Proceedings of the 3rd International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/23/20231011

Review of the effects of chronic stress on human insomnia

Leyi Kang

University of California San Diego, California, United States, 92092

Kangleyi1105@gmail.com

Abstract. While there are decent amounts of studies exploring the effects of chronic stress on sleep in animal models (e.g., rats), studies recruiting human subjects on this specific topic are rare in neuroscience and psychology. Thus, this paper aims to review the literature focusing on and mentioning chronic stress effects on human sleep, primarily based on experimental trials and clinical cases. Specifically, this review assesses the relationship between chronic stress (rather than acute stress and traumatic events) and insomnia in adult humans, the neurological and behavioral influence of chronic stress, and potential treatments for insomnia related to stress. The review was conducted using the PsycInfo database. Results from the reviewed literature show that chronic stress is associated with a decrease in neurogenesis and can be predicted by amygdala reactivity. Human subjects are likely to replicate results from rat models that show a decrease in REM sleep time under chronic stress and altered slow wave activities during sleep, and such deprivation of REM sleep can further alter hormonal levels in brain areas relating to stress and learning. Promisingly, there is evidence supporting the efficacy of cognitive and behavioral therapy for insomnia (CBT-I), conducted by professional therapists.

Keywords: chronic stress, insomnia, REM sleep, CBT.

1. Introduction

Insomnia is the most common sleep disorder that can present independently or with comorbidity with other physical or mental conditions. It is highly prevalent and can lead to many costly consequences on patients and society [1]. Multiple physiological causes for insomnia have been identified, including both acute stress (e.g., separation, illness) and chronic stressful events (e.g., occupational stress) and corresponding resolutions have been studied [2]. There is also abundant evidence for the hyperarousal theory, which suggests that insomnia occurs when both sleep and arousal are active [3]. However, studies on the neurological mechanism of how chronic stress affects insomnia presentations are rather scarce, while lots of people with stressful lifestyles face this problem. there has been evidence on the consequences of chronic stress on sleep quality and activities of rats, but only a few of them include comparisons and contrasts with humans, and research using only human subjects is rarer.

Even though there are ample amount of studies discussing the causes and mechanism of insomnia, few of them focuses on a more everyday setting and includes chronic stress as a factor – chronic stress is not as noticeable as acute stress caused by traumatic events or other psychiatric conditions, but it should be acknowledged, especially in a modern society where we all live under stress and may not be fully aware of it and lack proper knowledge to cope with it. Thus, this paper aims to review the literature

DOI: 10.54254/2753-8818/23/20231011

containing information on human subjects, draw conclusions on the neurological mechanisms of chronic stress on insomnia, and examine promising treatments for insomnia that are specifically due to stress.

2. Features of insomnia

The United States faces the heavy burden of insomnia: more than 50% of adults have difficulties sleeping, and 22.1% meet DSM-IV criteria for insomnia. The overall prevalence of insomnia in working people is 23.2%, and it is higher in women (27.1%) than men (19.7%) [4]. Insufficient sleep has also been declared a public health problem by The Centers for Disease Control and Prevention (CDC) and negatively affects society globally. Given an estimate based on a macro-economic model, up to $680 Billion is lost each year across five OECD countries due to insufficient sleep [5].

Besides the societal effects of insomnia, the neurological changes caused by it are also well-studied. In an fMRI study, insomnia patients presented higher amygdala responses to insomnia-related stimuli compared to healthy good sleepers and lacked the habituation of amygdala responses [6]. A resting-state fMRI study revealed abnormal spontaneous brain activities in regions such as the left orbitofrontal cortex and inferior frontal gyrus [7]. Regarding the aspect of neural development, worse insomnia was associated with smaller volumes of CA3 and dentate subfields of the hippocampus, consistent with the findings of studies using animal models [8].

3. Effects of chronic stress on sleep in rodent models: Dysfunctional REM sleep

Kant et al. designed a paradigm signaling intermittent foot shock to create chronic stress for rats, which were divided into a controllable stress group (CS) and an uncontrollable stress group (UCS) [9]. CS could pull on a chain to avoid the electrical shock, while UCS could not. Results showed that the total sleep time decreased significantly in CS during the first day of stress, and REM sleep was significantly more affected by stress even after the first day. Although both NREM and REM sleep time gradually increased after day 1 of stress, it was hard to return to the pre-stress level, demonstrating the persistent influence of chronic stress.

In another study conducted by Machado et al., all REM-sleep-deprived (PSD) rats exhibited REM sleep rebound, while PSD rats receiving multiple footshock (MFS) showed the highest rebound [10]. They also showed altered levels of hormones: intermediate levels of corticosterone, highest prolactin, and elevation of serotonin in the hypothalamus. The change in hormonal levels can be explained by the adaptation to stress, but it should also be noted that such a change in hormonal baseline can contribute to future sleep loss, which has been observed and reported by many insomnia patients.

Furthermore, the mice model presented comparable results, showing that chronic social stress induced by sleep deprivation disturbed homeostasis regulation and slow wave activities (SWA) during sleep [11].

The importance of REM sleep has been highlighted by numerous studies, and its relationship with insomnia has been acknowledged: the contribution of REM sleep to subjective wake time was significantly larger in insomnia patients than in good sleeper controls [12]. Feige et al. further concluded that REM sleep might be responsible for the subjectively disturbed sleep of primary insomnia patients, their perception of insomnia. On the other hand, the slow wave activity deficiency in insomnia patients is widely acknowledged, so it is reasonable to draw a connection between the finding of disrupted SWA in rats and that in humans [13]. Although for now there are not enough experiments in rats or human to draw any solid conclusion, it can be assumed that chronic stress leads to dysfunctional REM sleep and slow wave processes, which can then cause insomnia or aggravate the condition.

4. Effects of chronic stress on sleep in humans: Altered neurological responses

Some clinical symptoms of insomnia can be attributed to neurological abnormalities: some findings indicated that insomnia in humans was associated with volume loss in CA3/dentate subfields in the hippocampus [8]. They conformed with the results in a rat model presenting reduced neurogenesis in the hippocampus due to sleep fragmentation [14]. Fragmented sleep is also a result of chronic stress, so if more human participants are recruited and more data are gathered, we might be able to explore the

DOI: 10.54254/2753-8818/23/20231011

causal relationship between chronic stress and hippocampal neurogenesis reduction. Since dendritic branching is a crucial process for learning and memory, it is not surprising that rats' spatial learning and spatial reference memory were impaired under chronic stress conditions without arousal from fear, and we could assume that humans may fall under the same pattern [15].

There is also evidence shedding light on the relationship between amygdala responses and stress levels. fMRI results presented a significant association between amygdala reactivity to fearful facial stimuli and self-reported stress level in male poor sleepers [16]. This provides further support for the neurological consequences of the stress-insomnia interaction.

5. Promising treatments

Researchers in the realms of pharmacology, cognitive science, psychiatry, and psychology all work hard to develop numerous ways to improve the life quality of insomnia patients. Gladly, some experimental trials and case studies have proven the validity of Cognitive and Behavioral Therapy (CBT). Perlis et al. found a series of successes: in their cases, 33% of insomnia patients improved after the completion of four or more sessions of CBT and medical comorbidity did not influence their outcome [17].

It should be noted that CBT specifically written for insomnia and administered by a professional therapist produces the most significant reduction in insomnia, compared to self-help CBT procedures, even helping treat comorbid insomnia with depression [18].

6. Conclusions

Insomnia, as the most prevalent sleeping disorder, severely impairs patients' quality of life and brings heavy burdens to societies. More importantly, it produces long-lasting effects in cognition and neural development, which can in turn lead to more serious consequences in life. This paper reviews studies that can validate the association between chronic stress and insomnia, aiming to bring attention to the risky factor that has long existed under our noses. Overall, chronic stress disrupts brain wave activities (especially REM sleep) and hormones relating to stress in rats, which consequently elevates their stress level and impairs their sleep quality. There is potential relationship between chronic stress and insomnia, as the deficiency of slow wave activities in insomnia subjects is already acknowledged. Moreover, insomnia and chronic stress can worsen each other and cause long-lasting effects on the human brain, such as the loss of neuronal branching in the hippocampus and altered fear responses in the amygdala. We can expect impaired learning and memory in human participants with chronic-stress-induced insomnia.

Limited by the number of related articles, this paper might not be able to give the most holistic review of this topic. To understand more about how chronic stress affects human sleep, more clinical experiments recruiting human subjects are needed. For more reliable results and conclusions, we should consider the differences in gender, age, and social class, as the prevalence of insomnia differs among them.

References

[1] Leger, D., & Bayon, V. (2010b). Societal costs of insomnia. Sleep Medicine Reviews, 14(6), 379–389. https://doi.org/10.1016/j.smrv.2010.01.003

[2] Morin, C. M., & Benca, R. M. (2012). Chronic insomnia. The Lancet, 379(9821), 1129–1141. https://doi.org/10.1016/s0140-6736(11)60750-2

[3] Bonnet, M. H., & Arand, D. L. (2010). Hyperarousal and insomnia: State of the science. Sleep Medicine Reviews, 14(1), 9–15. https://doi.org/10.1016/j.smrv.2009.05.002

[4] Dopheide, J. A. (2020). Insomnia overview: epidemiology, pathophysiology, diagnosis and monitoring, and nonpharmacologic therapy. The American Journal of Managed Care, 26(Suppl 4), S76–S84. https://doi.org/10.37765/ajmc.2020.42769

[5] Hafner, M., Stepanek, M., Taylor, J., Troxel, W. M., & Van Stolk, C. (2017). Why sleep matters: The economic costs of insufficient sleep. In RAND Corporation eBooks. https://doi.org/10.7249/rb9962

[6] Baglioni, C., Spiegelhalder, K., Regen, W., Feige, B., Nissen, C., Lombardo, C., Violani, C., Hennig, J., & Riemann, D. (2014). Insomnia disorder is associated with increased amygdala reactivity to insomnia-related stimuli. Sleep: Journal of Sleep and Sleep Disorders Research, 37(12), 1907-1917. https://doi.org/10.5665/sleep.4240

[7] Li, C., Ma, X., Dong, M., Yin, Y., Hua, K., Li, M., Li, C., Zhan, W., Li, C., & Jiang, G. (2016). Abnormal spontaneous regional brain activity in primary insomnia: A resting-state functional magnetic resonance imaging study. Neuropsychiatric Disease and Treatment, 12, 8. https://www.proquest.com/scholarly-journals/abnormal-spontaneous-regional-brain-activity/docview/1812935487/se-2

[8] Neylan, T. C., Mueller, S. G., Wang, Z., Metzler, T. J., Lenoci, M., Truran, D., Marmar, C. R., Weiner, M. W., & Schuff, N. (2010). Insomnia severity is associated with a decreased volume of the CA3/dentate gyrus hippocampal subfield. Biological Psychiatry, 68(5), 494-496. https://doi.org/10.1016/j.biopsych.2010.04.035

[9] Kant, G. J., Pastel, R. H., Bauman, R. A., Meininger, G. R., Maughan, K. R., Robinson, T. N., Wright, W. L., & Covington, P. S. (1995). Effects of chronic stress on sleep in rats. Physiology & Behavior, 57(2), 359-365. https://doi.org/10.1016/0031-9384(94)00241-V

[10] Machado, R. B., Tufik, S., & Suchecki, D. (2008). Chronic stress during paradoxical sleep deprivation increases paradoxical sleep rebound: Association with prolactin plasma levels and brain serotonin content. Psychoneuroendocrinology, 33(9), 1211-1224. https://doi.org/10.1016/j.psyneuen.2008.06.007

[11] Olini, N., Rothfuchs, I., Azzinnari, D., Pryce, C. R., Kurth, S., & Huber, R. (2017). Chronic social stress leads to altered sleep homeostasis in mice. Behavioural Brain Research, 327, 167-173. https://doi.org/10.1016/j.bbr.2017.03.022

[12] Feige, B., Al-Shajlawi, A., Nissen, C., Voderholzer, U., Hornyak, M., Spiegelhalder, K., Kloepfer, C., Perlis, M. L., & Riemann, D. (2008). Does REM sleep contribute to subjective wake time in primary insomnia? A comparison of polysomnographic and subjective sleep in 100 patients. Journal of Sleep Research, 17(2), 180–190. https://doi.org/10.1111/j.1365-2869.2008.00651.x

[13] Tafti, M., Villemin, E., Besset, A., & Billard, M. (1993). Slow wave activity deficiency in sleep maintenance insomnia patients. Sleep Res, 22, 575.

[14] Guzman-Marin, R., Suntsova, N., Methippara, M., Greiffenstein, R., Szymusiak, R., & McGinty, D. (2005b). Sleep deprivation suppresses neurogenesis in the adult hippocampus of rats. European Journal of Neuroscience, 22(8), 2111–2116. https://doi.org/10.1111/j.1460-9568.2005.04376.x

[15] Conrad, C. D. (2010). A critical review of chronic stress effects on spatial learning and memory. Progress in Neuro-Psychopharmacology & Biological Psychiatry, 34(5), 742-755. https://doi.org/10.1016/j.pnpbp.2009.11.003

[16] Prather, A. A., Bogdan, R., & Hariri, A. R. (2013). Impact of sleep quality on amygdala reactivity, negative affect, and perceived stress. Psychosomatic Medicine, 75(4), 350-358. https://doi.org/10.1097/PSY.0b013e31828ef15b

[17] Perlis, M. L., Sharpe, M., Smith, M. T., Greenblatt, D., & Giles, D. (2001). Behavioral treatment of insomnia: Treatment outcome and the relevance of medical and psychiatric morbidity. Journal of Behavioral Medicine, 24(3), 281-296. https://doi.org/10.1023/A:1010770807823

[18] Ashworth, D. K., Sletten, T. L., Junge, M., Simpson, K., Clarke, D., Cunnington, D., & Rajaratnam, S. M. W. (2015). A randomized controlled trial of cognitive behavioral therapy for insomnia: An effective treatment for comorbid insomnia and depression. Journal of Counseling Psychology, 62(2), 115-123. https://doi.org/10.1037/cou0000059