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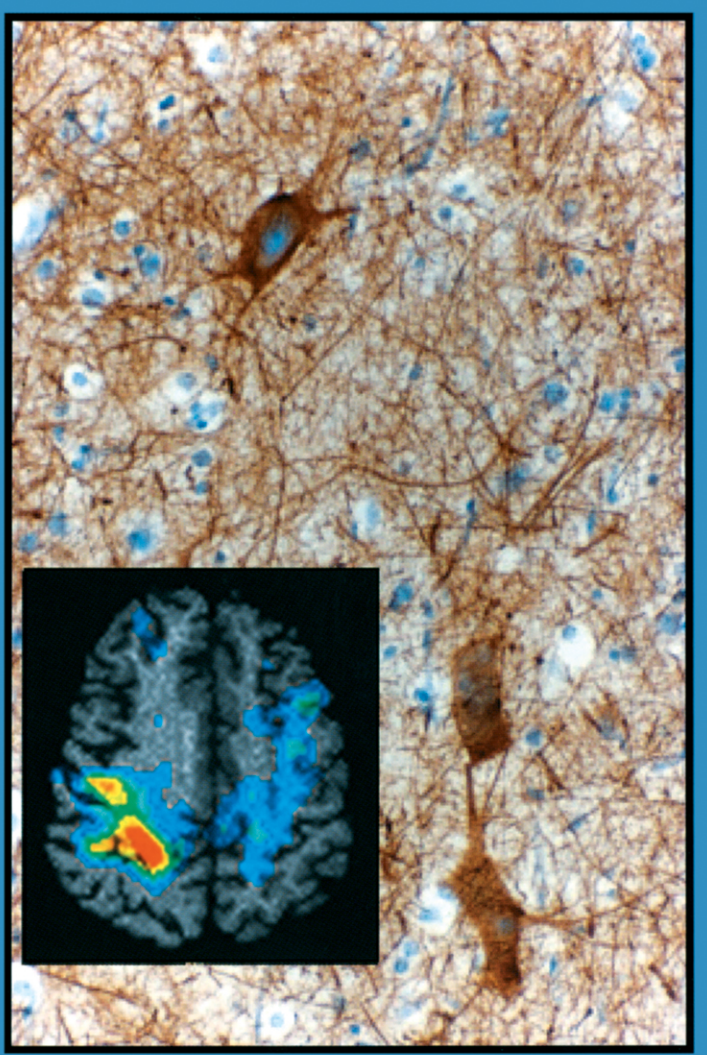
Magnetic Resonance in Epilepsy

Neuroimaging Techniques

Second Edition



Ruben I. Kuzniecky
Graeme D. Jackson

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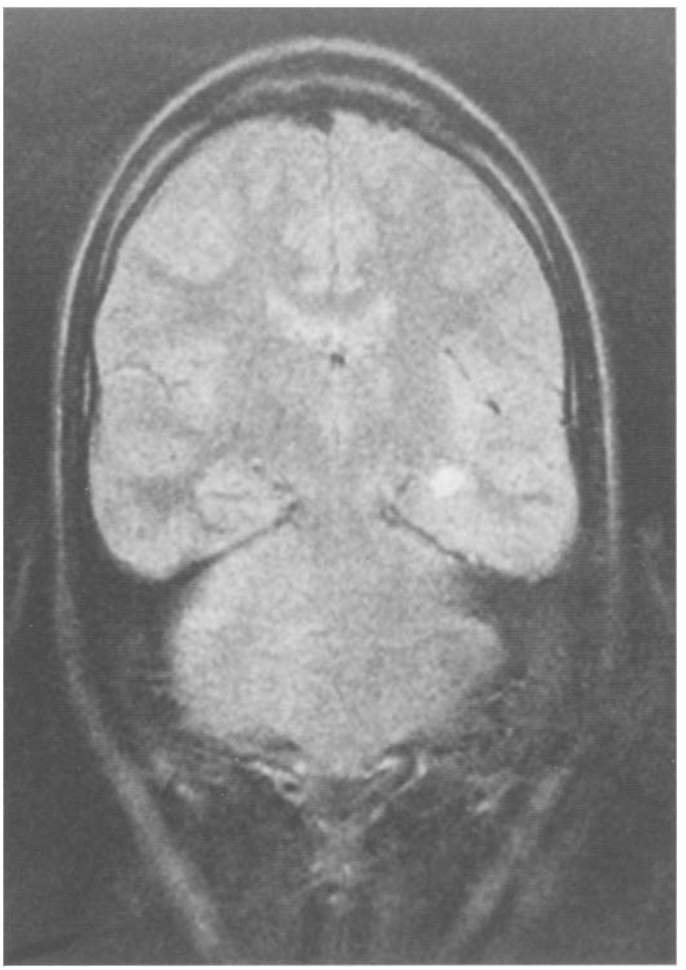

Frontispiece One of the earliest images of hippocampal sclerosis detected by magnetic resonance imaging. Coronal T2-weighted image showing increased signal abnormalities from the hippocampus. Pathologic analysis confirmed the diagnosis. Magnetic resonance image obtained at the Montreal Neurologic Institute on a Philips Gyroscan 0.5 T unit in 1986.

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Dedication

To my father whose eternal spirit lives in us.

Ruben Kuzniecky

To Ruth, Daniel, Hannah and Joseph for providing the meaning.

Graeme Jackson

Magnetic Resonance in Epilepsy

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Foreword

It is at times difficult to predict from the outset how our understanding of neurologic disease and of brain function may be enhanced by the development and application of a new technology. Roentgen's discovery of X-rays, for instance, allowed an initially unforeseen extension of our senses and opened a new era of modern medicine.

Despite the extraordinary insight of early neurologists like Jackson and Gowers, the mechanisms of epilepsy remained the subject of intuitive analysis and, even in the 1920s, there was still some question whether pyknolepsy was epileptic or not. All this changed with the discovery of the electroencephalogram by Hans Berger. It opened a window on the physiology of epilepsy that in turn fueled research and undreamed progress in our understanding of the working of the brain. The EEG complemented clinical localization, and the electroclinical correlation became the gold standard for our understanding and formulation of the different forms of epilepsy.

The advent of computed tomography revolutionized neurologic diagnosis and lightened the burden of neurologic dysfunction by removing the torture of pneumoencephalography. Then came magnetic resonance imaging! Previously, few neurologists were aware of it, and then only as an interesting exercise in physics. The early reports about its usefulness in epilepsy were disappointing. Excitement, however, was soon kindled when epileptologists, such as Sam Berkovic in our group and others as well, first realized that one could now actually see the amygdala and the hippocampus during life.

Ruben Kuzniecky was part of this early wave of enthusiasm and chose magnetic resonance imaging pathologic correlations in temporal lobe epilepsy as the subject of his debut in clinical research. On the other side of the globe, Graeme Jackson, working with Bladin and Berkovic, became similarly enthralled by the spell of modern imaging of epileptic disorders. Information mushroomed and our understanding of the mechanisms of epilepsy was greatly enhanced.

Since the first edition of this book there have been new technical developments such as diffusion and perfusion MRI. These, I hope, will be subjected to further clinical validation in the field of epilepsy and permit new approaches in patients with status epilepticus and should clarify also the spread of epileptic discharge. Spike-dependent FMRI permits the marriage of electrophysiology and imaging. Quite surprising results are emerging, which should lead to new insights on the mechanisms not only of focal, but also of generalized epilepsy.

The investigation of patients with epilepsy is in a continuous process of evolution. In particular, one can say without exaggeration that magnetic resonance imaging and now magnetic resonance spectroscopy have and continue to revolutionize our concepts of epilepsy. Recently, the indications and methods of presurgical evaluation have been completely altered by the utilization of magnetic resonance techniques, with reduction in morbidity, improved accessibility, and reduced costs.

Medical administrators and economists are still not always aware of the need for congruent information from the different imaging and other sources in the localization of the epileptic process. This should include, in addition to high-quality MRI, magnetoencephalography and positron emission tomography, highlighting the need for congruence of these different techniques in order to obtain the best possible localization. Important challenges remain: for instance, the demonstration of imaging changes in mild cortical dysplasia, a test of the ingenuity of the physicists working in this rapidly expanding field.

It seemed appropriate to bring together in one volume current concepts of epilepsy, the insights derived from the new technology, emerging approaches to investigation of patients, and the prospect of future technological advances and their clinical application. This timely volume will focus attention of imagers, physicists, and neuroradiologists on the problems of epilepsy and provide epileptologists, neurologists, and neurosurgeons with the information required to optimally use this technology for the benefit of epileptic patients.

Fred Andermann, M.D.
Montreal, Canada

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Preface to the Second Edition

When we wrote the first edition of this book it was a time when the role of magnetic resonance in epilepsy was still being defined. One major issue in the field was what role MR imaging had in the diagnosis of hippocampal sclerosis (the most common cause of intractable epilepsy). Amazingly, it was widely felt that MR imaging without crude volumetric analysis was unable to routinely detect hippocampal sclerosis. Functional MRI was only just being described. The first edition attempted to pull together the knowledge required to effectively use MR in answering clinical and research questions in epilepsy. In effect, we were just entering the imaging era of epilepsy. This field continues to grow and this has motivated us to undertake this second edition so that those beginning in the field and those who would like to review the wide range of techniques that can help with their clinical and research question can access a source for this. We have enlisted the help of more co-authors who can give deep insights into the relevant parts of these growing fields of MR as they are relevant to epilepsy.

Now it is abundantly clear what the development of high-resolution brain imaging techniques, particularly MR imaging, has meant to the study and treatment of epilepsy. The multiplanar capability and high-resolution MR imaging of brain structures remains unmatched by any other current imaging technique. Similarly, the sensitivity of MR for the detection of small brain lesions is unsurpassed. MR offers high-resolution anatomic imaging and also has the ability to provide dynamic information about brain regions activated during various physiologic tasks. In addition, metabolic imaging using MR spectroscopy has now emerged as a technology with wide applications in the study of brain function and disease states. The prospect for these technologies is great with the advent of routinely available high-field imaging systems. These MR technologies continue to evolve rapidly and will continue to modify the way we study the central nervous system, its functions, and its common disorders. As well as rapid changes in the available technology, the way we interpret and apply the findings obtained using this technology requires ever-increasing sophistication on the part of the interpreting specialist, and the analysis methods teams that are increasingly important in dealing with this wealth of data. It is important to understand that a 'routine study' may no longer be adequate for many problems, and that optimizing the MR investigation is necessary. Increasingly, patients will have many MR sessions, starting with a screening examination, returning for a focused study based on clear ideas of probable disease areas and epileptological hypotheses, and finally returning for advanced investigations that cannot be performed in all cases. This requires very close communication between the physician, the physicist, and the imaging specialist and the analysis team.

The aim of this second edition of *Magnetic Resonance in Epilepsy* is to update readers about this rapidly changing field and its application to human epilepsy. We have retained in part the organization of the first edition with the first three chapters devoted to an introduction to principles that we feel are needed to more fully understand the context of neuroimaging findings. The first chapter is an introduction to epilepsy, written largely for those not familiar with the field. Chapter 2 similarly deals with the principles of MR in a way that is intended to provide an overview of major issues that allow the non-physicist an understanding of how MR works. We hope this will help in understanding the specific findings of later chapters. We felt that Chapter 3 by Henry Duvernoy was a masterpiece in the first edition. There it dealt primarily with the anatomy of the hippocampus and temporal lobe. As the focus of MR has increasing expanded to deal with issues of abnormalities beyond the temporal lobe, so this chapter has been expanded to include anatomic and MRI details of the entire brain. We strongly believe that the detection of what is abnormal is based on a detailed and deep understanding of normal brain anatomy as demonstrated by classical sectional anatomy (almost equivalent to high-resolution MRI).

Chapters 4–7 discuss epilepsy first from the viewpoint of the site of seizure origin (Chapters 4 – temporal – and 5 – extratemporal). This reflects our clinical interest relevant to the investigation of patients with epilepsy. Chapters 6 and 7 approach the MR findings from an etiologic viewpoint. The common acquired causes for epilepsies (Chapter 6) are followed by a discussion of malformations of cortical development (Chapter 7). Chapter 8 is devoted to advances in structural analysis of MRI, which increasingly allows the detection of subtle cortical abnormalities that are often the basis of epilepsy .

Chaper 9 provides a discussion of language and memory from the viewpoint of the epilepsy neuropsychologist. While we could have placed this in the initial part of the book as essential principles, the advent of fMRI of language and memory (Chapter 10) needs to be understood along with this perspective.

The linkage of the spatial resolution and sensitivity of fMRI with the temporal resolution of electroencephalography (Chapter 11) promises to be revolutionary for our understanding of epilepsy process in the intact whole brain. This promises to have clinical applicability in many situations as well.

Techniques such as perfusion and diffusion imaging, DWI (Chapter 12) and MRS (Chapter 13), are important research tools in epilepsy that are rapidly developing and being applied to problems in clinical practice.

Chapters 14–16 discuss the role of other imaging techniques in epilepsy such as PET, SPECT, and magnetoencephalography. It is with wonder that we see how these new techniques have advanced the field.

We do not discuss computed tomography imaging in this book. CT technology continues to develop and, although we do not recommend CT studies for the investigation of epilepsy, it will be interesting to see how this technology develops in the next decade.

We hope that the reader will find in this book a valuable source of information on MR and the role of neuroimaging in epilepsy. The success of this book will only be measured by how helpful it is to those who use it for research, education, and clinical care. As we wrote in 1995 in the preamble to our first edition, 'MR technology is rapidly changing but we trust that the guiding principles of MR as described in this book may apply to technology and applications of this technology yet to come'. In retrospect, we think we were correct. We are confidently courageous to repeat the same message again. Ultimately, our hope is that the knowledge obtained from this book will be usefully applied to the investigation and treatment of those most afflicted: patients with epilepsy.

Welcome to the neuroimaging era of epilepsy!

Ruben I. Kuzniecky, New York, USA
Graeme D. Jackson, Melbourne, Australia
July 2004

Acknowledgments

We are indebted to the many teachers who inspired and encouraged us to undertake our paths in clinical research that led to the original project and the second edition of this book. We specially thank the individuals who have contributed their efforts to chapters in this second edition. We recognize them as authors and great authorities in their field.

We thank Richard Morawetz and James Hugg who provided assistance, advice and material for this book and the late Dr. John Whitaker, Chair of Neurology at UAB, who supported our initial MRI efforts.

We thank the directors of the Brain Research Institute; Chris Blake, Tom Buchan, Margaret Jackson, Anne Ward and Mark Jones, who have done much to encourage advanced MR research in Australia. Jennifer Williams supported the fledgling institute. John Balla and Peter Bladin were great early career teachers and mentors. Sam Berkovic, John Duncan and David Gadian have always given support and encouragement in research. Jewell Gardner and Lucy Holloway helped with many details of this second edition.

We also thank the MRI technical, clinical and research staff at UAB, the Brain Research Institute, and Austin Health for their many contributions to our work and aspects of this book.

Many thanks to Faye Clark and Perry Smith for graciously providing us with a most wonderful venue to retreat at Lake Martin, Alabama, to finish this book. Special thanks to Dr. Noelle Gracy from Academic Press who undertook the initiation of this project and completed it with us, Anne Russum who patiently finished the project and Claire Jennings who graciously organized and worked on many aspects of this book.

To our partners, Yvonne and Ruth, who supported without protest the many hours we spent away from home and our children. We love you dearly.

Finally, our thanks and thoughts go out to our patients and their families. We believe that what we have learned over the past decade has had an important impact on the life of many patients. Hopefully, their issues will further serve as inspiration to all of us to advance our understanding to the benefit of those affected by epilepsy.

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CHAPTER 1

Introduction to Epilepsy

Graeme D. Jackson, Ruben I. Kuzniecky and Samuel F. Berkovic

"Today, epilepsy has more secrets to confide to the neurologist or neurosurgeon who can understand the 'tongue' she speaks."
Wilder Penfield, 1974 (age 83).

The origin of the modern view of epilepsy is generally considered to have been the studies and work of John Hughlings Jackson (Fig. 1.1). He was appointed assistant physician to the National Hospital for the Relief and Cure of the Paralysed and Epileptic (now the National Hospital for Neurology and Neurosurgery), Queen Square, London in 1862 at the age of 27. Jackson's wife developed focal motor seizures following a cerebral thrombosis, and it is this form of epilepsy, with its typical march of symptoms, that became known as jacksonian epilepsy. This work was in the context of a developing view of neurology that was beginning to relate cortical functions to specific locations within the brain (1). In 1873 Jackson presented his classic definition of epileptic seizures, which was 'occasional sudden excessive, rapid and local discharges of gray matter (2, 3).' This view established partial seizures as being truly epileptic in origin. At that time William Gowers, J. Hughlings Jackson, Victor Horsley, and David Ferrier were developing concepts of cortical localization and of epilepsy, which were to have far reaching consequences. The combination of basic scientific research and clinical findings enabled Jackson's ideas to be confirmed by Ferrier in experiments in primates using techniques of cortical stimulation (4). As a consequence, brain functions were able to be localized and the view developed that localization of the site of origin of seizures was possible based on their clinical symptoms – in particular the symptoms at the start of the clinical seizure.

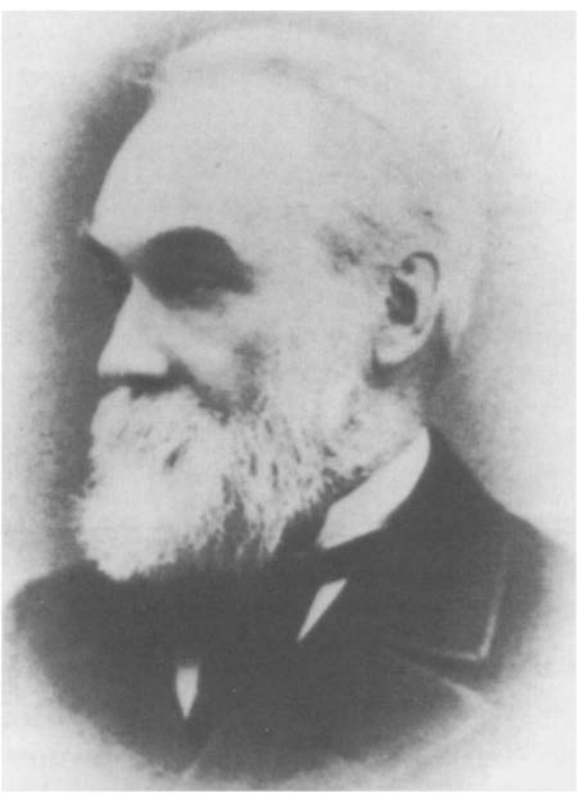

FIG. 1.1. John Hughlings Jackson, London (1835–1911).

ORIGINS OF SEIZURE SURGERY

Using this concept of brain localization and using clinical symptoms as a guide to the site of the seizure focus (jacksonian seizures), a neurosurgeon in Glasgow, William Macewen, correctly localized a frontal meningioma and operated in 1879 (5). Following tumor removal the patient both survived and became seizure-free. At the National Hospital

in London, Victor Horsley operated on three patients with epileptogenic lesions in 1886 (6). The first of these was a patient of Jackson's, and present in the operating theater were Horsley, Jackson, and Ferrier. This represents the origin of epilepsy surgery for the treatment of epilepsy. Although these early cases were successful, establishing the principle of seizure control by surgical removal of the 'seizure focus,' the overall success of surgery for epilepsy was poor and eventually operative treatment fell into disuse until the 'modern era' represented by Penfield and colleagues at the Montreal Neurologic Institute. What now seem like simple measures, such as anesthesia, antisepsis, and antibiotics, made a large impact on the feasibility and safety of neurosurgery for epilepsy, as they did in many other areas of medicine.

Despite major developments in the understanding of the process of epilepsy and the propagation and spread of seizures, the central issues and principles on which this surgery was based have, at their core, remained largely unchanged to the present day. That is, if the seizure focus can be accurately localized, then surgical removal of that focus will alleviate the occurrence of seizures. What has changed to a remarkable extent is the technological environment in which this work can be carried out. Major milestones have been the advent of the electroencephalogram (EEG) and more recently neuroimaging techniques, represented in their most dramatic form by magnetic resonance imaging (MRI). The data and criteria by which the diagnosis of seizure localization is made continues to develop and this book examines the role of MR in this evaluation process: this development has changed the face of epilepsy diagnosis, management and treatment. In addition to its initial revolutionary role in surgical treatment of epilepsy, MRI has altered the understanding of, and clinical approach to, many forms of focal and generalized epilepsy.

THE MODERN ERA

During the 20th century, Wilder Penfield (Fig. 1.2), who founded the Montreal Neurologic Institute in 1934, became the leading figure in the further development of both the surgical treatment of epilepsy and the structural localization of brain functions. In common with Jackson, his extensive writings, coupled with a clear, detailed, and objective skill in observation, provided a wealth of information, which is of relevance to this day. From his observations, Penfield recognized the dramatic vascular changes that occur during seizures (7). Despite the subsequent emphasis, as a consequence of the development of the powerful EEG technology, on the electrical events that occur during seizures, Penfield retained his interest in these vascular changes throughout his life (8). With the advent of ictal imaging technologies, such as SPECT (9) and functional MRI, the legacy of his observations remain relevant to the interpretation of blood flow changes during ictal events. Although he died in 1976 at the age of 85, before the development of medical nuclear magnetic resonance technology, he clearly foresaw that new technology would reveal many new aspects of epilepsy and brain functions.

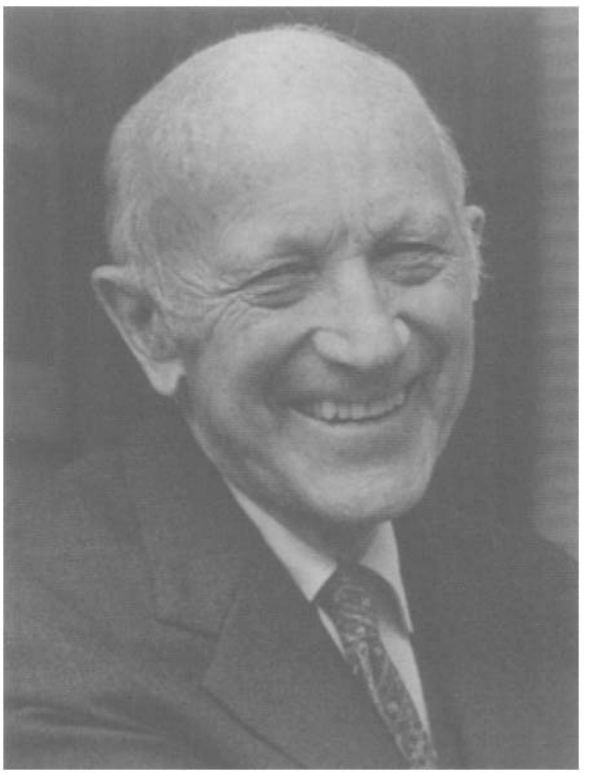

FIG. 1.2. Wilder Penfield, Montreal (1891–1976).

ELECTROENCEPHALOGRAM DEVELOPMENT

In 1929, Berger published the technique of EEG (10), which, in his study, was based on a single-electrode contact. This important technology was subsequently developed by many researchers to provide a means whereby seizures could be localized without characteristic and localizing ictal clinical symptoms. This was a very exciting development in neurology as it enabled the totally noninvasive investigation of brain function with an objective technique that provided information independent of the clinical examination. This eventually shifted the emphasis from epilepsy originating in eloquent areas of cortex such as the motor strip (because of the ability to localize these events) and enabled temporal lobe seizures to be localized on the basis of the electroencephalographic localization of the electrical activity associated with the seizure.

The EEG technology developed to the point that in 1951 Bailey (neurosurgeon) and Gibbs (electroencephalographer) published a series of 25 patients who underwent temporal lobe resection based only on EEG criteria (11) without supporting clinical localization. The results were encouraging and helped establish the EEG as the prime method of seizure localization, to the extent that epileptic syndromes

often became referred to as electro-clinical diagnoses (showing how important this investigation modality had become in the practice of epilepsy). Over the next 30 years the study of epilepsy was dominated by the technical development of, and understanding of the information obtained from, the EEG (12, 13). During this period, surgery, as a treatment of epilepsy, also gained considerable ground.

MAGNETIC RESONANCE IMAGING

Magnetic resonance techniques were first applied to human studies in the late 1970s (12) and the routine clinical availability of MRI began in the mid 1980s. MRI enables a detailed view of the fine structure of the living brain, which had previously only been possible after death (by post-mortem examination). It soon became apparent that MRI could add another powerful dimension to the problem of localizing where seizures originate by demonstrating the location and nature of structural brain abnormalities. Small tumors, many which had been undetected by CT scanning, were commonly found in these patients (13–17).

Less apparent, but especially important, lesions such as hippocampal sclerosis were initially thought to be largely undetectable using MR (14, 16, 18). The development of MR techniques for the detection of hippocampal sclerosis figured prominently in the first edition of this book and remains central to epilepsy practice. Even in the case of tumors, however, a new issue arose. There is an apparent dissociation in some cases between the site of the EEG abnormality and the imaging abnormality. The issue then becomes: which is most important; to resect the structural lesion or to resect the area of EEG abnormality? The answer to this could only have been addressed in the MR era of epilepsy surgery. Most studies suggest that removal of the structural abnormality, when it can be detected, is critical for good post-surgical outcome (19, 20).

Magnetic resonance also opened Pandora's box on malformations of cortical development, which are a major cause of hitherto unexplained epilepsies (21). While classical neuropathology on autopsy specimens had led to the recognition of severe developmental abnormalities, it was only with the advent of MR that more subtle varieties were properly appreciated. Understanding and interest in this area has exploded in the last few years, largely due to the impetus of MRI (Box 1.1).

Improvements in instrumentation, sequence development and interpretative skills have enabled ever more subtle lesions to be detected. MR is now an obligatory part of the investigation of all patients with epilepsy, although the yield may be low for certain clearly defined idiopathic syndromes.

BOX 1.1 Classification Scheme: Malformations of Cortical Development

- I. Malformations Due to Abnormal Neuronal and Glial Proliferation or Apoptosis
  - A. Decreased proliferation/increased apoptosis: microcephalies
    - 1. Microcephaly with normal to thin cortex
    - 2. Microlissencephaly (extreme microcephaly with thick cortex)
    - 3. Microcephaly with polymicrogyria/cortical dysplasia
  - B. Increased proliferation/decreased apoptosis (normal cell types): megalencephalies
  - C. Abnormal proliferation (abnormal cell types)
    - 1. Non-neoplastic
      - a. Cortical hamartomas of tuberous sclerosis
      - b. Cortical dysplasia with balloon cells
      - c. Hemimegalencephaly (HMEG)
    - 2. Neoplastic (associated with disordered cortex)
      - a. Dysembryoplastic neuroepithelial tumor (DNET)
      - b. Ganglioglioma
      - c. Gangliocytoma
- II. Malformations Due to Abnormal Neuronal Migration
  - A. Lissencephaly/subcortical band heterotopia spectrum
  - B. Cobblestone complex
    - 1. Congenital muscular dystrophy syndromes
    - 2. Syndromes with no involvement of muscle
  - C. Heterotopia
    - 1. Subependymal (periventricular)
    - 2. Subcortical (other than band heterotopia)
    - 3. Marginal glioneuronal
- III. Malformations Due to Abnormal Cortical Organization (Including Late Neuronal Migration)
  - A. Polymicrogyria and schizencephaly
    - 1. Bilateral polymicrogyria syndromes
    - 2. Schizencephaly (polymicrogyria with clefts)
    - 3. Polymicrogyria with other brain malformations or abnormalities
    - 4. Polymicrogyria or schizencephaly as part of multiple congenital anomaly/mental retardation syndromes
  - B. Cortical dysplasia without balloon cells
  - C. Microdysgenesis
- IV. Malformations of Cortical Development, Not Otherwise Classified
  - A. Malformations secondary to inborn errors of metabolism
    - 1. Mitochondrial and pyruvate metabolic disorders
    - 2. Peroxisomal disorders
  - B. Other unclassified malformations
    - 1. Sublobar dysplasia
    - 2. Others

Modified from reference 22.

STRUCTURAL VERSUS FUNCTIONAL ABNORMALITY

The distinction between the structural lesion that may underlie the epileptic process, the area that produces symptoms, and the epileptogenic zone has been clearly made (see Engel 1993 (1) and references therein). In addition to remarkable advances in structural imaging, MR spectroscopy (MRS), functional MRI (fMRI) of brain function and very recently, fMRI of epileptic activity have changed our understanding and clinical practice in epileptology. No one could have predicted the remarkable ability that MR

techniques have for investigating noninvasively brain structure, function biochemistry, and metabolism.

In 1967, Penfield, aged 76, published a paper with the title of 'Epilepsy, the great teacher: the progress of one pupil (23).' The sentiment of this paper is no less true today than ever, and MR technology may provide many new insights and lessons if we can learn to use and apply it well.

DEFINITIONS, TERMINOLOGY AND CLASSIFICATION

Epilepsy terminology can sometimes seem very difficult to understand. It is a field that has much confusing and residual outdated terminology. The terminology, and indeed the knowledge this terminology relates to, has changed rapidly over a relatively short time. It is therefore important to have at least a few clear concepts and to understand something about the current definition and significance of terms relating to epilepsy, in order to make any sense of the field.

An additional problem is the residue of many terms and concepts that no longer relate to current classifications and views of epilepsy. For example, the terms petit mal (meaning small seizure) and grand mal (meaning large seizure) date from the early concepts of epilepsy proposed by the French school of epileptology (which established an outstanding epilepsy tradition) and these terms are still often used. Many new meanings have been attached to these old concepts (often used in different ways even when referring to the same patient) and, as these concepts no longer fit our view of seizures, the use of these terms adds confusion rather than clarification. Terms such as 'grand mal' no longer have any part in a modern classification of seizures yet are a constant source of confusion to those who deal with epilepsy. (Generally 'tonic–clonic seizure,' a description of the seizure type, is what is meant by 'grand mal seizure;' see below.)

While this book does not take on fully the task of dealing with general concepts of epilepsy, a few essential definitions and the concepts on which they are based must be established in order to understand the context into which we place MR findings.

Important Concepts of Epilepsy

Epileptic seizures can be defined as the clinical manifestations of abnormal excessive neuronal activity in the gray matter of the cerebral cortex. Although abnormal electrical activity usually manifests itself through predictable clinical features, it may be silent (pure electrographic events) or it may exhibit clinical features (therefore a seizure), which may either relate to the site of this seizure or correspond to regions indirectly activated by a discharge beginning at some distant site. *Epilepsy* is a chronic disorder that has as its major symptom events (epileptic seizures) that are only manifested periodically. If we define epilepsy in this way it must be defined in terms not of fixed underlying damage to the cerebral cortex but of these transient functional events. This may not be the only possible definition of epilepsy; however, it is largely these episodic events that most trouble the patient and that treatment is designed to prevent.

While the first task of the practicing epileptologist is often to determine whether a transient event is an epileptic event or not (for example a pseudoseizure), we will not deal with this issue here. We now consider only those events that are epileptic in nature.

In general, epileptic conditions can be thought of in three broad categories. In the first place seizures can occur in a normal brain, precipitated by specific factors (such as hypoxia or hypoglycemia). This type of seizure may be experienced by anyone, depending on the circumstances. Second, seizures can occur in an apparently structurally normal brain, but with a known tendency to seizures, whether genetic, biochemical, or otherwise. Finally, seizures can occur in a brain that has a definite structural abnormality, either focally or diffusely (24). While this may seem an obvious distinction, it is essential to determine which category any given patient fits into, and it is not always immediately obvious which situation applies. In order to make this distinction the clinical history (the context) and investigations such as EEG (function) and MRI (brain structure) may be essential. To begin the process of analysis (and subsequently to be able to communicate our findings) the following definitions may be usefully applied:

Epilepsy is a general term that cannot be considered a diagnosis. To say that a person has epilepsy is not in any way specific, and should not be considered to be a complete diagnosis. While it may give a general indication of the nature of a problem, it is so nonspecific as to be almost meaningless in many contexts. 'Epilepsy' encompasses a large number of conditions that can manifest as a variety of seizure types.

Epileptic Seizures

Epileptic seizures are transient events consisting of abnormal brain function. Hughlings Jackson (2) proposed in 1870 that they were "occasional excessive and disorderly discharges of nervous tissue." With the advent of the EEG, this definition, in terms of electrical events in the brain, has become widely accepted, and many might consider a seizure to be an electroclinical event. It is clear, however, that an epileptic seizure consists of transient, complex alterations in blood flow, metabolism, and biochemistry, and changes in neurotransmitters as well as electrical events. With powerful new methods of noninvasive investigation of brain structure and function, our concepts of what an epileptic seizure is are starting to change as this information becomes increasingly available. The essential feature of an epileptic seizure is that it is a transient event, and it is the symptom of 'epilepsy' that troubles the patient. Regardless of what the underlying abnormality of the brain is, epileptic seizures are transient episodes that disturb the normal function of the brain.

BOX 1.2 Abridged Version of the International Classification of Seizures

1. Partial (focal, local) seizures
   A. Simple partial seizures
   B. Complex partial seizures
   C. Partial seizures evolving to secondary generalized seizures
2. Generalized seizures (convulsive or nonconvulsive)
   A. Absence seizures
   B. Myoclonic seizures
   C. Clonic seizures
   D. Tonic seizures
   E. Tonic–clonic seizures
   F. Atonic seizures
3. Unclassified epileptic seizures

From reference 26.

The international league against epilepsy (ILAE) classification of epileptic seizures proposed by the Commission on Classification and Terminology (1981) (25) divides seizures into those that are generalized from the beginning, and those that are partial or focal at the beginning. The partial seizures are divided, according to whether or not consciousness is disturbed, into simple partial and complex partial seizures (Box 1.2). This box gives a summary of the full classification.

The current classification system emphasizes features of the clinical seizure that can be used to make some assumptions or preliminary hypotheses about the underlying mechanism of the seizure disorder. Specifically, the presence of partial seizures implies that the seizures begin in a specific, possibly localized, site. The presence of generalized seizures provides no evidence to suggest a focal structural lesion (although it in no way excludes this) and it is more likely that either a widespread abnormality, or no detectable abnormality is present. Although the seizure type may suggest the likelihood of an underlying abnormality it must be considered as only a starting point. The type of seizure is not a diagnosis but a symptom and therefore the concept of an epilepsy syndrome is a useful one.

As noted above, epileptic seizures are transient episodes manifested as abnormal clinical behavior. As well as the clinical context of epilepsy, one can also define epilepsy in terms of functional events that occur at specific times. These events can be studied through EEG or estimating blood flow changes with positron-emission tomography (PET) or single-photon-emission computed tomographic (SPECT) techniques (or, more recently, fMRI). One can also view the process of epilepsy in terms of the underlying abnormality of the cerebral cortex that gives rise to these transient events. Using the simple concept of partial or generalized epilepsy (see below), one can presume that, in the first situation, a small area of dysfunction, either anatomical or biochemical, will be present. Conversely in generalized epilepsy, one may postulate that large brain areas are abnormal or that there are generalized underlying abnormalities that form the basis of these seizures.

While it may not always be possible to precisely define all these events, it can be proposed that a complete description of any epilepsy or epileptic disorder will require definition of the clinical episodes (demonstrated by the clinical semiology, video monitoring to demonstrate the seizure events), transient functional events (partly illustrated by the ictal EEG, ictal SPECT, and functional MRI), and the fixed underlying structural and biochemical abnormality of the brain (as shown in part by MRI, PET, SPECT, MRS, and the neuropsychological deficit).

Epilepsy Syndromes

The first 'modern' classification of epileptic seizures, as presented above (25), has proved to be very useful for the description of a patient's symptoms, but in the MR era the problem often is that is often only the first step in the diagnostic process. When the clinical and electrographic features are associated with a recognizable grouping of features such as age of onset, genetics, and course, they may constitute an epilepsy syndrome (27). Clear examples include juvenile myoclonic epilepsy, a form of idiopathic generalized epilepsy, and benign rolandic epilepsy, classified within the idiopathic partial epilepsies. In these conditions, a genetic defect may determine the clinical and EEG features. In the new approach to classification discussed below only certain defined, specified, and agreed syndromes are included. This is a work in progress but we believe that it is a very sensible development and one that we fully endorse. In the MR context we note that the syndrome of mesial temporal epilepsy (29) has been proposed as a good example of lesional epilepsy, although this is not fully accepted as an agreed syndrome by the ILAE commission.

Conceptually, the epilepsies are the diseases that cause recurrent epileptic seizures. Often these diseases are not known, or cannot be defined in terms of underlying pathophysiology and etiology. Therefore empirically defined clusters of the clinical and investigation features of these patients are collected into categories of classification known as epilepsy syndromes.

Epilepsy syndromes are symptom complexes that include information from the main investigation modalities such as EEG and now MRI. The International Classification of the Epilepsies and Epileptic Syndromes (30, 31) groups the epilepsies according to whether they are localization-related (partial) or generalized, and whether they are idiopathic or symptomatic (Box 1.3). As more detailed information becomes widely available from MRI and molecular genetics, the classification needs to change in recognition of knowledge of underlying basis of the epilepsy. As noted above, the defined list of epilepsy syndromes no longer tries to be inclusive but to list defined entities as these become more fully understood. The ILAE 1989 system needed to be fully