Sleep loss, executive function, and decision-making

Chapter · January 2019

DOI: 10.1016/B978-0-12-815373-4.00026-5

2 authors:

Brieann Satterfield
Washington State University
65 PUBLICATIONS **563** CITATIONS
SEE PROFILE

William D. S. Killgore
The University of Arizona
546 PUBLICATIONS **13,852** CITATIONS
SEE PROFILE

Sleep And Health

Edited by

Michael A. Grandner

ACADEMIC PRESS

An imprint of Elsevier

Academic Press is an imprint of Elsevier
125 London Wall, London EC2Y 5AS, United Kingdom
525 B Street, Suite 1650, San Diego, CA 92101, United States
50 Hampshire Street, 5th Floor, Cambridge, MA 02139, United States
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, United Kingdom

Notices
Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

ISBN 978-0-12-815373-4

Publisher: Stacy Masucci
Acquisition Editor: Katie Chan
Editorial Project Manager: Carlos Rodriguez
Production Project Manager: Punithavathy Govindaradjane
Cover Designer: Christian Bilbow

Typeset by SPi Global, India

Chapter 26

Sleep loss, executive function, and decision-making

Brieann C. Satterfield, William D.S. Killgore

Department of Psychiatry, College of Medicine, University of Arizona, Tucson, AZ, United States

ABBREVIATIONS

ACC	Anterior cingulate cortex
ADA	Adenosine deaminase
ADORA2A	Adenosine A2A receptor
BART	Balloon risk analog test
BDNF	Brain derived neurotrophic factor
DAT1	Dopamine transporter
DRD2	Dopamine D2 receptor
DTI	Diffusion tensor imaging
h	Hour
IGT	Iowa gambling task
mg	Milligram
min	Minute
OFC	Orbitofrontal cortex
PER3	PERIOD3
PFC	Prefrontal cortex
PVT	Psychomotor vigilance test
RT	Response time
SD	Standard deviation
SE	Standard error
sec	Second
TNFα	Tumor necrosis factor alpha
VWM	Visual working memory
WCST	Wisconsin card sorting task

INTRODUCTION

We live in a society that operates around the clock, often forgetting that sleep is important. In fact, insufficient sleep has become a public health epidemic and is often overlooked as a serious problem [1]. While the National Sleep Foundation recommends adults sleep >7 h per night [2], 35% of adults in the United States sleep less [3]. Most people have suffered from sleep loss, either chronic or acute, at some point in their lives whether it be due to a new baby, stress, studying for an exam, or other circumstances. However, many people fail to realize the negative impact sleep loss has on cognitive functioning and how this has far-reaching real-world implications. In fact, insufficient sleep is common in several safety-critical occupations, including medical professionals, military personnel, airline pilots, and truck drivers, just to name a few. Thus, it is important to understand how sleep loss impacts various aspects of cognition.

The present chapter provides an overview of the effects of sleep loss on several major cognitive domains. First, it is important to discuss the underlying neurobiological mechanisms that regulate sleep and wake, and thus modulate cognitive performance. We must also appreciate that human cognitive capacities are complex, with higher-order processes (e.g., executive functions, decision-making) building upon a foundation of elementary processes (e.g., attention). Therefore, this chapter will offer a discussion of how sleep loss impairs alertness, sustained attention, and vigilance. Additionally, we will discuss the importance of considering how inter-individual differences are related to relative resistance or vulnerability to cognitive impairment. We will then build upon these elementary capacities and focus on the consequences that sleep loss has on several complex executive function domains including working memory, inhibitory control, cognitive control, problem solving, risk-taking, and decision-making.

NEUROBIOLOGY OF SLEEP AND FATIGUE

There are two fundamental neurobiological processes that drive fatigue and alertness: the *homeostatic process* (Process S) and the *circadian process* (Process C) [4, 5]. The homeostatic process keeps track of prior amounts of sleep and wakefulness, and is conceptualized as an accumulating pressure for sleep with increasing time spent awake. This pressure is then dissipated over the course of a sleep period. The circadian process is the body's natural 24-h rhythm that keeps track of time of day. This process, modulated by the suprachiasmatic nucleus (SCN) of the hypothalamus, oscillates throughout a 24-h period to drive daytime alertness and nighttime sleepiness. During daytime hours, homeostatic sleep pressure accumulates

Sleep and Health. https://doi.org/10.1016/B978-0-12-815373-4.00026-5

with each hour awake, but is counteracted by the circadian drive for alertness. This interaction between the homeostatic and circadian pressures allows us to maintain normal daytime functioning at a fairly constant level. During nighttime hours, the homeostatic pressure for sleep is high and the circadian drive for alertness is low, promoting the onset and maintenance of sleep. Thus, waking performance is optimal during daytime hours and worst during nighttime hours (Fig. 26.1) [5, 6]. However, perturbations to this system (i.e., shift work, mistimed sleep, travel across time zones) can result in impaired neurobehavioral functioning. For example, the homeostatic and circadian processes become misaligned when an individual works during the night and sleeps during the day. In such a case, the homeostatic pressure for sleep mounts over the course of nighttime waking hours, but the circadian drive for alertness decreases, and hits the nadir during the early morning hours (Fig. 26.1). The net effect of this misalignment is increased fatigue, which can lead to cognitive performance impairment. Further, sleeping during the day is often difficult for a nightshift worker. This is because the circadian process increases the pressure for wakefulness throughout the day, forcing an individual to awaken before the homeostatic pressure is fully dissipated. This type of sleep curtailment can lead to a net accumulation of sleep debt [6].

ALERTNESS, SUSTAINED ATTENTION, AND VIGILANCE

In our day-to-day lives, the ability to maintain focus and attention is essential for effectively completing the task at hand and solving problems that require complex cognitive processing. Our ability to maintain attention and alertness fluctuates throughout the day as a function of the circadian and homeostatic processes, often without notice. However, when these two processes become misaligned due to extended wakefulness or mistimed sleep, attention begins to degrade. When wake is extended beyond 16 h or restricted to <6 h per night, individuals tend to show consistent and profound impairment in sustained attention.

Psychomotor vigilance

Sustained attention is typically measured using the psychomotor vigilance test (PVT) [7, 8]. The PVT is a simple computerized reaction time task that is considered to be the gold standard measure of behavioral alertness. It is sensitive to sleep loss and does not show an appreciable learning effect [9, 10]. In the standard version of the task, a visual stimulus is presented on the screen at random intervals between 2 and 10 s for a total of 10 min in duration. When the stimulus appears, the examinee presses a response button as quickly as possible, while avoiding false starts. Lim and Dinges [11] identified several distinct impacts that sleep deprivation has on PVT performance: (1) slowing of response times (RTs), (2) increases in attentional lapses, (3) exaggerated time-on-task effects, and (4) sensitivity to homeostatic and circadian influences.

In a typical sleep deprivation study, PVT RTs begin to slow around 16 h of wakefulness and degrade further across the night, with impairment being the most prominent during the early morning hours (i.e., the circadian nadir). *Slower responses* on

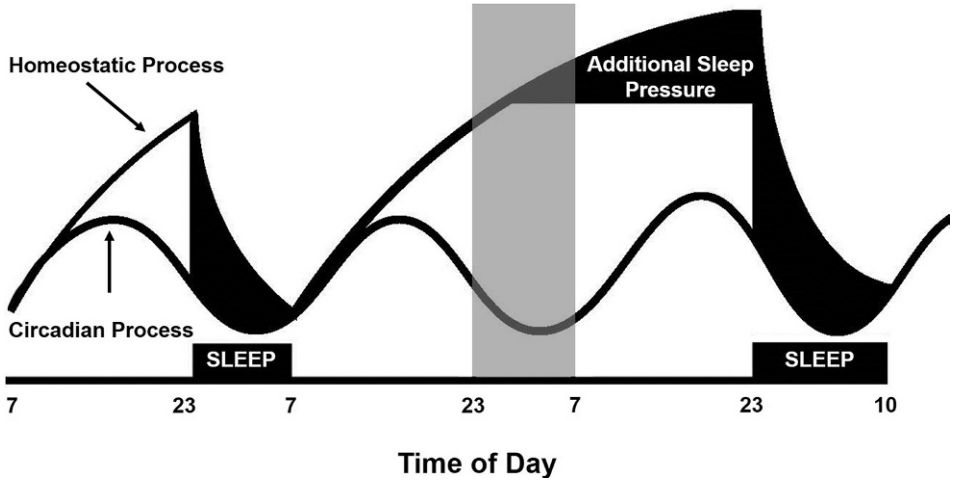

FIG. 26.1 The two process model of sleep regulation. The homeostatic process (S) and circadian process (C) interact to drive daytime alertness and nighttime sleepiness. Homeostatic pressure for sleep increases as a function of time spent awake and dissipates with time spent asleep. At the same time, circadian pressure oscillates across a 24-h period, with pressure for alertness highest in the early evening and lowest during the early morning hours. However, when an individual skips a night of sleep (shaded area) homeostatic pressure continues to build, while the circadian process continues to drive sleepiness during the earlier morning hours. At this point, the net effect of high homeostatic pressure and low circadian pressure is reduced alertness and increased fatigue, resulting in impaired cognitive functioning. Once an individual goes to sleep, homeostatic pressure decreases, and often results in increased sleep duration that is required to fully dissipate the homeostatic buildup. *Modified from File:Two-process model of sleep regulation.jpg [Internet]. WikiMedia. (2007). Available from: https://en.wikipedia.org/wiki/File:Two-process_model_of_sleep_regulation.jpg.*

the PVT are associated with reduced activation in the default mode network, a cortical system that includes the medial frontal and posterior cingulate cortex, regions that are most active when the brain is idle and not involved in complex cognitive processing [12]. While the average RT across trials increases during periods of sleep deprivation, there is also a significant slowing of both the fastest 10% and slowest 10% of RTs on the PVT. Albeit, the slowest RTs are disproportionately affected compared to the fastest 10% RTs (Fig. 26.2) [8, 10, 13, 14]. This indicates that sleep loss impacts not only the typical response, but also the best and worst performance. Decrements in PVT performance are not limited to conditions of total sleep deprivation. PVT performance is also substantially degraded when sleep is restricted by only a few hours each night. Belenky et al. demonstrated that when sleep is restricted to either 7, 5, or 3 h per night over the course of 1 week, response speeds (1/RT*1000) slowed in a cumulative manner across days [15]. Even when participants were allowed three 8 h nighttime recovery sleep periods, performance did not return to baseline levels (Fig. 26.3) [15].

Another characteristic of sleep loss is the increased frequency and duration of *attentional lapses* (RTs ≥ 500 ms) that occur within a single PVT bout, which are also accompanied by increases in errors of commission or false alarms (i.e., responding when no stimulus is present). Van Dongen and colleagues demonstrated that when sleep is restricted to either 6, 4, or 8 h over the course of 2 weeks the number of attentional lapses increases in a cumulative and

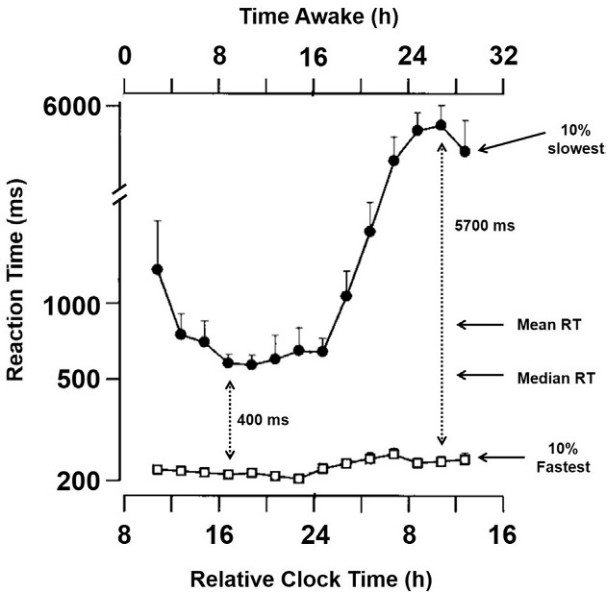

FIG. 26.2 Time course of PVT mean RTs across 32 h of sleep deprivation. PVT performance remained relatively stable until 16 h wake. Up until this point, only 400 ms separated the average 10% slowest (black circles) and 10% fastest (white squares) RTs. However, with increased time awake, RTs slowed dramatically. Just after 24 h wake, approximately 5700 ms separated the the fastest and slowest 10% of RTs. While not displayed in this figure, mean and median RTs are also significantly impacted by sleep loss and fall between the fastest and slowest curves shown here. *Modified from Cajochen C, Khalsa SB, Wyatt JK, Czeisler CA, Dijk DJ. EEG and ocular correlates of circadian melatonin phase and human performance decrements during sleep loss. Am J Physiol 1999;277:R640–9.*

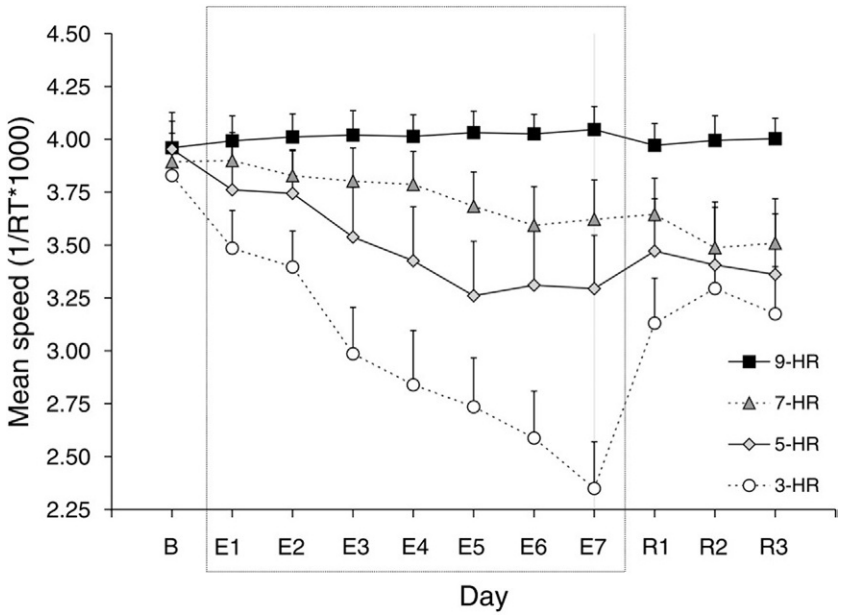

FIG. 26.3 Mean response speed (1/RT*1000) on the PVT over the course of a 7 day sleep restriction protocol as a function of sleep condition group. All groups had similar PVT performance at baseline (B). In the 9 h sleep group, PVT performance remained stable across sleep restriction days (E1–E7) and into the recovery days (R1–R3). When sleep was restricted to either 7, 5, or 3 h, there was a steady decline in PVT mean speed as days progressed. This decline was more pronounced in the 3 h sleep condition compared to the 7 h sleep condition. Additionally, 8 h sleep for three nights (recovery) was not sufficient to return PVT performance back to baseline levels. *Reproduced from Belenky G, Wesensten NJ, Thorne DR, Thomas ML, Sing HC, Redmond DP, Russo MB, Balkin TJ. Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-response study. J Sleep Res 2003;12(1):1–12, with permission from John Wiley and Sons.*

dose-dependent manner [16]. In fact, when sleep restriction was most severe (i.e., 4 h per night), the average number of lapses at the end of the 2 weeks was similar to the average number of lapses seen at the end of an 88 h sleep deprivation period [16]. Neuroimaging findings suggest that attentional lapses during sleep deprivation are related to reduced neural activation within the frontal, parietal and occipital regions, as well as the thalamus [17]. Together, imaging and behavioral studies have demonstrated how sleep loss disrupts normal functioning within the vigilant attention network, in turn hindering the ability to sustain attention.

The *time-on-task effect* is a phenomenon in which performance degrades as a function of time spent performing a cognitive task. That is, performance progressively declines the longer an individual is required to sustain attention necessary to perform the task [18]. This results in increased performance variability [19]. The time-on-task effect is apparent on several different types of cognitive tasks, however it is especially noticeable on tasks of vigilant attention, like the PVT. [20] On the PVT, the time-on-task effect manifests as a steady increase in the standard deviation of RTs across the task duration [10]. This phenomenon is present even under well-rested baseline conditions. Variability in PVT RTs is also a distinct characteristic of how vigilant attention is affected by sleep loss. Interestingly, the time-on-task effect interacts with sleep loss to amplify performance impairments when homeostatic pressure is high [8, 10, 21]. When faced with sleep loss, the time-on-task effect can be mediated by taking short breaks or switching tasks [6, 22, 23].

Last, PVT performance is sensitive to *homeostatic and circadian influences* [8, 24]. Fig. 26.4 shows the dynamic influence that the two neurobiological processes exert on performance. As described above, homeostatic pressure increases across hours awake, while the circadian process waxes and wanes across a 24-h period (Fig. 26.4, left). When these processes are considered in interaction, the sum of the two processes modulates PVT performance in a distinct manner. Fig. 26.4 (right) shows how the net effect of the two neurobiological processes impact PVT performance during 62 h of total sleep deprivation. Not only does PVT impairment increase with time spent awake, it also oscillates with the circadian process. Performance slightly improves during the early evening hours when the circadian pressure for wake is high, but further deteriorates after the circadian nadir and with mounting homeostatic pressure [25].

Wake state instability

Several aspects of PVT performance impairment, as described above, have been summarized into a single theory: the wake state instability hypothesis [10]. Sleep loss leads to a decrease in RTs, increase in attentional lapses and errors, and an increase in the time-on-task effect, all of which are influenced by mounting homeostatic pressure and manifesting as performance instability [8]. These moment-to-moment variations in performance are not gradual, linear, or predictable, but rather stochastic in nature. For example, Fig. 26.5 shows PVT responses from a single subject

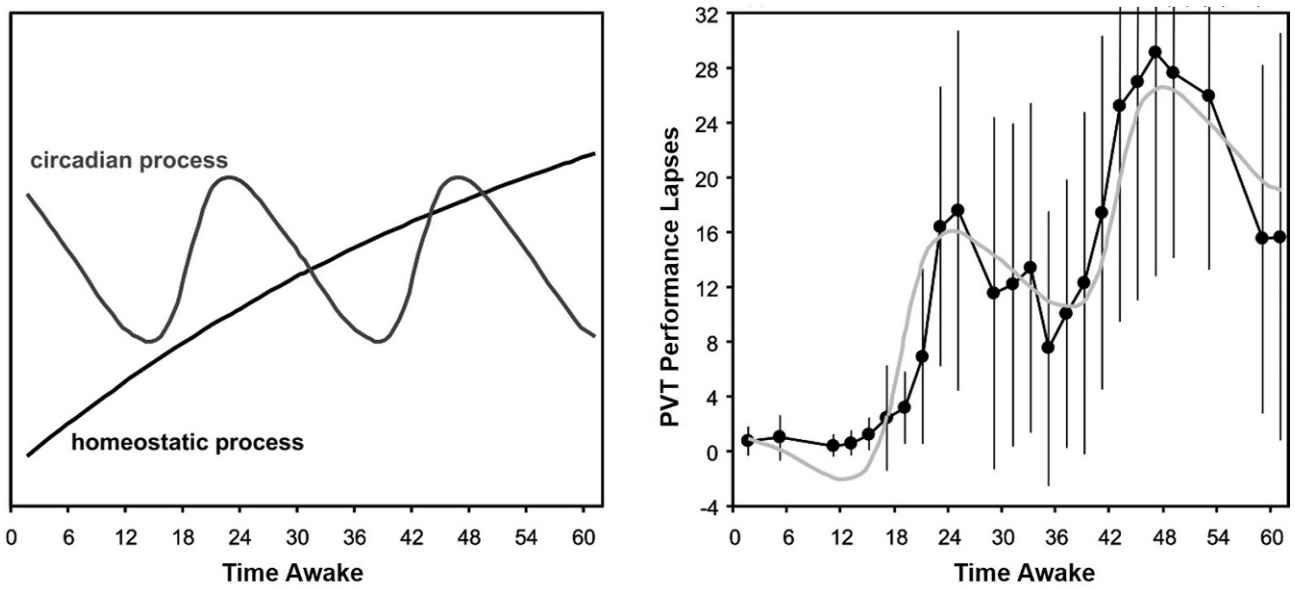

FIG. 26.4 The influence of the homeostatic and circadian processes on PVT performance during 62 h of extended wakefulness. The left panel shows the steady increase in homeostatic pressure across the sleep deprivation period in interaction with the waxing and waning of the circadian process. The right panel shows a mathematical derivation of the sum of the homeostatic and circadian processes (gray curve) overlaid on mean PVT lapses (± SD; *black curve*) collected from 12 healthy adults. *Reproduced from Van Dongen HPA, Belenky G. Individual differences in vulnerability to sleep loss in the work environment. Ind Health 2009;47(5):518–26, with permission.*

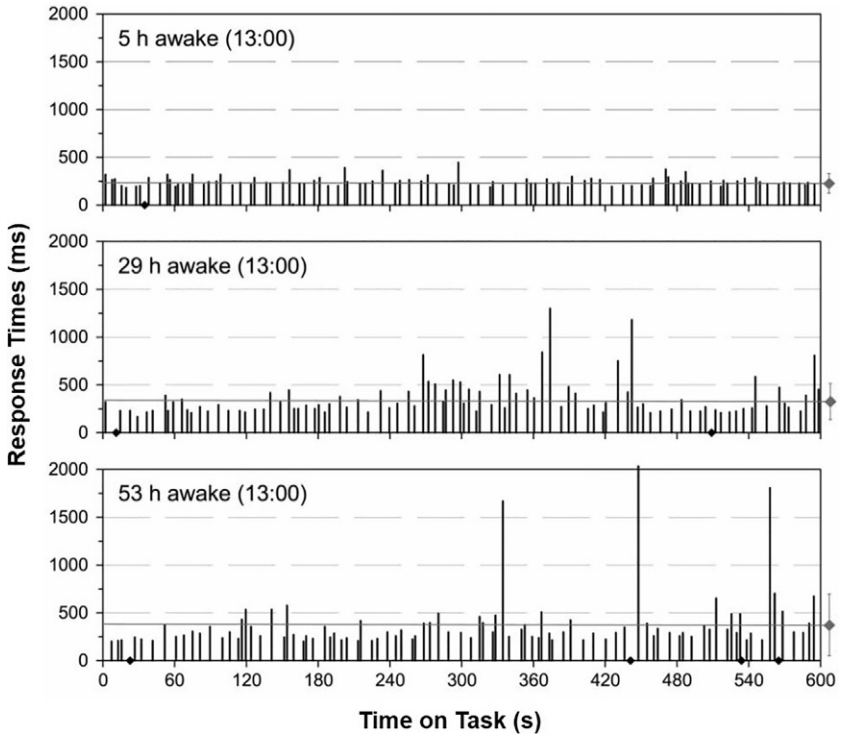

FIG. 26.5 Raw PVT RTs from a single subject collected over the course of a 62 h sleep deprivation period. RTs are plotted against time-on-task. PVT performance is shown at 5 h wakefulness (top panel), again 24 h later (middle panel), and another 24 h later (bottom panel). RTs become longer and more variable as a function of both time-on-task and time awake. Additionally, false starts (*black diamonds*) also increase. *Gray diamonds*: mean RT ± SD. *Reproduced from Satterfield BC, Van Dongen HPA. Occupational fatigue, underlying sleep and circadian mechanisms, and approaches to fatigue risk management. Fatigue Biomed Heal Behav 2013;246(3):118–36, with permission of Taylor & Francis Ltd. (http://www.informaworld.com).*

throughout the course of a 62 h sleep deprivation period. In the early afternoon when the subject has only been awake for 5 h, PVT performance is stable, with minimal variability in RTs and no attentional lapses. However, a different picture emerges 24 h later when the subject has been awake for 29 consecutive hours (Fig. 26.5, middle). At this point, there is moderate variability in RTs as time-on-task increases, and the occasional response exceeds the 500 ms attentional lapse threshold. Another 24 h later (Fig. 26.5, bottom), performance variability is further increased. At 53 h awake, attentional lapses become more frequent, RTs become longer, more errors are made, and the time-on-task effect is amplified. Together, these data illustrate that performance instability is a hallmark of sleep loss [6, 18, 23]. It is this unstable and unpredictable nature that makes fatigue so dangerous, especially in safety-critical operations. It has been posited that the stochastic nature of performance instability is the result of neuronal groups involved in the task expressing a local, use-dependent sleep like state. The local sleep theory suggests that activity from sustained use during a performance task and extended wakefulness pushes local neuronal groups to fall asleep. In turn, information processing in the task-specific pathway is interrupted, causing performance instability and increased attentional lapses [18, 26].

INDIVIDUAL DIFFERENCES

Research has shown that there are varying degrees of cognitive impairment during sleep loss across individuals. That is, not all individuals respond to sleep loss in the same manner [27–30]. These inter-individual differences are substantial and robust across a variety of manipulations, and constitute a trait [21, 31, 32]. As demonstrated by Van Dongen and colleagues [32], there are individuals who are resilient to the effects that sleep deprivation exerts on cognitive performance and individuals who are incredibly vulnerable. Fig. 26.6 shows that resilient individuals (triangles) are able to maintain stable performance across a 40 h sleep deprivation period, while vulnerable individuals (circles) show substantial impairment as wake extends past 16 h [33]. Due to the stable, trait nature of inter-individual differences, a number of biomarkers have been assessed to predict which individuals may be more or less susceptible to cognitive impairment due to sleep loss. These include personality and sensory markers [34, 35], neural markers [36], and genetic markers [37].

Several neuroimaging studies have sought to identify neural predictors of inter-individual differences in cognitive performance by assessing functional activation while performing a cognitive task [17, 38–40], functional

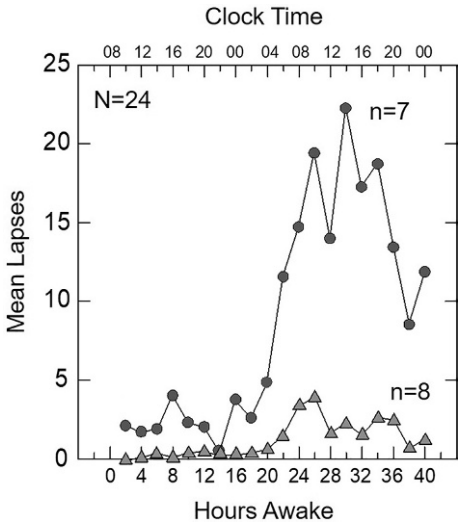

FIG. 26.6 Mean PVT lapses collected from 24 individuals during 40 h of total sleep deprivation. The number of PVT lapses remains low until about 16 h awake. At this point, the number of PVT lapses increases significantly for those most vulnerable ($n=7$) to impairment (*circles*). In contrast, the number of PVT lapses remains relatively stable for those most resilient ($n=8$) to impairment (*triangles*). Performance for the remaining nine individuals falls between these curves. *Modified from Van Dongen HPA, Maislin G, Dinges DF. Dealing with inter-individual differences in the temporal dynamics of fatigue and performance: Importance and techniques. Aviat Space Environ Med 2004;75(Suppl 3):A147–54, with permission.*

connectivity between brain regions [41], and white matter microstructure [42]. Chee and Tan found that sleep loss was associated with lower fronto-parietal activation compared to the rested state, and individuals most vulnerable to impaired selective attention had reduced activation in top-down cognitive bias regions (i.e., frontal and parietal cortices) [17]. In addition to measuring changes in neural activation, individual differences in neuroanatomical connectivity and structure have been identified. For example, our lab used diffusion tensor imaging (DTI) to assess the association between microstructure of the fronto-parietal attention system and PVT performance during a single night of sleep deprivation. We found that indirect measures of higher white matter integrity and higher myelination in the fiber pathways connecting the left frontal and left parietal regions were significantly correlated with resistance to PVT impairment [42]. Neural markers have the potential to help identify those individuals most vulnerable and those most resistant to impaired cognitive performance without having to expose them to any sleep loss paradigm. This affords us with a better understanding of the neural mechanisms underlying sleep loss related cognitive impairment.

Identifying genetic markers of inter-individual differences to performance impairments has become a large area of research in the last several years. Often, genetic polymorphisms are used as a tool to investigate how the functional differences brought about by the polymorphisms influence inter-individual differences in cognitive performance [43]. These studies have focused on polymorphisms associated with circadian pathways, adenosine (a marker of homeostatic pressure) pathways, neurotransmitters, neural signaling pathways, and immune responses [43].

PVT performance during sleep deprivation is mediated by several genetic variants, including those of the adenosine A_{2A} receptor (ADORA2A) gene [44], adenosine deaminase (ADA) gene, dopamine transporter (DAT1) gene [45, 46], and the tumor necrosis factor alpha (TNFα) gene [47]. For example, it was recently found that a variant of DAT1 mediates the time-on-task effect during sleep deprivation [45]. Study participants performed the PVT every 2 h over the course of a 38 h sleep deprivation period. Subjects homozygous for the 10-repeat variant of DAT1 were resilient to the time-on-task effect compared to subjects with the 9-repeat variant of the same gene. As Fig. 26.7 shows, performance between the two DAT1 genotype groups diverged as sleep deprivation progressed, with the most resilient individuals (i.e., the 10/10 group) maintaining stable performance with very little time-on-task effect [45]. Holst et al. also found that DAT1 genotype modulates PVT performance, specifically PVT lapses [46]. Genetic markers have also been found to influence performance on a variety of other cognitive tasks and will be discussed throughout the remainder of the chapter.

EXECUTIVE FUNCTIONS

The term "executive function" is used to describe a group of higher order cognitive processes that are necessary to coordinate and control deliberate actions toward future goals [48]. The term encompasses several cognitive processes including the ability to sustain attention while suppressing distractors, inhibit inappropriate actions, switch tasks, shift mental sets, think flexibly, plan and sequence events, and make appropriate and low-risk decisions, to name a few (Fig. 26.8). While these complex cognitive processes are mediated by several interacting cortical and subcortical regions, they rely heavily on the prefrontal cortex (PFC) which is sensitive to the effects of sleep loss [49]. Notably, the PFC shows reduced glucose metabolism following sleep deprivation (Fig. 26.9) [50], which is not fully reversed following a single night of recovery sleep [51]. This decline in prefrontal metabolic activity is thought to underlie some of the cognitive impairments seen during sleep loss.

To further complicate matters, not only are there inter-individual differences in cognitive performance as discussed in the previous section, these differences are also task-dependent [52], meaning that those most vulnerable to impairment on one task are not necessarily vulnerable to performance impairment on a different task. This is because cognitive performance, including executive functioning, is not a unitary concept. Most tasks designed to measure

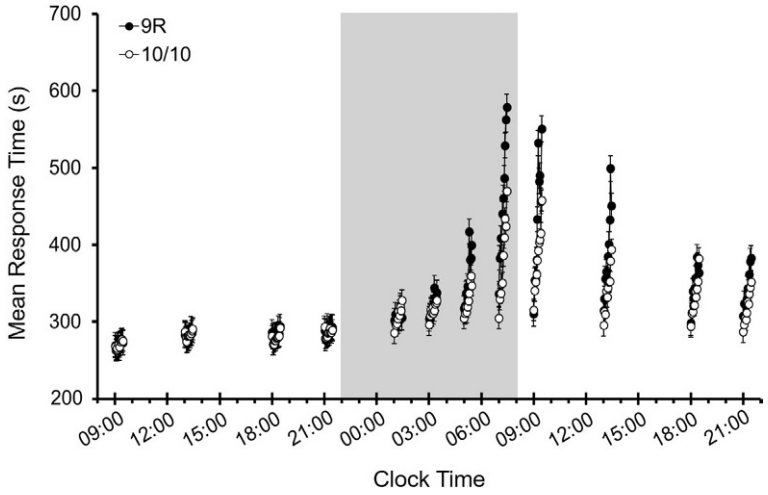

FIG. 26.7 Time-on-task performance for the DAT1 genotype groups across 38 h of total sleep deprivation. Mean RTs (±standard error) from 12 individual test bouts are plotted in 1-min bins for the 10-min PVT. Individuals carrying the 9-repeat allele, as either heterozygous or homozygous, were grouped together (9R). Data are plotted against the start time of the PVT test bout. As sleep deprivation progressed, time-on-task performance diverged between the 9R and 10/10 DAT1 genotype groups, such that those homozygous (10/10) for the DAT1 10-repeat allele were protected against severe time-on-task impairment. *Shaded area*: nighttime test bouts. *Modified from Satterfield BC, Wisor JP, Schmidt MA, Van Dongen HPA. Time-on-task effect during sleep deprivation in healthy young adults is modulated by dopamine transporter genotype. Sleep 2017;40(12):zsx167, with permission from Oxford University Press.*

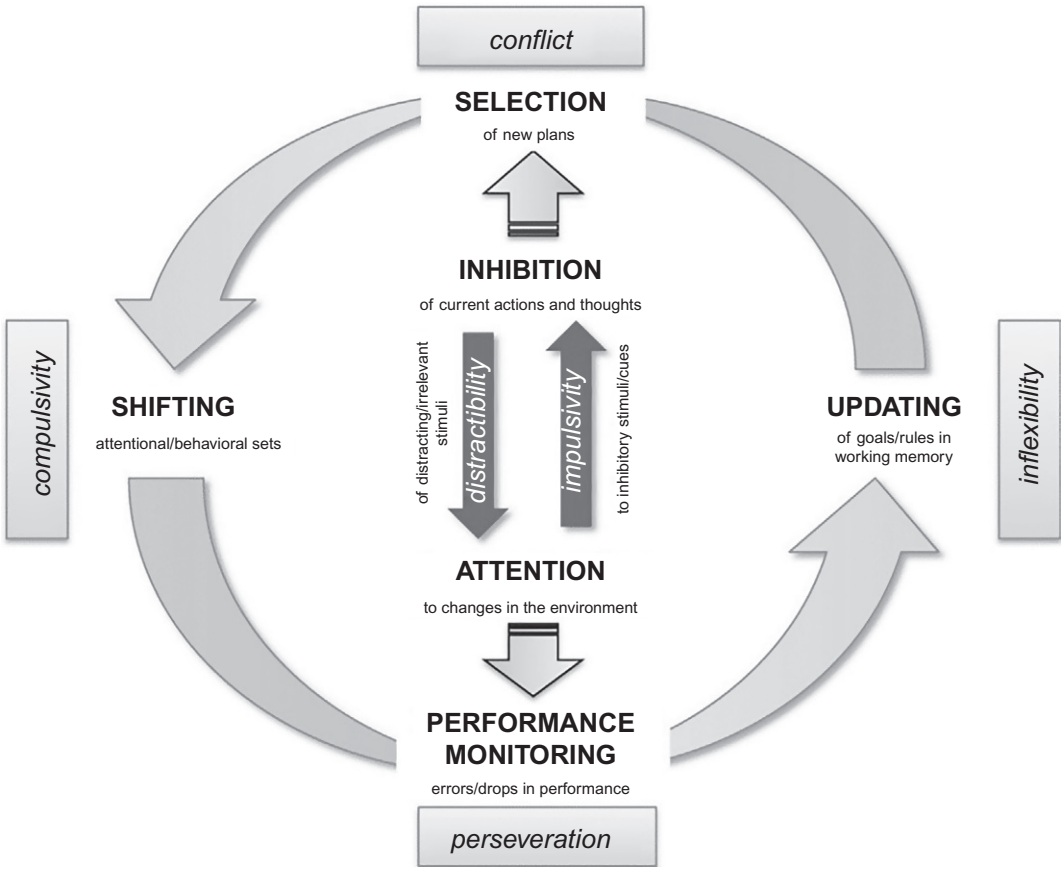

FIG. 26.8 A simplified schematic of the hypothesized relationship between the different executive functions. The ability to sustain attention and inhibit inappropriate responses are thought to be central components of executive function. A well-rested individual will pay *attention* to incoming information in order to respond appropriately to incoming stimuli, such as *inhibiting* the current course of action if needed. At the same time, the brain *monitors performance* based on internal and external feedback and triggers a signal that a new plan of action is required if performance levels drop and the number of errors increase. Then, behaviors are updated to reflect a change in goals and a new plan is *selected.* With the implementation of a new course of action, an individual must then *shift* both behavioral and attentional resources to continue with the new plan. However, sleep loss disrupts several points in this cycle leading to unfavorable actions and outcomes. For example, impairments in attention and inhibition may lead to distractibility and impulsivity, respectively. Further, impaired attention can lead to perseveration, or over focused behavior. In turn, relevant goals and rules are unable to be updated, resulting in inflexibility. Inflexible behavior does not allow for an individual to select a new course of action and could lead to compulsive behavior. Thus, one must be able to effectively integrate attention, inhibition, and flexibility in order to monitor performance and accurately update goals in response to environmental changes. *Reproduced from Bari A, Robbins TW. Inhibition and impulsivity: Behavioral and neural basis of response control. Prog Neurobiol 2013;108:44–79, with permission from Elsevier.*

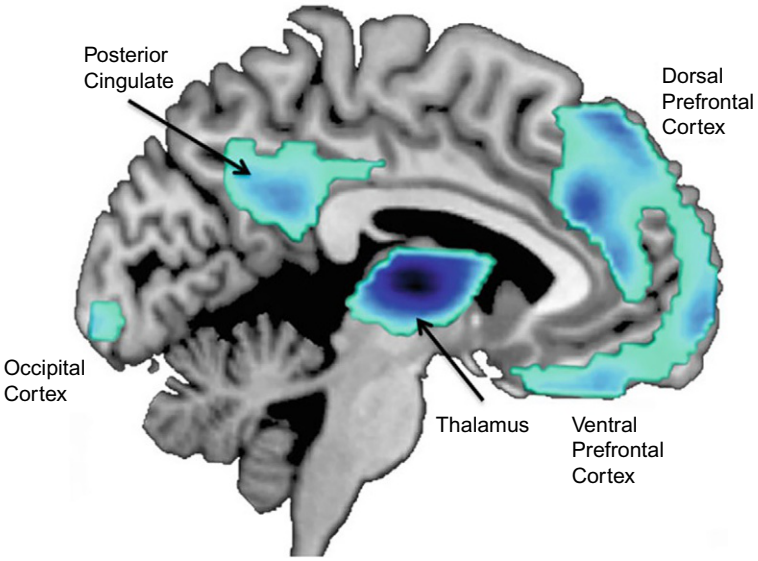

FIG. 26.9 A positron emission tomography (PET) image of regional cerebral glucose metabolism following 24 h of sleep deprivation. Sleep deprivation results in decreased glucose metabolism in areas of the prefrontal cortex, thalamus, and posterior cingulate. Reduced metabolism in these areas is thought to subserve some of the sleep loss induced impairments in cognitive performance we often see. *Reproduced from Killgore WDS, Weber M. Sleep deprivation and cognitive performance. In: Bianchi MT, editor, Sleep deprivation and disease: effects on the body, brain, and behavior. New York: Springer; 2014. p. 209–29.*

executive functions involve several integrated processes that are differentially impacted by sleep loss [53]. The complexity and multiple cognitive processes involved in many executive function tasks introduces a "task impurity problem." As Tucker and colleagues have demonstrated, performance on executive function tasks may not be attributable to global task impairments, but rather impairments in specific cognitive components of the task [54]. Thus, caution should be taken when administering and interpreting performance data from complex executive function tasks.

Working memory

Working memory can be described as the capacity to maintain and manipulate information in immediate memory, and underlies most executive functions. Working memory is conceptualized as having four components that include the storage of information, integration of information, regulation of information, and manipulation of information [55–57]. Working memory is distinct from short-term memory in that it requires both short-term storage of information *and* manipulation of that information [55]. There are several cognitive tasks that are used to measure various aspects of working memory, including digit span, word recall, number generation, serial addition, Sternberg, and *N*-back tasks [56].

In a meta-analysis, Lim and Dinges found that sleep loss impacts working memory performance with moderate effects sizes. Specifically, they found that both accuracy and RTs are impaired on these tasks [11]. Chee and colleagues conducted a series of studies using two different working memory tasks to investigate how sleep loss disrupts neural signaling specific to maintenance and manipulation of information. Following either 24 or 35 h of total sleep deprivation, both tasks showed reduced functional activation within bilateral parietal regions [58, 59], a common finding in studies of working memory and sleep loss [39, 60, 61]. However, Chee et al. [58, 59] found conflicting results in regard to activity within the PFC. In the latter study of the series [59], activity in the left PFC was *reduced* after sleep loss, while the first study [58] found that activation in the left PFC actually *increased* after 24 h of sleep deprivation. The increase in neural responsiveness of the PFC following sleep loss may reflect the initiation of compensatory mechanisms that are required to maintain stable performance. The compensatory recruitment hypothesis suggests that some individuals are able to sustain cognitive performance during sleep loss by recruiting areas of the cortex that are typically not engaged by the same task during rested wakefulness [62].

Working memory performance during sleep loss appears to also be mediated by a genetic polymorphism of the circadian clock gene PERIOD3 (PER3). Individuals with the 5-repeat allele for PER3 had better working memory performance on an *N*-back task than those with the 4-repeat allele. The difference in performance was significant only at the circadian nadir in the early morning hours [63]. Taken together, findings from neuroimaging studies show that sleep deprivation influences working memory through disruption to fronto-parietal networks, and performance is mediated by genetic polymorphisms of the circadian system.

While imaging studies have been able to identify brain regions involved in working memory performance during sleep loss, behavioral studies have found that sleep loss differentially impacts specific aspects of working memory performance [54, 59, 64], and in a sex-dependent manner [65, 66]. For example, Chee and Chuah found that sleep deprivation impairs general visual working memory (VWM) capacity, possibly due to degraded perceptual processing [67]. However, others have found that sleep loss does not impair VWM capacity, but rather impairs the ability to filter out VWM distractors [64]. Tucker et al. [54] also demonstrated that while sleep loss may show global decrements in working memory, the impairment is driven by specific working memory components. When dissociating a working memory task into "executive" and "non-executive" components, the non-executive working memory components (i.e., RTs) were the only elements impacted. "Executive" working memory scanning efficiency and resistance to proactive interference remained intact [54].

In a recent study, Rångtell and colleagues [65] administered a sequence-type working memory task following a single night of sleep loss, or 8 h sleep, which study participants performed in silence or with an auditory distraction. They were then asked to rate how confident they were in their performance. Overall, sleep loss impaired working memory performance in women, but not in men. Neither sex reported differences in subjective working memory performance. The auditory distraction impaired performance in both conditions and was not impacted by sex [65]. Overall, the accumulating data suggests that working memory impairments may actually be driven by degradation in alertness and vigilance, rather than the specific executive functions such as the ability to maintain and manipulate information, and these impairments are sex-specific.

Inhibitory control

Some actions may be adaptive under one set of circumstances, yet maladaptive in other circumstances. A key aspect of executive functioning is the ability to inhibit inappropriate responses or behaviors in a particular context. For instance, lack of inhibitory control can lead to impulsive decisions that may have negative consequences. Inhibitory control is typically assessed using response inhibition tasks, including the stop signal task or go/no-go paradigms. These tasks are designed to measure the ability to withhold a prepotent (i.e., automatic) response [68]. In a typical go/no-go task, individuals learn to respond to a specific set of stimuli (*go* stimuli) and learn to withhold a response for a different set of stimuli (*no-go* stimuli). Performance is assessed based on correctly responding to *go* stimuli (simple attention and response time) and correctly withholding a response to *no-go* stimuli (inhibitory control).

Neuroimaging studies using the go/no-go paradigm suggest that the task recruits several PFC regions. Specifically, the ability to correctly withhold a response most consistently activates the right lateral PFC and bilateral insula. In contrast, failure to withhold a response engages the right anterior cingulate cortex (ACC), medial frontal gyrus and portions of the parietal lobe. All of which are regions often associated with error detection and behavioral monitoring [69]. These are some of the same regions that show reduced metabolic activity following sleep loss [50]. Thus, it would be expected that sleep loss impairs the ability to withhold inappropriate responses, which has been observed. In fact, sleep deprived individuals who are unable to efficiently inhibit responses on the go/no-go have difficulty recruiting the ventrolateral PFC. Conversely, resilient individuals show increased activation within this region [70].

Drummond and colleagues [71] used the go/no-go to assess the effects of 64 h of sleep deprivation on inhibitory control. As expected, the ability to inhibit inappropriate responses decreased as a function of time awake. Interestingly, hit rates (correct *go* responses) remained unaffected for most of the sleep deprivation period, but rapidly declined at 55 h of wakefulness [71]. Another sleep deprivation study found similar results [72]. Additionally, these findings have been replicated under conditions of partial sleep restriction, where sleep was limited to 6 h per night for four nights. Study participants showed impaired inhibitory actions while maintaining correct responses [73]. Sleep loss causes a steady decline in response withholding with increasing time spent awake, while maintaining the ability to attend to incoming stimuli. These findings emphasize the fact that sleep deprivation does not result in a global degradation of cognitive performance due to impaired basic attention, thus cognitive impairment is task and domain-specific [32, 53, 74].

Cognitive control

A hallmark characteristic of executive function is the ability to modulate cognitive processes. In a broad sense, cognitive control is the ability to regulate and coordinate thoughts and actions in-line with behavioral goals or changes in situational demands [75]. This allows us to balance cognitive *stability*—the ability to actively focus on and maintain task-relevant information—with cognitive *flexibility*—the ability to update information according to changes in situational demands, while also suppressing irrelevant information in order to appropriately adapt behavioral actions to meet new goals [75–77]. For example, you may be driving down a long, straight highway when a large deer jumps out in front of your vehicle. Your current goal of driving down a straight highway is disrupted by the unexpected object in the road. You must update your goal in order to appropriately adapt your response to the situation (i.e., avoid hitting the deer).

Impairments in cognitive control can lead to perseverative, or over-focused, behaviors that can have serious consequences. These types of behaviors are often seen in psychiatric conditions such as obsessive compulsive disorder and schizophrenia [78].

Cognitive control encompasses the interaction of multiple cognitive processes, including working memory, attention, decision-making, response selection, response inhibition, and associated learning [78]. These processes underlie several behaviors such as multi-tasking/task-switching, changing behavior to fit a new rule, or suppressing distractions. Multi-tasking and task-switching are typically assessed using paradigms that require an individual to rapidly switch between response sets. The effect of *interference* (i.e., failure to suppress distractions) is often assessed using task paradigms that involve ignoring irrelevant information presented in order to stay focused on the task goal. Whereas *flexibility* (changing behavior to fit a new rule) is often measured using reversal learning tasks that require an individual to recognize changes in contingencies (changes in stimulus-response patterns) and update behavior accordingly.

In well-rested individuals, these task paradigms have been shown to reliably recruit areas of the PFC, specifically the orbitofrontal cortex (OFC) and dorsolateral PFC. There are also several reciprocal projections between the PFC and subcortical structures such as the ventral striatum, amygdala, and thalamus that are involved in maintaining cognitive control [78, 79]. Additionally, both the cortical and subcortical regions are highly sensitive to disruptions in the neurochemical environment. Dopamine is a primary neuromodulator in the fronto-striatal pathway that is quite sensitive to perturbations such as sleep loss. Even small variations in dopamine levels can result in cognitive impairment [78, 80]. Thus, alteration of functioning within the dopamine system may be one of the primary ways that sleep deprivation can affect cognition.

Multi-tasking and task-switching

In safety-critical operations, the ability to rapidly and efficiently switch between multiple tasks is paramount. Unfortunately, many of the occupations (e.g., airline pilots, truck drivers, medical personnel, military personnel, etc.) that require multi-tasking are also often subjected to chronic sleep loss. During a typical task-switching paradigm, individuals perform two types of tasks in succession in which numerical stimuli are presented. On one task type study participants are asked to identify which of the numbers is even or odd. On another task type study participants are asked to identify if the number presented is smaller or larger than a predetermined value. When two of the same task types are presented one after another, this is considered a repetition trial. When the trial switches from one task to the other this is considered a switch trial. Switch trials are used to calculate *switch cost*, or the change in reaction time and accuracy between the switch and repetition trials. Essentially, switch cost is a measure of the amount of time that is required to reconfigure the cognitive processes needed to perform the new task—a basic executive function.

A recent neuroimaging study found that while performing a task-switching paradigm following sleep deprivation, neural activation increased in the fronto-parietal network and cingulate gyrus as compared to the well-rested state. However, different brain regions were involved in the switch trials. Task-switching was associated specifically with increased activation in the superior temporal gyrus and thalamus. Based on the cerebral metabolic data described earlier, it would seem sensible to expect reduced activation in these key brain regions. However, the fact that sleep deprivation was associated with increased neural activation suggests that compensatory mechanisms may be initiated to maintain some level of information retrieval necessary for the task [81]. Nonetheless, from a behavioral perspective, sleep loss results in slowed RTs, especially during switch trials [81, 82]. A single night of sleep loss also reduces performance accuracy and increases switch costs [82].

Total sleep deprivation studies are extreme cases of sleep loss and often do not translate to real-world scenarios. Haavisto and colleagues [83] investigated how multi-tasking performance is affected by sleep restriction over the course of what some would consider a typical workweek. Individuals in the restricted condition were only allowed to sleep for 4 h per night for five consecutive nights, compared to those in the well-rested condition who were allowed to sleep for 8 h per night. A multi-tasking paradigm was used in which study participants performed a series of subtasks to assess short-term memory, arithmetic skills, and visual and auditory monitoring. Sleep restriction impaired the ability to multi-task as a function of the number of days of sleep restriction, with performance also degrading further as time-on-task increased. Additionally, it took two nights of recovery sleep (8 h) to return to baseline performance levels [83]. Because sleep loss degrades the ability to multi-task or rapidly switch between activities, the potential for errors and accidents significantly increases.

Cognitive interference

Another aspect of cognitive control is being able to suppress irrelevant or distracting information while maintaining focus on relevant task information. When the irrelevant aspects of the task cannot be ignored, this is known as *cognitive interference*. Typically, cognitive interference is measured using various forms of the Stroop paradigm. The goal of a Stroop task is to inhibit a common or "prepotent" response in favor of a less common response. For example, the brain naturally reads printed words it sees without any effort. This automatic tendency to read is known as a prepotent response. During a typical Stroop task, the participant

is presented with a series of words depicting color names (e.g., "RED", "GREEN", "BLUE"). In some conditions the words are printed in either congruent (e.g., "RED" in red letters) or incongruent (e.g., "RED" in blue letters) ink colors, while in the neutral condition the words are printed in black ink. Individuals are to state the color of the ink in which the word appears, but not the word itself. The goal is to suppress the prepotent response (i.e., reading the word) in favor of the less common response (i.e., saying the color of the ink in which the word appears). This induces cognitive interference. Interestingly, several studies using the Stroop task have found that sleep deprivation does not affect cognitive interference, but rather only causes a general slowing of RTs [84–86]. A recent study found that resilience to slowed RTs and increased errors on the Stroop during a 30 h sleep deprivation period was related to a genetic polymorphism of the brain derived neurotrophic factor (BDNF) gene. Those individuals with the common Val allele had fewer errors compared to those with the Met allele [87], suggesting that some aspects of cognitive interference are predictable by genetic markers.

However, Gevers and colleagues [88] recognized the importance of assessing task performance in relevant components rather than assessing performance across the task as a whole. The Stroop task was administered once after a full night of sleep and again following a night of sleep deprivation. The task was decomposed into three components for analysis: size of the interference effect, bottom-up modulation (facilitated processing after repetitions), and top-down modulation (cognitive control adjustments for incongruent trials). They found that sleep deprivation impaired top-down control such that there was a reduced ability to efficiently recognize and adapt to conflicts (i.e., incongruent trials) [88]. It is possible that earlier studies did not find an effect of cognitive interference because different aspects of the task, as demonstrated by Gevers et al. [88], are differentially impacted by sleep loss, further highlighting the importance of deconstructing a task into specific, well-defined cognitive components.

Flexible attentional control

As with multi-tasking, the ability to think flexibly and quickly adapt to changing environmental circumstances is important in safety-critical operations. Effective attentional control requires an individual to anticipate responses and outcomes based on a predetermined set of expectations. However, real-world situations place individuals in dynamic environments that often challenge set expectations. Thus, individuals must be able to effectively recognize a change in circumstances and appropriately update the behavioral response. Reversal learning paradigms are typically used to assess flexible attentional control. While there are a wide variety of reversal learning paradigms, in the simplest form these tasks involve learning specific stimulus-response mappings that are tied to a reward and those that are tied to an unfavorable outcome. At a point in the middle of the task, the stimulus-response contingencies are reversed, such that previously rewarding stimuli become unfavorable and vice versa. Those that are able to maintain flexible attentional control will quickly recognize a change has occurred and adapt their responses. In contrast, those that do not think flexibly tend to show perseverative behavior by responding to the old stimulus-response mappings.

Interestingly, impairments in cognitive flexibility mimic impairments seen in individuals suffering from damage to the OFC and the basal ganglia [78, 89–91]. Neuroimaging studies in well-rested adults show that reversal learning recruits the ventrolateral PFC when a subject stops responding to the previously correct stimuli and starts responding to the new, relevant stimuli. When a subject makes a reversal error (i.e., responding to the incorrect stimulus following the stimulus-response reversal), there is neural activation within the ventral striatum [92]. Until recently, flexible attentional control had not been thoroughly explored under conditions of sleep deprivation. Whitney and colleagues [93, 94] conducted a series of sleep deprivation studies to assess how sleep loss impacts the ability to maintain flexible attentional control. In the first study, research participants were exposed to a 62 h sleep deprivation period. These individuals performed a modified version of the basic go/no-go paradigm during well-rested baseline, after 55 h of extended wakefulness, and following recovery sleep. During this novel task, participants were required to respond to a specific set of numeric stimuli (*go* stimuli) and withhold their response from a different set of numeric stimuli (*no-go* stimuli). However, they were required to learn which stimuli were *go* and which were *no-go* based on monetary reward feedback. Halfway throughout the task, the stimulus-response contingencies were reversed. Stimuli that were previously *go* stimuli became *no-go* stimuli and stimuli that were previously *no-go* stimuli became *go* stimuli. Participants were unaware of the reversal, and were again required to use monetary reward feedback to determine the correct stimulus-response mappings [93]. Sleep deprivation degraded pre-reversal performance, and even further degraded post-reversal performance (Fig. 26.10). Importantly, the profound impairment seen on the reversal learning task was distinct from vigilant attention impairment [93]. Further, it was found that the Val165Met genetic polymorphism of catechol-*O*-methyltransferase (i.e., the enzyme that degrades dopamine in the PFC) was associated with resilience to impairment on the go/no-go reversal learning task. Specifically, individuals carrying the Met allele were protected from the post-reversal performance impairment described above [76].

In a follow-up study, Whitney and colleagues [94] used a novel adaptation of the continuous performance task (AX-CPT) in which previous cue-probe contingencies were switched halfway throughout the task. They again

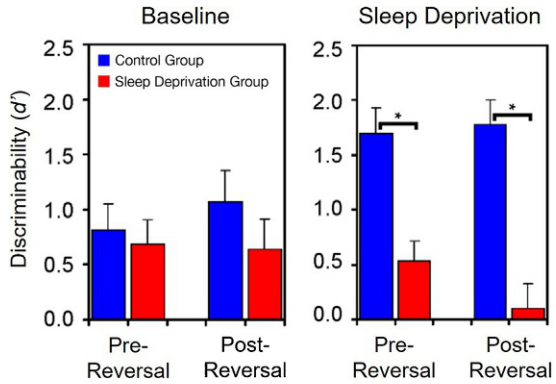

FIG. 26.10 Discriminability scores (±SE) on the go/no-go reversal learning paradigm. At baseline (left), there were no significant differences in pre- or post-reversal performance between the well-rested control and the sleep deprived groups. However, performance was profoundly degraded in the sleep deprived group (right). Impairment was further impaired following the stimulus-response reversal. Asterisks (*) indicate statistically significant pairwise differences. *Modified from Whitney P, Hinson JM, Jackson ML, Van Dongen HPA. Feedback blunting: Total sleep deprivation impairs decision making that requires updating based on feedback. Sleep 2015;38(5):745–54, with permission from Oxford University Press.*

demonstrated that sleep deprivation diminishes flexible attentional control, and also found that top-down control does not efficiently prevent errors [94]. They also found that a polymorphism that affects the binding potential of the dopamine D_2 receptor (DRD2) is associated with protection from impairment. Specifically, individuals homozygous for the C allele were resilient to impaired flexible attentional control. Together, these findings demonstrate that sleep deprivation profoundly degrades the ability to maintain flexible attention control, which can lead to maladaptive behaviors, including perseveration. Further, resilience to cognitive control impairment seems to be mediated by functional dopaminergic polymorphisms involved in the frontostriatal pathways.

Problem solving

The ability to solve problems is a core aspect of nearly any job. Depending on the operational environment, the kinds of problems that workers may encounter can range from simple mundane challenges to those that can be mission critical or even life threatening. Because many occupations require individuals to remain awake for extended periods or during times that are out of phase with their circadian rhythm, it is important to understand how various aspects of problem-solving ability can be impacted by lack of sleep.

Convergent thinking and logical deduction

Different kinds of problems require different kinds of solutions. One type of problem can be solved through the process of *convergent thinking*. This type of problem solving involves the step-by-step application of logical deductive reasoning and the use of established rules to reach a solution. These kinds of problems can be solved by beginning with an established set of information or major premise, adding a second minor premise, and finally arriving at a logical conclusion. For example, given the major premise that "every A is B" and the minor premise that "this C is A," then it is logical to conclude that "therefore this C is B." Concretely, we could apply this to a real-life example such as "all bulldogs are animals. Baxter is a bulldog. Therefore, Baxter is an animal." While this process sounds complex, evidence suggests that this form of convergent thinking is not significantly degraded by sleep deprivation [49]. Most studies that have specifically tested outcome measures such as logical deduction, intellectual functioning, grammatical reasoning, reading comprehension, and nonverbal problem solving have found negligible effects of sleep deprivation on these capacities [11, 49].

Divergent and innovative thinking

In contrast to the convergent thought processes discussed above, the ability to think laterally, innovatively, and flexibly *does* appear to be particularly susceptible to sleep deprivation [49]. In one study, a single night without sleep was associated with fewer creative responses and greater difficulty letting go of unsuccessful strategies [95]. Similarly, sleep deprivation has also been shown to adversely affect the ability to generate lists of novel words and produces slower and less efficient performance on the Tower of London, a task that requires planning, forethought, and cognitive flexibility [49]. The ability to generate and vocalize a series of random numbers is also degraded by sleep deprivation, leading to increased redundancy and stereotypy of responses and frequent rule violations [96]. On the other hand, inconsistent effects of sleep deprivation have been reported for the Wisconsin Card Sorting Test (WCST), a clinically based test of concept formation, set shifting, and mental flexibility [97]. It is important to keep in mind, however, that the WCST is a clinical task that was designed to detect relatively severe brain injuries and may not be sensitive enough to detect the subtle effects produced by sleep loss.

One particularly interesting study attempted to mimic real life decision-making during sleep deprivation by using a complex marketing strategy game. The task required participants to engage in several high level executive function tasks during a prolonged period of sleep loss. In particular, participants had to continuously monitor ongoing activities, revise their marketing strategies in light of periodically appearing new information, and apply available information to develop creative and innovative solutions under severe time constraints [98]. When normally rested, participants were able to think flexibly and innovatively, but once sleep deprived, they showed rigid thinking and perseverated on poor and ineffective strategies. As they reached the end of the game, these sleep deprived individuals had exhausted

their financial resources and were in a significantly worse financial position than compared to playing the same game in a rested state [98]. While such tasks can be incredibly ecologically valid and applicable to real-world situations, these types of complex tasks also suffer from the previously described task impurity problem [53, 54]. These types of tasks are not designed to deconstruct the component processes most affected by sleep loss, but do provide important understanding of how lack of sleep may actually be manifested in real-world situations.

RISK-TAKING, JUDGMENT, AND DECISION-MAKING

Can sleep deprivation increase the tendency to engage in high-risk activities or does it affect decisions that involve risk? While these questions seem simple, the answers appear to be complex and depend on a number of factors. We will address several issues, including how sleep loss affects self-reported risk-taking propensity, decision-making under conditions of uncertainty, the role of effort on risky behavior, implicit cognitive biases, aggressive behaviors, and moral decision-making.

Self-rated risk propensity

People can engage in high risk activities for a number of reasons. The construct of *risk-taking* is often confused with the closely related construct of *sensation seeking*, a preference for seeking out novel experiences and other thrilling activities that produce high levels of physiological arousal [99]. In contrast to sensation seeking, *Risk-Taking Propensity* represents the tendency to engage in activities that include a high level of risk, danger, or uncertainty of outcome [100, 101]. Although risk taking can occur because an individual is sensation seeking, risky behavior can also occur for reasons other than the pursuit of thrills or excitement. Accordingly, these two constructs are only modestly correlated with one another [102].

Interestingly, sleep deprivation has been shown to affect scores on measures of both sensation seeking and risk-taking, but the associations are typically inverse. For instance, one night of total sleep deprivation has been shown to significantly reduce scores on measures of self-reported sensation-seeking and self-reported risk-taking propensity [103, 104]. Similar findings have also been reported following two nights without sleep [35, 105]. Such findings are not surprising when considered in light of the fact that one of the most common symptoms of sleep loss is increased fatigue and reduced physical and mental energy [106]. It seems sensible that increased fatigue would lead to a reduction in activities requiring energy expenditure or exertion of mental or physical effort. Interestingly, longer periods of total sleep deprivation (i.e., 75 h awake) have been associated with a reversal of this trend, with participants showing greater interest in risky activities by the third night without sleep [35]. It is not entirely clear why this upsurge in risky preferences may occur, but it is conceivable that severe extended sleep deprivation may (1) substantially alter judgment, (2) lead to a burst of hypomanic disinhibition due to altered prefrontal functioning, or (3) be an attempt of participants to seek out stimulation as a means to behaviorally induce arousal. Notably, repeated doses of caffeine (200 mg every 2 h) appeared to be protective against this sudden surge in self-reported risk-seeking. Overall, these findings suggest that short term sleep deprivation (one or two nights) reduces interest in high-risk sensational activities, whereas that interest may show a rebound when sleep deprivation becomes extreme (≥3 nights).

Risky decision-making

While it is clear that sleep loss can lead to altered risk-related perceptions, it is also important to understand how sleep deprivation can affect actual risk-taking behavior. These types of effects are often revealed by gambling or other similar game-like risk tasks. As discussed below, sleep deprivation can lead to altered perception of risk, which will alter behavioral outcomes.

Cognitive framing

Sleep deprivation can affect how a person responds to the way in which a risk is presented to them, a phenomenon known as "framing." In most circumstances, risks can be framed as a potential gain (e.g., would you rather have an 80% chance of winning $4000, or a 100% chance of winning $3000) or as a potential loss (e.g., would you prefer an 80% chance of losing $4000 or a 100% chance of losing $3000). In such cases, it is well established that most people are risk avoiding when considering possible gains (i.e., they would prefer the "sure thing") and risk seeking when considering possible losses (i.e., they would prefer the "long shot") [107]. Interestingly, sleep deprivation appears to shift this basic cognitive bias. For example, in one study using a gambling game, when possible outcomes were described in terms of potential gains, sleep deprivation produced an increase in risk-taking above baseline. However, when possible outcomes were framed as potential losses, sleep deprivation caused participants to become more risk averse than when normally rested [108]. These findings suggest that sleep deprivation modifies the typical framing effect, increasing risk-taking when gains are emphasized and increasing risk-aversion when losses are emphasized, thus magnifying our typical tendencies.

Altered expectations of reward

Sleep deprivation appears to alter the cognitive assessment of risk by changing functioning within brain regions that

assign value to objects or situations. For example, one study examined the effects of sleep deprivation on brain activation while participants completed a roulette-style gambling task [109]. During a neuroimaging session, participants completed a series of roulette gambles that ranged from certain wins to highly risky bets. One night of sleep deprivation led to increased activation within the nucleus accumbens during high-risk decisions. This brain structure is involved in the anticipation of rewards and the increased responsiveness of this area following sleep loss suggests that it may be increasing the expected value of the risky bets. Simultaneously, sleep deprivation also blunted activation within the insular cortex during losses. Together, these findings suggest that sleep deprivation alters brain activation in a way that could bias an individual toward risky-behavior (i.e., increasing expectation of rewards and minimizing responses to losses).

The same research team conducted a follow-up study to examine the effects of sleep deprivation on complex reward-based decision-making [110]. Research participants completed a series of trials, some of which focused on gains and others that focused on losses. For instance, during the gain-focused trials, participants could choose to increase the potential amount of money that could be won or increase the probability of winning a particular amount. On the other hand, loss-focused trials permitted the participant to either reduce the amount of money that could be lost or lower the probability of losing a specified amount. Rested individuals showed a bias toward minimizing losses, but this pattern shifted toward maximizing gain after sleep deprivation. These changes were associated with increased activation of reward processing regions, including the ventromedial PFC, and a decline in activation of the insular cortex, which is generally associated with aversion and negative affective experiences [110]. Together, these findings suggest that sleep deprivation alters functional activation in brain regions associated with reward and punishment, which may increase the expectation that risky decisions will lead to reward.

Reward-based learning

Poor decision-making is often characterized by a preference for short-term gains that ultimately lead to long-term losses. Everyday life is full of choices that involve deciding whether to forgo immediate satisfaction in service of longer lasting benefits. One experimental paradigm that seems to get to the heart of these kinds of decisions is the Iowa Gambling Task (IGT), a computerized gambling game-like task that involves selecting cards from four decks with varied, but unstipulated, payout schedules. Two of the decks are high risk because of their widely variable payouts that lead to a net loss, and two of the decks are low risk because they have very consistent but small payouts that reliably lead to a net gain. When healthy normal individuals play this game, they rapidly learn to maximize long-term profits over short-term gains by sticking with the low risk decks. In contrast, patients with focal lesions to the ventromedial PFC, a region critical to learning from rewards and punishments, tend to become selectively attracted to the short-term gains associated with the high-risk decks, which eventually leads them to progressively lose money throughout the course of the game [111, 112].

The IGT has been studied in several studies of sleep deprivation, which have consistently demonstrated that lack of sleep is associated with a pattern of performance that is qualitatively similar to that of patients with lesions in the ventromedial region of the PFC [113–115]. In short, sleep deprivation leads to a short-term focus on immediate gains to the detriment of longer-term outcomes, a pattern that appears to be more severe with greater durations of sleep deprivation. This effect is mediated, in part, by the DAT1 polymorphism, such that individuals with the 9-repeat allele have elevated responsivity to gain anticipations [116]. Interestingly, stimulant countermeasures such as caffeine, modafinil, and dextroamphetamine have not been effective at restoring performance on the IGT (Fig. 26.11), despite normalizing performance on psychomotor vigilance [113, 114]. This lack of effect of stimulants suggests that the deficits on the IGT are probably not due to problems with attention and vigilance and are brought about by alteration

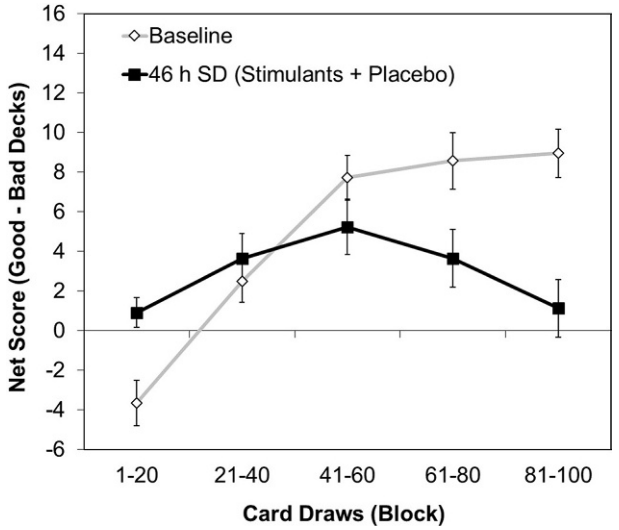

FIG. 26.11 Net scores on the IGT for each block of the task. Study participants performed the task following 46 h of extended wakefulness. Stimulants (600 mg caffeine, 20 mg dextroamphetamine, 400 mg modafinil, or placebo) were administered at 44 h wakefulness. Stimulants did not affect IGT performance, and are thus grouped with the placebo group here. Stimulants (*black squares*) were not effective at restoring IGT performance back to baseline levels (*white diamonds*). *Modified from Killgore WDS, Grugle NL, Balkin TJ. Gambling when sleep deprived: don't bet on stimulants. Chronobiol Int 2012;29(1):43–54, with permission from Taylor & Francis Ltd. (http://www.informaworld.com).*

in the process of integrating information about rewards and punishments with ongoing decision-making processes. Furthermore, we also recently showed that daytime sleepiness reduces the psychological weight that individuals give to more temporally distant versus more recent trials on the IGT in their decision-making strategy [117]. These data suggest that sleepiness may shorten the "time horizon" over which decision information is integrated into the decision-making process. Thus, a sleep deprived individual could also make risky choices because they base decisions on a limited amount of information.

Impulsive behavior

While risk taking often involves deciding between high and low risk options, another form of risk-taking involves "pressing one's luck" beyond the point where the benefits of success are outweighed by the costs of failure. A task that assesses the tendency to push the limits and behave impulsively is known as the Balloon Analog Risk Task (BART). The BART is a computerized task that presents a series of 30 virtual balloons that must be inflated on the screen to win money. To inflate each balloon, the participant presses the spacebar on the keyboard. With each key press, or "pump," the balloon increases in size slightly and gains an additional five cents in value. The larger the balloon becomes, the greater its potential monetary value. The participant can "bank" the accumulated value of a balloon at any time, as long as it has not exploded. If the balloon is inflated too much, the balloon will explode and all accumulated value for that balloon will be lost. Each balloon has a different breaking point that is not known to the participant. In order to win the most money possible, the participant must make a judgment about how much to inflate each balloon and then attempt to cash in before reaching the unknown explosion point. A commonly used output variable from this task is mean number of key presses for the unexploded balloon trials (i.e., those trials that were "banked" without popping the balloon), which is commonly known as the Adjusted Average Number of Pumps. Some studies have also calculated a "Cost/Benefit Ratio," which considers both the Cost (i.e., proportion of exploded balloons) versus the Benefit (i.e., the proportion of all potential money that was actually banked) [35, 104, 105]. Higher Cost/Benefit Ratio scores suggest greater risk-taking.

Several sleep deprivation studies have used the BART to examine the effects of sleep loss on risky behavior. The first published study to examine the BART during sleep deprivation showed that one night without sleep led to a decline in the Cost/Benefit Ratio, suggesting a tendency toward less behavioral risk-taking [104]. A second study published around the same time also found that a single night of sleep deprivation was associated with reduced risk-taking (i.e., lower Adjusted Average Number of Pumps) among women but not men [118]. Later work further confirmed that risk taking on the BART was reduced with two nights of sleep deprivation, but was returned to baseline levels with a 20 mg dose of dextroamphetamine, but not by similarly alerting doses of 400 mg modafinil, or 600 mg of caffeine [105]. In contrast, Killgore and colleagues found that BART Cost/Benefit scores were generally unaffected by two nights of sleep deprivation, but this was followed by a surge in behavioral risk-taking after three nights without sleep [35]. The cause of this surge in risk-taking after extreme sleep deprivation is not clear, but it is possible that inhibitory capacity eventually fails after several nights awake, or that the increased risk taking is simply a way for participants to stimulate arousal [35].

The fact that the BART typically shows reduced risk-taking during sleep loss seems to stand in contradiction to the increased risk-taking that is consistently found on the IGT. One explanation for this discrepancy may involve the difference in effort required by these two tasks [104]. While both the IGT and BART involve risky decision-making, risky choices on the IGT require no more effort than the safe options (i.e., a single button press is required regardless of which option is selected), while greater risk taking on the BART requires the expenditure of additional physical and cognitive effort (i.e., more button presses are required to be risky, while fewer button presses are safer). This explanation was given further support by a study that showed that sleep deprivation leads to "effort discounting," a willingness to accept less reward if it requires only minimal effort rather than expend greater effort to obtain higher value rewards [119]. Sleep deprived individuals appear to be less willing to expend effort to engage in risky activities.

Aggressive/punitive responses

Negative mood states are common during sleep deprivation and evidence suggests that individuals may become more easily frustrated by even minor hassles or interpersonal slights. For instance, sleep deprivation appears to increase the willingness to blame others for frustrating problems and makes people less willing to work with others to achieve mutually satisfying outcomes [120]. Without sleep, people often feel picked on or targeted for persecution [121]. Sometimes, this can even lead to aggressive behaviors [122]. In one study, participants played a series of "bargaining" and "trust" games that required them to interact with other players to earn various levels of money [123]. On these games, sleep deprivation increased the tendency to engage in aggressive exchanges with the other players. Moreover, sleep deprived individuals were less trusting of their partners and more often rejected monetary offers that were perceived as unfair, even when rejecting the offer would come at a financial cost to themselves. Sleep deprivation appears to have an adverse effect on trust and normal social discourse.

Moral judgment

Our stable moral precepts and beliefs dictate our responses to difficult situations where the appropriate decision is not obvious. A few studies have demonstrated moral judgment and moral decision-making can be affected by sleep deprivation. In the earliest published study to examine moral judgment following sleep loss, participants completed a series of moral and non-moral dilemmas when fully rested and again following 53 h of sleep deprivation [124]. The findings showed that most decision-making processes were relatively unaffected by sleep deprivation, including non-moral decisions and moral decisions that were generally low in emotional intensity. However, sleep deprivation appeared to significantly slow responses to difficult moral decisions that involved high levels of emotional conflict. Compared to the speed of decisions at baseline, the time to respond to emotionally challenging situations was much slower, suggesting that sleep deprivation does not affect all decisions equally—sleep deprivation specifically impairs the ability to make emotionally based decisions. Moreover, sleep deprivation also altered the qualitative direction of the judgments. Specifically, sleep deprived individuals were more likely to make utilitarian type judgments that violated their own moral beliefs compared to when they were well rested [124]. However, this effect was not significant in a second study of only a single night of sleep loss [125], suggesting that deficits in moral judgments may only emerge with prolonged periods without sleep. Other evidence also suggests that moral reasoning may be affected by partial sleep restriction as well. For instance, when sleep was restricted to approximately 2.5 h per night over 5 days, military personnel showed significant reductions in principle-oriented moral reasoning [126]. Among this sample of military cadets, their moral decisions became more rules-focused and self-oriented over the course of sleep restriction, and they showed progressively greater difficulty with higher-level principle-oriented reasoning. Overall, it appears clear that sleep deprivation affects the speed and quality of moral decisions and judgments.

PRACTICAL IMPLICATIONS

Extreme cases of acute sleep deprivation often fail to be generalizable to real-word situations. However, a common occurrence in everyday life is that of chronic sleep restriction. It is common for individuals to repeatedly, and regularly, obtain insufficient amounts of sleep. Individuals that are chronically sleep-restricted often have difficulty with day-to-day tasks, and they may not even realize it until it is too late. For example, individuals that are leaving a night shift often drive drowsy. While drowsy driving may not always lead to a direct negative consequence, under the right circumstances the results can be catastrophic due to the unpredictable nature of sleep loss induced impairments. For instance, if an individual experiences even a single lapse in attention at the same moment a stop light turns red, the result could be disastrous. Further, the inability to effectively inhibit responses and make rational decisions can significantly impact work performance and interpersonal relationships. As sleep loss impairs inhibitory control, individuals that are sleep-restricted may make decisions or act in ways that are out of character or inappropriate to the context due to a diminished capacity to inhibit responses. This could prove harmful to an individual's social or professional reputation or could damage close interpersonal relationships. Additionally, sleep loss alters reward expectation in such a way that individuals do not realize the consequences of their actions, as they expect to be rewarded by their choices, regardless of the quality of the decisions. This exaggerated expectation of reward may lead individuals to make risky decisions, which could affect economic choices such as gambling or selecting risky investments. Of course, these same unrealistic expectations of reward could potentially affect other behaviors as well, including social, interpersonal, and professional decisions. Overall, it is important for individuals to recognize the range of cognitive consequences of sleep loss and the downstream effects that insufficient sleep can have on basic day-to-day activities and interpersonal relationships.

Often times, the effects of sleep loss can be mitigated with effective countermeasure strategies, including caffeine and strategic napping [6], although there is some evidence that widely used stimulants, such as caffeine, may improve some executive functions [35, 127, 128] while having no discernable effects on others [113, 114]. However, many of the negative consequences associated with sleep loss can be avoided all together with a proactive approach. Those who are often faced with chronic sleep loss should take the steps necessary to educate themselves on causes and consequences of fatigue. It is also important to become educated about and implement proper sleep hygiene techniques, including making sleep a priority, standardizing sleep schedules, creating a good sleep environment, and "unplugging" from technology and other forms of stimulation at least 30 min before bed [129]. Additionally, individuals should attempt to align lifestyle choices with their work and social schedules to maximize sleep opportunities [6].

CONCLUSIONS

Sleep loss appears to have a multifaceted impact on both neural and behavioral measures. These impacts affect both global and domain-specific aspects of cognition. This, in part, is due to the differential responsiveness of the interconnected brain regions underlying each specific cognitive task. Sleep loss consistently impairs vigilant attention performance, resulting in increased lapses of attention and slowed response times. However, the literature is mixed as

to if, and how, insufficient sleep influences performance on higher-order executive function and decision-making tasks. For example, the executive and non-executive components of working memory are differentially impacted by sleep loss. Further, other complex executive functions, such as cognitive control, are negatively impacted by sleep loss, yet impaired vigilant attention does not seem to be the underlying cause. For some higher-level tasks that involve judgment and decision-making, the effects of sleep loss on emotional systems may be particularly important. While research into the underlying mechanisms of cognitive impairment due to sleep loss has increased in recent years, more work is needed in order to fully elucidate how sleep loss specifically impacts various aspects of cognition. Identification of task-specific impairments, and the mechanisms subserving these impairments, can aid in the development of appropriate countermeasures and fatigue risk management strategies for those most at risk for experiencing chronic and acute sleep loss.

REFERENCES

[1] Center for Disease Control and Prevention. Insufficient sleep is a public health epidemic [Internet]. Insufficient sleep is a public health problem. Available from: http://www.cdc.gov/features/dssleep/; 2015.

[2] Bayon V, Leger D, Gomez-Merino D, Vecchierini MF, Chennaoui M. Sleep debt and obesity. Ann Med 2014;46(5):264–72.

[3] Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, Hazen N, Herman H, Katz ES, Kheirandish-Gozal L, Neubauer DN, O'Donnel AE, Ohayon M, Peever J, Rawding R, Sachdeva RC, Setters B, Vitiello MV, Ware JC, Adams Hillard PJ. National sleep foundation's sleep time duration recommendations: methodology and results summary. Sleep Heal 2015;1(1):40–3.

[4] Borbély AA. A two process model of sleep regulation. Hum Neurobiol 1982;1(3):195–204.

[5] Daan S, Beersma DG, Borbély AA. Timing of human sleep: recovery process gated by a circadian pacemaker. Am J Physiol 1984;246:R161–83.

[6] Satterfield BC, Van Dongen HPA. Occupational fatigue, underlying sleep and circadian mechanisms, and approaches to fatigue risk management. Fatigue Biomed Heal Behav 2013;246(3):118–36.

[7] Dinges DF, Powell JW. Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. Behav Res Methods Instrum Comput 1985;17(6):652–5.

[8] Lim J, Dinges DF. Sleep deprivation and vigilant attention. Ann N Y Acad Sci 2008;1129:305–22.

[9] Dorrian J, Rogers NL, Dinges DF. Psychomotor vigilance performance: neurocognitive assay sensitive to sleep loss. In: Kushida CA, editor. Sleep deprivation: clinical issues, pharmacology and sleep loss effects. New York: Marcell Dekker; 2005. p. 39–70.

[10] Doran SM, Van Dongen HPA, Dinges DF. Sustained attention performance during sleep deprivation: evidence of state instability. Arch Ital Biol 2001;139(3):253–67.

[11] Lim J, Dinges DF. A meta-analysis of the impact of short-term sleep deprivation on cognitive variables. Psychol Bull 2010;136(3):375–89.

[12] Drummond SPA, Bischoff-Grethe A, Dinges DF, Ayalon L, Mednick SC, Meloy MJ. The neural basis of the psychomotor vigilance task. Sleep 2005;28(9):1059–68.

[13] Wesensten NJ, Killgore WDS, Balkin TJ. Performance and alertness effects of caffeine, dextroamphetamine, and modafinil during sleep deprivation. J Sleep Res 2005;14(3):255–66.

[14] Cajochen C, Khalsa SB, Wyatt JK, Czeisler CA, Dijk DJ. EEG and ocular correlates of circadian melatonin phase and human performance decrements during sleep loss. Am J Physiol 1999;277:R640–9.

[15] Belenky G, Wesensten NJ, Thorne DR, Thomas ML, Sing HC, Redmond DP, Russo MB, Balkin TJ. Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-response study. J Sleep Res 2003;12(1):1–12.

[16] Van Dongen HPA, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep 2003;26(2):117–26.

[17] Chee MWL, Tan JC. Lapsing when sleep deprived: neural activation characteristics of resistant and vulnerable individuals. Neuroimage 2010;51(2):835–43.

[18] Van Dongen HPA, Belenky G, Krueger JM. A local, bottom-up perspective on sleep deprivation and neurobehavioral performance. Curr Top Med Chem 2011;11(19):2414–22.

[19] Bills AG. Blocking: a new principle of mental fatigue. Am J Psychol 1931;43(2):230–45.

[20] Kribbs NB, Dinges DF. Vigilance decrement and sleepiness. In: Ogilvie RD, Harsh JR, editors. Sleep onset: normal and abnormal processes. Washington, DC: American Psychological Association; 1994. p. 113–25.

[21] Van Dongen HPA, Dinges DF. Investigating the interaction between the homeostatic and circadian processes of sleep-wake regulation for the prediction of waking neurobehavioural performance. J Sleep Res 2003;12(3):181–7.

[22] Bills AG. Fatigue in mental work. Physiol Rev 1937;17:436–53.

[23] Van Dongen HPA, Belenky G, Krueger JM. Investigating the temporal dynamics and underlying mechanisms of cognitive fatigue. In: Ackerman PL, editor. Cognitive fatigue: mulitidisciplinary perspectives on current research and future applications. Washington, DC: American Psychological Association; 2011. p. 127–47.

[24] Van Dongen HPA, Dinges DF. Sleep, circadian rhythms, and psychomotor vigilance. Clin Sports Med 2005;24:237–49.

[25] Van Dongen HPA, Belenky G. Individual differences in vulnerability to sleep loss in the work environment. Ind Health 2009;47(5):518–26.

[26] Krueger JM, Rector DM, Roy S, Van Dongen HPA, Belenky G, Panksepp J. Sleep as a fundamental property of neuronal assemblies. Nat Rev Neurosci 2008;9(12):910–9.

[27] Wilkinson RT. Interaction of lack of sleep with knowledge of results, repeated testing, and individual differences. J Exp Psychol 1961;62(3):263–71.

[28] Leproult R, Colecchia EF, Berardi AM, Stickgold R, Kosslyn SM, Van Cauter E. Individual differences in subjective and objective alertness during sleep deprivation are stable and unrelated. Am J Physiol Regul Integr Comp Physiol 2003;284:R280–90.

[29] Tucker AM, Dinges DF, Van Dongen HPA. Trait interindividual differences in the sleep physiology of healthy young adults. J Sleep Res 2007;16(2):170–80.

[30] Grant DA, HPA VD. Individual differences in sleep duration and responses to sleep loss. In: Shaw P, Tafti M, Thorpy M, editors. The genetic basis of sleep and sleep disorders. Cambridge: Cambridge University Press; 2013. p. 189–96.
[31] Rupp TL, Wesensten NJ, Balkin TJ. Trait-like vulnerability to total and partial sleep loss. Sleep 2012;35(8):1163–72.
[32] Van Dongen HPA, Baynard MD, Maislin G, Dinges DF. Systematic interindividual differences in neurobehavioral impairment from sleep loss: evidence of trait-like differential vulnerability. Sleep 2004;27(3):423–33.
[33] Van Dongen HPA, Maislin G, Dinges DF. Dealing with inter-individual differences in the temporal dynamics of fatigue and performance: importance and techniques. Aviat Space Environ Med 2004;75(Suppl 3):A147–54.
[34] Killgore WDS, Richards JM, Killgore DB, Kamimori GH, Balkin TJ. The trait of introversion-extraversion predicts vulnerability to sleep deprivation. J Sleep Res 2007;16(4):354–63.
[35] Killgore WDS, Kamimori GH, Balkin TJ. Caffeine protects against increased risk-taking propensity during severe sleep deprivation. J Sleep Res 2011;20(3):395–403.
[36] Chee MWL, Van Dongen HPA. Functional imaging of inter-individual differences in response to sleep deprivation. In: Nofzinger E, Maquet P, Thorpy M, editors. Neuroimaging of sleep and sleep disorders. Cambridge: Cambridge University Press; 2013. p. 154–62.
[37] Goel N. Genetic markers of sleep and sleepiness. Sleep Med Clin 2017;12(3):289–99.
[38] Mu Q, Mishory A, Johnson KA, Nahas Z, Kozel FA, Yamanaka K, Bohning DE, George MS. Decreased brain activation during a working memory task at rested baseline is associated with vulnerability to sleep deprivation. Sleep 2005;28(4):433–46.
[39] Mu Q, Nahas Z, Johnson KA, Yamanaka K, Mishory A, Koola J, Hill S, Horner MD, Bohning DE, George MS. Decreased cortical response to verbal working memory following sleep deprivation. Sleep 2005;28(1):55–67.
[40] Lythe KE, Williams SCR, Anderson C, Libri V, Mehta MA. Frontal and parietal activity after sleep deprivation is dependent on task difficulty and can be predicted by the fMRI response after normal sleep. Behav Brain Res 2012;233(1):62–70.
[41] Yeo BTT, Tandi J, Chee MWL. NeuroImage functional connectivity during rested wakefulness predicts vulnerability to sleep deprivation. Neuroimage 2015;111:147–58.
[42] Cui J, Tkachenko O, Gogel H, Kipman M, Preer LA, Weber M, Divatia SC, Demers LA, Olson EA, Buchholz JL, Bark JK, Rosso IM, Rauch SL, WDS K. Microstructure of frontoparietal connections predicts individual resistance to sleep deprivation. Neuroimage 2015;106:123–33.
[43] Goel N. Neurobehavioral effects and biomarkers of sleep loss in healthy adults. Curr Neurol Neurosci Rep 2017;17(11):89.
[44] Bodenmann S, Hohoff C, Freitag C, Deckert J, Rétey JV, Bachmann V, Landolt H-P. Polymorphisms of ADORA2A modulate psychomotor vigilance and the effects of caffeine on neurobehavioural performance and sleep EEG after sleep deprivation. Br J Pharmacol 2012;165(6):1904–13.
[45] Satterfield BC, Wisor JP, Schmidt MA, Van Dongen HPA. Time-on-task effect during sleep deprivation in healthy young adults is modulated by dopamine transporter genotype. Sleep 2017;40(12):zsx167.
[46] Holst SC, Müller T, Valomon A, Seebauer B, Berger W, Landolt H-P. Functional polymorphisms in dopaminergic genes modulate neurobehavioral and neurophysiological consequences of sleep deprivation. Sci Rep 2017;7:45982.
[47] Satterfield BC, Wisor JP, Field SA, Schmidt MA, Van Dongen HPA. TNFα G308A polymorphism is associated with resilience to sleep deprivation-induced psychomotor vigilance performance impairment in healthy young adults. Brain Behav Immun 2015;47:66–74.
[48] Miller EK, Wallis JD. Executive function and higher-order cognition: definition and neural substrates. Encycl Neurosci 2010;4:99–104.
[49] Harrison Y, Horne JA. The impact of sleep deprivation on decision making: a review. J Exp Psychol Appl 2000;6(3):236–49.
[50] Thomas ML, Sing HC, Belenky G, Holcomb HH, Mayberg HS, Dannals RF, Wagner Jr. J, Thorne D, Popp K, Rowland L, Welsh A, Balwinski S, Redmond D. Neural basis of alertness and cognitive performance impairments during sleepiness I. Effects of 48 and 72 h of sleep deprivation on waking human regional brain activity. J Sleep Res 2000;9:335–52.
[51] Wu JC, Gillin JC, Buchsbaum MS, Chen P, Keator DB, Wu NK, Darnall LA, Fallon JH, Bunney WE. Frontal lobe metabolic decreases with sleep deprivation not totally reversed by recovery sleep. Neuropsychopharmacology 2006;31(12):2783–92.
[52] Van Dongen HPA, Bender AM, Dinges DF. Systematic individual differences in sleep homeostatic and circadian rhythm contributions to neurobehavioral impairment during sleep deprivation. Accid Anal Prev 2012;45(Suppl):11–6.
[53] Jackson ML, Gunzelmann G, Whitney P, Hinson JM, Belenky G, Rabat A, Van Dongen HPA. Deconstructing and reconstructing cognitive performance in sleep deprivation. Sleep Med Rev 2013;17(3):215–25.
[54] Tucker AM, Whitney P, Belenky G, Hinson JM, Van Dongen HPA. Effects of sleep deprivation on dissociated components of executive functioning. Sleep 2010;33(1):47–57.
[55] Reichert C, Maire M, Schmidt C, Cajochen C. Sleep-wake regulation and its impact on working memory performance: the role of adenosine. Biology 2016;5(1):11.
[56] Frenda SJ, Fenn KM. Sleep less, think worse: the effect of sleep deprivation on working memory. J Appl Res Mem Cogn 2016;5(4):463–9.
[57] Baddeley AD. Working memory: theories, models, and controversies. Annu Rev Psychol 2012;63:1–29.
[58] Chee MWL, Choo WC. Functional imaging of working memory after 24 hr of total sleep deprivation. J Neurosci 2004;24(19):4560–7.
[59] Chee MWL, Chuah LYM, Venkatraman V, Chan WY, Philip P, Dinges DF. Functional imaging of working memory following normal sleep and after 24 and 35 h of sleep deprivation: correlations of fronto-parietal activation with performance. Neuroimage 2006;31(1):419–28.
[60] Choo WC, Lee WW, Venkatraman V, Sheu FS, Chee MWL. Dissociation of cortical regions modulated by both working memory load and sleep deprivation and by sleep deprivation alone. Neuroimage 2005;25(2):579–87.
[61] Bell-McGinty S, Habeck C, Hilton HJ, Rakitin B, Scarmeas N, Zarahn E, Flynn J, DeLaPaz R, Basner R, Stern Y. Identification and differential vulnerability of a neural network in sleep deprivation. Cereb Cortex 2004;14(5):496–502.
[62] Drummond SPA, Meloy MJ, Yanagi MA, Orff HJ, Brown GG. Compensatory recruitment after sleep deprivation and the relationship with performance. Psychiatry Res Neuroimaging 2005;140(3):211–23.
[63] Groeger J, Viola A, Lo J, von Schantz M, Archer SN, Dijk D-J. Early morning executive functioning during sleep deprivation is compromised by a PERIOD3 polymorphism. Sleep 2008;31(8):1159–67.

[64] Drummond SPA, Anderson DE, Straus LD, Vogel EK, Perez VB. The effects of two types of sleep deprivation on visual working memory capacity and filtering efficiency. PLoS One 2012;7(4):1–8.
[65] Rångtell FH, Karamchedu S, Andersson P, Liethof L, Olaya Búcaro M, Lampola L, Schiöth HB, Cedernaes H, Benedict C. A single night of sleep loss impairs objective but not subjective working memory performance in a sex-dependent manner. J Sleep Res 2019;28:1–8.
[66] Santhi N, Lazar AS, McCabe PJ, Lo JC, Groeger JA, Dijk D-J. Sex differences in the circadian regulation of sleep and waking cognition in humans. Proc Natl Acad Sci 2016;113(19):E2730–9.
[67] Chee MWL, Chuah YML. Functional neuroimaging and behavioral correlates of capacity decline in visual short-term memory after sleep deprivation. Proc Natl Acad Sci 2007;104(22):9487–92.
[68] Bari A, Robbins TW. Inhibition and impulsivity: behavioral and neural basis of response control. Prog Neurobiol 2013;108:44–79.
[69] Taylor SF, Stern ER, Gehring WJ. Neural systems for error monitoring: recent findings and theoretical perspectives. Neuroscientist 2007;13(2):160–72.
[70] Chuah YML, Venkatraman V, Dinges DF, Chee MWL. The neural basis of interindividual variability in inhibitory efficiency after sleep deprivation. J Neurosci 2006;26(27):7156–62.
[71] Drummond SPA, Paulus MP, Tapert SF. Effects of two nights sleep deprivation and two nights recovery sleep on response inhibition. J Sleep Res 2006;15(3):261–5.
[72] Sagaspe P, Taillard J, Amieva H, Beck A, Rascol O, Dartigues J-F, Capelli A, Philip P. Influence of age, circadian and homeostatic processes on inhibitory motor control: a Go/Nogo task study. PLoS One 2012;7(6):e39410.
[73] Demos KE, Hart CN, Sweet LH, Mailloux KA, Trautvetter J, Williams SE, Wing RR, McCaffery JM. Partial sleep deprivation impacts impulsive action but not impulsive decision-making. Physiol Behav 2016;164:214–9.
[74] Killgore WDS. Effects of sleep deprivation on cognition. In: Kerkhof G, HPA VD, editors. Progress in brain research. Elsevier B.V.; 2010. p. 105–29.
[75] Braver TS. The variable nature of cognitive control: a dual mechanisms framework. Trends Cogn Sci 2012;16(2):106–13.
[76] Satterfield BC, Hinson JM, Whitney P, Schmidt MA, Wisor JP, Van Dongen HPA. Catechol-O-methyltransferase (COMT) genotype affects cognitive control during total sleep deprivation. Cortex 2017;99:179–86.
[77] Cools R. The costs and benefits of brain dopamine for cognitive control. WIREs Cogn Sci 2016;7:317–29.
[78] Klanker M, Feenstra M, Denys D, Lo C, Tsing N. Dopaminergic control of cognitive flexibility in humans and animals. Front Neurosci 2013;7:201.
[79] Botvinick M, Braver TS. Motivation and cognitive control: from behavior to neural mechanism. Annu Rev Psychol 2015;66:83–113.
[80] Cools R, Robbins TW. Chemistry of the adaptive mind. Philos Trans R Soc A Math Phys Eng Sci 2004;362(1825):2871–88.
[81] Nakashima A, Bouak F, Lam Q, Smith I, Vartanian O. Task switching following 24 h of total sleep deprivation. Neuroreport 2018;29(2):123–7.
[82] Couyoumdjian A, Sdoia S, Tempesta D, Curcio G, Rastellini E, De Gennaro L, Ferrara M. The effects of sleep and sleep deprivation on task-switching performance. J Sleep Res 2010;19:64–70.
[83] Haavisto ML, Porkka-Heiskanen T, Hublin C, Härmä M, Mutanen P, Müller K, Virkkala J, Sallinen M. Sleep restriction for the duration of a work week impairs multitasking performance: sleep restriction and multitasking. J Sleep Res 2010;19(3):444–54.
[84] Sagaspe P, Sanchez-Ortuno M, Charles A, Taillard J, Valtat C, Bioulac B, Philip P. Effects of sleep deprivation on color-word, emotional, and specific stroop interference and on self-reported anxiety. Brain Cogn 2006;60(1):76–87.
[85] Cain SW, Silva EJ, Chang AM, Ronda JM, Duffy JF. One night of sleep deprivation affects reaction time, but not interference or facilitation in a stroop task. Brain Cogn 2011;76(1):37–42.
[86] Bratzke D, Steinborn MB, Rolke B, Ulrich R. Effects of sleep loss and circadian rhythm on executive inhibitory control in the stroop and simon tasks. Chronobiol Int 2012;29(1):55–61.
[87] Grant LKL, Cain SW, Chang A-M, Saxena R, Czeisler CA, Andersaon C. Impaired cognitive flexibility during sleep deprivation among carriers of the brain derived neurotrophic factor (BDNF) Val66Met allele. Behav Brain Res 2018;338:51–5.
[88] Gevers W, Deliens G, Hoffmann S, Notebaert W, Peigneux P. Sleep deprivation selectively disrupts top-down adaptation to cognitive conflict in the stroop test. J Sleep Res 2015;24(6):666–72.
[89] Frank MJ, Claus ED. Anatomy of a decision: Striato-orbitofrontal interactions in reinforcement learning, decision making, and reversal. Psychol Rev 2006;113(2):300–26.
[90] Fellows LK. The role of orbitofrontal cortex in decision making: a component process account. Ann N Y Acad Sci 2007;1121(1):421–30.
[91] Pauli WM, Hazy TE, O'Reilly RC.. Expectancy, ambiguity, and behavioral flexibility: separable and complementary roles of the orbital frontal cortex and amygdala in processing reward expectancies. J Cogn Neurosci 2011;24(2):351–66.
[92] Cools R, Clark L, Owen AM, Robbins TW. Defining the neural mechanisms of probabilistic reversal learning using event-related functional magnetic resonance imaging. J Neurosci 2002;22(11):4563–7.
[93] Whitney P, Hinson JM, Jackson ML, Van Dongen HPA. Feedback blunting: total sleep deprivation impairs decision making that requires updating based on feedback. Sleep 2015;38(5):745–54.
[94] Whitney P, Hinson JM, Satterfield BC, Grant DA, Honn KA, Van Dongen HPA. Sleep deprivation diminishes attentional control effectiveness and impairs flexible adaptation to changing conditions. Sci Rep 2017;7(1):16020.
[95] Horne JA. Sleep loss and "divergent" thinking ability. Sleep 1988;11(6):528–36.
[96] Cade BE, Gottlieb DJ, Lauderdale DS, Bennett DA, Buchman AS, Buxbaum SG, De Jager PL, Evans DS, Fülöp T, Gharib SA, Johnson WC, Kim H, Larkin EK, Lee SK, Lim AS, Punjabi NM, Shin C, Stone KL, Tranah GJ, Weng J, Yaffe K, Zee PC, Patel SR, Zhu X, Redline S, Saxena R. Common variants in DRD2 are associated with sleep duration: the CARe consortium. Hum Mol Genet 2016;25(1):167–79.
[97] Jones K, Harrison Y. Frontal lobe function, sleep loss and fragmented sleep. Sleep Med Rev 2001;5(6):463–75.
[98] Harrison Y, Horne JA. One night of sleep loss impairs innovative thinking and flexible decision making. Organ Behav Hum Decis Process 1999;78(2):128–45.
[99] Hoyle RH, Stephenson MT, Palmgreen P, Lorch EP, Donohew RL. Reliability and validity of a brief measure of sensation seeking. Pers Individ Dif 2002;32(3):401–14.
[100] Killgore WDS, Vo A, Castro C, Hoge C. Assessing risk propensity in American soldiers: preliminary reliability and validity of the evaluation of risks (EVAR) scale—english version. Mil Med 2006;171(3):233–9.

[101] Sicard B, Jouve E, Blin O. Risk propensity assessment in military special operations. Mil Med 2001;166(10):871–4.
[102] Killgore WDS, Grugle NL, Killgore DB, Balkin TJ. Sex differences in self-reported risk-taking propensity on the evaluation of risks scale. Psychol Rep 2010;106(3):693–700.
[103] Chaumet G, Taillard J, Sagaspe P, Pagani M, Dinges DF, Pavy-Le-Traon A, Bareille MP, Rascol O, Philip P. Confinement and sleep deprivation effects on propensity to take risks. Aviat Space Environ Med 2009;80(2):73–80.
[104] Killgore WDS. Effects of sleep deprivation and morningness-eveningness traits on risk-taking. Psychol Rep 2007;100:613–26.
[105] Killgore WDS, Grugle NL, Killgore DB, Leavitt BP, Watlington GI, McNair S, Balkin TJ. Restoration of risk-propensity during sleep deprivation: caffeine, dextroamphetamine, and modafinil. Aviat Space Environ Med 2008;79(9):867–74.
[106] Dinges DF, Pack F, Williams K, Gillen K, Powell J, Ott G, Aptowicz C, Pack AI. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. Sleep 1997;20(4):267–77.
[107] Kahneman D. A perspective on judgment and choice: mapping bounded rationality. Am Psychol 2003;58(9):697–720.
[108] Mckenna BS, Dickinson DL, Orff HJ, Drummond SPA. The effects of one night of sleep deprivation on known-risk and ambiguous-risk decisions. J Sleep Res 2007;16(3):245–52.
[109] Venkatraman V, Chuah LY, Huettel SA, Chee MW. Sleep deprivation elevates expectation of gains and attenuates response to losses following risky decisions. Sleep 2007;30(5):603–9.
[110] Venkatraman V, Huettel SA, Chuah LYM, Payne JW, Chee MWL. Sleep deprivation biases the neural mechanisms underlying economic preferences. J Neurosci 2011;31(10):3712–8.
[111] Bechara A, Damasio H, Tranel D, Damasio AR. Deciding advantageously before knowing the advantageous strategy. Science 1997;275(5304):1293–5.
[112] Bechara A, Damasio AR, Damasio H, Anderson SW. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 1994;50(1–3):7–15.
[113] Killgore WDS, Grugle NL, Balkin TJ. Gambling when sleep deprived: don't bet on stimulants. Chronobiol Int 2012;29(1):43–54.
[114] Killgore WDS, Lipizzi EL, Kamimori GH, Balkin TJ. Caffeine effects on risky decision making after 75 hours of sleep deprivation. Aviat Sp Environ Med 2007;78(10):957–62.
[115] Killgore WDS, Balkin TJ, Wesensten NJ. Impaired decision making following 49 hours of sleep deprivation. J Sleep Res 2006;15(1):7–13.
[116] Greer SM, Goldstein AN, Knutson B, Walker MP. A genetic polymorphism of the human dopamine transporter determines the impact of sleep deprivation on brain responses to rewards and punishments. J Cogn Neurosci 2016;28(6):803–10.
[117] Olson EA, Weber M, Rauch SL, Killgore WDS. Daytime sleepiness is associated with reduced integration of temporally distant outcomes on the Iowa gambling task. Behav Sleep Med 2016;14(2):200–11.
[118] Acheson A, Richards JB, de Wit H. Effects of sleep deprivation on impulsive behaviors in men and women. Physiol Behav 2007;91(5):579–87.
[119] Libedinsky C, Massar SAA, Ling A, Chee W, Huettel SA, Chee MWL. Sleep deprivation alters effort discounting but not delay discounting of monetary rewards. Sleep 2013;36(6):899–904.
[120] Kahn-Greene ET, Lipizzi EL, Conrad AK, Kamimori GH, Killgore WDS. Sleep deprivation adversely affects interpersonal responses to frustration. Pers Individ Dif 2006;41(8):1433–43.
[121] Kahn-Greene ET, Killgore DB, Kamimori GH, Balkin TJ, Killgore WDS. The effects of sleep deprivation on symptoms of psychopathology in healthy adults. Sleep Med 2007;8(3):215–21.
[122] Kamphuis J, Meerlo P, Koolhaas JM, Lancel M. Poor sleep as a potential causal factor in aggression and violence. Sleep Med 2012;13(4):327–34.
[123] Anderson C, Dickinson DL. Bargaining and trust: the effects of 36-h total sleep deprivation on socially interactive decisions. J Sleep Res 2010;19:54–63.
[124] Killgore WDS, Killgore DB, Day LM, Li C, Kamimori GH, Balkin TJ. The effects of 53 hours of sleep deprivation on moral judgement. Sleep 2007;30(3):345–52.
[125] Tempesta D, Couyoumdjian A, Moroni F, Marzano C, De Gennaro L, Ferrara M. The impact of one night of sleep deprivation on moral judgments. Soc Neurosci 2012;7(3):292–300.
[126] Olsen OK, Pallesen S, Eid J. The impact of partial sleep deprivation on moral reasoning in military officers. Sleep 2010;33(8):1086–90.
[127] Killgore WDS, Kamimori GH, Balkin TJ. Caffeine improves the efficiency of planning and sequencing abilities during sleep deprivation. J Clin Psychopharmacol 2014;34(5):660–2.
[128] Killgore WDS, Kahn-Greene ET, Grugle NL, Killgore DB, Balkin TJ. Sustaining executive functions during sleep deprivation: a comparison of caffeine, dextroamphetamine, and modafinil. Sleep 2009;32(2):205–16.
[129] National Sleep Foundation. Healthy sleep tips. [Internet]. Available from: https://sleepfoundation.org/sleep-tools-tips/healthy-sleep-tips; 2018.