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Short Sleep Duration and the Risk of Hypertension and Diabetes

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By

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Introduction

"Health is the first muse, and sleep is the condition to produce it"-Ralph Waldo Emerson. Sleep is a vital component necessary for all humans to maintain health, yet over 50% of Americans sleep less than seven hours a night.[1] Is less than seven hours unhealthy? For many, a good night's sleep is the difference between whether one has a productive day or not. At the cellular level, sleep is a time when the body restores and repairs itself. For many in society today, getting adequate sleep inherently becomes an afterthought to time spent at school, work, and with loved ones. Before examining the impact of sleep on health, understanding the basic terms and concepts about sleep in humans is necessary.

Sleep is a complex physiologic process characterized by different stages. At its most basic level, "Sleep is a naturally recurring state characterized by altered consciousness, inhibited sensory activity, and inhibition of voluntary muscle movement".[2] Sleep consists of two types: rapid eye movement (REM) and non-rapid eye movement (NREM). Healthy and restorative sleep consists of 4 to 5 cycles of NREM and REM sleep each night, with each cycle lasting approximately 90 minutes. Sleep begins with NREM sleep, when active muscle tone is maintained. As the cycle continues, the NREM sleeper becomes less responsive to external stimuli and is harder to wake. REM sleep follows in which the sleeper experiences rapid eye movements and atonia of the skeletal muscles. In the human body, two basic regulatory mechanisms are inherently in place in the human body to monitor sleep, the circadian process and the homeostatic drive for sleep, both of which within reason, can be nullified with voluntary sleep restriction.[2]

Despite these mechanisms, sleep for millions of people is not a simple endeavor. Both physiological and psychological barriers exist for millions of people, impairing their ability to

regulate and follow their circadian and homeostatic drives for sleep. A common problem resulting from disordered sleep is insomnia. Per the current Diagnostic and Statistical Manual of Mental Disorders (DSM-5) the diagnostic criteria for insomnia disorder, are that one must have all items A thru E:

A	A predominant complaint of dissatisfaction with sleep quantity or quality, associated with one (or more) of the following symptoms: 1) Difficulty initiating sleep 2) Difficulty maintaining sleep, characterized by frequent awakenings or problems returning to sleep after awakenings 3) Early morning awakening with inability to return to sleep
B	The sleep disturbance causes clinically significant distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning
C	The sleep difficulty occurs at least 3 nights per week
D	The sleep difficulty is present for at least 3 months
E	The sleep difficulty occurs despite adequate opportunity for sleep
F	The insomnia is not better explained by and does not occur exclusively during the course of another sleep-wake disorder (narcolepsy, a breathing-related sleep disorder, a circadian rhythm sleep-wake disorder, a parasomnia)
G	The insomnia is not attributable to the physiological effects of a substance
H	Coexisting mental disorders and medical conditions do not adequately explain the predominant complaint of insomnia

From:Black, D. and Grant, J. (2014). DSM-5 TM Guidebook. Washington, DC: American Psychiatric Publishing

In essence, insomnia is difficulty sleeping or maintaining sleep long enough for one to feel the restoring effects of sleep. In a report by Depner et al., approximately 8-10% of the population experiences chronic insomnia, but as many as 20-30% of the population are affected by some symptoms of insomnia. [1] Putting these numbers into perspective, it is concerning that numerous people are negatively affected by something so integral to their health, sleep.

As mentioned, the majority of Americans are sleeping less than seven hours per night. Among health academicians, 7-8 hrs of sleep per night is considered by consensus as the gold standard for the duration of sleep necessary to achieve a "full night's rest". Many terms are used to describe less than optimal (7-8 hours) sleep per night, including insomnia and insufficient sleep syndrome. Insufficient sleep syndrome is simply the inability to remain alert with sufficient wakefulness as a result of inadequate or insufficient nocturnal sleep[1]. Unfortunately, this definition lacks quantitative stipulations for hours slept each night. This limitation notwithstanding, insufficient sleep has been linked with numerous health problems, including but not limited to, inflammation, depression, stress, anxiety, obesity, diabetes and cardiovascular disease. [1] Based on this information, chronic health issues prevalent in Americans, such as obesity and cardiovascular disease (CVD), appear to be explained in part by insufficient sleep.

The correlation between disease and insufficient sleep becomes significant in view of the large number of people who do not obtain at least seven hours of sleep per night or achieve "a full-night's rest." Furthermore, the highly prevalent and burdensome diseases, hypertension and diabetes, seem to be associated with insufficient sleep. These associations suggest that over the majority of Americans are at risk for diabetes and hypertension based on insufficient sleep alone. Therefore, whether adults (persons >18 years old) who sleep less than seven hours a night, compared with those who sleep seven or more hours, actually have a greater risk for developing diabetes or hypertension is critical information for preventative care.

Specifically, the morbidities of hypertension and diabetes mellitus become significant because of their increasing prevalence throughout the American population. According to the CDC (Center for Disease Control), the rate of diabetes nearly doubled in the United States between the years 1980 to 2006, and increased similarly throughout the world. The CDC also

reports that about 1 in 3 adults, or roughly 75 million Americans have high blood pressure, while another in 1 in 3 adults has prehypertension.[4] It is alarming how quickly the rate of type 2 diabetes is increasing. That two thirds of American adults are either hypertensive or pre-hypertensive is also disturbing.

Per the CDC, in the year 2016, essential hypertension as a primary diagnosis lead to 1 million emergency department visits. Outpatient visits with that same diagnosis and year were staggering as well, at 32.8 million visits.[5] Mortality in 2016 exceeded 35,000 deaths due to primary hypertension.[5] The numbers are just as concerning for diabetes, per the CDC's report that 11.4% and 11.5% of emergency department visits and physician office visits, respectfully, involved diabetes in 2016. In addition, diabetes was responsible for more than 83,000 deaths in 2016.[6]

These statistics highlight the importance of determining the relationship of short sleep durations and development of either hypertension or diabetes. Furthermore, the high prevalence of insufficient sleep and these diseases assure that primary care providers will frequently encounter patients who struggle to control one, two, or even all three of these conditions. For these reasons, it is essential to investigate the association, if any, between insufficient sleep, and hypertension and diabetes. If a direct relationship between a lack of sleep and an increased risk of either hypertension or diabetes were found, then future providers could educate patients accordingly and thus, prevent suffering from these mostly preventable diseases.

Discussion: Hypertension & Sleep

The relationship between short sleep durations and the risk of hypertension has been examined in several studies. In 2015 a meta-analysis by Wang et al. investigated whether sleep duration was associated with hypertension. This meta-analysis consisted of 13 studies that

examined self-reported sleep duration (less than 7 hours was considered deficient sleep) and the frequency of hypertension (defined as those with blood pressure readings >140/90mm Hg or who had been diagnosed with hypertension and use antihypertensive drugs). The results revealed a direct correlation between short sleep duration of less than seven hours and an increased risk of hypertension. In fact, it was discovered that essentially any amount of sleep outside the gold standard of seven hours per night, i.e., more or less than seven hours, lead to an increased risk of developing hypertension. Strengths of this meta-analysis included not only the diversity of publishing countries included (USA, Brazil, Spain, China, Australia), but also the broad age ranges in each study, spanning from age 18 to 86 years. In total, the study population in the meta-analysis consisted of over three hundred thousand individuals, further lending to the credibility and strength of its argument that sleep duration has a direct correlation with development of hypertension. However, almost all the studies relied on self-reported sleep durations, thus potentially limiting the reliability of the data.[7]

In corroboration with these findings, Shulman et al., compared 24-hour ambulatory blood pressure measurements with sleep durations. In those participants with shorter sleep durations (<7 hrs), the mean 24-hour systolic blood pressure was elevated more than 12 mmHg compared with those who had at least 7 hours of sleep in a night. In addition, patients with short sleep durations had increased risks of uncontrolled and/or sustained hypertension and faster 24 hr mean heart rates compared with those who slept at least 7 hours per night.[8] Table 2 from this study is included below for further illustration of these results.

Table 2.

Ambulatory blood pressure monitoring characteristics by sleep duration in LIMBS and PISA

	LIMBS Study N=66			PISA Study N=153		
	Short Sleep (<7 hours) N=21	**Long Sleep (≥7 hours) N=45**	**P-value**	**Short Sleep (<7 hours) N=84**	**Long Sleep (≥7 hours) N=69**	**P-value**
24-hour mean SBP (SD), mmHg	146.3 (14.0)	133.6 (10.1)	<0.001	131.5 (10.6)	126.8 (9.6)	0.005
24-hour SBP variability (SD), mmHg	9.3 (1.9)	8.6 (1.6)	0.121	8.9 (2.0)	9.0 (1.9)	0.777
24-hour heart rate (SD), bpm	65.8 (11.6)	57.8 (12.4)	0.027	76.2 (9.1)	74.3 (8.6)	0.182
Dippers, n (%)	11 (65%)	21 (47%)	0.205	55 (65%)	45 (65%)	0.973
White coat hypertension, n (%)	0 (0%)	3 (6%)	0.275	9 (11%)	5 (7%)	0.459
Masked hypertension, n (%)	4 (24%)	10 (22%)	0.913	15 (18%)	18 (26%)	0.218

	LIMBS Study N=66			PISA Study N=153		
	Short Sleep (<7 hours) N=21	**Long Sleep (≥7 hours) N=45**	**P-value**	**Short Sleep (<7 hours) N=84**	**Long Sleep (≥7 hours) N=69**	**P-value**
Uncontrolled hypertension, n (%)	8 (47%)	9 (20%)	0.033	21 (25%)	9 (13%)	0.064

Abbreviations: LIMBS = Lifestyle Modification in Blood Pressure Lowering Study; PISA = Penn Iceland Sleep Apnea Study; SD = standard deviation; SBP = systolic blood pressure; bpm = beats per minute
From: Shulman R, Cohen DL, Grandner MA, et al. Sleep Duration and 24-hour ambulatory blood pressure in adults not on antihypertensive medications. *The Journal of Clinical Hypertension*. 2018; 20(12):1712-1720. doi:10.1111/jch.13416.

Using 24-hour mean systolic blood pressure measurements, Schulman et al. corroborated findings in other studies that link high blood pressures with insufficient sleep. However, a limitation similar to other studies was the self-reported duration of sleep. Additionally, this cross-sectional study did not include the length of time (days, months, years) that participants were exposed to short sleep durations.

Grimaldi et. al examined the effects that sleep restriction had on the circadian rhythm and whether circadian misalignment increased the chance of developing hypertension. The term circadian misalignment is traditionally encountered with sleep restriction as sleep wake cycles are desynchronized and/or interrupted. The results of the study showed that consistent sleep restriction (<5 hrs per night) of participants was associated with increased heart rates as well as

increased urine norepinephrine excretions both nocturnally and in the morning. The increases in both nocturnal and morning catecholamines indicates an impairment in normal autonomic physiology throughout the sleep/wake cycle. This impairment can potentially lead to increased baseline blood pressure throughout the duration of those elevations, known as "nocturnal sympathetic activation".[9] The major strength of this nonrandomized parallel group was that participants had their sleep duration tracked via polysomnography, rather than self-reporting. In contrast, the major limiting factor included the small sample size of only 26 participants.

Discussion: Diabetes & Sleep

Correlations between short sleep durations of less than seven hours and the development of type 2 diabetes mellitus have been found in relatively recent research. In 2015 their meta-analysis, Shan et. al. found in their meta-analysis that the risk of developing type 2 diabetes mellitus increased with every one-hour shorter sleep duration of less than 7 hours. One of the strengths of this meta-analysis was the fact that the authors examined research from several countries on different continents, including USA, Germany, Australia, and Japan. Secondly, the inclusion criteria for the meta-analysis resulted in more than 450,000 participants.[10]

When examining the relationship between sleep duration and glucose intolerance in 2007, Chaput et al. found in the cross-sectional study that the chance of developing impaired glucose tolerance increased with decreased sleep duration (<7 hours sleep). Markers of glucose intolerance (fasting plasma glucose, insulin concentrations, and total insulin levels) were elevated. This study's strength was its objective measures of glucose intolerance or insulin resistance. However, the sample size of only several hundred participants may have limited the evidence, and thus its generalizability. Nonetheless, a strength was the plausible physiological explanation for the increased insulin resistance associated with short sleep duration, which

theory would also explain increased appetite concomitant with a lack of sleep. The authors do note that limitations of the study included its relatively small sample size (740 participants), as well as researcher's inability to quantify potential confounding effects of impaired glucose tolerance such has OSA or depression.[11]

Additional research by Ferrie et al. further supports the notion that short sleep duration (<7 hrs) increases the risk of diabetes mellitus. Using common markers for diagnosing diabetes, such as fasting plasma glucose, 75-gram glucose tolerance test, and Hemoglobin A1C, Ferrie et. al. found that those participants with consistent sleep duration levels equal to or less than (<5.5 hours) developed diabetes more frequently than the persistent 7-hour sleepers. The reverse "J" shaped curve formed by the data illustrated that both short sleep durations and long sleep durations increased the likelihood of developing diabetes mellitus. The large sample size of over 10,000 participants and the objective measures of diabetes strengthened the evidence quality and generalizability, whereas the self-reporting of sleep durations by the participants potentially limited the internal validity of this study. Nonetheless, external validity was strengthened by the sample size as well as the diversity of its participants.[12] These findings agree with those from other studies.

Summary

Several questions arise concerning these results that may require further study to help better understand these relationships between disease and short sleep durations. The theory of nocturnal sympathetic activation is likely to become the main emphasis of research for exploring the relationship between insufficient sleep and the risk of hypertension. To summarize this theory, sleep deprivation leads to an autonomic sympathetic response, thus activating the renin-angiotensin aldosterone system as well as the increased production of catecholamines. The

resulting vasoconstriction leads to increased blood pressure.[7] Further research measuring these markers would confirm this theory.

Future areas of investigation that might explain the correlation between diabetes and sleep duration include the concept of chronic inflammation resulting from the alteration of neurohormones due to eating habits. Specifically, sleep restriction has been closely associated with an increased appetite, especially for calorie dense foods, via mechanisms of upregulation of appetite stimulating hormones.[12] Moreover, sleep deprivation in lab rats promoted a chronic proinflammatory state, which led to increased levels of inflammatory markers such as interleukin-6 and C-reactive protein.[12] These possible explanations for the associations between short sleep durations and increased risks of hypertension and diabetes seem to be based in known pathophysiology.

Conclusion

The evidence in available studies confirms the increased risk of developing either hypertension or diabetes mellitus due to chronic sleep insufficiency. Furthermore, specific and plausible pathophysiologic mechanisms have been proposed to explain the relationships between short sleep durations and the development of these diseases. Future research may establish these mechanisms as the causes for the increased risks. In the meantime, the high prevalence of hypertension and diabetes necessitates due diligence in promoting preventive measures. Therefore, the important relationship between sleep, and both hypertension and diabetes need to be recognized by clinicians so that they can caution their patients to plan for adequate sleep as a means of decreasing or eliminating the risk of developing these diseases.

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