Neuropsychopharmacology www.nature.com/npp

EDITORIAL

Sleep and neuropsychiatric illness

Neuropsychopharmacology (2020) 45:1–2;
https://doi.org/10.1038/s41386-019-0514-5

Sleep and neuropsychiatric illness are entwined. Disturbances of sleep are DSM-5 diagnostic features for major depressive disorder, generalized anxiety disorder, post-traumatic stress disorder, and bipolar disorder, and are consistent features of psychoses and most neurodegenerative disorders. Pharmacologic or psychological treatment of these disorders often improves the sleep impairment, and medications used to treat neuropsychiatric disorders may also be used as primary treatments for sleep disorders.

The most promising aspect of this relationship was explicitly postulated 30 years ago for mood disorders: not only is sleep disturbance a phenotypic feature of many neuropsychiatric illnesses, but it may in fact predispose, contribute to, and dare we say it, cause them [1, 2]. The Epidemiologic Catchment Area study was the first high-profile data demonstrating that insomnia was a strong predictor of incident mood disorders, suggesting that sleeplessness was thus "an opportunity for prevention". This type of "bidirectional" relationship with insomnia has been demonstrated (although not equivocally) over the last 30 years for a number of neuropsychiatric disorders, including bipolar disorder [3], anxiety disorders [4], PTSD [5], substance use disorders [6], and Alzheimer's disease [7]. Sleep disturbance has also been established as a risk for transdiagnostic symptoms such as suicidality and pain [8, 9]. Further, circadian rhythm dysregulation (independent of sleep disturbance) may be a risk for neuropsychiatric illness, including bipolar disorder, neurodegenerative disorders, and schizophrenia [10, 11]. Many of the papers in the current issue of Neuropsychopharmacology Reviews discuss the bidirectional relationship of sleep disturbance/circadian rhythms and neuropsychiatric illness, and their potential underlying neurobiological mechanisms.

As recognition of the complex role that sleep disturbance plays in psychiatric illness, DSM-5 mitigated the nearly impossible task for clinicians of determining whether insomnia was caused by psychiatric illness or vice-versa. This continued the evolution of previous DSM editions in eliminating distinctions between primary vs secondary, and subsequently primary vs comorbid, insomnia; instead insomnia diagnosis in DSM-5 is primarily based on symptom features, frequency, and duration. As a result, it encourages independent treatment of insomnia, as well as facilitating further research into the role of sleep disturbance in the etiology and natural history of psychiatric illness.

Multiple approaches to the analysis of sleep function exist, many of which are addressed in this special issue. Whereas the EEG has been the standard method to determine differences in brain activity during vigilance states, fMRI, DTI, and other imaging methods have added information about the role of specific networks in sleep/wake dysfunction and hyperarousal conditions. Further, multimodal and longitudinal recordings of physiological parameters using wearables will add precision to the characterization of the arousal dysfunctions [12].

Significant advances in systems neuroscience have generated a much more detailed picture of the neuronal circuitry underlying sleep/wake control (reviewed by Jones et al. in this issue), and hyperarousal [13, 14]. For instance, Eban-Rothschild et al. [15] described a causal role of mesocorticolimbic dopaminergic activity in sleep and wakefulness. Alterations of dopaminergic neurons have long been associated with hyperarousal, PTSD [14], autism [16], and alcoholism and drug abuse [17]. Also, advances in molecular genetics of memory [18], cognitive performance, and circadian oscillations have dramatically increased our understanding of such connections [19, 20]. Hypocretin/orexin release in the brain correlates with accumulation of beta amyloid peptides, providing a molecular connection between sleep circuits and sleep dysfunction in Alzheimer's disease [21]. In addition to AD, sleep disruption accompanies the progression of several neurodegenerative disorders including Parkinson's and newly described autoimmune disorders [22, 23]. Genetic variants associated with the neuronal activity associated with these circuits will likely predict risk for neuropsychiatric disorders.

Together, this special issue highlights the role of sleep in maintaining a healthy brain. We expect that a comprehensive characterization of sleep and arousal circuits will increase the arsenal of methods to precisely increase sleep quality, thereby increasing quality of life in neuropsychiatric patients.

FUNDING AND DISCLOSURE

The authors declare no competing interests.

John W. Winkelman[1] and Luis de Lecea[2]
[1]*Professor of Psychiatry, Harvard Medical School, Departments of Psychiatry and Neurology, Massachusetts General Hospital, Boston, USA and* [2]*Professor of Psychiatry and Behavioral Sciences. Dept. of Psychiatry and Behavioral Sciences, Stanford University Medical School, Stanford, USA*
Correspondence: John W. Winkelman (jwwinkelman@partners.org) or Luis de Lecea (llecea@stanford.edu)

ADDITIONAL INFORMATION

REFERENCES

1. Wehr TA, Sack DA, Rosenthal NE. Sleep reduction as a final common pathway in the genesis of mania. Am J Psychiatry 1987;144:201–4.
2. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention?. JAMA 1989;262:1479–84.
3. Harvey AG. Sleep and circadian functioning: critical mechanisms in the mood disorders? Annu Rev Clin Psychol 2011;7:297–319.
4. Chung KH, Li CY, Kuo SY, Sithole T, Liu WW, Chung MH. Risk of psychiatric disorders in patients with chronic insomnia and sedative-hypnotic prescription: a nationwide population-based follow-up study. J Clin Sleep Med 2015;11:543–51.
5. Wang HE, Campbell-Sills L, Kessler RC, Sun X, Heeringa SG, Nock MK, et al. Predeployment insomnia is associated with post-deployment post-traumatic stress disorder and suicidal ideation in US Army soldiers. Sleep. 2019;42.

Received: 27 August 2019 Accepted: 27 August 2019
Published online: 5 September 2019

6. Dolsen MR, Harvey AG. Life-time history of insomnia and hypersomnia symptoms as correlates of alcohol, cocaine and heroin use and relapse among adults seeking substance use treatment in the United States from 1991 to 1994. Addiction 2017;112:1104–11.
7. Irwin MR, Vitiello MV. Implications of sleep disturbance and inflammation for Alzheimer's disease dementia. Lancet Neurol 2019;18:296–306.
8. Pigeon WR, Pinquart M, Conner K. Meta-analysis of sleep disturbance and suicidal thoughts and behaviors. J Clin Psychiatry. 2012;73:e1160–7.
9. Finan PH, Goodin BR, Smith MT. The association of sleep and pain: an update and a path forward. J Pain 2013;14:1539–52.
10. Leng Y, Musiek ES, Hu K, Cappuccio FP, Yaffe K. Association between circadian rhythms and neurodegenerative diseases. Lancet Neurol 2019;18:307–18.
11. Wulff K, Dijk DJ, Middleton B, Foster RG, Joyce EM. Sleep and circadian rhythm disruption in schizophrenia. Br J Psychiatry 2012;200:308–16.
12. Goldstein-Piekarski AN, Williams LM. New technologies for precision psychiatry. Neuropsychopharmacology. 2019.
13. Jones BE. Arousal and sleep circuits. Neuropsychopharmacology. 2019.
14. Neylan TC. Sleep disturbance across anxiety-related disorders: an updated review and a discussion about the transdiagnostic role of arousal and threat. Neuropsychopharmacology. 2019.
15. Eban-Rothschild A, Rothschild G, Giardino WJ, Jones JR, de Lecea L. VTA dopaminergic neurons regulate ethologically relevant sleep-wake behaviors. Nat Neurosci 2016;19:1356–66.
16. Missig G, McDougle CJ, Carlezon WA, Jr. Sleep as a translationally-relevant endpoint in studies of autism spectrum disorder (ASD). Neuropsychopharmacology. 2019.
17. Koob GF, Colrain IM. Alcohol use disorder and sleep disturbances: a feed-forward allostatic framework. Neuropsychopharmacology. 2019.
18. Born J. Neurochemical mechanisms for memory processing during sleep – basic findings in humans and neuropsychiatric implications. Neuropsychopharmacology. 2019.
19. Hudson AN, Van Dongen HPA, Honn KA. Sleep deprivation, vigilant attention, and brain function: a review. Neuropsychopharmacology. 2019.
20. Ashbrook L, Krystal A, Fu YH, Ptacek LJ. Genetics of the human circadian clock and sleep homeostat. Neuropsychopharmacology. 2019.
21. Holtzman DM. Bidirectional relationship between sleep and Alzheimer's disease: role of amyloid, tau, and other factors. Neuropsychopharmacology. 2019.
22. Stefani A, Hogl B. Sleep in Parkinson's disease. Neuropsychopharmacology. 2019.
23. Iranzo A. Sleep and neurological autoimmune diseases. Neuropsychopharmacology. 2019.