Neuronal Substrates of Sleep and Epilepsy

Contrary to the conventional wisdom that sleep is a resting state of the brain, with negligible activity of cortical neurons, the author brings evidence favoring the idea that, during this behavioral state, memory traces acquired during waking are consolidated. Many physiological correlates of waking and sleep states as well as diverse types of epileptic seizures are discussed. The author focuses on the coalescence of different sleep rhythms in interacting corticothalamic networks and on three types of paroxysmal disorders; namely spike-wave seizures as in absence epilepsy, Lennox–Gastaut seizures, and temporal lobe epilepsy. Profusely illustrated with figures from *in vivo, in vitro* and "*in computo*" studies, the majority coming from the author's own laboratory, *Neuronal Substrates of Sleep and Epilepsy* is essential reading for neuroscientists and clinical researchers.

MIRCEA STERIADE has held the position of Professor and Head of the Laboratory of Neurophysiology at Laval University, Quebec since 1968 and is a Fellow of the Royal Society of Canada (Academy of Sciences). His main areas of interest have focused on states of vigilance, epilepsy, the cerebral cortex, the thalamus, and brainstem, and has employed intracellular studies of all of these. He has published over 300 scientific articles. He is co-author of *Thalamic Oscillations and Signaling* (1990), *Brainstem Control of Wakefulness and Sleep* (1990), *The Visual Thalamocortical System and its Modulation by the Brainstem Core*, *Thalamus* (Vol. 1, 1997), and co-editor of *Brain Cholinergic Systems* (1990) and *Thalamus* (Vol. 2, 1997). His most recent book is *The Intact and Sliced Brain* (2001).

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This book is dedicated to my daughters, Donca and Claude, and to Jacqueline.

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Preface

This monograph is a synthesis of the ongoing efforts toward the understanding of neuronal mechanisms underlying sleep stages and different forms of paroxysmal (epileptiform) activities that preferentially occur during the states of drowsiness and slow-wave sleep. I have been interested in the neurophysiological basis of electrographic seizures since the 1960s, and this interest intensified during the early 1970s when I investigated spike-wave seizures during light sleep in behaving monkeys. This work inspired my idea that such seizures originate within the neocortex and set the scene for our recent intracellular work *in vivo*, throughout the 1990s. The journey continues this century, along the same conceptual lines, with new collaborators who have joined my team.

The two major topics of my laboratory are the neocortical and thalamic neuronal bases of sleep and of paroxysmal activities that mimic different forms of epilepsy in humans, more particularly absence seizures and Lennox–Gastaut syndrome. This is why sleep and these two forms of paroxysmal activities found a place of choice in the present monograph. Nonetheless, I have also attempted to relate these topics with a series of other forms of epilepsy. There are some edited volumes in which many authors express their views, sometimes discrepant, on sleep and/or epilepsy, but I decided to write a monograph because this may allow an expression of coherence, even if the views in this book might be, of necessity, biased by my ideas and personal experimental data. Let the reader judge the soundness of data and whether they support my concepts in this field. I have also included related clinical data but, of course, the reader may find more complete clinical phenomenology in handbooks of epilepsies. This monograph is for those basic neuroscientists and clinicians that want to spend some time over the text and figures to decipher the neuronal basis of normal and pathological phenomena.

The reader will find, as in my previous monograph on *The Intact and Sliced Brain* (The MIT Press, 2001), significant dissimilarities between the results from *in vivo* and some *in vitro* experiments, especially when the latter arise from work on isolated thalamic

slices. Although I consider that the work *in vitro* led to important discoveries of the ionic nature of different voltage-gated currents and the identification of receptors implicated in synaptic transmission, and that every laboratory should have electrophysiological setups for both *in vivo* and *in vitro* experiments, I remain allergic to extrapolations from single cells and simple networks recorded in a 0.4-mm tissue to global notions such as "sleep" and "absence epilepsy", when even our animals with intact brain connectivity are quite absent during experimental procedures. This is why I refrain from using the clinical term of epilepsy when describing the neuronal basis of electrographic seizures. I hope, however, that the stereotyped events we are exploring in animal models may be similar to what future investigators will be able to detect by using intracellular recordings from different forms of epileptic diseases in humans.

Acknowledgments

The memory of my mentor Frédéric Bremer continues to be an inspiration for me.

The personal work described in this monograph would not have been possible without the skillful and creative collaboration of my young colleagues. Among the many Ph.D. students and postdoctoral fellows that have worked in my laboratory at Laval University since 1968, I mention here (in order of appearance in my laboratory) the most prominent, with whom work on sleep and/or epilepsy was performed: V. Apostol, P. Wyzinski, G. Yossif, M. Deschênes, N. Ropert, L.L. Glenn, L. Domich, B. Hu, D. Paré, R. Curró Dossi, A. Nuñez, F. Amzica, D. Contreras, I. Timofeev, D. Neckelmann, and F. Grenier. Collaboration with T.J. Sejnowski, A. Destexhe, M. Bazhenov, and W.W. Lytton was instrumental in the computational studies of cortical and thalamic networks implicated in sleep and epilepsy.

Since 1968, my work has been continuously supported by grants from the Medical Research Council of Canada (now Canadian Institutes for Health Research), Natural Science and Engineering Research Council of Canada, Human Frontier Science Program, National Institute of Health (U.S.A.), Savoy Foundation for Epilepsy Research, and the Research Fund of Laval University.

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