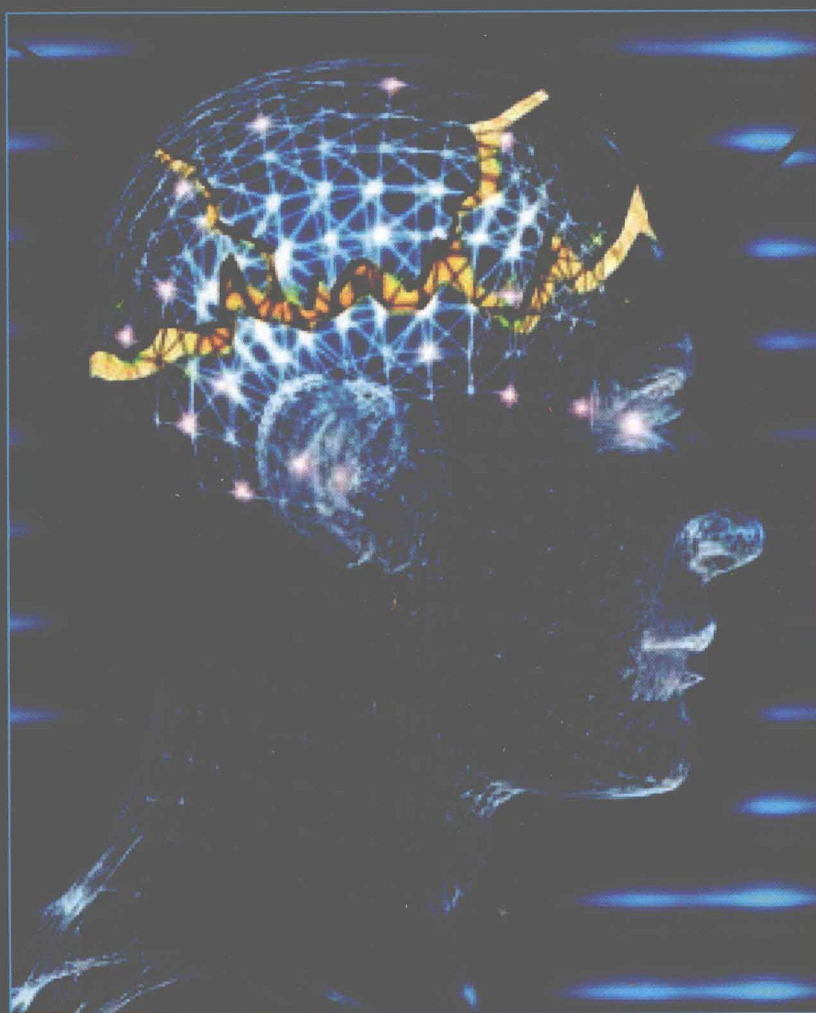


ENCYCLOPEDIA OF

BASIC EPILEPSY RESEARCH

VOLUME 1 A-H



PHILIP A. SCHWARTZKROIN
EDITOR-IN-CHIEF



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INTRODUCTION

Research in today's epilepsy laboratories is exciting, evolving, and full of interesting twists and turns. Epilepsy has been recognized as a common human disorder for thousands of years. But modern research into its underlying bases has been ongoing, I would argue, only since the middle of the 20th century. Nonetheless, the epilepsy research field boasts an intriguing and productive history. As with most disorders, and certainly for disorders of the nervous system, discovery of mechanisms and improvement in treatment have been a function of technical advances – which in turn have moved research efforts toward ever more detailed and revealing analysis. Because of the complexity of the nervous system, and because of the many different forms that epilepsy may take, research in this field lends itself to different conceptual and technical approaches. It attracts the involvement of those with interests at very basic levels of analysis (e.g., the “hard-core” basic scientists who are interested in “explanations” at the level of genes and molecules) as well as those whose interests are more “clinical” in nature (i.e., those interested in “net output” behaviors, both normal and pathological). Any search of current research activities in the epilepsy field confirms the breadth and variety of epilepsy-related laboratory work. In addition, even a superficial reading of the literature shows the value of epilepsy-related research for opening windows to normal brain function – through which one can begin to see the connections between, and shared mechanisms of, normality and pathology. For anyone interested in the brain, in the general area of neuroscience, and in an opportunity to explore an endlessly fascinating set of puzzles, epilepsy research provides many rewards.

My initial introduction to epilepsy research was in the laboratory. It didn't take long for me to be “hooked,” but it did require some hands-on experimental time. Given the need for such exposure, I've struggled with the question of how one can convey that experimentally-generated enthusiasm to someone who's never been in a laboratory, who is in the initial stages of considering a commitment to research or is pondering a focus for his/her laboratory efforts. For a number of years, I've also been frustrated by my inability to provide a satisfying response to an all-too-common question: “Where can I find out about what's going on in epilepsy research?” This type of query comes regularly from students and fellows, from clinical colleagues, from potential colleagues and collaborators outside the epilepsy field who are seeking a reference to current basic research activities. One could, of course, simply direct these individuals to PubMed or to one of the excellent “textbooks” on epilepsy (mostly clinically oriented). But neither of these alternatives is very helpful, especially if one would like to encourage the questioner to become more interested and involved in the laboratory.

My solution to this frustration has been to try to bring many of the current studies in basic epilepsy under one roof – thus, this volume. We've called it an “encyclopedia,” but it certainly isn't an encyclopedia in the classical sense. In particular, it does not pretend to be a comprehensive overview of everything (A-Z) in the epilepsy research field. Rather, the collected articles cover a broad selection of topics, contributed by some of the most active epilepsy research groups in the world. These selections were solicited specifically to answer the question “What's going on in epilepsy research today?” My goal is not to cover all potentially relevant themes, but rather to offer representation in this “encyclopedia” to those who have contributed significantly to the field – to share their goals, insights, and progress.

It might be interesting for the reader to note that my preliminary table of contents did not look like the Table of Contents that now introduces this encyclopedia. The initial version was more like something one might see in a textbook, starting with articles at the “micro” level (cellular/molecular features of cells), progressing through synaptic and circuit considerations, and ending with articles focusing on the “net output.” I believed that this type of organization could present a rationally-ordered overview of the field. However, as I began to go through the articles that were eventually submitted, I was reminded of my starting motivation – to offer the reader a volume that reflects the major areas of today's research effort in the epilepsy research arena. The current Table of Contents does mirror current research emphases. And the encyclopedia offers the interested reader (including non-experts) a collection of short and focused articles that provide a real sense of the modern research field – What's exciting? What are the key technical approaches? What are the important questions?

We sent out invitations to hundreds of the most active investigators in the field. Each author was asked to frame the question or issue that drives his/her research, to provide some background that puts the research into an historical context, and to describe (briefly) some of the methods that are currently used for this line of work. Authors were then encouraged to identify recent results – from their own laboratories or from others – that are exciting and promising, and to discuss where this line of research should go in the future – the goals, challenges, and potential for clinical application. In short, I asked each author to write an article as though he/she were talking to a prospective laboratory recruit (a graduate student, a postdoctoral fellow, or a collaborative colleague) in a way that would convey the interest and excitement that draws us (as epilepsy scientists and clinicians) toward a career in this area of research. As one might predict, each author has approached this charge in a way that reflects his/her own interests, approach to research, and laboratory personality. While we've tried to make the format of these articles relatively uniform, the style and substance of each article are unique to the laboratory of origin.

Of course, as with any project of this sort, there are always hurdles, objections, and problems. One significant problem – a major concern for me in thinking about the magnitude of this effort – is that much of material collected in these articles is likely to be out of date in a few years. To address this issue, we plan to produce this Encyclopedia in an easily accessible and readily update-able electronic form. My hope from the start was that the material presented here will be updated on a regular 2–3 year cycle, with new results entered, and new areas of research described on a regular basis. Another equally thorny problem was what to include – or exclude. As you can see from the title of the encyclopedia, the emphasis has been on “basic research.” But determining exactly what “basic” (and “research”) means is a little tricky, especially in a field like epilepsy in which basic and clinical aspects are so intertwined; indeed, epilepsy research has always been what it is now fashionable to call “translational.” The coverage of the current volume therefore expresses, in large measure, my own scope of interests; perhaps more accurately, the topics are very much a function of my circle of professional colleagues – those who agreed to participate and the topics they chose to write about. The holes in the current volume – and there certainly are some – include areas in which there is little current activity, but also topics that might have been covered by “other” sets of authors.

We anticipate that this encyclopedia will serve as a useful reference tool for a broad range of readers – laboratory scientists and clinicians, students, fellows, and well-established investigators. Students and young investigators should be able to use this volume to discover potential areas for establishing their own research efforts. Scientists and clinicians with already-established research programs can use the Encyclopedia as a tool for guiding their students and trainees, as an easy way of “keeping up,” and even as a source of practical hints that will help them plan their own future studies.

I hope you find this Encyclopedia of Basic Epilepsy Research useful and informative. I've certainly learned a lot from putting it together. For those of you who have contributed to the volume, I thank you for your interest and involvement – and I look forward to your support when I approach you for updates and/or additions. For those of you who have ideas for new articles, whether stemming from your own research or from other laboratories, please contact me with your suggestions. If this Encyclopedia is to fulfill its mission, it needs to be a dynamic, evolving, interactive tool. We are committed to making it work that way.

Philip A. Schwartzkroin
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GUIDE TO USE OF THE ENCYCLOPEDIA

Structure of the Encyclopedia

The material in the Encyclopedia is arranged as a series of articles within a certain topic in alphabetical order. The topics are also arranged in alphabetical order.

There are four features to help you easily find the topic you're interested in: an alphabetical contents list; cross-references at the end of each article to other relevant articles in the Encyclopedia; a full subject index; and a list of volume contributors for each volume.

1. Alphabetical Contents List

The alphabetical contents list, which appears at the front of all volumes, lists the entries in the order that they appear in the Encyclopedia. It includes both the volume number and the page number of each entry.

2. Cross-references

All of the entries in the Encyclopedia have been cross-referenced. The cross-references which appear at the end of an entry serve three different functions:

- i. To draw the readers attention to parallel discussions in other entries
- ii. To indicate material that broadens the discussion
- iii. To direct readers to other articles by the same author(s)

Example

The following list of cross-references appears at the end of the entry Genetic Determinants of Temporal Lobe Epilepsy

See also. **Ion Channels:** Intrinsic Properties of Neocortical Neurons Relevant to Seizure Discharges; The Lesson of Epileptogenic Channelopathies; **Models:** Model Characterization in Relationship to Human Disorders; **Genetics:** Single Gene Mutations Causing Epileptogenic Malformations of the Cerebral Cortex; **Genetics:** Genetic Contributions to Brain Structure and Epileptogenesis; **Interneurons:** Plasticity and Reorganization of GABA Neurons in Epilepsy; **Ion Channels:** Channelopathies in Epilepsy; **Development/Malformations:** Epilepsy-Associated Reelin Dysfunction Induces Granule Cell Dispersion in the Dentate Gyrus; **Temporal Lobe Epilepsy:** Morphological Abnormalities Associated with Genetic Epilepsies

3. Index

The index includes page numbers for quick reference to the information you're looking for. The index entries differentiate between references to a whole entry, a part of an entry, and a table or figure.

4. Contributors

At the start of each volume there is list of the authors who contributed to that volume.

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