Survey of progress

Epileptic seizure disorders

Developments in diagnosis and therapy

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Summary. There has been considerable progress in various segments of epileptology over the past two to three decades. The diagnostic sector has benefited from more advanced and sophisticated EEG-related techniques. The advent of computerized tomography has expedited the clinical evaluation of epileptic patients and new high-technology methods have been introduced. A new type of diagnostic subdivision (based on age-determined epileptic conditions and certain epileptic syndromes) is of great practical significance because of its prognostic implications (distinction of basically benign and severe forms of epileptic seizure disorders). The therapeutic sector has been stimulated by the introduction of new antiepileptic medications and particularly by profound insights into metabolic and pharmacokinetic characteristics of anticonvulsants; this has resulted in the introduction of techniques for serum level determinations. There have been new developments in the field of neurosurgical treatment of epileptic seizure disorders.

Key words: Epileptology – Anticonvulsants

Introduction

Epileptology has emerged over the past 50 years as a neurological subspecialty. In addition to a constant expansion and improvement of the therapeutic armamentarium, several important milestones have highlighted the development of epileptology: (1) the advent of electroencephalography with its neurophysiological and clinical-epileptological implications (also developing into special methods in the service of the neurosurgical treatment of epilepsies); (2) the introduction of reliable determinations of anticonvulsant serum level; and (3) the advent of CT scanning and even more sophisticated methods of cerebral imaging.

In the course of this development, the pharmacokinetics and modes of actions of antiepileptic drugs have been extensively investigated. These few remarks attempt to set the stage for a more focused review of epileptological progress. The reader, however, must understand that lack of space precludes a comprehensive overview.

I. New diagnostic developments

1) Electroencephalography and related methods

a) Conventional electroencephalography. The standard scalp EEG with the use of hyperventilation, intermittent photic stimulation and brief sleep (natural or medicated) remains a centerpiece in the diagnosis of seizure disorders. This test is strictly function-orientated and uniquely demonstrates normal and abnormal electrical cerebral activity. The usefulness and limitations in epileptic patients have been pointed out [32, 41, 83, 96, 128, 172, 174, 223]; a recent review of this topic [60] deserves special attention. It is correct that even ongoing epileptic seizures may escape EEG detection but such cases are rare and limited mainly to the motor cortex.

b) EEG activation methods. The underlying mechanisms of hyperventilation are quite complex; it has been theorized that induced hemodynamic and arterial pCO₂ changes act on subcortical CO₂ chemoreceptors which, in turn, affect nonspecific cortical afferences [219]. The mechanisms involved in intermittent photic stimulation have been reassessed [166, 196] and the role of genetic predisposition has been stressed. Emphasis has been placed on the use of red light and special patterns as special activators [236]. Hemifield stimulation has also been employed [234, 235].

The use of pentylenetetrazole has greatly diminished because of its nonspecific convulsive effects. More encouraging results have been reported on the use of bemegride [28, 66].

The use of sleep deprivation as a special activating condition for generalized as well as partial epileptic discharges has been advocated by a growing number of contributors [47, 154, 212, 218]. A critical review of the diagnostic benefits and pitfalls of the sleep activation methods was presented by Rodin [209].

The sleep EEG is not an activation method since it implies physiological states. Brief sleep recordings in a routine EEG provide additional and epileptologically valuable information [87, 175].

c) Depth electroencephalography (stereo-electroencephalography). Depth EEG is limited to candidates for seizure surgery. The technical aspects of EEG have been vastly improved [10, 11, 61, 141, 257, 259]. The combined use of computer analysis [25, 140, 148, 152, 210], neuropsychological methods [257], and video-split screen observation [257] has provided additional insight into ictal mechanisms.
The search for a primary focus by means of depth EEG often proves unsuccessful [173]. According to Gloor [98], “...depth EEG is no panacea for difficult localization problems.”

d) Electrocorticography. In the wake of earlier major studies [1, 13, 17, 96], there has been relatively sparse activity in the field of intraoperative electrocorticography. The work of Graf et al. [100] demonstrates the frequent occurrence of multiple and dissipated spike foci (instead of expected single epileptogenic zones).

e) Video-EEG monitoring. EEG evaluation in the laboratory is usually limited to a period of 20–90 min. This time window is fully utilized when a brief sleep portion is included in the recording. The limitations in time, however, have prompted the demand for more prolonged EEG recording (usually at the expense of limited numbers of available EEG channels).

An additional problem has been the unavailability of behavioral documentation during an ictal attack. The use of prolonged split-screen video-EEG techniques has gradually enhanced the capacity to correlate behavior and EEG over significant periods of time.

Telemetric recording with radio transmission of the EEG signal over short distances has made it possible to record from a free-moving patient. Miniaturized amplifiers may be worn on the head along with attached transmitters. Of course, most of the time the patient has to remain in full view of the television camera in order to obtain video documentation. This documentation may or may not be videotaped in continuity.

Ample use is also being made of cable-connected video-EEG monitoring. In general, this type of monitoring is carried out for 6–12 h, but it is sometimes prolonged for several days around the clock, especially in depth EEG studies.

Following earlier pioneering work [91, 186, 231] it became apparent that video-EEG monitoring would also provide valuable information on the clinical semiology of seizures [188, 192].

The principal advantage of video-EEG monitoring lies in the investigation of behavioral and EEG correlation during a seizure and especially in the differentiation of epileptic seizures from nonepileptic organic (syncopal) and psychogenic seizures.

f) Combined EEG-cinematography. This technique is expensive and has been sparingly utilized [232]. The masterful atlas of epileptic seizures of Oller-Daurella and Oller-Ferrer-Vidal [181] is based on this type of seizure documentation.

g) Ambulatory EEG monitoring (mobile long-term EEG monitoring). This type of EEG monitoring follows the principles used in ambulatory electrocardiography (Holter monitoring). The ambulatory EEG is based on a miniature cassette tape recorder, which stores the EEG data derived from differential preamplifiers placed on the patient's head with a rather limited number of electrodes. A video playback unit is used by the electroencephalographer in order to read and interpret the recording. In general, 4- and 8-channel systems are in use, sometimes supplemented with a dedicated ECG or event-marker channel.

The patients may pursue their regular activities at home or at work during the 24-h recording. With this technique, the patients' ictal and interictal abnormalities can be evaluated in their natural environment.

The development in this field is reflected by a sizable number of studies [48, 56, 115, 116, 137, 138, 154, 192, 195, 199, 213, 225, 233]. In spite of its limitations (number of electrodes and available montages, problems of time coding), this method has yielded remarkable insights into a patient's real number of ictal episodes and interictal spiking during a 24-h period.

h) Automatic spike detection. The automatic detection of spikes in an EEG tracing with paroxysmal features has been attempted during the past decade [99, 148]. These methods, however, have not been widely utilized.

i) Magnetoencephalography. Biomagnetic fields arising from the brain were recorded by Cohen [33]. The recorded fluctuations are similar, but not identical, to those found in the EEG [110, 111]. A recent review of magnetoencephalography has been presented by Hughes [109]. The application of magnetoencephalography is presently limited by unfavorable signal-to-noise ratios, lack of data on sensitivity, specificity and artifacts, as well as expense. Nevertheless, hope has been raised [12] that extracranial magnetic recordings may detect the sources of deeply situated abnormal discharges, without the use of depth electrodes.

2) Structural neurodiagnostic methods

a) Computer tomography (CT scan, CAT scan). In clinical practice, the neurologist-epileptologist has greatly appreciated the availability of a noninvasive method of demonstrating the brain structures as well as the presence or absence of local or diffuse pathology. Bygone are the days when progressive pathology had to be ruled out by pneumoencephalography and/or arteriography.

According to Gastaut and Gastaut [81], normal CT scan findings were obtained in 89% of patients diagnosed as having primary generalized epilepsy, but in only 37% of patients with partial epilepsies. In 16% of epilepsies above age 16 years, CT scan revealed a brain tumor. In 50% of the total epileptic patient population, the CT scan was abnormal. CT scan abnormalities are present in around 50% of epilepsies with Lennox-Gastaut syndrome [265] and in 54% of patients with partial epilepsies [14]. Atrophic changes in epileptics are mostly diffuse [120]. The presence of mesial temporal lobe herniation in temporal lobe epilepsies has been studied with CT scan enhanced with metrizamide [23].

With the radiation-free method of nuclear magnetic resonance, the quality of cerebral imaging has surpassed the capacities of CT scanning, but its role in diagnosis of lesions underlying epilepsy remains to be determined.

b) Positron emission tomography (PET scanning, positron scanning). The epileptogenic focus and its ictal and interictal metabolic conditions have been the topic of several publications employing PET scanning [59, 63–65, 129]; enhanced local metabolism in focal seizures has been demonstrated. A local hypometabolic state in the interictal period is common. This expensive method relies on the availability of radioactive substances of short half-life and may even necessitate the vicinity of a cyclotron. PET scanning is still in the research phase and has not been used yet on a fee-for-service basis.

Unlike PET, single photon emission computed tomography is based on gamma-emitting radioactive substances. This