Imaging Biomarkers in Epilepsy

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To our dear mentors, Frederick Andermann and Dieter Janz

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Preface

Epilepsy is one of the most common and disabling neurological disorders, affecting 50 million people worldwide. Its prevalence appears to be increasing and is double that of multiple sclerosis, Parkinson's disease, and autism spectrum disorders combined. In nearly 30% of patients with epilepsy, seizures remain insufficiently controlled despite the availability of numerous antiseizure drugs. No treatments exist to prevent the development of epilepsy, despite an increasing understanding of its underlying molecular and cellular pathways. Major barriers in these areas are the complex and multifactorial nature of epilepsy and its heterogeneity. No tests exist for measuring the presence or severity at any stage of the disease, other than counting seizures, and no tools are available for predicting response to therapeutic interventions, be it medical or surgical, other than waiting for the next seizure to occur. Thus, the vision of new treatments relies upon the development of biomarkers that would ultimately allow individualized treatments.

Epilepsy may broadly be defined as a state of recurrent spontaneous seizures that arise when balance between neuronal excitation and inhibition is disrupted. Epileptogenesis, the gradual process by which a brain develops epilepsy after diverse pathogenetic insults, can be examined at different levels of the nervous system: ions and membranes, cells and circuits/synapses, and large-scale neuronal networks. Importantly, there have been two recent paradigm shifts in our conceptualization and understanding of these phenomena, which make this book particularly timely. Indeed, epilepsy is now defined as a disorder characterized by an enduring predisposition to generate epileptic seizures and associated cognitive, psychological, and social consequences. This widened approach is mirrored by the generally accepted view that epileptogenesis includes both the development of an epilepsy condition and its progression.

During the last few decades, we have witnessed unprecedented advances in imaging techniques, particularly MRI, which has revolutionized epileptology by shifting the field from prevailing electroclinical correlations to a multidisciplinary practice. Importantly, neuroimaging provides a broad spectrum of research and clinical tools with the capacity to identify biomarkers, namely objectively measurable characteristics of biological processes that identify the development, presence, severity, progression, and localization of epileptogenic abnormalities. In this regard, epilepsy research, with its established animal models that recapitulate many syndromes seen in human subjects, provides a unique opportunity to assess the validity of preclinical biomarkers in clinical settings and vice versa. The ideal biomarker should be sensitive, specific, and reproducible, as well as non-invasive, easily repeatable, and cost-effective. It is fair to say that imaging markers, particularly MRI-derived indicators of the "epileptic state," meet the majority of these criteria.

We wanted this book to be truly translational and provide both clinicians and researchers with a series of chapters that integrate in one medium state-of-the-art science on imaging biomarkers aimed at capturing the development and progression of various epilepsies, as well as their neurobiological and cognitive consequences. The central concept to this work is that clinically relevant topics, such as mapping epileptogenic lesions, tracing disease consequences, or predicting therapy responses, should be linked with multidisciplinary research that takes advances from basic science directly into the medical arena, with the ultimate goal to tailor the right diagnostic and therapeutic strategy for the right person at the right time. We anticipate that the discovery of novel imaging-derived biomarkers for prediction and monitoring of treatment response and outcome (including comorbidities) will have a fundamental impact not only on the way we treat epilepsy but also on associated conditions, such as stroke and neurodegeneration.

The book is divided into four sections. Part I includes a series of chapters focused on imaging of

early disease stages. Part II discusses lesion detection and network analysis methods. Part III focuses on imaging methods used to predict response to antiepileptic drugs and surgery. Finally, Part IV presents imaging techniques used to evaluate disease consequences. The hope of the editors and contributors, who are worldwide recognized experts in the field, is that this book will provide a unique tool to guide the selection of imaging platforms in everyday clinical practice, to improve understanding of the pathophysiology of epilepsy, and to set the stage for future research in neuroimaging of epilepsy.

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