

Partial Epilepsies – A Brief Overview

Fernando Cendes

Department of Neurology, FCM/UNICAMP – Campinas, SP, Brazil

ABSTRACT

Introduction: The epilepsies represent a heterogeneous group of disorders with diverse etiologic, electrographical and behavioral seizure patterns. **Objectives:** To review recent concepts about epileptogenesis and seizure-induced damage in partial epilepsies. **Methods:** Critical review and discussion of some of the relevant papers in this topic. **Results:** Mechanisms that are responsible for, or influence, the development of an epileptic condition, as well as its progression, are quite complex, and data on literature are sometimes apparently contradictory. **Conclusion:** This brief overview serves as an introductory remark to the review papers in this supplement.

Key words: epilepsy, partial seizures, epileptogenesis, brain damage, structural lesions.

RESUMO

Epilepsias parciais – uma breve revisão

Introdução: As epilepsias representam um grupo heterogêneo de doenças com etiologias e padrões de EEG e comportamento ictal bastante variados. **Objetivos:** Rever conceitos recentes sobre epileptogênese e dano neuronal induzido por crises em epilepsias parciais. **Métodos:** Revisão crítica e discussão de alguns trabalhos relevantes para este tópico. **Resultados:** Os mecanismos responsáveis, ou que influenciam, o desenvolvimento de um processo epileptogênico, bem como sua eventual progressão, são bastante complexos, e os dados na literatura são às vezes aparentemente contraditórios. **Conclusão:** Esta breve revisão serve como introdução para os artigos de revisão deste suplemento.

Palavras-chave: epilepsia, crises parciais; epileptogênese; dano cerebral, lesões estruturais.

The epilepsies represent a heterogeneous group of disorders with diverse etiologic, electrographical and behavioural seizure patterns. The subtype termed partial epilepsy⁽¹⁾ is one of the most devastating forms of human epilepsy. Complex partial seizures (CPS) constitute the single most common seizure type, accounting for approximately 40% of all cases in adults⁽²⁾. CPS are often quite resistant to available anticonvulsant drugs; only 40% of adults with CPS experience complete seizure control despite optimal clinical treatment^(3,4).

Mechanisms that are responsible for, or influence, the development of an epileptic condition differ from

those that actually precipitate acute or chronic epileptic seizures^(5,6). It is well known from clinical studies and experimental animal models that there is a latent period between induction of a localized cerebral insult and the appearance of a chronic seizure disorder^(5,7-13). Penfield and Jasper⁽¹⁰⁾ referred to this period as “ripening of the scar”. Presumably, the acute structural change produced in a region of cortical tissue is not in itself adequate to cause chronic seizures.

Animal models of partial epilepsy (in particular, of limbic epilepsy) reveal a characteristic course in the development of chronic epileptogenic lesions^(5-8,12). First,

localized interictal EEG spikes occur in cortical areas immediately adjacent to the experimental intervention; and latter, in some but not all cases, spontaneous seizures are seen. The process does not necessarily stop at that point; epileptic seizures may become progressively more elaborate, with larger areas of brain involvement. Mechanisms related to neuronal plasticity in temporal lobe epilepsy (TLE) are discussed by Guedes et al. in this issue (p. 10-17).

Limbic pathways in rats and a variety of other species are particularly vulnerable to activation with high-frequency trains of stimulation, or excitotoxins, that evoke brief electrographic and behavioral seizures with many features of complex partial seizures. Repeated activation results in progressive seizure activity that eventually evolves into spontaneous seizures and a permanent epileptic state, referred to as *kindling*^(6,7,14,15). The period of time between the initial insult and the development of spontaneous seizures depends on many factors, including the choice of epileptogenic intervention, the brain region manipulated, the degree of phylogenetic and ontogenetic development of the experimental animal, and hereditary predisposition of the animal for specific types of epilepsy^(6,7). The *kindling* process involves a variety of brain changes, and it is still unclear which are salient - or even how to determine which are critical. The data can be quite confusing. Indeed, results from different models are apparently contradictory^(6,14,16).

Secondary epileptogenesis is readily demonstrated in animals by *kindling*^(5,7,15). However, arguments for the clinical relevance of secondary epileptogenesis in man must account for discrepancies between the *kindling* animal model and human partial epilepsy^(5-7,15,17,18).

Information on the natural history of the epilepsies is confounded by almost inevitable therapeutic intervention that alters the clinical course. However, in some situations the timing of this therapeutic intervention itself provides important information. A major study on prognosis in epilepsy listed the following among the risk factors for an adverse outcome: a young age at onset, more seizures prior to the first visit to a physician, and a longer duration of illness⁽¹⁹⁾. Most subsequent studies have confirmed these findings⁽²⁰⁾. It can be argued, however, that the poor prognosis for patients whose seizures take longer to control, or who have more frequent seizures, is due to more severe epilepsy initially, rather than the occurrence of seizures *per se*⁽²¹⁾. Prognosis in these studies also depended on other features such as neurological deficits and an organic etiology, which clearly reflect the severity of the epileptogenic process from start. Consequently, these data do not directly address the issue of the possible progressive nature of epilepsy.

ARE RECURRENT SEIZURES HARMFUL TO THE HUMAN BRAIN?

One of the major controversies in epileptology concerns the issue of whether recurrent seizures do cause additional progressive brain damage⁽²²⁾. If isolated seizures do cause harm, it can be argued that all seizures should be prevented, either by medication or by early surgical intervention when adequate anticonvulsant trials do not render seizure freedom. Conversely, if the risk of brain injury is slight, it could be argued that seizures do not always require treatment. Because anticonvulsant drugs are associated with cognitive and behavioural impairment, and also are potentially teratogenic, this is a very important question to be solved.

Modern neuroimaging techniques such as MRSI allow non-invasive *in vivo* monitoring of neuronal integrity and thus may help to clarify the issue of whether the epileptogenic damage is a cause or consequence of repeated seizures.

STRUCTURAL LESIONS & MRI

In recent years, there has been increasing appreciation of the role of structural lesions due to injury to the central nervous system. By far the most common example of this is mesial temporal atrophy associated with neuronal loss and gliosis, which was described as mesial temporal sclerosis (MTS)^(11-13,23,24). This entity is strongly associated with febrile seizures and other insults during early development (usually under age 4), is very likely to produce a mesial temporal ictal onset, and is amenable to treatment by selective mesial temporal resection. Other pathologic substrates associated with intractable temporal lobe seizures include small lesions, such as neuronal migration disorders, vascular malformations, hamartomata and low-grade gliomas. In older series of patients who had resective surgery for epilepsy, these lesions were most often occult and only discovered at operation or in the surgical specimen. Modern neuroimaging techniques however, particularly MRI, have revolutionized this field.

The demonstration by MRI of atrophy and signal changes suggesting MTS has streamlined the presurgical evaluation of patients with TLE⁽²⁵⁻²⁸⁾. Other pathologies causing temporal lobe epilepsy are readily identified on MR images, though again, as the lesions are often small, fine contiguous slices should be used. Volumetric imaging provides information suited to the detection of both hippocampal and neocortical temporal disease, and is rapidly becoming the MR technique of choice for assessment of TLE^(25,29-32).

CLINICAL TREATMENT, PRESURGICAL INVESTIGATION AND SURGICAL TREATMENT

In this issue, the history and principles of anti-epileptic drug (AED) treatment⁽³³⁾, and current issues about presurgical investigation in children are reviewed⁽³⁴⁻³⁶⁾.

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Address correspondence to:
 Fernando Cendes
 Departamento de Neurologia – FCM/UNICAMP
 CEP 13083-970, Campinas, SP, Brasil
 E-mail: fcendes@unicamp.br