Preface

Sleep is truly one of the biggest mysteries in behavioral neuroscience. Humans spend a substantial portion of their lives asleep, as do all other mammalian and bird species that have been studied to date, yet the functions of sleep remain elusive and continue to be a topic of debate among sleep researchers. This debate is complicated by the fact that there are two completely different forms of sleep, slow-wave sleep and rapid-eye-movement sleep, each of which may have its own function. Many of the modern hypotheses on the possible functions of sleep presume that it serves some crucial roles in neuronal recovery, maintenance, and plasticity, which ultimately are important for brain function in terms of alertness, information processing, memory formation, and emotional regulation. Indeed, while we are only beginning to understand how sleep supports brain function at the molecular and cellular level, sleep loss has an undeniable negative impact on behavioral performance and well-being. Moreover, accumulating evidence suggests that chronically restricted or disrupted sleep may contribute to age-related cognitive decline and psychiatric disorders such as schizophrenia and depression. This book reviews current knowledge on the importance of sleep for brain function, from molecular mechanisms to behavioral output, with special emphasis on the question of how sleep and sleep loss ultimately affect cognition and mood.

The opening chapters of this book describe sleep at the behavioral and electrophysiological level and define the different forms and stages of sleep. They also explain the principles of sleep homeostasis, which suggests that a need for sleep builds up as a consequence of the brain's activity during wakefulness.

One proposed homeostatic function of sleep is to globally downscale the strength of synapses that have been potentiated as a consequence of neuronal activity during waking. The core claim of this hypothesis is that experience and input during wakefulness are associated with a net increase in synaptic strength. In turn, sleep is thought to provide synaptic renormalization and this reset of synaptic strength would then enable processing of new information next day. However, sleep does not appear to have a single effect on synaptic strength. An unbiased review of the literature indicates that effects of sleep vary depending on, for example, the type of waking experience that precedes sleep and the type of neuronal

synapse under examination. In fact, another popular theory proposes that sleep is crucially involved in certain forms of Hebbian plasticity, which include input-specific strengthening of synapses that presumably underlie the formation of memory and long-term storage of information in the brain. Data in support of these different views on the role of sleep in synaptic plasticity are presented and discussed.

Several chapters in this book together provide an extensive overview of the latest insights into the role of sleep in regulating gene expression, synaptic plasticity, and neurogenesis, and how that in turn is linked to learning and memory processes. State-of-the-art techniques such as optogenetics and pharmacogenetics are being employed in rodent models to unravel the molecular and cellular mechanisms underlying sleep-related memory processes. Brain imaging methods in humans are used to characterize the functional neuroanatomy of sleep stages and to assess regional changes in brain activity during learning and subsequent memory processing during sleep. These imaging methods provide an important window on the brain that helps to bridge the gap between established and well-developed behavioral learning paradigms in humans and molecular measurements in model species such as rats, mice, birds, and flies. Together, these different methods and approaches applied in a variety of different mammalian and non-mammalian species have clearly established that sleep helps to transform newly learned information or skills into robust memories. In humans, even a properly timed nap may have positive effects on the formation of memories. Moreover, beyond helping to store information, sleep may also promote the flexible combination of information and thereby contribute to insightful behavior.

Obviously, the notion that sleep plays an important role in the regulation of neuronal plasticity and synaptic strength implies that insufficient sleep may have serious repercussions for brain function. Given the high incidence of restricted and disrupted sleep in our society this is an extremely pressing issue. Many people experience insufficient sleep on a regular basis due to our modern around-the-clock lifestyle, high work pressure, psychosocial stress, or sleep disorders. While acute sleep disruption can have a major and immediate impact on cognitive function and reduce the capacity to learn and form new memories in otherwise healthy subjects, chronic and progressive changes in sleep architecture and sleep quality may contribute to the cognitive decline that is seen with both normal aging and, to a much greater extent, neurodegenerative diseases.

Disturbed sleep may also explain symptoms of specific psychiatric disorders. One of the chapters discusses the dysfunction of sleep-mediated plasticity in schizophrenia patients and offers suggestions on how the study of sleeping brain activity can shed light on the pathophysiological mechanisms of this disorder. The relationship between sleep complaints and mental illness is particularly strong in the case of depression. Sleep complaints often precede the onset of depression and constitute an independent risk factor for the development of this mood disorder. Instead of being a symptom, insufficient sleep may act as a causal factor that sensitizes individuals, contributes to the development of depression, exacerbates the symptoms, and reduces the efficacy of pharmacological treatment. Because sleep is

considered to play a crucial role in regulating neuronal plasticity and synaptic strength, chronically insufficient sleep may contribute to psychiatric disorders through an impairment of these plasticity processes, leading to altered connectivity and communication within and between brain regions involved in the regulation of mood and cognitive function. Yet, a major unresolved issue in the field of sleep research is the paradox of sleep deprivation therapy discussed in one of the final chapters. While evidence is accumulating that chronically insufficient sleep may be a causal factor that increases the risk for depression, once people are depressed many of them respond positively to a night of sleep deprivation. Although this phenomenon seems contradictory, it clearly underscores the importance of sleep-related processes in the regulation and dysregulation of mood.

The closing chapter provides an extensive overview of the pharmacological treatment of sleep complaints and sleep disorders, particularly in relation to drug effects on neuronal plasticity processes. Various lines of evidence suggest that sleep disorders may negatively affect neuronal plasticity and cognitive function. Pharmacological treatments may alleviate these effects but may also have adverse side effects by themselves. Understanding the complex processes underlying neuroplasticity may lead to targeted pharmacotherapy and help in the design of drugs that can restore and enhance brain function in patients with sleep disorders.

All together, the chapters in this volume provide an extensive overview of the relationship between sleep, neuronal plasticity, and brain function and they illustrate the exciting developments and progress being made in the fields' attempts to unravel the mysteries of sleep. This book will be of interest to students, researchers, and clinicians with a general interest in brain function or a specific interest in sleep and sleep disorders.

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http://www.springer.com/978-3-662-46877-7

Sleep, Neuronal Plasticity and Brain Function
Meerlo, P.; Benca, R.M.; Abel, T. (Eds.)
2015, X, 559 p. 59 illus., 34 illus. in color., Hardcover
ISBN: 978-3-662-46877-7