2 The Functional Impact of Sleep Deprivation, Sleep Restriction, and Sleep Fragmentation

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Paradigms of sleep deprivation, sleep restriction, and sleep fragmentation have been utilized to answer fundamental questions about sleep, including how much sleep adults need and the deficits and recuperation associated with sleep loss. While definitive answers to many of these core questions remain, this work has highlighted how sleep is crucial for healthy functioning. Absent, insufficient, or fragmented sleep has widespread neurobehavioral and physiological consequences, and also broader social and economic ramifications. The present chapter will compare and contrast the functional impacts of sleep deprivation, sleep restriction, and sleep fragmentation in adults, then discuss the implications that this research has on our understanding and conceptualization of sleep need and sleep debt.

Sleep Deprivation

The first sleep deprivation study was published over 100 years ago [1] and since then many studies have examined the impact of sleep deprivation on healthy functioning. A meta-analysis by Pilcher and Huffcutt [2] highlighted the impact of sleep deprivation; with their data showing cognitive performance and self-rated mood of sleep-deprived individuals below the 9th percentile of non-sleep-deprived subjects. In a seminal study by Dawson and Reid [3], alcohol was used to illustrate the deleterious impact of sleep deprivation on performance. They found that cognitive ability following 17 h of sustained wakefulness was equivalent to that of a person with a blood alcohol concentration of 0.05 % (the legal driving limit in many countries), while performance following 24 h of wakefulness was equivalent to that with a blood alcohol concentration of 0.10 % [3]. Sleep deprivation is common in many occupations that demand 24 h operations, such as nursing, mining, trucking, and aviation and tragically sleep deprivation has been implicated in several catastrophic incidents and accidents [4, 5].

Sleep Deprivation, Cognition, and Neurobehavioral Functioning

Changes to sleepiness and alertness are among the most robust and frequently examined consequences of sleep deprivation [6–11]. During sleep deprivation, the drive for sleep builds [12], resulting in decreased subjective alertness and increased self-reported and objective sleepiness. There are numerous ways to measure sleepiness, ranging from subjective self-report, EEGs markers, such as the latency to slow wave sleep (SWS) (shorter latencies reflect greater sleep pressure) and objective sleepiness measures, such as the Multiple Sleep Latency Test (MSLT) and the Maintenance of Wakefulness Test (MWT). These tests measure the time taken to fall asleep, or

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M.T. Bianchi (ed.), *Sleep Deprivation and Disease: Effects on the Body, Brain and Behavior*,
DOI 10.1007/978-1-4614-9087-6_2, © Springer Science+Business Media New York 2014

sleep latency, using EEG to monitor brain activity. The MSLT objectively measures the time taken to fall asleep in a sleep-conducive environment, while the MWT measures sleep latency under conditions where an individual is trying to *resist* falling asleep. Both MSLT and MWT values decline during sleep deprivation, indicating that individuals fall asleep much more quickly when trying to sleep, and they also fall asleep faster even when they are attempting to stay awake [13, 14]. Just one night of sleep deprivation can reduce MSLT sleep latencies to well within a pathologically sleepy range of 5 min or less [15] and reduce the latency to deep sleep by 50 % [16]. Franzen and colleagues [7] compared a group of 15 healthy, young adults following 1 night of sleep deprivation with 14 who had normal sleep. Sleep deprivation led to a range of performance and mood deficits; however, it had the largest impact on subjective and objective sleepiness. Faster MWT sleep latencies highlighted the increased likelihood of unintended sleep onset following sleep deprivation, a problem with substantial ramifications to safety.

The ability to sustain attention and maintain vigilance is reduced following even 1 night without sleep, another factor which increases the risk for accidents. Reaction times slow, behavioral lapses (the failure to respond to a stimulus within a timely fashion) increase, and failure to inhibit an incorrect response increases with sleep deprivation [7, 17–22]. Lapsing of attention (failing to respond to a stimulus) is believed to occur when microsleeps intrude into the waking state [23]. A commonly used task of vigilant attention task that is very sensitive to sleep loss is the psychomotor vigilance test (PVT). In a sleep deprivation study involving 88 h of sleep deprivation (3 nights without sleep), Doran and colleagues [23] found that, after 18 h of wake, PVT performance progressively deteriorated in terms of both reaction time and response errors. Over time, they also witnessed greater between-subject variance in vigilant attention, with the magnitude of performance deficits varying significantly among subjects. Lim and Dinges [24] suggest that sleep deprivation leads to a general slowing in response times (responses >500 ms), an increase in incorrect responses, and an amplification of the time-on-task effect (whereby performance deteriorates during a test as a result of boredom, fatigue, or lack of novelty). While the PVT is a basic task, vigilance and attention are functions that are important to and subserve a multitude of higher-order cognitive tasks. They argue that sustained attention deficits, as a prerequisite for upstream cognitive processing, are responsible for many of the performance deficits in memory and executive functioning tasks following sleep deprivation [24].

Many simple and complex cognitive tasks and domains show deficits following sleep deprivation. These include working memory [6, 25], memory consolidation, mental arithmetic [22], reasoning [22, 26], tracking [26, 27], innovative thinking and strategic planning [28–31], creative thinking [32, 33], verbal fluency [28, 32, 34], temporal memory [35], planning [32], creative and flexible thinking, decision making, speech articulation, language, and judgement [28–30, 34, 36, 37]. These deficits can begin as early as the first night of sleep deprivation [38, 39] and continue to increase significantly with extended wakefulness [9, 40, 41].

While these neurobehavioral deficits are commonly found in response to sleep loss, there is substantial variance among people in terms of individual vulnerability to sleep loss [9]. In addition, there is also substantial variance within individuals in regard to which domains are most affected by sleep loss [42]. This pattern of response was illustrated by a study by Van Dongen and colleagues [43]. They exposed 21 healthy, young participants to 36 h of sleep deprivation on three separate occasions. Results revealed a remarkable consistency in their response to sleep loss across different occasions. Surprisingly, however, this consistency did not hold across different neurobehavioral domains. So participants who reported a high level of subjective sleepiness did not necessarily show cognitive processing deficits or poor sustained attention, and individuals particularly vulnerable to cognitive deficits following sleep loss were not necessarily sleepier or less behaviorally alert. This differing pattern of individual response is illustrated in Fig. 2.1. One of the important ramifications of

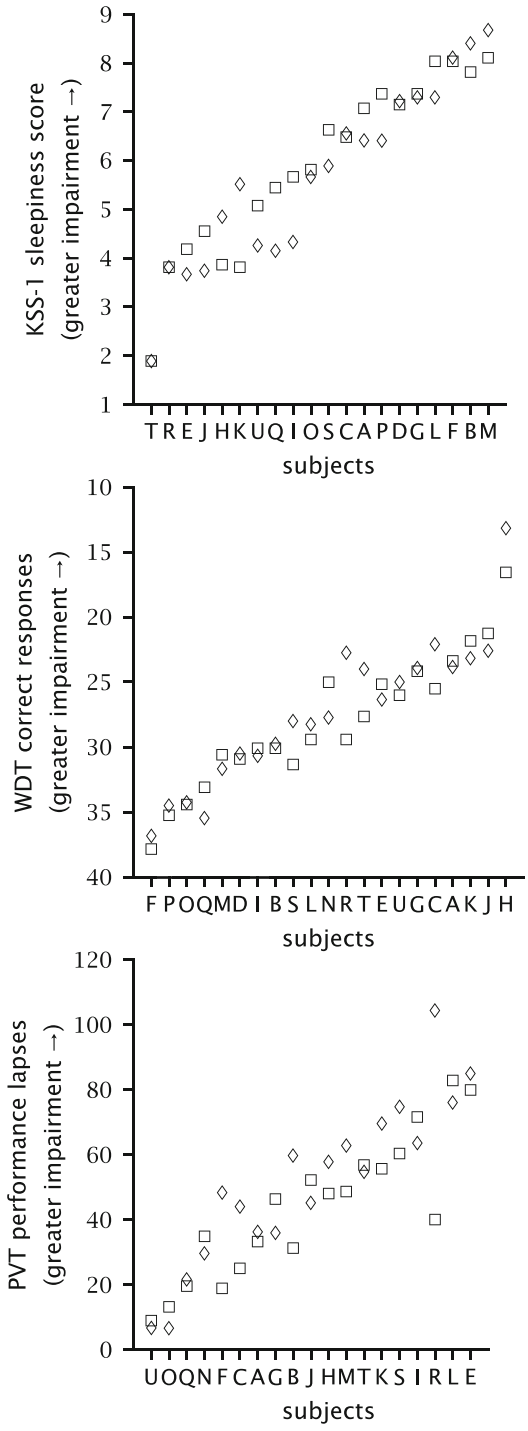

Fig. 2.1 Trait like neurobehavioral responses to total sleep deprivation. Data are shown for the Karolinska Sleepiness Scale (KSS-1), the word detection task (WDT), and the psychomotor vigilance task (PVT). The abscissa of each panel shows the 21 individual subjects, labeled A–U, in arbitrary order with the same label being used for the same subject across the three panels. Within each panel, the subjects are ordered by the magnitude of their impairment (averaged over 2, 36 h sleep deprivation periods), with the most resistant subjects on the left and the most vulnerable subjects on the right. Responses in the first exposure to sleep deprivation following 7 days of sleep extension are marked by boxes; responses in the second exposure to sleep deprivation following 7 days of sleep extension are marked by diamonds. The data show that subjects differed substantially in their responses to sleep deprivation, while the responses were relatively stable within subjects between the 2 exposures to sleep deprivation. (Reproduced with permission from Van Dongen et al. [43])

this work is that it highlights the shortcomings of relying upon an individual's subjective feelings of sleepiness and alertness to evaluate their cognitive or behavioral impairments. Indeed, the authors of this study argued that individuals are not well equipped to introspect their performance deficits following sleep deprivation.

Sleep Deprivation and Mood

Sleep deprivation has been associated with an increase in negative mood states [6, 44] and diminished positive mood [44]. These findings span discrete emotions including excitement, happiness, cheerfulness, activation, pride, and delight, as well as intensified symptoms of dissociation [45, 46]. Sleep deprivation has been linked to potentially serious changes to emotion, mood states, and their regulation [47, 48]. Changes with sleep deprivation to the brain's serotonergic system (low serotonin is associated with depression), in particular a desensitization of the serotonin (5-HT) 1A receptor system, could be a mechanism underlying this dysregulation of mood [49].

It has also been found that following 1 night of sleep deprivation, healthy young adults report increased negative mood and decreased positive affect [7]. In this study objective affect reactivity was measured using pupil dilation in response to emotional pictures [7]. Sleep deprivation led to elevated pupillary responses to negative pictures and the authors hypothesized that this reflected

heightened emotional reactivity to negative emotional information. Another study by Minkel et al. [50] examined stress and mood response following 1 night of sleep deprivation in either a low stress or high stress environment. Stressor intensity was altered by increasing the difficulty of the cognitive task, providing negative feedback about performance, and increasing time pressure. Sleep deprivation increased subjective stress, anxiety, and anger ratings following exposure to the low-stressor condition, but not in response to the high-stressor condition. Sleep deprivation elevated negative mood and stress about equally for both sleep conditions. These data suggest that sleep deprivation lowers the psychological threshold for the perception of stress, but does not change the magnitude of negative affect in response to high-stress, cognitive demands.

Sleep Deprivation and the Brain

The impact of sleep deprivation on cognition, sustained attention, and mood is likely to reflect the effect that sleep deprivation has on the neural systems that subserve these functions. Numerous and diverse cortical and subcortical structures and systems have been shown to be sensitive to sleep loss [8, 43, 51, 52]. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies have revealed significant decreases in global glucose metabolism throughout the brain during sleep deprivation [8, 53–57]. It has been argued that these reductions in brain glucose metabolism underlie functional deficits following sleep deprivation because of resource depletion [58–60]. While the relationship between attention, cognition, and neurophysiology following sleep deprivation is reasonably well explored, less is known about the neural mechanisms associated the changes in affect occurring after sleep deprivation [7]. Yoo and colleagues [61] found reduced functional connectivity between the medial frontal cortex (which exerts top-down control over limbic areas and has a role in emotional and behavioral regulation [62–64]) and the amygdala following sleep deprivation and a 60 % increased amygdala response during sleep deprivation compared to when rested. Accordingly, following sleep deprivation individuals are more likely to display inappropriate behaviors and act impulsively [35].

Close examination of the EEG spectra is another way to investigate the brain mechanisms that might mediate the relationship between sleep deprivation, increased sleepiness, and poor cognitive performance. Past studies have also consistently demonstrated a drowsiness-related pattern of changes in the spectral composition of the resting state EEG. In one study [65], spectral analysis of the EEG during 21 h of wakefulness revealed that power in the delta band increased (2 and 4 Hz) in the parietal region, while alpha in the occipital region (measured as the average power in a 1-Hz band around the peak frequency in the 8- and 12-Hz range) was significantly reduced by extended wakefulness. These changes paralleled those observed in subjective sleepiness ratings (Karolinska Sleepiness Scale). These data suggests that sleep deprivation has demonstrable effects on brain activity, with subsequent impact on feeling and functioning.

After a period of extended wakefulness, the stability of one of the brain regions responsible for the transition between sleep and wake becomes unstable, resulting in the uncontrollable intrusion of sleep into wakefulness [66]. The main region involved in this transition is the ventrolateral preoptic (VLPO) nucleus and it is sometimes referred to as the "flip-flop" switch between sleep and wake [66] The VLPO receives diminished inhibition following sleep loss [24], which increases the likelihood of both behavioral lapses and sleep onset. Research has shown that lapses are more likely to occur when the waking EEG shows signs of transition to sleep onset [67].

More recently, research has shown the importance of sleep to the generation and survival of new neurons [68]. In an adult rat model, 96 h of sleep deprivation led to a 50 % reduction in new cells in the hippocampal dentate gyrus, a brain region involved in the formation of new memories. Three weeks subsequent to the sleep deprivation period, the development of mature, functioning cells was reduced by 35 %. Taking into account both suppressed neurogenesis and

failure to develop to functional maturity, the authors estimate that sleep deprivation reduced the new neurons in this region by 60 %, supporting the role of sleep in enabling the development of the structural substrates of brain plasticity. This suggests that recovery from sleep deprivation may not be quick and the effects of sleep deprivation on neurogenesis are not readily reversible.

Sleep Restriction

Typically it is recommended that adults obtain about 8 h sleep per night [69], however restricting sleep below this amount is common practice. Lifestyle and occupational factors such as long hours of work, commuting, shift work, family and social commitments, and the increased use of technology in the evening, all impact sleep duration and can cause chronic sleep restriction [70–72]. In a sample of more than 1.1 million American adults, 20 % reported obtaining less than 6.5 h sleep per night [73].

Early studies of sleep restriction reported few adverse effects [74, 75], but many of these studies were limited by methodological difficulties including lack of a non-sleep-restricted control group, lack of experimental control over key variables, such as sleep duration, use of caffeine or exposure to light, or use of tests that were insensitive to sleep loss, or the results of which were confounded by practice effects or circadian timing [76]. Now the deleterious effects of sleep restriction are better documented and well recognized.

Sleep Restriction and Neurobehavioral Function

A wide range of neurobehavioral functions have been shown to be sensitive to sleep loss. Sleep restriction to less than 6 h per night for a number of consecutive nights leads to increased objective sleepiness as measured on the MSLT, and faster night time sleep onset [77, 78]. The effects of sleep restricted to 5 h time in bed (TIB) for 7 nights on measures of subjective and objective sleepiness were measured in ten healthy, young adults [78]. On the second day of sleep restriction, the MSLT showed increases in sleepiness which continued to rise and a visual analogue scale showed an increase in sleepiness following sleep restriction, which leveled off after 4 days of sleep restriction. This discrepancy between subjective sleepiness, which tapers off, and objective sleepiness, which continues to rise, may indicate greater adaptation to sleep restriction in subjective sleepiness than objective sleepiness. This finding of dissociation between subjective and objective sleepiness and performance has been replicated in other studies [9, 79].

Van Dongen and colleagues [9] conducted a seminal study examining the impact of sleep deprivation and sleep restriction on sleep and performance in a strictly controlled laboratory environment. Sleep deprivation was examined across 3 days, together with sleep restricted to 4, 6, or 8 h TIB per night for 14 nights, in 48 healthy, young adults aged 21–38 years. Subjective sleepiness showed an initial increase, but then plateaued. While subjective responses showed a saturating exponential response, lapses in behavioral alertness (PVT) were near-linearly related to the length of accumulated wakefulness in excess of 16 h. The time course of these deficits is shown in Fig. 2.2. The dissociation between subjective and objective sleepiness and performance indicates that individuals are unaware of their level of cognitive and behavioral impairments, a finding that has significant ramifications for individuals' self-management of fatigue and safety under conditions of sleep restriction (Fig. 2.2).

This study also compared sleep restriction with sleep deprivation. While the 4 and 6 h TIB conditions showed significant, cumulative, dose-dependent impairments across all cognitive tasks, total sleep deprivation over 3 nights led to performance deficits and changes to EEG delta power relative to sleep lost that were disproportionately greater. This study supports the notion that individuals do not adjust to chronic sleep restriction, but that performance deficits continue to accrue with successive nights. Further, the estimated maximum length of continuous wakefulness per

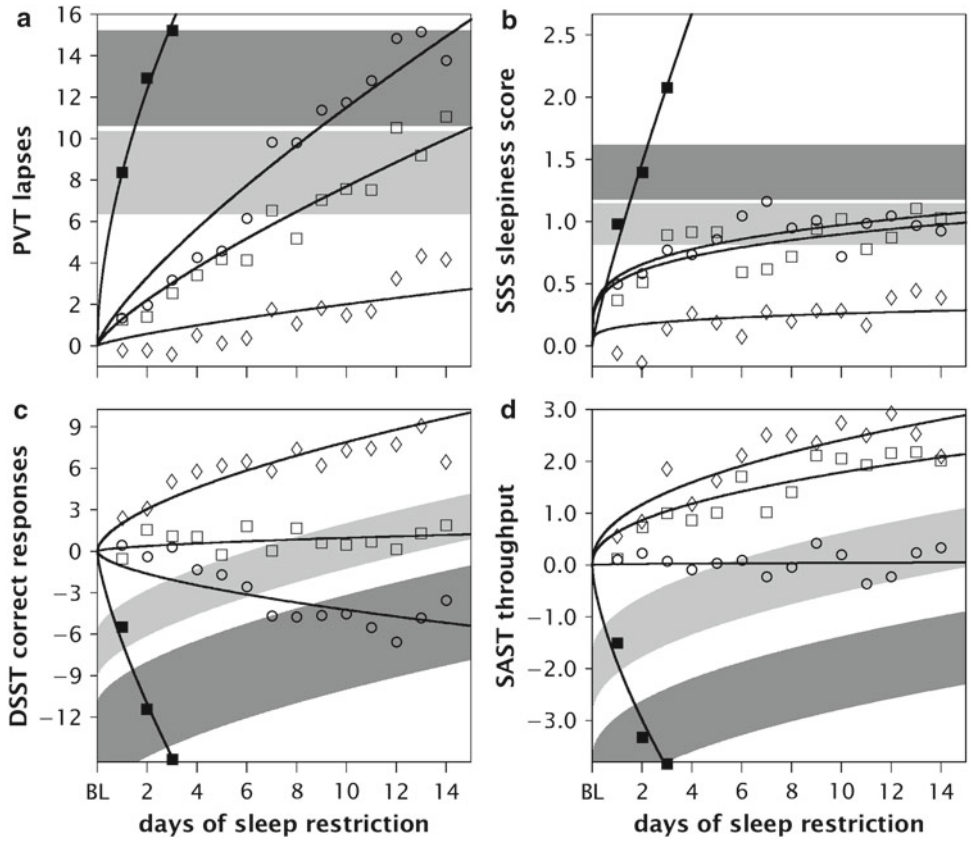

Fig. 2.2 Neurobehavioral responses to varying doses of nightly sleep. Four different neurobehavioral tests were used to measure cognitive performance and subjective sleepiness. *Panel A* shows psychomotor vigilance task (PVT) performance lapses; *panel B* shows Stanford Sleepiness Scale (SSS) self-ratings; *panel C* shows digit symbol substitution task (DSST) correct responses; and panel D shows serial addition/subtraction task (SAST) correct responses per min. Upward corresponds to worse performance on the PVT and greater sleepiness on the SSS, and to better performance on the DSST and the SAST. Each panel displays group averages for subjects in the 8 h (*open circles*), 6 h (*open squares*), and 4 h (*open diamonds*) chronic sleep period conditions across 14 days, and in the 0 h (*filled squares*) sleep condition across 3 days. The curves through the data points represent best-fitting profiles of the response to sleep deprivation. The mean ± SE ranges of neurobehavioral functions for 1 and 2 days of 0 h sleep (total sleep deprivation) are shown as *light* and *dark gray bands*, respectively, allowing comparison of the 3-day total sleep deprivation condition and the 14-day chronic sleep restriction conditions. (Reproduced with permission from Van Dongen et al. [9])

day to maintain optimal functioning and prevent the accumulation of neurobehavioral deficits was just under 16 h per day.

It has been suggested that neurobehavioral and cognitive functions show the least adaptation to chronic sleep restriction [80], with a number of studies reporting decreased PVT performance, in terms of both lapses and speed [77, 79, 81, 82]. Tasks including the digit symbol substitution task and serial addition and subtraction task, which measure working memory and cognitive throughput, also show declines in performance following sleep restriction [9].

Mood and sociability are also reduced with sleep restriction [47, 48, 76]. Dinges and colleagues [47] restricted 16 healthy, young adults to 7 nights of 4–5 h sleep per night. Sleep restriction resulted in cumulative deficits in subjective sleepiness, and an increase in fatigue, confusion, tension, mental exhaustion, and stress. While the

effects of sleep restriction on attention, sleepiness, cognitive performance, and mood are clear, there are marked differences both within individuals and between individuals regarding the magnitude and time course of these deficits [9, 43, 83].

Sleep Restriction and the Brain and Body

Core features of sleep EEG change following sleep restriction. Reductions occur in sleep onset latency, Stage N2, wake after sleep onset, REM and latency to REM, while SWS remains unchanged [9, 76, 77, 79, 81, 84, 85]. The conservation of SWS has led some to speculate that SWS may be "protected" during sleep restriction, due to the crucial role of SWS in restoring brain function [86]. But data suggests that while sleep EEG changes occur rapidly in response to sleep restriction, they do not seem to accumulate with successive days of sleep restriction, unlike performance deficits [9]. Slow wave activity (power in the EEG delta band), the putative marker of sleep homeostasis, has however been found to increase with successive nights of sleep restriction [76], suggesting that there is some response in the brain during sleep to chronic shortening of sleep time.

Sleep restriction also has been found to impact upon a range of physiological functions. These changes include an increased stress response [49, 87], altered immune function [88] such as changes to killer cell activity [89], impaired glucose metabolism [90], increased blood pressure [91], heightened sympathetic nervous system activation [92], increased inflammatory markers [93] such as interleukin-6 [94, 95], altered appetite through reduced leptin and increased ghrelin [96, 97], neurogenesis [98], and poorer outcomes such as increased body mass index, and heightened risk of cardiovascular disease and diabetes [99, 100]. Vgontaz and coauthors [77] reduced the sleep of 25 healthy adults to 6 h per night for 7 days and found that this relatively mild dose of sleep restriction lowered morning peak cortisol secretion and significantly increased the daily secretion of the inflammatory cytokine, IL-6. These are markers of systemic inflammation and have been linked to the development of cardiovascular disease, osteoporosis, and insulin resistance [77]. In another study, 6 nights of sleep restricted to 4 h per night led to a significant decrease in glucose tolerance, most acutely in response to the initial meal following wake (breakfast) [87]. Even shorter periods of sleep restriction also have implications for metabolic regulation. Spiegel and colleagues [96] found that just 2 nights of short sleep (4 h TIB) led to higher glucose levels and lower insulin levels. They also examined ghrelin (a peptide that stimulates appetite) and leptin (an adipocyte-derived hormone that suppresses appetite) and found an increase of over 70 % in the ghrelin-to-leptin ratio and a 30 % increase in self-reported appetite for calorie-dense, high-carbohydrate foods. Thus, when these hormones are out of balance, appetite is increased which could lead to weight gain and possibly type 2 diabetes.

Population-based studies support these laboratory results (for review see Killick et al. [101]). For example in the Wisconsin Sleep Cohort sleep was measured in 1,024 adults using sleep diaries, surveys, and overnight PSG [99]. Fasting blood samples were taken subsequent to the PSG night. Among participants sleeping less than 8 h per night (nearly three quarters of the sample), there was a negative relationship between sleep duration and BMI. Short sleep was also associated with decreased leptin and increased ghrelin, although no significant association was found between sleep duration and insulin or glucose.

Sleep Fragmentation

Sleep fragmentation, like sleep restriction, is commonplace in the community. Sleep fragmentation frequently arises due to sleep disorders, such as obstructive sleep apnea (OSA), periodic limb movements in sleep (PLMS), and sleep maintenance insomnia, as well as other medical conditions involving chronic pain or urinary frequency. Studies have been conducted that experimentally fragment sleep to examine in a controlled way its impact on health functioning.

Experimental Sleep Fragmentation and Cognitive Function

Studies experimentally inducing sleep fragmentation have used a number of techniques, from waking individuals from sleep and requiring a behavioral response, to producing a brief EEG arousal by administering an auditory or vibration stimulus to elicit increased EEG frequency [102]. Irrespective of the paradigm used, studies frequently find that sleep fragmentation results in increased subjective and objective sleepiness [103–105], decrements in attention [103, 104, 106], slowed reaction time [103, 107], less cognitive flexibility [108], decreased working memory [107], and impaired mood [105, 106, 109, 110]. Sleep continuity therefore appears to be important for cognitive functions and memory consolidation [111]. Studies in which the frequency of arousals was experimentally manipulated found that performance deficits on a simple addition task, completed during a brief awakening, as well as longer latencies to respond, occurred sooner and increased more rapidly with more frequent arousal schedules, suggesting a dose–response relationship [104, 112]. The magnitude of stimulus required to elicit wake also increased with more frequent arousals [112], suggesting that individuals may habituate to the stimulus, or perhaps their pressure for sleep was such that they were more difficult to arouse. Participants who were woken every minute showed performance levels equivalent to individuals performance following 64 h of sleep deprivation [112]. Sleep appears to have a reduced recuperative value when significantly fragmented.

Challenges in interpreting studies that have completely woken participants, and particularly those that have measured performance during these arousals, include, (1) difficulty in teasing apart the impact of sleep fragmentation and that of sleep inertia, and (2) fully waking also introduces greater disruption to sleep parameters and sleep architecture. More recent studies of sleep fragmentation have used auditory tones to produce brief EEG arousal without requiring a full waking response [104, 109, 113]. These studies have been able to examine the effect of sleep fragmentation and non-fragmented sleep in conditions where total sleep time is the same [113], or at least very similar [104, 109]. These studies have found that sleep fragmentation causes greater sleepiness, even when sleep duration is near equivalent. Stepanski and colleagues [103] conducted a within-subjects experiment examining three sleep fragmentation conditions: 8–9 arousals per hour, 4–5 arousals per hour, or 8–9 arousal per hour for the first 4 h of sleep and then uninterrupted sleep for the remainder of the sleep period [103]. They used auditory tones to induce brief arousals and ran each condition for 2 nights. After 2 nights, individuals in all conditions showed significantly increased sleepiness on the MSLT the next day (fell asleep more quickly), but surprisingly, there were no significant differences between conditions, suggesting that perhaps the difference in the arousal frequency was not sufficient to result in significant differences in objective sleepiness [103]. However, even when total sleep is unaffected by sleep fragmentation, some studies have still found changes to sleep architecture, including increased Stage N1 sleep and decreased SWS and REM [106, 114, 115]. It appears, therefore, that changes in sleep stage dynamics and the constant disruption of the normal sleep process are major contributing factors to the cognitive deficits seen with sleep fragmentation.

Sleep Fragmentation and Health

Given the prevalence of sleep and medical conditions which can cause fragmented sleep, it is possible that sleep fragmentation may contribute to the morbidity associated with these conditions. In one study of healthy subjects, sleep fragmentation alone resulted in alterations to blood pressure, heart rate, glucose metabolism, and O_2/CO_2 metabolism [114, 116]. Stamatakis and Punjabi subjected 11 healthy, young volunteers to 2 nights of sleep fragmentation using auditory and mechanical stimuli at a rate of 30 or more EEG micro-arousals per hour, which is similar to mild to moderate sleep apnea [114]. Two nights of sleep fragmentation were associated with

increased morning cortisol, decreased insulin sensitivity and glucose effectiveness, and a significant increase in sympathetic nervous system activation, but no changes in inflammatory markers.

Carrington and Trinder found that sleep fragmentation inhibited the normal dip in blood pressure that occurs during sleep onset [116]. The absence of normal blood pressure dipping at sleep onset, coupled with transient increases in blood pressure following arousals from sleep [117, 118], may translate into higher diurnal blood pressure. These experimental data are also supported by a population-based study of sleep fragmentation [119]. The association between blood pressure during wake and a PSG-derived sleep fragmentation index was examined in 1,021 healthy, middle aged adults, without sleep apnea from the Wisconsin Sleep Cohort. It was found that, after controlling for demographic variables, BMI, and use of blood pressure medication, individuals with a higher sleep fragmentation index were found to have higher levels of systolic blood pressure [119]. Taken together these data suggest that sleep fragmentation could lead to the development of hypertension and increase the risk for cardiovascular disease.

Sleep Deprivation, Restriction, and Fragmentation: Comparison and Implications for our Theoretical Understanding of Sleep

Many of the waking effects of sleep deprivation, sleep restriction, and sleep fragmentation on neurobehavioral response and physiology are similar, hinting at common underlying mechanisms. Deficits common to all three include increased subjective and objective sleepiness, deficits of vigilance, attention and cognition, mood degradation, and changes to glucose metabolism and heart rate. Despite many qualitative similarities between these conditions, the magnitude and time course of these deficits varies substantially. It is these differences, as well as the similarities, that have the potential to add to our understanding of human sleep need, its purpose for function, what accounts for the pattern and time course of neurobehavioral and physiological changes observed, and the recuperative value of sleep.

Early sleep restriction experiments tended to reveal few waking deficits associated with sleep restriction, but more significant effects following sleep deprivation. This observation led to the core sleep hypothesis [120]. This hypothesis posits that only a core sleep of 4–5 h per night is physiologically required to maintain healthy functioning and that additional sleep is optional, often used purely to fill the quiet hours until morning. However more recent, controlled sleep restriction experiments have shown significant functional deficits after sleep is reduced to 7 h or less TIB per night [9, 79]. In addition, sleep fragmentation experiments in which total sleep time has been minimally reduced have shown substantial waking deficits, sometimes comparable to that seen following partial or total sleep deprivation. Therefore, the core sleep hypothesis does not adequately account for these cognitive impairments.

Given the conservation of SWS during sleep restriction, it has been argued that SWS or deep sleep must have a primary recuperative value. This would help to explain why sleep deprivation has a much greater and more immediate impact on human functioning than sleep restriction, because individuals are deprived of the recuperative value of SWS. This could also account for some of the findings from sleep fragmentation experiments in which SWS was reduced and functioning was diminished. However, in sleep restriction paradigms, while SWS is preferentially preserved across different total sleep conditions, performance deficits still vary according to these conditions, with less sleep, but not always less SWS associated with greater and faster accumulating deficits [9, 79]. Additionally, sleep fragmentation studies, while reducing SWS, do not eliminate it entirely, yet they have shown deficits akin to that of total sleep deprivation, which is inconsistent with the hypothesis that SWS is the only recuperative component of sleep.

Sleep restriction studies, showing dose-dependent responses to sleep restriction, have led to the concept of sleep debt. Sleep debt is the

accumulated deficit of sleep time relative to individual sleep need and has intuitive appeal relative to a basic understanding of sleep restoration: that the deficits in waking function will be relative to the quantity of sleep lost. However, studies that have compared sleep restriction with sleep deprivation do not support this notion [9]. Participants who obtained 4 h of sleep per night for 14 nights sustained a cumulative sleep debt (totally amount of sleep lost) much greater than participants who were deprived of sleep for 88 h; however, those in the sleep deprivation condition showed much greater deficits of waking performance [9]. This suggests that it is not sleep loss, per se, that accounted for these patterns of waking deficits, but rather that there are neurobehavioral costs associated with extended wakefulness [9].

More recently, a theory positing the importance of bottom-up processes as an explanation for patterns of deficits following sleep loss has been suggested [121]. This theory emphasizes the importance of use-dependent sleep occurring in localized neuronal groups to explain performance deficits. Thus, localized areas develop a heightened homeostatic sleep drive in response to *both* sleep loss and also to sustained use. Beyond a certain point, these local areas "fall asleep," and thus brain area-specific performance is impaired. The sustained use of a localized area may occur when a cognitive task is performed that loads heavily on that brain area. While generalized homeostatic sleep pressure builds across the whole brain as a function of sleep loss, localized homeostatic sleep drive is use-dependant. Thus, this theory offers a potential mechanism to explain the differences within individuals in terms of their performance deficits across different cognitive domains. It also has the potential to explain why performance across sleep deprivations studies is more degraded than during an equivalent accumulated sleep loss during sleep restriction. Presumably this is because sleep deprivation involves both accumulated wakefulness and greater local use of neuronal networks with repeated task performance. However, while this bottom-up theory provides a reasonable account of performance deficits witnessed in sleep deprivation and sleep restriction studies, as well as accounting for within-subjects variability in response to sleep loss, it is less clear how it can accommodate findings from sleep fragmentation research. In particular, the findings showing deficits following sleep fragmentation without substantial reductions in total sleep or extensions in total wake. It follows then that perhaps sleep fragmentation may cause cognitive performance deficits and physiological derangement through a different mechanistic pathway than total sleep deprivation or sleep restriction. The important component of this type of sleep loss may therefore be the fragmentation itself and the lack of sleep continuity, rather than reductions in sleep time per se.

It seems likely that there are aspects of both the waking period (in particular the length of prior wake and local use of neuronal networks) and the sleep period (especially sleep length and sleep continuity) that explain performance deficits and the restoration of function. However, more theoretical understanding of these different forms of sleep loss would be gained by comparing them together, in a single experiment.

Conclusion

This chapter has reviewed results from studies examining the impact of sleep deprivation, sleep restriction, and sleep fragmentation on healthy functioning. Limiting or disrupting sleep opportunities in adults has significant negative effects on cognitive performance, sleepiness, and neurophysiologic functioning. These findings are highly relevant in modern society, with sleep loss increasingly common in the general population, and where the ramifications of poor sleep extend into general safety, health, and well-being.

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