

Insomnia and Depression

Commentary on Buysse et al. Prevalence, Course, and Comorbidity of Insomnia and Depression in Young Adults. *SLEEP* 2008;31:473-80; on Pigeon et al. Is insomnia a perpetuating factor for late-life depression in the IMPACT cohort? *SLEEP* 2008;31:481-8; and on Manber et al. Cognitive behavioral therapy for insomnia enhances depression outcome in patients with comorbid major depressive disorder and insomnia. *SLEEP* 2008;31:489-95.

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CAN INSOMNIA INSTIGATE, PERPETUATE, OR EXACERBATE DEPRESSION? AS WITH MUCH OF CLINICAL SCIENCE, THIS QUESTION CAN NEVER BE ANSWERED definitively. A traditional or “true” experimental study is not possible; it is unethical and/or impossible to randomly assign healthy subjects to have insomnia induced or not, and then measure depression. The only way to approximate a “true” experimental design is to rely upon quasi-experimental methods (i.e., observational epidemiology) or randomized clinical trials treating insomnia and seeing if depression decreases. Variations on these methods were used in three studies appearing in this issue of *SLEEP*, and the results suggest that insomnia may indeed have a negative effect on depression in some cases.

Buysse and colleagues¹ present an epidemiological study that involved 6 interviews of 591 Swiss adults over 20 years. Participants were divided (based on the answer to a single self-report question) into insomnia duration/frequency subtypes (e.g., 1 month with distress, occasional brief insomnia) versus those without insomnia. When the insomnia subtypes were grouped together, participants with insomnia lasting ≥ 2 weeks were at greater risk for onset of major depressive disorder (MDD) at a later interview (95% C.I. 1.3-2.6, $P = 0.001$). Although not new, these findings are consistent with mounting evidence that insomnia is a risk factor for onset of MDD.²

In a related article, Pigeon and colleagues³ report the results of secondary data analyses of a large ($N = 1801$), multisite randomized control trial of “enhanced” depression treatment versus treatment as usual in a primary care setting in older adults (60+) with MDD or dysthymia. The goal was to determine if “insomnia–status” predicted increased risk for worse depression treatment response. Elderly patients with persistent insomnia had worse depression treatment outcomes (1.8 to 3.5 times as likely to remain depressed), and the results were strongest in the MDD group. This study provides the best evidence to date

that untreated insomnia exacerbates or perpetuates depression, at least in those aged 60 years and older.⁴⁻⁶

In the third study in this issue, Manber and colleagues⁷ performed a pilot placebo controlled randomized clinical trial comparing cognitive behavioral therapy of insomnia (CBTi) to a systematic desensitization control (CTRL) in MDD patients with insomnia receiving open-label escitalopram. The CBTi group was significantly more likely than the CTRL group to have insomnia remission (50% vs. 8%), indicating targeted treatment of insomnia is more effective than depression treatment alone at reducing insomnia. One would think that if insomnia were being “caused” by depression, targeted insomnia treatment should not result in significant change. This provides some evidence that insomnia has uncoupled from the depression in these individuals and become an independent and treatable disorder. Further, patients in the CBTi group were more likely than the CTRL group to have depression remission (61.5% vs. 33.3%). This second result was nonsignificant, likely due to inadequate power, but argues strongly that in a portion of depressed patients, targeted insomnia treatment may improve depression response. This implies that the “independent” insomnia mentioned above was serving to maintain the comorbid depression. These results are in line with other research showing that treatment of insomnia in patients with depression is possible and can result in positive depression outcomes.^{8,9}

While important additions to a better scientific understanding of the relationship between insomnia and depression, there are noteworthy limitations to the study designs used in these 3 reports. Because the first 2 studies^{1,3} used quasi-independent variables (i.e., not actively manipulating insomnia status), one cannot unequivocally say that some other variable was not causing both the insomnia and depression. In addition, these studies suffered from limited definitions of insomnia, which weaken the confidence that can be placed in the results. Further, within the randomized controlled trial,⁷ there is the problem of not knowing the exact mechanism of action. It is possible that some of the interventions aimed at insomnia (e.g., sleep restriction) were inadvertently targeting depression (i.e., consistent wake time might result in daytime efficiency, which in turn improves accomplishment, thus decreasing dysphoria).

Overall, however, these three studies^{1,3,7} are in agreement with much, if not most, of the longitudinal data examining the relationship between insomnia and depression, by showing that insomnia is a risk factor for onset of depression and for worsening depression. However, insomnia and depression do

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not follow a typical cause-and-effect relationship; sometimes insomnia precedes depression, sometimes depression comes first, sometimes they are unrelated, and other times they are comorbid. Thus, it can never be said that either disorder causes the other disorder in all cases. However, the data from these studies add to a growing amount of evidence that supports the idea that *in some cases*, insomnia may be instigating, perpetuating, or exacerbating depression.

How might insomnia cause depression? Below are some potentially testable hypotheses.*

- Insomnia is related to decreased quality of life, social and interpersonal functioning, and workplace performance, and any of these could result in levels of distress or life events that may trigger, maintain, or worsen MDD.¹⁰⁻¹²
- Lying awake in the dark presents a tabula rasa for depressive rumination that may trigger a depressive episode.
- Loss of control of sleep may trigger thoughts of helplessness and hopelessness, which might “activate” the template for helpless/hopeless schema common to depression.
- Insomnia promotes a level of circadian misalignment that may also contribute to decrements in diurnal mood and performance.
- Sleep loss or sustained wakefulness may cause alterations in neurobehavioral functions that may result in depression.

Future directions in this area of research might involve a variety of variations on the designs used above. Certainly better longitudinal studies of insomnia and depression are needed, where careful definition of insomnia and depression occur as well as more frequent and intensive assessments over time. Other studies might involve randomized controlled trials comparing treatments of insomnia only, depression only, and placebo only in patients with comorbid insomnia and depression, to determine the relative effect of each independent treatment. Clearly there is much research yet to be done to improve our understanding of insomnia in relation to depression.

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REFERENCES

1. Buysse JD, Angst J, Gamma A, Ajdacic V, Eich D, Rössler W. Prevalence, course and comorbidity of insomnia and depression in young adults. *Sleep* 2008;31:473-80.
2. Taylor DJ, Lichstein KL, Durrence HH. Insomnia as a health risk factor. *Behav Sleep Med* 2003;1:227-47.
3. Pigeon WF, Hegel M, Unützer J, et al. Is insomnia a perpetuating factor for late-life depression in the IMPACT cohort? *Sleep* 2008;31:481-8.
4. Buysse DJ, Frank E, Lowe KK, Cherry CR, Kupfer DJ. Electroencephalographic sleep correlates of episode and vulnerability to recurrence in depression. *Biol Psychiatry* 1997;41:406-18.
5. Dew MA, Reynolds CF 3rd, Houck PR, et al. Temporal profiles of the course of depression during treatment. Predictors of pathways toward recovery in the elderly. *Arch Gen Psychiatry* 1997;54:1016-24.
6. Reynolds CF 3rd, Frank E, Houck PR, 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.
7. Manber R, Edinger JD, Gress JL, San Pedro-Salcedo MG, Kuo TF, Kalista T. Cognitive behavioral therapy for insomnia enhances depression outcome in patients with comorbid major depressive disorder and insomnia. *Sleep* 2008;31:489-95.
8. Fava M, McCall WV, Krystal A, et al. Eszopiclone co-administered with fluoxetine in patients with insomnia coexisting with major depressive disorder. *Biol Psychiatry* 2006;59:1052-60.
9. Taylor DJ, Lichstein KL, Weinstock J, Sanford S, Temple J. A pilot study of cognitive-behavioral therapy of insomnia in people with mild depression. *Behav Ther* 2007;38:49-57.
10. Hatoum HT, Kong SX, Kania CM, Wong JM, Mendelson WB. Insomnia, health-related quality of life and healthcare resource consumption. A study of managed-care organisation enrollees. *Pharmacoeconomics* 1998 Dec;14:629-37.
11. Katz DA, McHorney CA. Clinical correlates of insomnia in patients with chronic illness. *Arch Intern Med* 1998;158:1099-107.
12. McCall WV, Reboussin BA, Cohen W. Subjective measurement of insomnia and quality of life in depressed inpatients. *J Sleep Res* 2000;9:43-8.