DOI: 10.14744/DAJPNS.2026.00333
Dusunen Adam J Psychiatr Neurol Sci
2026;39:169-172

INVITED EDITORIAL

Sleep as a psychiatric vital sign, not just a symptom

Umit Haluk Yesilkaya[1–3], Clifford B. Saper[1,2]

[1]Beth Israel Deaconess Medical Center, Harvard Medical School, Department of Neurology, Boston, USA
[2]Harvard Medical School, Division of Sleep Medicine, Boston, USA
[3]Istanbul Nisantasi University Faculty of Medicine, Department of Psychiatry, Istanbul, Turkiye

Every clinician who treats psychiatric illness knows that patients sleep badly. The usual assumption is that poor sleep is a consequence of the illness and will improve once the depression, mania, or psychosis is treated. Over the past three decades, work on the brain circuits that generate sleep, together with large clinical studies, has overturned that assumption (1). Disturbed sleep is not simply a by-product of psychiatric illness; it is often part of its cause and, unlike much of what we assess in psychiatry, it can be measured. We argue here that sleep deserves to be treated as a vital sign, recorded and acted upon as routinely as blood pressure.

HOW DOES THE BRAIN SWITCH BETWEEN SLEEP AND WAKING?

To see why sleep can serve as a vital sign, it helps to understand how the brain produces it. Sleep and wakefulness are not simply the brain slowing down and speeding up; they are two stable states, each actively generated, with rapid transitions between them (1, 2). On one side are the monoaminergic arousal cell groups that keep us awake: the noradrenergic locus coeruleus, the serotonergic raphe nuclei, and the histaminergic tuberomammillary nucleus. On the other are sleep-promoting neurons of the ventrolateral preoptic nucleus (VLPO) of the hypothalamus, which release the inhibitory transmitters γ-aminobutyric acid (GABA) and galanin. Each side inhibits the other, so the circuit behaves like an electrical flip-flop switch. It settles firmly into waking or sleep and resists the drowsy middle ground (2). Orexin (also called hypocretin) neurons in the lateral hypothalamus act on the waking side of the switch and hold it steady; when they are lost, as in narcolepsy, the switch becomes unstable, and patients fall abruptly between states (3). That VLPO neurons are genuinely sleep-active was demonstrated directly when they were found to fire in step with sleep (4). Two points matter for psychiatry. First, this circuit produces outputs that can be counted: how quickly a patient falls asleep, how consolidated the night is, how the sleep stages are arranged, and when they occur. Second, the waking side of the switch is built from the very monoamine systems that psychiatry implicates in mood and anxiety and targets with its drugs. Thus, disturbances of sleep and mood are, in part, two views of the same circuitry.

IS THE SLEEP PROBLEM IN PSYCHIATRY ONLY INSOMNIA?

When psychiatrists speak of sleep, they usually mean insomnia. But insomnia is only the most visible part of a larger disturbance. When sleep is recorded overnight, patients across a range of psychiatric diagnoses show changes in its architecture, with reduced continuity and efficiency and shifts in the amount and timing of slow-wave and rapid-eye-movement (REM) sleep; few disorders leave sleep entirely normal (5). In major depression, the oldest and best-established findings are that REM sleep begins too early in the night and becomes too

How to cite this article: Yesilkaya UH, Saper CB. Sleep as a psychiatric vital sign, not just a symptom. Dusunen Adam J Psychiatr Neurol Sci 2026;39:169-172.

Correspondence: Umit Haluk Yesilkaya, Beth Israel Deaconess Medical Center, Harvard Medical School, Department of Neurology, Boston, USA
E-mail: uyesilka@bidmc.harvard.edu

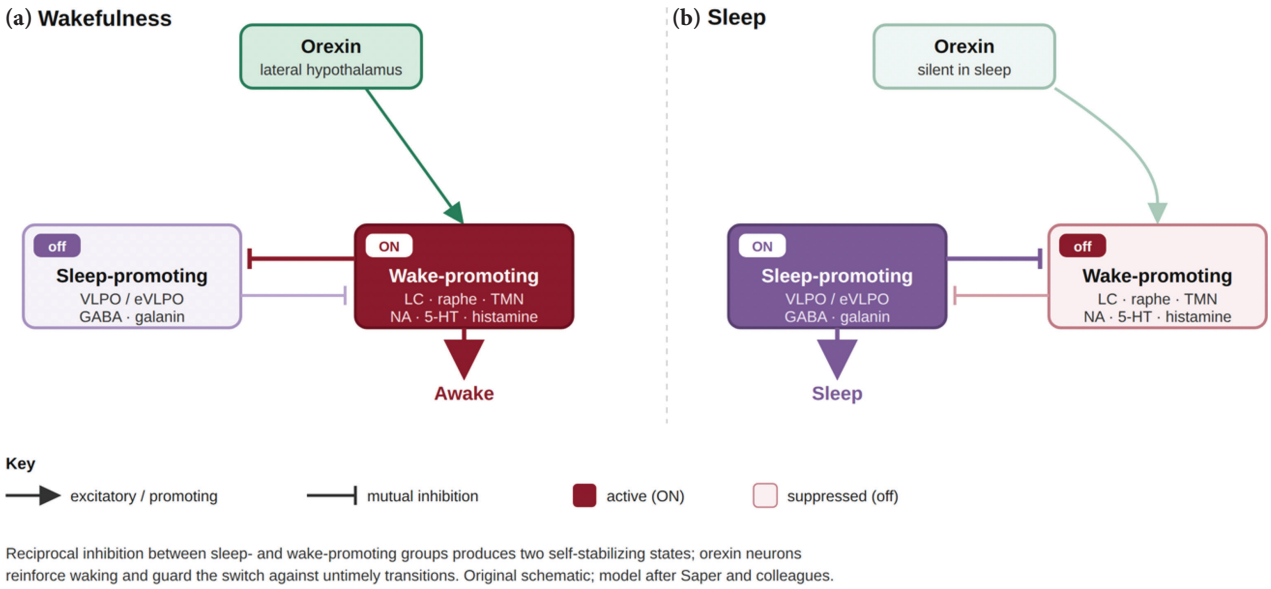

Figure 1. The sleep–wake flip-flop switch. Sleep-promoting neurons of the ventrolateral preoptic nucleus (VLPO) and the wake-promoting monoaminergic arousal system (locus coeruleus, raphe nuclei, tuberomammillary nucleus) inhibit each other, generating two self-stabilizing states; orexin neurons reinforce the arousal side and hold the switch steady. In wakefulness **(a)**, the arousal groups are active and the sleep-promoting group is suppressed; in sleep **(b)**, the balance reverses.

GABA: γ-aminobutyric acid; His: Histamine; LC: Locus coeruleus; NA: Noradrenaline; 5-HT: Serotonin; TMN: Tuberomammillary nucleus; VLPO: Ventrolateral preoptic nucleus. Original schematic; model adapted from Saper et al. (1, 3).

intense, while deep slow-wave sleep is reduced (6). These are not complaints; they are measurable features of the night.

The disturbance reaches down to the fine structure of sleep as well. Sleep spindles, the brief bursts of oscillation generated by the thalamus during non-REM sleep, are strikingly reduced in schizophrenia, both in patients who have never taken medication and in those who have, and, to a lesser degree, in their unaffected relatives (7). The magnitude of the spindle deficit tracks how poorly patients consolidate memories overnight, making spindles both a candidate biomarker and a potential treatment target (8). Schizophrenia also disturbs the timing of sleep, producing a misalignment of the sleep–wake cycle that persists even when medication and daytime inactivity are taken into account (9). Sleep pathology in psychiatry is therefore both coarse- and fine-grained, and it carries information that a single question about difficulty sleeping cannot capture.

DOES POOR SLEEP COME BEFORE THE ILLNESS?

If disturbed sleep were only a symptom, it would arrive with the illness and leave with it. Often, it does neither. Sleep disturbance cuts across diagnostic boundaries, recurring in mood, anxiety, psychotic, and substance use disorders and sharing mechanisms with them, which has led to its description as a transdiagnostic process rather than a symptom of any one disease (10). Its timing is more telling still. In long-term studies, insomnia roughly doubles the chance that a person will later experience a first episode of depression (11), and it also forecasts the later appearance of anxiety, psychosis, and substance use disorders (12). In many patients, the sleep problem appears before the rest of the illness and lingers between episodes, behaving less like a passenger and more like an early, and often modifiable, part of the disorder (13).

DOES SLEEP CAUSE THE TROUBLE, OR ONLY REFLECT IT?

Prediction is not proof of cause, and sleep and mood plainly influence each other. Two lines of evidence, however, point to sleep as a genuine contributor. The first comes from genetics. Mendelian-randomization studies use inherited variants as natural experiments that approximate the random assignment of a trial and reduce the influence of confounding and reverse causation; these analyses suggest that insomnia contributes to depression and related conditions, and

not merely the reverse (14). The second comes from treatment. In the largest trial of its kind, improving sleep in people with insomnia reduced paranoia and hallucinations, and the analysis showed that the benefit was mediated by the improvement in sleep itself (15). Adding treatment for insomnia to the treatment of depression also improves depressive symptoms beyond treating mood alone (16). In the same vein, poor sleep is associated with the occurrence and severity of delusions and hallucinations and often precedes relapse in psychosis (17). Even a single sleepless night weakens the control that the prefrontal cortex normally exerts over the amygdala, demonstrating in the laboratory how lost sleep can unsettle emotional regulation (18).

WHAT SHOULD THE CLINICIAN DO?

The practical message is simple. Sleep should be asked about and documented at every psychiatric visit (its duration, continuity, timing, and the patient's natural rhythm) as routinely as we record blood pressure. A sleep diary and a brief questionnaire such as the Insomnia Severity Index take little time and provide a number that can be followed over weeks (19); actigraphy and, increasingly, validated wearable devices bring objective measurement within reach. When sleep is abnormal, it should be treated in its own right rather than set aside until the main diagnosis improves. Cognitive behavioral therapy for insomnia is now recommended as first-line treatment for chronic insomnia (20). Attention to circadian timing, through scheduled light exposure and a regular sleep–wake pattern, addresses the clock; when medication is needed, drugs aimed at the arousal system, such as dual orexin-receptor antagonists, may suit the problem better than general sedation (21). Because sleep and psychiatric illness feed one another, improvement in either tends to help the other.

WHY DOES THIS MATTER BEYOND PSYCHIATRY?

There is a final reason to take sleep seriously. Sleep does more than rest the mind; during deep non-REM sleep, the brain clears metabolic waste more efficiently than during wakefulness (22). This finding links chronic sleep loss to neurodegenerative and other medical diseases and reminds us that broken sleep is seldom harmless in any illness. Clinicians already ask their patients whether they sleep. What is usually missing is the habit of measuring the answer, attending to its detail, and acting on it. To treat sleep as a vital sign (something to be measured, followed, and corrected rather than noted and excused) would be a small change in practice with potentially large returns. Making it real will require simple measurement standards, a place for sleep in the medical record, and trials that ask whether treating sleep to a target improves the outcomes of psychiatric illness.

Conflict of Interest: The authors declare that there is no conflict of interest.

Use of AI for Writing Assistance: The authors declared that artificial intelligence was not used in the study.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Saper CB, Scammell TE, Lu J. Hypothalamic regulation of sleep and circadian rhythms. Nature 2005;437:1257-1263. [CrossRef]
2. Saper CB, Chou TC, Scammell TE. The sleep switch: hypothalamic control of sleep and wakefulness. Trends Neurosci 2001; 24:726-731. [CrossRef]
3. Saper CB, Fuller PM, Pedersen NP, Lu J, Scammell TE. Sleep state switching. Neuron 2010; 68:1023-1042. [CrossRef]
4. Sherin JE, Shiromani PJ, McCarley RW, Saper CB. Activation of ventrolateral preoptic neurons during sleep. Science 1996; 271:216-219. [CrossRef]
5. Baglioni C, Nanovska S, Regen W, Spiegelhalder K, Feige B, Nissen C, et al. Sleep and mental disorders: A meta-analysis of polysomnographic research. Psychol Bull 2016; 142:969-990. [CrossRef]
6. Palagini L, Baglioni C, Ciapparelli A, Gemignani A, Riemann D. REM sleep dysregulation in depression: state of the art. Sleep Med Rev 2013; 17:377-390. [CrossRef]
7. Ferrarelli F, Huber R, Peterson MJ, Massimini M, Murphy M, Riedner BA, et al. Reduced sleep spindle activity in schizophrenia patients. Am J Psychiatry 2007; 164:483-492. [CrossRef]
8. Manoach DS, Stickgold R. Abnormal sleep spindles, memory consolidation, and schizophrenia. Annu Rev Clin Psychol 2019; 15:451-479. [CrossRef]
9. Wulff K, Dijk DJ, Middleton B, Foster RG, Joyce EM. Sleep and circadian rhythm disruption in schizophrenia. Br J Psychiatry 2012; 200:308-316. [CrossRef]
10. Harvey AG, Murray G, Chandler RA, Soehner A. Sleep disturbance as transdiagnostic: consideration of neurobiological mechanisms. Clin Psychol Rev 2011; 31:225-235. [CrossRef]
11. Baglioni C, Battagliese G, Feige B, Spiegelhalder K, Nissen C, Voderholzer U, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. J Affect Disord 2011; 135:10-19. [CrossRef]

12. Hertenstein E, Feige B, Gmeiner T, Kienzler C, Spiegelhalder K, Johann A, et al. Insomnia as a predictor of mental disorders: A systematic review and meta-analysis. Sleep Med Rev 2019;43:96-105. [CrossRef]

13. Freeman D, Sheaves B, Waite F, Harvey AG, Harrison PJ. Sleep disturbance and psychiatric disorders. Lancet Psychiatry 2020; 7:628-637. [CrossRef]

14. Gibson MJ, Lawlor DA, Millard LAC. Identifying the potential causal role of insomnia symptoms on 11,409 health-related outcomes: a phenome-wide Mendelian randomisation analysis in UK Biobank. BMC Med 2023; 21:128. [CrossRef]

15. Freeman D, Sheaves B, Goodwin GM, Yu LM, Nickless A, Harrison PJ, et al. The effects of improving sleep on mental health (OASIS): a randomised controlled trial with mediation analysis. Lancet Psychiatry 2017; 4:749-758. [CrossRef]

16. 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; 31:489-495. [CrossRef]

17. Reeve S, Sheaves B, Freeman D. The role of sleep dysfunction in the occurrence of delusions and hallucinations: A systematic review. Clin Psychol Rev 2015; 42:96-115. [CrossRef]

18. Yoo SS, Gujar N, Hu P, Jolesz FA, Walker MP. The human emotional brain without sleep--a prefrontal amygdala disconnect. Curr Biol 2007;17:R877-878. [CrossRef]

19. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001; 2:297-307. [CrossRef]

20. Qaseem A, Kansagara D, Forciea MA, Cooke M, Denberg TD; Clinical Guidelines Committee of the American College of Physicians. Management of chronic insomnia disorder in adults: a clinical practice Guideline from the American College of Physicians. Ann Intern Med 2016; 165:125-133. [CrossRef]

21. Rocha RB, Bomtempo FF, Nager GB, Cenci GI, Telles JPM. Dual orexin receptor antagonists for the treatment of insomnia: systematic review and network meta-analysis. Arq Neuropsiquiatr 2023; 81:475-483. [CrossRef]

22. Xie L, Kang H, Xu Q, Chen MJ, Liao Y, Thiyagarajan M, et al. Sleep drives metabolite clearance from the adult brain. Science 2013; 342:373-377. [CrossRef]

AUTHORS' BIOGRAPHIES

Umit Haluk Yesilkaya, MD, PhD, is a Postdoctoral Research Fellow in the Department of Neurology at Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA. A psychiatrist with a PhD in neuroscience, his research focuses on peripheral inflammatory and neurotrophic biomarkers in first-episode psychosis and mania, sleep-dependent memory consolidation in schizophrenia, and hypothalamic circuits regulating sleep and circadian rhythms in neurodegenerative and mood disorders. He is a recipient of the NARSAD Young Investigator Award (National Alliance for Research on Schizophrenia and Depression) and multiple European College of Neuropsychopharmacology (ECNP) Excellence Awards.

Clifford B. Saper, MD, PhD, is the James Jackson Putnam Professor of Neurology and Neuroscience at Harvard Medical School and served as Chairman of the Department of Neurology at Beth Israel Deaconess Medical Center from 1992 to 2021. He is a member of the National Academy of Medicine and a former Editor-in-Chief of Annals of Neurology and the Journal of Comparative Neurology. His research focuses on the hypothalamic and brainstem circuitry controlling sleep and wakefulness, circadian rhythms, thermoregulation, and responses to immune stimulation and stress. His work includes the identification of the ventrolateral preoptic nucleus as a sleep-promoting center and preoptic EP3 receptor neurons as a switch controlling fever and torpor.