., Jolesz, F., & Walker, M. (2006). (See References). An innovative study that addresses the impact of sleep deprivation on brain functioning, with implications for emotional functioning.

Acknowledgments—This research is supported by NARSAD. I gratefully acknowledge N. Dagys, P. Eidelman, R. Dahl, A. Gershon, J. Gruber, I. Hairston, K. Kaplan, E. McClinchey, L. Talbot, and M. Walker.

REFERENCES

American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorders (4th ed., text revision). Washington, DC: Author.

Barbini, B., Colombo, C., Benedetti, F., Campori, E., Bellodi, L., & Smeraldi, E. (1998). The unipolar–bipolar dichotomy and the response to sleep deprivation. *Psychiatry Research*, *79*, 43–50.

Benca, R.M., Obermeyer, W.H., Thisted, R.A., & Gillin, J.C. (1992). Sleep and psychiatric disorders: A meta-analysis. *Archives of General Psychiatry*, *49*, 651–668.

Breslau, N., Roth, T., Rosenthal, L., & Andreski, P. (1996). Sleep disturbance and psychiatric disorders: A longitudinal epidemiological study of young adults. *Biological Psychiatry*, *39*, 411–418.

Dahl, R.E. (1996). The regulation of sleep and arousal: Development and psychopathology. *Development and Psychopathology*, *8*, 3–27.

Dahl, R.E., & Harvey, A.G. (2007). Sleep in children and adolescents with psychiatric or emotional disorders. *Sleep Medicine Clinics*, *2*, 501–511.

Dinges, D.F., Pack, F., Williams, K., Gillen, K.A., Powell, J.W., & Ott, G.E., et al. (1997). Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. *Sleep*, *20*, 267–267.

Fairburn, C.G., Cooper, Z., & Shafran, R. (2003). Cognitive behaviour therapy for eating disorders: a "transdiagnostic" theory and treatment. *Behaviour Research and Therapy*, *41*, 509–528.

Harvey, A.G. (2001). Insomnia: Symptom or diagnosis? *Clinical Psychology Review*, *21*, 1037–1059.

Harvey, A.G., Mullin, B.C., & Hinshaw, S.P. (2006). Sleep and circadian rhythms in children and adolescents with bipolar disorder. *Development and Psychopathology*, *18*, 1147–1168.

Harvey, A.G., Watkins, E., Mansell, W., & Shafran, R. (2004). *Cognitive behavioural processes across psychological disorders: A transdiagnostic approach to research and treatment*. Oxford: Oxford University Press.

Krakow, B., Johnston, L., Melendrez, D., Hollifield, M., Warner, T.D., Chavez-Kennedy, D., et al. (2001). An open-label trial of evidence-based cognitive behavior therapy for nightmares and insomnia in crime victims with PTSD. *American Journal of Psychiatry*, *158*, 2043–2047.

Manber, R., Edinger, J., Gress, J.L., San-Pedro-Salcedo, M.G., Kuo, T.F., & Kalista, T. (2008). Cognitive behavioral therapy for insomnia enhances depression outcome in patients with comorbid major depressive disorder and insomnia. *Sleep*, *31*, 489–495.

Nielsen, T.A. (2004). Chronobiological features of dream production. *Sleep Medicine Review*, *8*, 403–424.

Perlis, M.L., Smith, L.J., Lyness, J.M., Matteson, S.R., Pigeon, W.R., Jungquist, C., et al. (2006). Insomnia as a risk factor for onset of depression in the elderly. *Behavioral Sleep Medicine*, *4*, 104–113.

Roth, T., & Ancoli-Israel, S. (1999). Daytime consequences and correlates of insomnia in the United States: Results of the 1991 National Sleep Foundation Survey. II. *Sleep*, *22*(Supl. 2), S354–S358.

Smith, M.T., Huang, M.I., & Manber, R. (2005). Cognitive behavior therapy for chronic insomnia occurring within the context of medical and psychiatric disorders. *Clinical Psychology Review*, *25*, 559–592.

Van Dongen, H.P., Maislin, G., Mullington, J.M., & Dinges, D.F. (2003). The cumulative cost of additional wakefulness: Dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep*, *26*, 117–126.

Walker, M.P., & Stickgold, R. (2006). Sleep, memory, and plasticity. *Annual Review of Psychology*, *57*, 139–166.

Wehr, T.A. (1990). Effects of wakefulness and sleep on depression and mania. In J. Montplaisir & R. Godbout (Eds.), *Sleep and biological rhythms: Basic mechanisms and applications to psychiatry* (pp. 42–86). London: Oxford University Press.

Yoo, S., Gujar, N., Hu, P., Jolesz, F., & Walker, M. (2007). The human emotional brain without sleep: A prefrontal–amygdala disconnect? *Current Biology*, *17*, R877–R878.