

**EXCITATORY AMINO
ACIDS AND EPILEPSY**

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EXCITATORY AMINO ACIDS AND EPILEPSY

Edited by

Robert Schwarcz

Maryland Psychiatric Research Center
University of Maryland School of Medicine
Baltimore, Maryland

and

Yehezkel Ben-Ari

INSERM-U29
Hôpital de Port-Royal
Paris, France

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FOREWORD

Human epilepsy is a major public health problem affecting approximately 2 persons per 1000. It is particularly frequent in children where convulsions may lead to brain damage and subsequent seizure activity in adulthood. Temporal lobe epilepsy (synonyms include limbic epilepsy, psychomotor epilepsy and complex partial epilepsy) is the most devastating form of epilepsy in the adult population since: a) it is often extremely resistant to currently available anticonvulsant drugs (i.e., it is more resistant than tonico-clonic or grand mal seizures) and b) it includes loss of consciousness, thereby limiting performance of many normal functions and leaving the individual susceptible to bodily injury. It is also associated with nerve cell loss, in particular in the hippocampus and other structures of the temporal lobes.

In order to promote an appropriate therapy it is essential to understand the etiology of seizures and its relationship to brain damage. Basic research on epilepsy also provides a very useful vehicle to learn about the way the brain functions under normal conditions. For instance, much of our present understanding of the mechanisms of action of GABA and benzodiazepines, control of neuronal activity, etc. has been derived from such studies.

Until recently, basic and applied research in this field has been focused primarily on the role of GABA-mediated inhibition in the prevention of epileptogenesis and the removal of GABA (i.e., disinhibition) as a necessary condition to induce paroxysmal discharge. However, in the past few years considerable evidence has accumulated, which suggests that an enhancement of the activity of excitatory amino acids (EAA) could play a central role in the pathogenesis of the epilepsies. Following the initial observation of Hayashi in 1954, namely that the topical application of glutamic acid produces paroxysmal discharge in animals and man, it is now clear that several endogenous and exogenous EAA can produce epilepsy and brain damage - notably in limbic structures - and that EAA can be used to provide suitable experimental models of human temporal lobe epilepsy.

This book contains the Proceedings of the first symposium devoted to EAA and seizure disorders. The international meeting, held at the Chateau de Fillerval, France, September 1-5, 1985, was attended by approximately 100 participants who provided both basic science and clinical perspectives. While many contributions centered on the hippocampus and other limbic structures, the meeting was truly multidisciplinary in nature: it included sessions on the neurochemistry, pharmacology and physiology of EAA and seizures, the contributions of ion shifts to paroxysmal discharges elicited by EAA, and the mechanistic relationships between epilepsy and brain damage. In addition, sessions were devoted to the anatomy of the limbic system, the problem of the blood-brain barrier with special reference to EAA and EAA-induced seizures, and on the possible

contributions of trace metals, notably zinc, to the epileptic actions of EAA. For this volume, the session chairmen have prepared a brief commentary, which has been printed as an appendix following the respective scientific papers in order to provide the reader with an insight into the lively discussions which took place in Fillerval.

The meeting at Fillerval could not have been held without the generous contribution of the Monsanto Co., St. Louis, MO. The symposium was also supported by the Centre National de la Recherche Scientifique (CNRS), the Institute National de la Sante et de la Recherche Medicale (INSERM), and by the following pharmaceutical companies: ASTRA, Ciba-Geigy, Ferrosan, E. Merck, Merck, Sharp and Dohme, Nova, Sanofi, Upjohn, Wander, and the Wellcome Foundation.

We are particularly grateful to P. Wolyniec for her excellent editorial assistance and to G. Charton for his outstanding help with the organization of the symposium. We also thank Drs. W.O. Whetsell, Jr. and J.L. Price for providing the 'official' Fillerval photograph enclosed in this volume. Last but not least, we are highly indebted to Niki, Yasmina, Tamara, Damian and Constance for their patience and understanding.

Baltimore and Paris, June 1986

R. Schwarcz
Y. Ben-Ari

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