Trabajos de Revisión

Epilepsias del Lóbulo Frontal: Estrategias Diagnósticas

Américo C. Sakamoto
Department of Neurology, Ribeirao Preto School of Medicine, University of Sao Paulo, Brazil.
sakamoto@fmrp.usp.br

RESUMEN

Las epilepsias del Lóbulo Frontal (ELF) son el segundo tipo más frecuente de epilepsia focal, sobrepasadas solamente por las epilepsias del lóbulo temporal (ELT). Ellas presentan más variabilidad clínica y más comportamientos ictales complejos que cualquier otra forma de epilepsia focal, y estos hechos explican la mayoría de sus desafíos diagnósticos. Ellas responden pobremente a fármacos antiepilép-ticos y tienen pronósticos menos favorables bajo tratamiento clínico y/o quirúrgico. Aunque en las últimas dos decadas han existido avances metodoló-gicos, especialmente de las técnicas de monitorea-miento electroencefalográfico y de las tecnologías de neuroimagen funcional y estructural, la localiza-ción precisa del área epileptogénica y el diagnóstico etiológico aún no son siempre alcanzados. En términos de estrategias diagnósticas es importante enfocar tres puntos principales: 1. Diagnóstico diferencial de crisis del lóbulo frontal y pseudocrisis; 2. Diagnóstico diferencial entre ELF y otros tipos de epilepsias focales no generadas en el lóbulo frontal, y 3. Diagnóstico preciso y localización de las áreas epileptogénicas del lóbulo frontal de relevancia para propósitos de plan quirúrgico. En este artículo revisaremos y discutiremos la fenomenología ictal clínica de las ELF, el papel y las limitaciones de los registros de EEG de superficie, indicaciones de técnicas invasivas, contribución de las técnicas de imagen funcional y estructural convencionales y avanzadas para los diagnósticos de ELF. Delinea-remos las principales estrategias diagnósticas aplicadas a pacientes con ELF y presentaremos nuestra estrategia quirúrgica y todos los resultados de nuestra serie quirúrgica involucrando dos subgrupos de pacientes operados entre 1995 y 1999:
a) pacientes con área epileptogénica restringida a uno de los lóbulos frontales; b) pacientes con área epileptogénica solamente localizada en forma parcial en el lóbulo frontal.

INTRODUCCION

Frontal Lobe Epilepsies (FLE) represent the second largest group within the focal epilepsies, immediately after the temporal lobe epilepsies (TLE). In contrast to this later group which has more predictable clinical and pathological picture (hippocampal-atrophy in most cases) the FLE group is more heterogeneous and complex in terms of clinical presentation and etiological profile. In this paper we will focus on the diagnosis of FLE which obviously stands on a whole set of clinical and laboratory data. We will briefly discuss the most useful diagnostic methodologies and more importantly, we will discuss the rationale and the diagnostic strategy that should be applied to approach FLE. In this strategy it is important to consider at least three main points that need to be addressed:

1. Differentiation between frontal lobe seizures (frontal lobe epilepsy) and pseudoseizures (psychiatric disease);
2. Differentiation between frontal lobe epilepsy and temporal and other extratemporal lobe epilepsies (ETLE);
3. Precise identification of the frontal lobe epileptogenic zones (limits and boundaries) of relevance for the definition of the surgical planning.

All three points represent real challenges in everyday practice. While most of TLE patients present a clear clinical and laboratory picture which easily allow the establishment of the diagnosis of mesial temporal lobe epilepsy, FLE in the other hand, is a much more heterogeneous and complex clinical entity, and has in addition a different etiological profile. The diagnostic tools currently available however are common to all focal epilepsies and the most relevant ones include Video-EEG monitoring, non-invasive and invasive electrophysiological recordings, cortical stimulation, structural and functional imaging, and

neuropsychological testing. How helpful each of these tools is, and what each individual test can acomplish in clarifying the diagnosis of FLE and particularly those above mentioned points constitute the essence of this diagnostic strategy.

ICTAL PHENOMENOLOGY

FLE ictal phenomenology is quite variable and complex. Bancaud & Talairach (1992) based on stereoelectroencephalography (SEEG) individuali-zed eight cortical epileptogenic areas within the frontal lobes, each generating different subtypes of focal seizures: areas 4 and 6, inferior frontal gyrus, intermediate medial frontal region, intermediate dorsolateral frontal region, anterior cingulate gyrus, frontopolar region, orbitofrontal region, operculo-insular region. The main seizure types generated in these areas were: simple motor seizures, complex motor seizures, complex partial seizures (CPS), “absences” and “generalized convulsions”.

VIDEO-EEG MONITORING

Continuous video-EEG monitoring is the gold standard methodology to record and characterize ictal behaviors from the clinical and electrophysiological standpoint. Invasive and non-invasive studies can be performed allowing detailed analysis of clinical semiology, of interictal and ictal EEG characteristics, and cortical stimulation and identification of brain eloquent areas. Invasive monitoring through intracranial electrodes can be recorded directly from the cortical convexity (subdural electrodes) as well as from structures situated in the depth of the brain (depth electrodes).

STRUCTURAL IMAGING

Magnetic resonance imaging (MRI) is the most powerful technique to detect structural lesions in the brain frequently allowing the identification of most of the pathological substrates associated to FLE: tumors, abnormalities of cortical development, scars, porencephalic cysts, gliosis, etc. High resolution MRI (minimum 1.5 T) and special processing methodolo-gies such as 3-D reconstruction, curvilinear reconstruction, etc. are frequently helpful, specially in cases of discrete abnormalities of cortical development.

FUNCTIONAL IMAGING

Positron emission tomography (PET) and single-photon emission tomography (SPECT) are the main functional imaging techniques applied to epilepsy. More recently new MRI techniques such as functional MRI (FMRI), spectroscopy (MRS), difusion techniques, etc. have been applied but at this point are still not critical for the investigation of FLE. SPECT has been particularly helpful when early ictal injections are obtained, and when multiple ictal SPECTs can be performed.

DIFFERENTIAL DIAGNOSIS BETWEEN FRONTAL LOBE SEIZURES AND PSEUDOEPILEPTIC SEIZURES

The differential diagnosis between pseudoepileptic events and complex motor seizures expressing bizarre automatisms and complex motor behaviors of probably anterior cingulate origin is usually very difficult. Video-EEG monitoring is essential for this differentiation. Careful examination and review of each detail of the ictal semiology through the video is a key point, and the correct interpretation of the clinical signs, of the sequence and clustering of behaviors that compose the ictal phenomenology usually require high level of expertise. Not very long ago this subtype of FLE was wrongly diagnosed as pseudoepileptic events, and its correct identification as true epileptic events represented a major advance in clinical epileptology and a direct evidence of the positive contribution of Video-EEG to the diagnosis of epilepsy.

Interictal and ictal EEG in counterpart is frequently not very helpful. Surface electrodes do not sample adequately the whole volume of the frontal lobes, and many areas such as orbitofrontal cortex, medial frontal areas and cingulate cortex are relatively “invisible” to surface EEG. In addition, the phenomenon of bilateral synchrony and the trend for fast spread of epileptic discharges within the frontal lobes cause the “generalization” of the discharges, even if they have a focal generator. This is particularly true for the ictal recordings that frequently are of difficult localization, or even lateralization. Another serious problem is related to the complex motor automatisms and behaviors that frequently produce artifacts that overwrite the EEG activity and make it

non-interpretable. Despite all these limitations occasionally surface EEG can demonstrate exquisitely localized interictal spikes and consistent ictal patterns that are very helpful in localizing the epileptogenic zone. Structural and functional imaging are frequently not critical in this differential diagnosis.

DIFFERENTIAL DIAGNOSIS BETWEEN FLE AND OTHER FOCAL EPILEPSIES

The main difficult here is related to the differentiation between complex partial seizures of frontal and non-frontal origin. Classically CPS is more frequently associated to TLE. However, it has also been recognized that the temporal lobes are preferentially involved in the spread of ictal discharges originating in extratemporal structures, particularly from the posterior cortex, but also from the orbital and cingulate cortex. In other words, the temporal lobes could act as the symptomatogenic zone of CPS originating elsewhere, producing seizures whose ictal phenomenology is indistinguishable from CPS of temporal lobe origin. Early feelings or symptoms (aura), occurring before impairment or loss of consciousness could give some hints regarding the origin of the ictal discharge, in particular epigastric and psychic auras would favor temporal lobe origin. MRI scans demonstrating structural lesions in the frontal lobes would strongly suggest FLE. Video EEG recordings capturing patients' habitual seizures would also help in differentiating FLE from other focal epilepsies.

LOCALIZATION OF THE EPILEPTOGENIC ZONE WITHIN THE FRONTAL LOBES

Localization of the epileptogenic zone within the frontal lobes is obviously important for the diagnosis of FLE, but unquestionably much more crucial for the definition of the surgical planning of medically intractable epilepsy patients. In this case it is essential to define as precisely as possible the limits and boundaries of the epileptogenic zone to be resected, its relationship to the eloquent cortex in its surroundings, as well as to identify the pathological substrate and the nature of the detected lesion. Optimization of the use of structural and functional imaging, Video-EEG monitoring, and neuropsychological tests is extremely important to achieve these goals.

DIAGNOSTIC STRATEGY

For the distinction between frontal lobe seizures and pseudoepileptic events the capability of careful review of ictal phenomenology through high-quality Video-EEG monitoring is essential. Not only the examination of the clinical signs of each individual event, but also the detailed phenomenological analysis across multiple episodes to additionally check for stereotypy, consistency, clustering of signs and ictal reactivity. Laboratory tests are usually not helpful unless clear ictal andior postictal EEG changes are observed. Although controversial induction tests can sometimes be helpful especially when non-epileptic events are successfully provoked under suggestion in the laboratory.

If the diagnosis of focal epilepsy is already established, then the distinction of FLE from other types of focal epilepsies, and moreover, the precise localization of the cpileptogenic zone require multiple tests that are normally grouped under the label of presurgical evaluation. The rationale of this evaluation is to gather convergent information from these independent tests that could help to localize/lateralize the epileptic focus. In this endeavor electrophysiological and imaging data are equally important in demonstrating structural lesions and epileptogenesis, respectively. In individual cases one test can be more helpful than the other, but generally speaking, both frequently complement each other and contribute to the final diagnosis of FLE. In terms of diagnostic strategy it is more rewarding to invest initially in gathering reliable information from high resolution structural imaging, and to divide patients in two subgroups, with and without structural lesions.

In the subgroup of epilepsies with focal lesions, the other tests become simply confirmatory and are usually sufficient to answer the question whether the detected lesion is or is not associated to the epilepsy being considered. This confirmation could come from interictal and ictal EEG, ictal SPECT, etc. In the subgroup of epilepsies without focal lesions, information from other laboratory tests become even more critical for the final diagnosis, and interictal and ictal EEG, ictal SPECT can demonstrate very focal abnormalities that could be very helpful. Occasionally EEG provides the single localized information for the patient, while in other cases multiple ictal SPECTS provide additional diagnostic evidences of focal epileptogenesis.

Implantation of intracranial electrodes and invasive recordings are indicated when the results of the

noninvasive tests are non-convergent, and when the lesions are close to or overlap to eloquent cortex, and inc knowledge of the limits and boundaries of the epileptogenic zone is critically needed for the surgical strategy.

FRONTAL LOBE EPILEPTOGENICITY

Frontal lobes can be the exclusive site of focal epileptogenesis (FLE) in a number of patients or be involved in a wider epileptogenic process (multilobar, multifocal or generalized epilepsies). Frontal lobe focal epileptogenicity was observed in a series of 31 consecutive cases of medically intractable FLE surgically treated at our center from 1994-2000. There were 19 males and 12 females, ages ranging from 11 months to 52 years old, median of 21 years. The main etiologies were: tumors 10 cases, cortical dysgenesis 10 cases, gliosislatrophic lesions 6 cases, tuberous sclerosis 3 cases, and Rasmussen Encephalitis 1 case.

Frontal lobes constituted part of a wider epileptogenic zone involving one of the cerebral hemispheres in another 27 surgical cases, 17 males and 10 females, ages ranging from ly 4m to 44 years old, mean of 14.7 yrs. The main etiologies were porencephalic cysts 9 cases, Rasmussen Encephalitis 8 cases, gliosislatrophic lesions 8 cases, cortical dysgenesis 2 cases, and inc surgical procedures consisted of functional hemispherectomies, and hemispherotomies. All these patients in both subgroups were evaluated according to the above described methodologies.

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