Neuroimaging of Sleep and Sleep Disorders

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CAMBRIDGE UNIVERSITY PRESS

CAMBRIDGE UNIVERSITY PRESS
Cambridge, New York, Melbourne, Madrid, Cape Town,
Singapore, São Paulo, Delhi, Mexico City

Cambridge University Press
The Edinburgh Building, Cambridge CB2 8RU, UK

Published in the United States of America by Cambridge University Press, New York

www.cambridge.org
Information on this title: www.cambridge.org/9781107018631

First published 2013

Printed and bound in the United Kingdom by the MPG Books Group

A catalog record for this publication is available from the British Library

ISBN 978-1-107-01863-1 Hardback

Contents

Contents

Section 4 Sleep and memory

Section 5 Neuroimaging of sleep disorders

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Foreword

The daily cycle of wake and sleep is a fundamental adaptation of vertebrates to their environment. Wake and sleep are each composed of two components. Wake is made up of active waking with an ongoing stimulus-response interaction, and quiet waking with reduced environmental interaction and activation of a set of specific cortical structures, often designated the default mode network. Sleep, long a biological mystery, became amenable to experimental investigation with the development of EEG. This was followed by a long and productive period in which REM sleep was characterized, demonstrating for the first time that sleep is an active process and that all components of sleep are more complex than had even vaguely been surmised. This left two important questions to be resolved. The first is the function of sleep. It was generally accepted that sleep was important, even essential, but how? The sledgehammer approach to the question was prolonged sleep deprivation over time, resulting in death of experimental animals and, in the human, a similar fate in fatal familial insomnia. In each instance, the events leading to death are similar and attributable to prolonged stress, not an informative result. Although these studies proved a point, the question, particularly for humans with our complex behavior dominated by language and verbal memory with the capacity for time binding, is not approachable by invasive experimental methods that can be used in animals. Equally important, how does the brain generate the complex states of sleep; how does this further inform us about adaptive waking behavior; and how are the brain mechanisms of wake and sleep affected in sleep disorders and other disease states?

Until relatively recently in this long saga, the answers to these questions were not approachable with the methodology available. There is an appropriate nineteenth-century German saying, *teknik ist alles* (technology is everything). Most major problems in neuroscience have been formulated long before answers are reached. In this case, solutions to the problem of understanding brain mechanisms of wake and sleep have become approachable using functional imaging methods that have evolved over the last 20 years. Advanced EEG methodology has provided functional maps, but a downside of this is that EEG analysis is restricted to surface cortex, a serious limitation. Other early techniques methods were Single Photon Emission Computerized Tomography (SPECT) and Positron Emission Tomography (PET). These have the shortcomings of limited spatial and temporal resolution. At the same time, structural and functional magnetic resonance imaging (MRI, fMRI) were developed, with an ongoing refinement of the technology. Another method with great potential, not yet fully realized, is Magnetoencephalogaphy (MEG). The importance of these methods, particularly fMRI with its high spatial and temporal resolution, cannot be overemphasized. In another context, fMRI has become the essential methodology of cognitive neuroscience.

In this book, *Neuroimaging of Sleep and Sleep Disorders*, a detailed review is presented with a third alloted to methodology and data from normal individuals, and two-thirds to data from disease states. Three well-known authorities in the field are editors, and the authors also are well recognized for their work. No other publication is available that covers this topic and the topics covered are extremely broad. It might be argued that the field is so new, and growing so rapidly that this is not the time for such a book, but its very size rebuts that view. My judgment is that *Neuroimaging of Sleep and Sleep Disorders* is an invaluable compendium marking the status of the field as of 2013, and will be in every medical library and on the desk, near at hand, of every worker in the field.

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Preface

Sleep is still largely a mysterious state that is not well understood in terms of its function and purpose. New studies indicate that it is important not only for the brain, but also for the whole body, particularly as it regulates circadian gene activity that influences most body systems. In order to understand the physiology and pathophysiology of sleep, new techniques are being developed that include new imaging methods to tell us not only about the physical structure of brain regions that are activated or deactivated by sleep and alertness, but also to help us understand the neurotransmitter mechanisms involved. This book, *Neuroimaging of Sleep and Sleep Disorders* details the important advances in the imaging of sleep disorders that holds promise to help us understand the underlying physiology and pathophysiology of sleep that will also aid in the diagnosis of sleep disorders.

The chapters presented here represent the cumulative integrated knowledge to date from several key developments in science over the past six decades. First, since the 1950s, fuelled by seminal findings in the explorations of the nature of sleep, basic science research has led to a rich understanding of the neural underpinnings of the global states of consciousness defined largely by the EEG, including waking, NREM, and REM sleep. As a result of this research, sleep is no longer impervious to scientific study, but now is understood to be a rich tapestry and integration of discrete behavioral states, each with well-defined interactions in neural circuitry. Second, at the human level, sleep has been shown to play a fundamental role in human behavior, involving interactions between homeostatic, circadian, and cognitive functions. Third, a clinical field of sleep medicine has evolved that has defined how sleep is disrupted in humans, leading to significant detrimental impacts on function, resulting in human suffering. Much of this pathology and its manifestations involves how the brain functions either normally or abnormally in clinically recognized sleep disorders, such as the insomnias, sleep apnea, narcolepsy, and the parasomnias. Fourth, a field of cognitive neuroscience has fluorished in which the brain is now understood, at its highest level of organization, to have regional brain specificity for particular behaviors and cognitive processes, such as motor behavior, sensory processing, thought, and emotion. Much of this new knowledge has come from brain imaging studies performed during waking. Fifth, there have been enormous technical developments in ways to "image" the human brain, at both the structural and functional levels, such as MR imaging, PET, and fMRI, making possible the testing of hypotheses at a regional brain level in relation to human behavior, health, and pathology. This book represents the first major overview of the wisdom generated from these cumulative scientific developments toward the study of sleep and sleep disorders.

No previous book has been published that focuses solely on neuroimaging of sleep and its disorders. This book accumulates the most recently available information on neuroimaging and is written by top specialists in the field: radiologists, sleep disorders physicians, and sleep researchers, from the USA, Europe, Canada, and Japan. The chapters are arranged in five major sections: an introduction; neuroimaging of sleep and wakefulness; neuroimaging of sleep loss and circadian misalignment; sleep and memory; and neuroimaging of the sleep disorders. The introductory section comprises chapters on the neurophysiology and the role of neuroimaging of sleep, with chapters on the fundamentals and methodology of imaging techniques. The second section specifically presents the neuroimaging of the sleep wake states, including NREM, REM, and wakefulness. Sections 3 and 4 discuss the role of neuroimaging in the understanding of sleep deprivation, and assessment of the functional responses to sleep deprivation, and how sleep is affected by circadian processes, as well as the assessment of memory by neuroimaging techniques. Section 5 presents the available information on neuroimaging of the sleep disorders, including insomnia, hypersomnias, narcolepsy, sleep-related breathing disorders, and parasomnias that includes several case presentations and the neuroimaging of alerting and sedative medications.

This volume is intended primarily for sleep disorder specialists, sleep researchers, and radiologists; however, it is suitable for neurologists, psychiatrists, and any professionals and researchers interested in the interdisciplinary field of sleep medicine. It will be of use to neurology, psychiatry and radiology residents and fellows, clinical psychologists, advanced

graduate medical students, neuropsychologists, house officers, and other mental health and social workers who want to get an understanding the physiology of sleep and pathophysiological and diagnostic features of sleep disorders.

We are greatly indebted to all the authors who have contributed to this book and are appreciative of the help from the staff of the University of Cambridge Press in getting this book in print so quickly, so that the contents are up to date and current. As findings in this area are rapidly advancing, it is anticipated that future editions of this volume, *Neuroimaging of Sleep and Sleep Disorders*, will take these developments into account.

Eric, Pierre, and Michael