

“Comorbid” Insomnia

Rest is a basic biological need. Sleep is a vital, highly organized process regulated by complex systems of neuronal networks and neurotransmitters. Sleep has an important role in the regulation of CNS and body physiologic functions, regulating metabolism, catabolism, temperature, learning, and memory consolidation.^[1] Sleep architecture is easily susceptible to external and internal disruption.

Insomnia is a symptom that arises from multiple environmental, medical, and psychological and mental disorders.^[2] Insomnia can be transient, short-term, or chronic in its presentation. In a typical psychiatric practice, 50-80% of adult patients experience significant problems with falling or staying asleep during any year.^[3] While 30-48% individuals report some problem in sleeping in a year, when diagnostic criteria were used for insomnia syndrome, 6% of the respondents indicated a disorder of insomnia that impaired daytime function.^[4] The insomnia syndrome becomes chronic when it is present for a month or longer and is defined by whether it is primary or associated with comorbid disorders. It is estimated that 10-15% of patients who have chronic insomnia are of primary origin. Insomnia that is comorbid with psychiatric disorders, medical disorders, circadian rhythm disorders, or substances or medications accounts for nearly 85-90% of chronic insomnia.^[4]

The Sleep Disorders Workgroup of the Diagnostic and Statistical Manual Committee of the American Psychiatric Association defines diagnostic criteria as problems of sleep onset, maintenance, early awakening, or nonrestorative sleep on more than half of the days for at least 1 month that are associated with significant daytime dysfunction that impair the performance of activities at home or work.^[5] The DSM-IV-TR^[14] segments chronic insomnia into primary insomnia or insomnia related to other conditions. A state-of-the-science conference held at the National Institute

of Health in 2005 described the circular rather than the linear association among insomnia, psychiatric disorders, and medical illness, suggesting the term “comorbid insomnia” to describe the association.^[6] Primary insomnia subsumes several insomnia diagnoses in the International Classification of Sleep Disorders^[7] including psychophysiologic insomnia, sleep-state misperception, idiopathic insomnia, and some cases of inadequate sleep hygiene.

In 2004, a workgroup of the American Academy of Sleep Medicine published criteria to be used in research trials for the insomnia syndrome.^[8] Research trials generally require a reported sleep-latency of 30 or more minutes to be eligible for enrollment. If the problem of sleep maintenance is to be studied, at least 30 minutes of wakefulness after sleep onset may be required, with many recent trials using 60 or more minutes of wakefulness. Sleep efficiency (time asleep while in bed) must be less than 85%. Although 1 month of sleep disturbance is required in the DSM-IV-TR for chronic sleep disturbance, many patients experience transient and short-term insomnia.^[9] Transient insomnia presents and then passes after a few days, typically developing during a brief adjustment reaction, rotating shifts, or international travel. Short-term insomnia is characterized by 4-28 days of poor sleep. The common precipitants for short-term insomnia include illness, job change, bereavement, dissolution of a relationship, or other significant life stressor.^[10]

Although the duration of the insomnia complaint is relevant to psychiatrists, the selection of therapeutic intervention may be better based upon the time of night that patients complain of sleep disturbance,^[11] namely, along a continuum of sleep onset, sleep maintenance and early awakening.

In the last decade, the view of the relationship between sleep and psychiatric disorders has undergone a radical change. There is an emerging perspective that unlike previously thought, there may be a more complex and bidirectional relationship between them.^[12] Sleep disturbances occurring in those who have psychiatric disorders have long been viewed as secondary symptoms of the associated psychiatric conditions.^[13] As the sleep problems are seen only as symptoms, this model focuses on the treatment of the underlying psychiatric illness while actually discouraging the treatment of the sleep difficulties present.

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SLEEP AND PSYCHIATRIC ILLNESSES

Major depression

Ninety percent of patients report insomnia or daytime sleepiness and it is one of the diagnostic criteria for the disorder.^[5,15] Consistent with the traditional model, non-sedating antidepressant treatment of patients who have insomnia co-occurring with depression resolves the sleep difficulty in majority of the cases.^[16-18]

Mania

Eighty percent of manic patients experience a decrease in the ability to sleep and a decreased need for sleep.^[5,19] Therapies for mania generally tend to be sedating, and sleep generally increases with treatment.^[20,21]

Anxiety disorders

Most commonly associated disorders are GAD and PTSD. It is a diagnostic criteria for these disorders, with majority of patients reporting problems in initiating or maintaining sleep.^[5,22] There is some evidence that SSRIs improve sleep in GAD^[23] while the data on sleep improvement after treatment in PTSD are inconsistent.^[12]

Schizophrenia

Sleep disturbances are not a diagnostic criteria for schizophrenia; however, sleep difficulties are common in this group.^[24,25] Most primary schizophrenia treatments generally enhance sleep, but there are no data on the effects of treatment on sleep in this population.^[12]

The challenge to the traditional symptom model comes from data that suggest a bidirectional relationship between sleep and psychiatric disorders, and the greatest evidence for the failure of the symptom model that has been obtained is related to sleep problems co-occurring with major depression. This evidence suggests that insomnia is not just a symptom and also has independent importance in terms of clinically relevant outcomes and the course of the disorder. Sleep disturbance seems to be associated with an independent increase in the risk of suicidal ideation and completed suicide.^[26,27] Insomnia also seems to predict a greater future risk of depression (and anxiety disorders and alcoholism).^[28-30] Residual insomnia after the otherwise successful antidepressant therapy is associated with an increased risk of depression relapse.^[31]

Data on the treatment of insomnia co-occurring with depression are the strongest blow to the symptom model. Initiating antidepressant treatment with a hypnotic agent in addition to an antidepressant medication leads not only to a greater improvement in sleep but also a faster and more complete antidepressant response.^[32,33] A placebo-controlled study of 545 patients identified

that the addition of eszopiclone (3 mg) to fluoxetine had a significant therapeutic effect not only on sleep but also on non-sleep features of depression.^[32] In addition, treatment of residual insomnia after the otherwise successful SSRI therapy with zolpidem (10 mg) resulted in a significant improvement in sleep and ratings of daytime function.^[34] If sleep were merely a symptom, targeting treatment of sleep difficulties with hypnotic therapy would not be expected to improve the antidepressant outcome over the administration of a therapeutic antidepressant regimen.

Despite the emergence of this new bidirectional approach, there are some key issues that need to be addressed. The evidence of hypnotics as cotherapy is limited to a few agents and the efficacy of other insomnia therapies including other medications and nonpharmacological therapies needs to be studied. It also appears that insomnia agents vary in the degree to which they are effective as cotherapies for depression.^[33] Also, another unresolved issue is whether benefits depend upon the antidepressant therapy implemented, as the current large-scale placebo-controlled trial was performed only with fluoxetine.^[32] Also important to determine is whether or not the same beneficial effects noted with cotherapy with antidepressants and hypnotics can be achieved with single-agent treatment with a sedating antidepressant like mirtazapine or TCA. Also, the timing of initiating insomnia therapy needs to be determined: whether to add insomnia treatment to the initial treatment regimen or wait to see if there is an incomplete response to the initial antidepressant therapy before initiating insomnia therapy. Ideally, the means should be developed to predict before initial therapy who is most likely to benefit from insomnia cotherapy. Also what needs to be established is the duration that cotherapy should continue for. Also, all the studies currently have been performed in patients with major depression; the same needs to be replicated in other psychiatric disorders. One objection to cotherapy may come from those practicing sleep deprivation as a treatment for major depression. The answer may lie in the fact that it is effective only in a subpopulation of cases and one of the side-effects of sleep deprivation therapy is actually worsening of depressive symptoms which actually supports the cotherapy model indirectly.

In patients diagnosed with chronic insomnia, major depression (14% of all cases), dysthymia (9% of all cases), and anxiety disorders (24% of all cases) are commonly comorbid with insomnia.^[35] When patients report disturbances in their sleep, its significance in relation to frequency, duration, and daytime impairment must be assessed, and a psychiatrist must determine whether the sleep disturbance affects

mood, motor performance, or cognitive function. Thus it is fair to say that disturbances of sleep and wakefulness can no longer be viewed only as symptoms or markers of psychiatric disease. Data from research support the additional viewpoint that they can be independent contributors to psychiatric phenomena, related to psychiatric illness in a bidirectional fashion. The understanding of these conditions is, therefore, crucial for psychiatrists and the clinical evaluation and treatment of sleep disorders in addition to psychiatric diagnoses should be the professional focus.

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REFERENCES

- Jones BE. Basic mechanism of Sleep-Wake States. In: MH Kryger, T Roth, WC Dement (editors), Principles and Practice of Sleep Medicine (4th ed). Philadelphia: Saunders, 2005;136-53.
- Kupfer DJ, Reynolds CF 3rd. Management of insomnia. *N Engl J Med* 1997;336:341-6.
- Smith MT, Perlis ML, Park A, Smith MS, Pennington J, Giles DE, et al. Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *Am J Psychiatry* 2002;159:5-11.
- Ohayon MM. Epidemiology of insomnia: What we know and what we still need to learn. *Sleep Med Rev* 2002;6:97-111.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed, text revision. Washington DC: American Psychiatric Press; 2004.
- National Institutes of Health. National Institutes of Health State of the Science Conference statement on Manifestations and Management of Chronic Insomnia in Adults, June 13-15, 2005. *Sleep*. 2005;28:1049-57.
- American Academy of Sleep Medicine. International classification of sleep disorders. 2nd ed. Diagnostic and coding manual. Westchester (IL): American Academy of Sleep Medicine; 2005.
- Edinger JD, Bonnet MH, Bootzin RR, Doghramji K, Dorsey CM, Espie CA, et al. American Academy of Sleep Medicine Work Group. Derivation of research diagnostic criteria for insomnia: Report of an American Academy of Sleep Medicine Work Group. *Sleep*. 2004;27:1567-96.
- Czeisler CA, Winkelman JW, Richardson GS, Sleep disorders. In: Braunwald E, Fauci AS, Kasper DL, editors. Harrison's principles of internal medicine. 15th ed. New York: McGraw Hill; 2001. p. 155-63.
- Vallières A, Ivers H, Bastien CH, Beaulieu-Bonneau S, Morin CM. Variability and predictability in sleep patterns of chronic insomniacs. *J Sleep Res* 2005;14:447-53.
- Becker PM. Pharmacologic and nonpharmacologic treatments of insomnia. *Neurol Clin* 2005;23:1149-63.
- Krystal AD. Sleep and psychiatric disorders: Future directions. *Psychiatr Clin North Am* 2006;29:1115-30; abstract xi.
- NIH Consensus Conference. Drugs and Insomnia. The use of medications to promote sleep. *JAMA* 1984;251:2410-4.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th edition, text revision. Washington DC: American Psychiatric Press; 2004.
- Thase ME. Antidepressant treatment of the depressed patient with insomnia. *J Clin Psychiatry* 1999;60 (Suppl 17):28-31
- Hirschfeld RM, Mallinckrodt C, Lee TC, Detke MJ. Time course of depression-symptom improvement during treatment with duloxetine. *Depress Anxiety* 2005;21:170-7
- Nelson JC, Wohlreich MM, Mallinckrodt CH, Detke MJ, Watkin JG, Kennedy JS. Duloxetine for the treatment of major depressive disorder in older patients. *Am J Geriatr Psychiatry* 2005;13:227-35
- Nierenberg AA, Keefe BR, Leslie VC, Alpert JE, Pava JA, Worthington JJ 3rd, et al. Residual symptoms in depressed patients who respond acutely to fluoxetine. *J Clin Psychiatry* 1999;60:221-5
- Hudson JI, Lipinski JF, Keck PE Jr, Aizley HG, Lukas SE, Rothschild AJ, et al. Polysomnographic characteristics of young manic patients. Comparison with unipolar depressed patients and normal control subjects. *Arch Gen Psychiatry* 1992;49:378-83
- Wehr TA, Goodwin FK, Wirz-Justice A, Breitmaier J, Craig C. 48-hour sleep-wake cycles in manic-depressive illness: Naturalistic observations and sleep deprivation experiments. *Arch Gen Psychiatry* 1982; 39:559-65.
- Zimanova J, Vojtechovsky M. Sleep deprivation as a potentiation of antidepressant pharmacotherapy? *Acta Nerv Super (Praha)* 1974;16:188-9.
- Monti JM, Monti D. Sleep disturbance in generalized anxiety disorder and its treatment. *Sleep Med Rev* 2000;4:263-76.
- Rosenthal M. Tiagabine for the treatment of generalized anxiety disorder: A randomized, open-label, clinical trial with paroxetine as a positive control. *J Clin Psychiatry* 2003;64:1245-9.
- Chouinard S, Poulin J, Stip E, Godbout R. Sleep in untreated patients with schizophrenia: a meta-analysis. *Schizophr Bull* 2004;30:957-67
- Doi Y, Minowa M, Uchiama M, Okawa M, Kim K, Shibui K, et al. Psychometric assessment of subjective sleep quality using the Japanese version of the Pittsburgh Sleep Quality Index (PSQI-J) in psychiatric disordered and control subjects. *Psychiatry Res* 2000;97:165-72.
- Turvey CL, Conwell Y, Jones MP, Phillips C, Simonsick E, Pearson JL, et al. Risk factors for late-life suicide: A prospective community based study. *Am J Geriatr Psychiatry* 2002;10:398-406
- Agargun MY, Kara H, Solmaz M. Sleep disturbances and suicidal behavior in patients with major depression. *J Clin Psychiatry* 1997;58:249-51.
- Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders; An opportunity for prevention? *JAMA* 1989;262:1479-84.
- Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: A longitudinal epidemiologic study of young adults. *Biol Psychiatry* 1996;39:411-8
- Chang PP, Ford DE, Mead LA, Cooper-Patrick L, Klag MJ. Insomnia in young men and subsequent depression. *Am J Epidemiol* 1997;146:105-14
- Reynolds CF 3rd, Frank E, Houck PR, Mazumdar S, Dew MA, Cornes C, et al. Which elderly patients with remitted depression remain well with continued interpersonal psychotherapy after discontinuation of antidepressant medication? *Am J Psychiatry* 1997;154:958-62.

32. Fava M, McCall WV, Krystal A, Wessel T, Rubens R, Caron J, *et al.* Eszopiclone co-administered with fluoxetine in patients with insomnia co-existing with major depressive disorder. *Biol Psychiatry* 2006;59:1053-60.
33. Nolen WA, Haffmans PM, Bouvy PF, Duivenvoorden HJ. Related hypnotics as concurrent medication in depression. A placebo-controlled, double-blind comparison of flunitrazepam and lormetazepam in patients with major depression, treated with a (tri)cyclic antidepressant. *J Affect Disord* 1993;28:179-88.
34. Asnis GM, Chakrabarty A, DuBoff EA, Krystal A, Londeborg PD, Rosenberg R, *et al.* Zolpidem for persistent insomnia in SSRI-treated depressed patients. *J Clin Psychiatry* 1999;60:668-76.
35. Becker PM. Insomnia: Prevalence, impact, pathogenesis, differential diagnosis, and evaluation. *Psychiatr Clin North Am* 2006;29:855-70.

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