Sleep disorders and depression: brief review of the literature, case report, and nonpharmacologic interventions for depression

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Abstract: Sleep disorders are so frequently associated with depression that, in the absence of sleep complaints, a diagnosis of depression should be made with caution. Insomnia, in particular, may occur in 60%–80% of depressed patients. Depressive symptoms are important risk factors for insomnia, and depression is considered an important comorbid condition in patients with chronic insomnia of any etiology. In addition, some drugs commonly prescribed for the treatment of depression may worsen insomnia and impair full recovery from the illness. The aim of this paper is to review briefly and discuss the following topics: common sleep disturbances during depression (in particular pavor nocturnus, nightmares, hypersomnia, and insomnia); circadian sleep disturbances; and treatment of depression by manipulation of the sleep-wake rhythm (chronotherapy, light therapy, cycles of sleep, and manipulation of the sleep-wake rhythm itself). Finally, we present a case report of a 65-year-old Caucasian woman suffering from insomnia associated with depression who was successfully treated with sleep deprivation.

Keywords: sleep disorders, depression, insomnia, sleep-wake rhythm

Introduction

Sleep disorders occur frequently in patients with depression. The co-occurrence of depression and sleep disorders is so frequent that some authors have suggested that, in the absence of sleep complaints, a diagnosis of depression should be made with caution.¹ In fact, insufficient/excessive sleep, as well as dysfunctions of sleep rhythm, are likely to occur during depression. The sleep-wake cycle is regulated by two interacting processes, the circadian process and the homeostatic (or recovery) process. The former regulates the daily rhythms of the body and the brain; this is mainly due to the suprachiasmatic nucleus of the hypothalamus which provides an oscillatory pattern of activity regulating fundamental mechanisms, eg, sleep-wake activity, hormone release, and liver function. Indeed, this (circadian) process is strongly influenced by stimuli from social and environmental cues, and is “independent of wake and tiredness”. In addition, circadian rhythm sleep disorders are common among depressed patients and relate to an alteration of the circadian process or to a misalignment between sleep and the 24-hour social and physical environment.² On the contrary, the latter (homeostatic or recovery process) is wake-dependent and regulates the drive to sleep. When sleep has been shorter than usual, there is a “sleep debt”, that leads to an increase in the homeostatic drive, resulting in longer hours of deep sleep. In depression, both homeostatic and circadian rhythms are altered.³ The most common sleep disorders in depression are pavor nocturnus, nightmares, insomnia, and hypersomnia.

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Pavor nocturnus (night terror episodes) is a parasomnia characterized by sudden arousal from deep sleep (polysomnographic stage 4) during which the individual may have a constricted awareness of his/her surroundings.⁴ Its manifestation includes a terrified scream followed by an intense autonomic discharge, frequently associated with motor activity that is typically stereotyped, persevering, and less purposive than that of sleepwalking.⁵ Night terror patients showed anxiety, depression, obsessive-compulsive tendencies, and phobia.⁶ Episodes of night terror in adults are similar to the ones described in children, and seem to occur in adults with a history of psychopathology.⁷

With regard to the nightmare, the *Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition, Text Revision*⁸ defines it as an “extremely frightening dream” from which a person wakes up abruptly. Once awake, the individual quickly recovers orientation, preserves a detailed memory of the complicated plot of the nightmare (usually involving threats to survival, to security, or to self-esteem), and can hardly return to sleep. Nightmares occur in the general population with a prevalence of between 1%⁹ to 8%.^{9,10} They are more common in women and are associated with an increase in nocturnal awakenings, sleep onset insomnia, daytime memory impairment, and anxiety due to poor nocturnal sleep.¹¹ However, stressful experiences even occurring during childhood could influence the development of depression with sleep complaints, such as oppressive and bad dreams.¹² In addition, they can be related to the use of medications, primarily those modifying the levels of neurotransmitters in the central nervous system, such as antidepressants, narcotics, or barbiturates. Intense frightening dreams may also occur during withdrawal of drugs, such as ethanol, barbiturates, and benzodiazepines, causing rebound rapid eye movement (REM) sleep.¹³

The etiopathogenesis of nightmares is controversial, with neopsychoanalytic theories,^{14,15} as well as personality,¹⁶ evolutionary,^{17,18} and neurobiologic models,^{19,20} having been advanced to provide a possible explanation for these phenomena.

According to these models, dreaming represents an emotionally adaptive function (image contextualization, desomatization of feelings, mood regulation, or extinction of fear). Nightmares are widely seen to be either an intensified expression of an emotionally adaptive function or, conversely, as evidence of its breakdown. A recent study has proposed an affective network dysfunction model that integrates the tenets of many prior models suggesting that nightmares are related to problems with the fear extinction function of dreaming.²¹

Nightmares are the most common parasomnia occurring in depression, and frequently pertain the themes of masochism and poor self-image.²² In addition, a recent meta-analysis supports an association between sleep disturbances and suicidal thoughts and behaviors.²³ A constellation of psychosocial and personality factors, baseline sleep disturbances, and comorbid anxiety symptoms may account for the residual sleep disturbances after recovery from depression.²⁴ Melancholic depressed patients present a high rate of nightmares, as well as middle and terminal insomnia. Indeed, feeling worse in the morning than later in the day may be related to the intervening dream content and may affect and predict suicidal tendency. Melancholia may be associated with an increased risk of suicide attempts due to repetitive and frightening dreams.²⁵

Insomnia is considered a difficulty in initiating/maintaining sleep and/or nonrestorative sleep accompanied by decreased daytime functioning and persisting for at least 4 weeks.⁹ The most common form of insomnia (24.4%) was difficulty maintaining sleep (middle insomnia), while difficulty initiating sleep (initial insomnia) and early morning awakening (terminal insomnia) had a prevalence of about 23%.²⁶ Insomnia may occur in 60%–80% of patients with major depression.²⁷ Depressive symptoms are important risk factors for insomnia; in fact, depression is considered an important comorbid condition in patients with chronic insomnia of any etiology, also taking into account that some drugs commonly prescribed for the treatment of depression may worsen insomnia and impair full recovery from the illness.²⁸ In particular, it has been demonstrated that serotonin neurons of the dorsal raphe nucleus project to the cholinergic laterodorsal and pedunculopontine tegmental areas inhibiting REM sleep;²⁹ consequently, REM sleep suppression has been observed in patients treated with tricyclic antidepressants,³⁰ selective serotonin reuptake inhibitors, and serotonin-norepinephrine reuptake inhibitors.³¹ Polysomnography has indeed revealed that selective serotonin reuptake inhibitors are associated with increased awakenings after sleep onset and sleep percentage, increased sleep latency, and increased REM latency.³² Moreover, insomnia is considered a risk factor for depression. Some studies have suggested that eating and sleep irregularities during early childhood may represent possible risk factors for depression in later life.³³ The treatment of insomnia associated with depression can be carried out with benzodiazepines and should be balanced judiciously against possible harms, including the development of dependence and proneness to accidents.³⁴ An important clinical problem is the high incidence of insomnia in the elderly; probably, the

pattern of polyphasic sleep is not sufficiently considered³⁵ in the elderly who, in wanting to pursue a monophasic sleep, demand urgent pharmacotherapy for insomnia. On the other hand, there is a positive association between sleep problems and suicidal ideation, especially in the elderly, showing further that insomnia is a risk factor for death by suicide despite recovery from other depressive symptoms.³⁶ In these cases, a drug-free psychoeducational intervention could represent an important and safe therapeutic approach for insomnia. A meta-analysis found moderate to large effects of behavioral treatment (ie, cognitive-behavioral therapy, relaxation, behavioral only) in sleep quality, sleep latency, and waking after sleep onset in older individuals.³⁷

Hypersomnia is characterized by excessive daytime sleepiness and daytime naps that do not result in a more refreshed or alert feeling. Hypersomnia does not include a lack of night-time sleep. Indeed, it is less common among depressed patients, but tends to be a feature of atypical depression and is more prevalent in youngsters (about 40% of depressed patients under 30 years of age and 10% of those in their 50s) and in females of all ages. Some patients experience both insomnia and hypersomnia during the same depressive episode.³⁸ Although hypersomnia is more prevalent in bipolar depression than in unipolar depression,³⁹ even during interepisode periods,⁴⁰ it occurs in approximately 30% of unipolar depressed patients⁴¹ and is associated with long-term, severe, and treatment-resistant depression.⁴² The complaint of sleepiness in hypersomnic bipolar depressed patients seems to be related to an anergic depressive condition (characterized by withdrawal, lack of interest, psychomotor retardation, and decreased energy) rather than to an increase in true sleep or REM sleep propensity.⁴³

Treatment of depression by manipulation of the sleep-wake rhythm

Treatment of depression relies on so-called “somatic therapy”, which includes both pharmacologic tools and manipulative interventions on the stimuli received by the subject, such as chronotherapy, light therapy, cycles of sleep, and manipulation of the sleep-wake rhythm. These interventions are readily available, and their effectiveness does not seem to be less than that of drugs.⁴⁴ Light therapy was initially developed as a treatment of choice in seasonal affective disorder,⁴⁵ antepartum depression,⁴⁶ and eating disorders.⁴⁷ Indeed, during the first week of treatment, light therapy, especially in the morning, seems to have modest antidepressant efficacy that increases when it is administered to patients who respond

to sleep deprivation.⁴⁸ The effects of light depend on the time of administration. Due to the fact that the biological clock in older adults is often advanced to an earlier time, in case of difficulty in falling asleep at night and difficulty in waking up in the morning because of a delayed biological clock, bright light treatment in the morning may anticipate bedtime.⁴⁹ If in the first 15 days of treatment, medications and psychotherapy are not efficacious, treatment of sleep cycles, administered all night or partially (ie, second half of the night) produces stunning effects in just a few hours in 60% of the patients with major depression.⁵⁰ Despite the rapid action of sleep deprivation, one must not forget that the antidepressant effect is usually short, because there is often a full or partial relapse after recovery sleep or after small naps. Further, depressed patients, especially the melancholic ones who have experienced treatment of sleep cycles, are surprised by the rapidity and extent of antidepressant efficacy but are subject to rapid relapse. In order to optimize such treatment and prevent relapse, some authors recommend the association of sleep cycles every night with lithium salts or selective serotonin reuptake inhibitors.⁵¹ The antidepressant efficacy of sleep deprivation seems to be influenced by patient characteristics, with a meta-analysis showing that the presence of baseline diurnal variation in mood contributes significantly to prediction of depression levels after total sleep deprivation.⁵² The therapeutic effect of sleep deprivation is also fully enhanced by the association of this method with light therapy performed in the morning.⁵³ Individual genetic characteristics of the molecular mechanism of the biological clock are involved in the manifestation of mood disorders, including age at onset, risk of recurrence, response to treatment of sleep cycles, and drug treatment. Further, some authors have suggested the presence of functional associations between mood adjustment and the biological clock systems that regulate diurnal preference; in particular, it seems that evening preference might increase susceptibility to development of mood disorders.⁵⁴ These considerations lead us to think that there is an intimate connection between the neurotransmitter system (on which drug treatments act) and circadian rhythm (on which chronotherapy acts).

There is probably a bidirectional relationship between regulation of daytime affect and night-time sleep; indeed, disturbances in affect regulation during the day interfere with night-time sleep/circadian functioning. On the other hand, the effects of sleep deprivation contribute, in an escalating vicious cycle, towards difficulty in affect regulation on the following day.⁵⁵ Circadian timing in mammals is based upon the cell-autonomous clockwork located in the

suprachiasmatic nuclei of the hypothalamus. Individual cells from the suprachiasmatic nucleus and many other tissues express 24-hour molecular rhythmicity, resulting from a transcriptional-translational feedback loop. The transcription factors, CLOCK and BMAL1, form heterodimers and are bound to E-box elements in the promoters of the *Period (Per) 1* and *Per2*, *Cryptochrome (Cry) 1*, and *Cry2* genes. The proteins produced form complexes which, in the nucleus, interact with the CLOCK/BMAL1 complex, with repression of its transactivational activity. Post-translational events modify the timing of this negative feedback, providing a fine control over the cycle length of the molecular oscillations.⁵⁶ The integration of these oscillations, with the synchronizing effect of light, controls the secretion of melatonin, especially during the dark phase of the circadian rhythm. In fact, melatonin generally is not secreted during the day; however, not only does it increase about 2 hours before sleep onset, but it also declines in the early morning hours. Furthermore, its circadian rhythms are frequently of low amplitude in depressed patients.⁵⁷

Shifting the focus from sleep cycles to circadian regulation, some authors have compared the levels of melatonin in pregnant depressed women versus post-partum depressed women. Compared with those who are pregnant without depression, melatonin levels decrease in pregnant depressed women during the night, whereas in post partum depressed women these levels increase, particularly in the early morning hours. However, pregnant women with a personal history of depression have earlier melatonin offset times and do not show a physiologic increase during pregnancy. These observations may be due to the less sensitive effect of estradiol or progesterone on melatonin receptors. As a result, the increase in gonadal hormones during pregnancy would increase melatonin secretion in pregnant women without depression but not in those who are depressed. On the contrary, in postpartum women, the declining levels of gonadal hormones would decrease melatonin levels in women without depression, but not in depressed ones, thus resulting in higher melatonin levels in postpartum depressed women versus healthy postpartum women.

These findings have important treatment implications. The low melatonin levels in depressed pregnant women may compromise their ability to use melatonin as a regulator of other circadian rhythms. As a result, desynchronization of circadian rhythms may predispose pregnant women to further depressive mood changes. Because melatonin treatment can alter reproductive function, light therapy would be a better strategy to synchronize circadian rhythms and

thereby mitigate depression.⁵⁸ These findings complement previous studies indicating a reduced level of melatonin in women with premenstrual dysphoric disorder⁵⁹ and an increased level in women with menopausal depression.⁶⁰ Low levels of melatonin were also found in patients with schizophrenia (in both drug-free patients and after treatment with neuroleptic drugs).⁶¹

It would be interesting to find out the reasons for these differences between groups in the secretion of melatonin and also whether these differences are related to a different sleep time or duration. In any case, the results of these studies provide additional important information about the role that dysfunction of circadian rhythms may have in the pathophysiology of depression. In conclusion, there are reasonable grounds to study the cycles of sleep and circadian dysfunction, also taking into consideration the therapeutic potential connected with them.

Case report

A 65-year-old Caucasian woman was referred to our Psychiatry Unit for consultation. She told us that since childhood, every year in spring and in the evening towards bedtime, she suffered from mental illness with feelings of guilt about her daily activities. Awareness of the recurrence of these periods meant that, since she was young, she feared the month of April because it coincided precisely with her subjective and objective behavioral disorder. At school, she often felt so ill and impatient that one day she obtained the teacher's permission to go home before the end of the lesson. This made her feel guilty. On another occasion, again in spring, she recalled that while she was walking along the main road, she suddenly experienced a strong "sense of loss" and was nearly run over by a car. She also remembered having often felt envious of a classmate who always had lots of sweets and coins. Indeed, on one occasion, she tried to steal a few coins from her school friend because of a strong desire to buy sweets. The girl was therefore scolded by the teacher in front of the whole class and this provoked a deep sense of guilt and shame. These episodes of guilt and awkwardness in interpersonal relationships associated with depressive feelings were present every spring. Indeed, she remembered having suffered from severe pain in her eyes and having feared becoming blind; this discomfort disappeared alone after a few weeks. At the age of 40 years, the patient reported her problems to her general practitioner who prescribed paroxetine, but the patient refused it.

This peculiar pathologic phenomena continued to occur until the discomfort perceived by the patient obliged her to contact our Unit. We decided to adopt a psychoeducational

approach because of her refusal to take drugs. We advised her to get out of bed immediately, and go to a secluded area of her house and do some housework if she were to wake up in the middle of the night with negative thoughts. She usually woke up between 2 am and 4 am, and as soon as she left her bed, the negative thoughts vanished and were replaced by her household duties. After performing these activities, she was able to go to work and be productive. She returned home at 2.30 pm, and after lunch had a nap. Once she was in bed, she plunged into a deep sleep and woke up around 6.30 pm, still feeling drowsy. This feeling disappeared after about 15 minutes. In the following days, at times she would wake up during the night, while other nights she slept peacefully. In any case, whenever she woke up in the middle of the night, she performed some domestic activities.

This patient, even though she felt different from other people because of the peculiarities in her sleep-wake cycle, did not complain of any depressive symptoms. In this case the wakefulness by itself (accompanied by some goal-directed activities such as washing, cooking, and ironing) probably improved her mood. It is well known that if a patient with major depression is stimulated to be active, their mood can improve at least for a short period.⁶² That said, the emerging hypothesis is that “the early morning awakening” is a form of biological remedy against depression. Hence, sleep deprivation could be a strategy to apply, especially in senile depression. In the elderly, sleep is frequently polyphasic. Finally, given that the clinical value of insomnia should not be underestimated, it would be natural to question whether the aim to treat insomnia with the objective to observe a socially agreed circadian rhythm is correct or whether insomnia should be “accepted” and considered a spontaneous expression of a biological remedy against depression.

Conclusion

The proposed clinical case report made it possible to observe how in our patient each depressive episode was characterized by middle insomnia and feelings of anxiety and worry. In the case of depression, the literature data put in evidence the therapeutic value of manipulating cycles of sleep and sleep deprivation. In our case report, the advice to get out of bed once awake and perform some housework, even though it was night-time, led to inhibition of anxiety by physical activity and defocused the issue, thereby dissolving the affective experience of crisis. Based on such experience, repeated over several years, during which the only discomfort experienced by the patient and her family was a feeling of not being

“chronobiologically coordinated”, it could be assumed that insomnia represents a spontaneous therapeutic trial. Rather than treating insomnia, the patient started to indulge it. This attitude is more “natural” than performing a chronotherapy with artificially imposed rhythms. Obviously, this hypothesis requires future rigorous trials.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Jindal RD, Thase ME. Treatment of insomnia associated with clinical depression. *Sleep Med Rev*. 2004;8:19–30.
2. Lu BS, Zee PC. Circadian rhythm sleep disorders. *Chest*. 2006;130:1915–1923.
3. Borbely AA. A two-process model of sleep regulation. *Hum Neurobiol*. 1982;1:195–204.
4. Hartman D, Crisp AH, Sedgwick P, Borrow S. Is there a dissociative process in sleepwalking and night terrors? *Postgrad Med J*. 2001;77:244–249.
5. Crisp AH, Matthews BM, Oakey M, Crutchfield M. Sleepwalking, night terrors, and consciousness. *BMJ*. 1990;300:360–362.
6. Kales JD, Kales A, Soldatos CR, Caldwell AB, Charney DS, Martin ED. Night terrors. Clinical characteristics and personality patterns. *Arch Gen Psychiatry*. 1980;37:1413–1417.
7. Llorente MD, Currier MB, Norman SE, Mellman TA. Night terrors in adults: phenomenology and relationship to psychopathology. *J Clin Psychiatry*. 1992;53:392–394.
8. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*. Washington, DC: American Psychiatric Association; 2000.
9. American Academy of Sleep Medicine. *The International Classification of Sleep Disorders*. Rochester, MN: Allen Press; 1997.
10. Klink M, Quan S. Prevalence of reported sleep disturbances in a general population and their relation to obstructive airway disease. *Chest*. 1987;91:540–546.
11. Ohayon MM, Morselli PL, Guilleminault C. Prevalence of nightmares and their relationship to psychopathology and daytime functioning in insomnia subjects. *Sleep*. 1997;20:340–348.
12. Csóka S, Simor P, Szabó G, Kopp MS, Bódizs R. Early maternal separation, nightmares, and bad dreams: results from the Hungarian Epidemiological Panel. *Attach Hum Dev*. 2011;13:125–140.
13. Pagel JF. Nightmares and disorders of dreaming. *Am Fam Physician*. 2000;61:2037–2042.
14. Solms M. Dreaming and REM sleep are controlled by different brain mechanisms. *Behav Brain Sci*. 2000;23:843–850.
15. Germain A, Krakow B, Faucher B, Hollifield M, Warner TD, Koss M. An increase in mastery characterizes imagery rehearsal treatment for nightmares in sexual assault survivors with PTSD. *Dreaming*. 2004;14:195–206.
16. Hartmann E, Elkin R, Garg M. Personality and dreaming: the dreams of people with very thick or very thin boundaries. *Dreaming*. 1991;1:311–324.
17. Malcolm-Smith S, Solms M. Incidence of threat in dreams: a response to Revonsuo's threat simulation theory. *Dreaming*. 2004;14:220–229.
18. Schredl M, Hofmann F. Continuity between waking activities and dream activities. *Conscious Cogn*. 2003;12:298–308.
19. Fisher C, Byrne J, Edwards A, Kahn E. A psychophysiological study of nightmares. *J Am Psychoanal Assoc*. 1970;18:747–782.
20. Kramer M. The selective mood regulatory function of dreaming: an update and revision. In: Moffitt A, Kramer M, Hoffmann R, editors. *The Functions of Dreaming*. Albany, NY: State University of New York; 1993.

21. Nielsen T, Levin R. Nightmares: a new neurocognitive model. *Sleep Med Rev.* 2007;11:295–310.
22. Beauchemin KM, Hays P. Dreaming away depression: the role of REM sleep and dreaming in affective disorders. *J Affect Disord.* 1996;41:125–133.
23. Pigeon WR, Piquart M, Conner K. Meta-analysis of sleep disturbance and suicidal thoughts and behaviors. *J Clin Psychiatry.* 2012;73:1160–1167.
24. Li SX, Lam SP, Chan JW, Yu MW, Wing YK. Residual sleep disturbances in patients remitted from major depressive disorder: a 4-year naturalistic follow-up study. *Sleep.* 2012;35:1153–1161.
25. Agargun MY, Besiroglu L, Cilli AS, et al. Nightmares, suicide attempts, and melancholic features in patients with unipolar major depression. *J Affect Disord.* 2007;98:267–270.
26. Gureje O, Kola L, Ademola A, Olley BO. Profile, comorbidity and impact of insomnia in the Ibadan Study of Ageing. *Int J Geriatr Psychiatry.* 2009;24:686–693.
27. Winokur A, Gary KA, Rodner S, Rae-Red C, Fernando AT, Szuba MP. Depression, sleep physiology, and antidepressant drugs. *Depress Anxiety.* 2001;14:19–28.
28. Santos Moraes WA, Burke PR, Coutinho PL, et al. Sedative antidepressants and insomnia. *Rev Bras Psiquiatr.* 2011;33:91–95.
29. McCarley RW, Hobson JA. Neuronal excitability modulation over the sleep cycle: a structural and mathematical model. *Science.* 1975;189:58–60.
30. Kupfer DJ, Spiker DG. Nortriptyline and EEG sleep in depressed patients. *Biol Psychiatry.* 1982;17:535–546.
31. Sharpley AL, Cowen PJ. Effect of pharmacological treatments of depressed patients. *Biol Psychiatry.* 1995;37:85–98.
32. Holshoe JM. Antidepressants and sleep: a review. *Perspect Psychiatr Care.* 2009;45:191–197.
33. Ong SH, Wickramaratne P, Tang M, Weissman MM. Early childhood sleep and eating problems as predictors of adolescent and adult mood and anxiety disorders. *J Affect Disord.* 2006;96:1–8.
34. Furukawa TA, Streiner DL, Young LT. Antidepressant and benzodiazepine for major depression. *Cochrane Database Syst Rev.* 2002;1:CD001026.
35. Campbell SS, Murphy PJ. The nature of spontaneous sleep across adulthood. *J Sleep Res.* 2007;16:24–32.
36. McCall WV, Batson N, Webster M, et al. Nightmares and dysfunctional beliefs about sleep mediate the effect of insomnia symptoms on suicidal ideation. *J Clin Sleep Med.* 2013;9:135–140.
37. Irwin MR, Cole JC, Nicassio PM. Comparative meta-analysis of behavioural interventions for insomnia and their efficacy in middle-aged adults and in older adults. *Health Psychol.* 2006;25:3–14.
38. Posternak MA, Zimmerman M. Symptoms of atypical depression. *Psychiatry Res.* 2001;104:175–181.
39. Benazzi F. Symptoms of depression as possible markers of bipolar II disorder. *Prog Neuropsychopharmacol Biol Psychiatry.* 2006;30:471–477.
40. Kaplan KA, Gruber J, Eidelman P, Talbot LS, Harvey AG. Hypersomnia in inter-episode bipolar disorder: does it have prognostic significance? *J Affect Disord.* 2011;132:438–444.
41. Kaplan KA, Harvey AG. Hypersomnia across mood disorders: a review and synthesis. *Sleep Med Rev.* 2009;13:275–285.
42. Matza LS, Revicki DA, Davidson JR, Stewart JW. Depression with atypical features in the national comorbidity survey: classification, description, and consequences. *Arch Gen Psychiatry.* 2003;60:817–826.
43. Nofzinger EA, Thase ME, Reynolds CF 3rd, et al. Hypersomnia in bipolar depression: a comparison with narcolepsy using the multiple sleep latency test. *Am J Psychiatry.* 1991;148:1177–1181.
44. Wirz-Justice A. Temporal organization as a therapeutic target. *Dialogues Clin Neurosci.* 2012;14:335–337.
45. Magnusson A, Partonen T. The diagnosis, symptomatology, and epidemiology of seasonal affective disorder. *CNS Spectr.* 2005;10:625–634.
46. Epperson CN, Terman M, Terman JS, et al. Randomized clinical trial of bright light therapy for antepartum depression: preliminary findings. *J Clin Psychiatry.* 2004;65:421–425.
47. Krysta K, Krzystanek M, Janas-Kozik M, Krupka-Matuszczyk I. Bright light therapy in the treatment of childhood and adolescence depression, antepartum depression, and eating disorders. *J Neural Transm.* 2012;119:1167–1172.
48. Tuunainen A, Kripke DF, Endo T. Light therapy for non-seasonal depression. *Cochrane Database Syst Rev.* 2004;2:CD004050.
49. Buysse DJ. Insomnia. *JAMA.* 2013;309:706–716.
50. Berger M, van Calker D, Riemann D. Sleep and manipulations of the sleep-wake rhythm in depression. *Acta Psychiatr Scand Suppl.* 2003;418:83–91.
51. Benedetti F, Barbini B, Campori E, Fulgosi MC, Pontiggia A, Colombo C. Sleep phase advance and lithium to sustain the antidepressant effect of total sleep deprivation in bipolar depression: new findings supporting the internal coincidence model? *J Psychiatr Res.* 2001;35:323–329.
52. Bouhuys AL. Towards a model of mood responses to sleep deprivation in depressed patients. *Biol Psychiatry.* 1991;29:600–612.
53. Tuunainen A, Kripke DF, Endo T. Light therapy for non-seasonal depression. *Cochrane Database Syst Rev.* 2004;2:CD004050.
54. Kitamura S, Hida A, Watanabe M, et al. Evening preference is related to the incidence of depressive states independent of sleep-wake conditions. *Chronobiol Int.* 2010;27:1797–812.
55. Harvey AG. Sleep and circadian rhythms in bipolar disorder: seeking synchrony, harmony, and regulation. *Am J Psychiatry.* 2008;165:820–829.
56. LeSauter J, Lambert CM, Robotham MR, Model Z, Silver R, Weaver DR. Antibodies for assessing circadian clock proteins in the rodent suprachiasmatic nucleus. *PLoS One.* 2012;7:e35938.
57. Srinivasan V, Smits M, Spence W, et al. Melatonin in mood disorders. *World J Biol Psychiatry.* 2006;7:138–151.
58. Parry BL, Meliska CJ, Sorenson DL, et al. Plasma melatonin circadian rhythm disturbances during pregnancy and postpartum in depressed women and women with personal or family histories of depression. *Am J Psychiatry.* 2008;165:1551–1558.
59. Parry BL, Berga SL, Kripke DF, et al. Altered waveform of plasma nocturnal melatonin secretion in premenstrual depression. *Arch Gen Psychiatry.* 1990;47:1139–1146.
60. Parry BL, Meliska CJ, Sorenson DL, et al. Increased melatonin and delayed offset in menopausal depression: role of years past menopause, follicle-stimulating hormone, sleep end time, and body mass index. *J Clin Endocrinol Metab.* 2008;93:54–60.
61. Rotenberg VS. Sleep in patients with schizophrenia on and off melatonin treatment: contradictions and hypothesis. In: Bosch P, van den Noort, editors. *Schizophrenia, Sleep and Acupuncture.* Göttingen, Germany: Hogrefe and Huber; 2008.
62. Rotenberg VS. Sleep deprivation in depression: an integrative approach. *Int J Psychiatry Clin Pract.* 2003;7:9–16.

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