

## Temporal Lobe Epilepsy with Unilateral Hippocampal Sclerosis and Contralateral Temporal Scalp Seizure Onset: Report of Four Patients with “Burned-out Hippocampus”

Luís Otávio Sales Ferreira Caboclo\*, Eliana Garzon\*, Flávia Saori Miyashira\*, Henrique Carrete Jr.\*, Ricardo da Silva Centeno\*, Elza Márcia Targas Yacubian\*, Americo Ceiki Sakamoto\*\*

Unidade de Pesquisa e Tratamento das Epilepsias – UNIPETE/UNIFESP, São Paulo, SP

### ABSTRACT

**Objectives:** Patients with temporal lobe epilepsy (TLE) and unilateral severe hippocampal sclerosis (HS) may have contralateral temporal scalp ictal onset. This has recently been called “burned-out hippocampus”, which is believed to be a rare entity. In this study we report four patients with unilateral hippocampal sclerosis and contralateral ictal onset registered by scalp electrodes. We discuss the importance of such cases in pre-surgical evaluation of patients with TLE, as well as possible strategies used for evaluation of these particular cases. **Patients and methods:** We reviewed charts from all patients with TLE submitted to pre-surgical evaluation, which included high resolution MRI and prolonged video-electroencephalogram (video-EEG) monitoring with scalp and sphenoidal electrodes, during a three-year period (2002-2004). We looked for patients who only had seizures that were clearly contralateral in location to the atrophic hippocampus. **Results:** Four patients fulfilled the criteria above. Two of these patients had semi-invasive video-EEG monitoring with foramen ovale (FO) electrodes, which revealed seizures originating from the temporal lobe with the atrophic hippocampus, hence confirming false lateralization in the scalp-sphenoidal EEG. These patients were submitted to surgical treatment and had favorable prognosis after surgery. **Conclusions:** Burned-out hippocampus syndrome may not be as rare as it was previously believed. Further studies will be necessary before one can affirm that patients with unilateral HS and scalp ictal EEG showing contralateral ictal onset may be operated without confirmation of the epileptogenic zone by invasive monitoring. In these patients, semi-invasive monitoring with FO electrodes might be an interesting alternative.

**Key words:** temporal lobe epilepsy, hippocampal sclerosis, false lateralization, foramen ovale electrode.

### RESUMO

*Epilepsia do lobo temporal com esclerose hipocámpal unilateral e início ictal contralateral no registro de superfície: relato de quatro pacientes com “burned-out hippocampus”*

**Objetivos:** Pacientes com epilepsia do lobo temporal (ELT) e esclerose hipocámpal (EH) unilateral acentuada podem apresentar início ictal contralateral à EH no registro com eletrodos de superfície. Esta situação foi recentemente chamada de “burned-out hippocampus”, que pode corresponder a uma entidade rara. Nesse estudo, nós relatamos os casos de quatro pacientes com EH unilateral marcada e início ictal contralateral à EH nas crises registradas com eletrodos de escalpo. Nós discutimos a importância desses casos na avaliação pré-cirúrgica de pacientes com ELT, bem como as possíveis estratégias utilizadas na avaliação desses pacientes. **Pacientes e métodos:** Nós revisamos os dados de todos os pacientes com ELT submetidos a avaliação pré-cirúrgica, que incluiu ressonância magnética (RM) de encéfalo de alta definição e monitorização prolongada com vídeo-eletroencefalograma (vídeo-EEG) com eletrodos de superfície, em um período de 3 anos (2002-2004). Procuramos por pacientes que apresentaram apenas crises com início ictal contralateral ao lado da EH. **Resultados:** Quatro pacientes preencheram os critérios acima. Dois desses pacientes foram

\* Universidade Federal de São Paulo – UNIFESP, São Paulo, SP.

\*\* Faculdade de Medicina da Universidade de São Paulo – Ribeirão Preto, SP.

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submetidos a monitorização semi-invasiva com eletrodos de forame oval (FO), que mostraram crises com origem no lobo temporal com o hipocampo atrofico, confirmando assim a falsa lateralização no EEG com os eletrodos de superfície. Esses pacientes foram submetidos a tratamento cirúrgico e apresentaram prognóstico pós-operatório favorável com relação ao controle das crises. **Conclusão:** “*Burned-out hippocampus*” pode não ser tão raro quanto se acreditava antes. Mais estudos serão necessários antes que seja possível afirmar que pacientes com EH unilateral e crises com início ictal contralateral à EH no registro com eletrodos de superfície podem ser operados sem confirmação da zona epileptogênica através de monitorização invasiva. Nesses pacientes, a monitorização semi-invasiva com eletrodos de FO pode ser uma alternativa.

**Unitermos:** epilepsia do lobo temporal, esclerose hipocampal, falsa lateralização, forame oval.

## INTRODUCTION

Temporal lobe epilepsy (TLE) due to hippocampal sclerosis (HS) is considered to be, in most cases, a bilateral disease, with variable degrees of neuronal loss in both hippocampi<sup>(1)</sup>. Patients with TLE frequently present bilateral independent interictal epileptiform discharges<sup>(2)</sup>. Seizures may originate from both temporal lobes; in such cases, surgery is often denied to the patient, although this is still a matter of debate<sup>(3,4)</sup>.

In some patients, magnetic resonance imaging (MRI) may show signs of severely atrophic hippocampus. Mintzer et al.<sup>(5)</sup> have recently reported five patients with unilateral severe hippocampal sclerosis and contralateral temporal scalp ictal onset. The authors referred to such cases as “burned-out hippocampus”. In the cases reported by the authors, invasive monitoring led to the diagnosis of false lateralization in scalp EEG. In any case, however, discordance among imaging and neurophysiologic data may raise concerns about bilateral epileptogenicity, and thus compromise indication of surgical treatment.

Burned-out hippocampus syndrome is believed to be a rare entity. In this article we report four patients with unilateral hippocampal sclerosis and contralateral ictal onset registered by scalp electrodes. We discuss the importance of such cases in pre-surgical evaluation of patients with TLE, as well as possible strategies used for evaluation of these particular cases.

## METHODS

We reviewed charts from all patients with TLE submitted to pre-surgical evaluation and prolonged video-EEG monitoring during a two-year period (April 2002 to March 2004). Patients were referred to the video-EEG unit from the outpatient clinic in our hospital, which is a tertiary care center for patients with epilepsy in São Paulo. The clinic privileges selection of patients with refractory epilepsy, particularly of patients with TLE who are likely suitable for surgical treatment.

All patients had MRI exams, following a standard protocol for study of temporal lobes.

Video-EEG monitoring was performed using a 32-channel digital equipment. Electrodes were placed according

to 10-20 International System, plus additional intermediary temporal electrodes and bilateral sphenoidal electrodes in all patients. During prolonged video-EEG monitoring, antiepileptic drug (AED) withdrawal was conducted according to the decision of treating physicians. All seizures were analyzed by the medical staff. Reports included detailed clinical and electroencephalographical characteristics, such as time, duration and type of each of the seizures

Patients with conflicting data in non invasive evaluation were selected for semi-invasive monitoring.

## RESULTS

All patients with refractory TLE submitted to prolonged video-EEG monitoring were initially identified. Eighty-six patients met these criteria. Of these, 72 had unilateral HS diagnosed by MRI.

Among these patients, four had seizures recorded by scalp-sphenoidal EEG that were clearly contralateral in location to the atrophic hippocampus. Two of them were further submitted to a new video-EEG monitoring with scalp electrodes plus foramen ovale electrodes.

The clinical, neuroradiological and neurophysiological features in each case are described below.

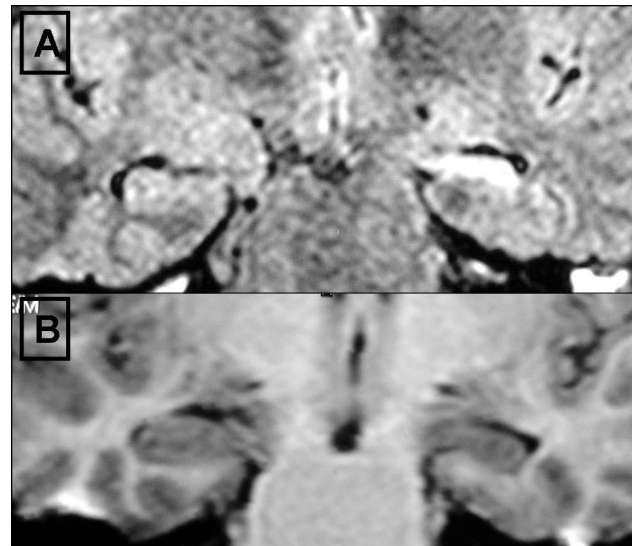
### CASE 1:

A 29-year-old right-handed man had several generalized non-febrile seizures between the ages of 2 and 13 years. Some of the seizures had lateralized features, although his mother was incapable of recalling which side showed most prominent clonic activity. At the age of 13 he started to have seizures with aura characterized by a rising epigastric sensation, followed by loss of consciousness, staring, oral and hand automatisms and, in some of the seizures, ictal spitting.

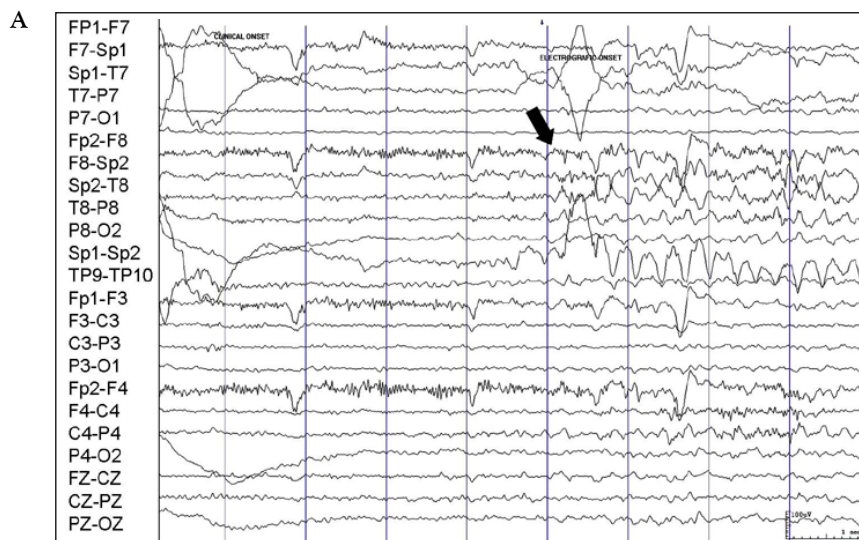
MRI scan revealed increased signal and marked atrophy of the left hippocampus (Figure 1). Interictal EEG analysis showed sharp waves over both temporal lobes. Twelve seizures were registered during prolonged video-EEG monitoring with scalp-sphenoidal electrodes. Dystonic posturing of the left arm could be observed in four seizures. Comprehensible ictal speech was present in three seizures.

Ictal spitting was observed in one seizure. In 11 of the seizures, ictal onset was clearly localized in the right temporal region or in the right hemisphere (Figure 2). In the remaining seizure, ictal onset could not be lateralized. Due to discordant neurophysiologic and imaging data, foramen ovale (FO) electrodes were implanted bilaterally for a new prolonged video-EEG monitoring. With FO electrodes, baseline EEG showed marked slowing over left basal temporal region. Bitemporal sharp waves were registered. The patient had three seizures. In all three ictal onset consisted of desynchronization or brain electric activity in the contacts of the left FO electrode, followed by emergence of a fast rhythm captured by the contacts of the right FO electrode (Figure 3).

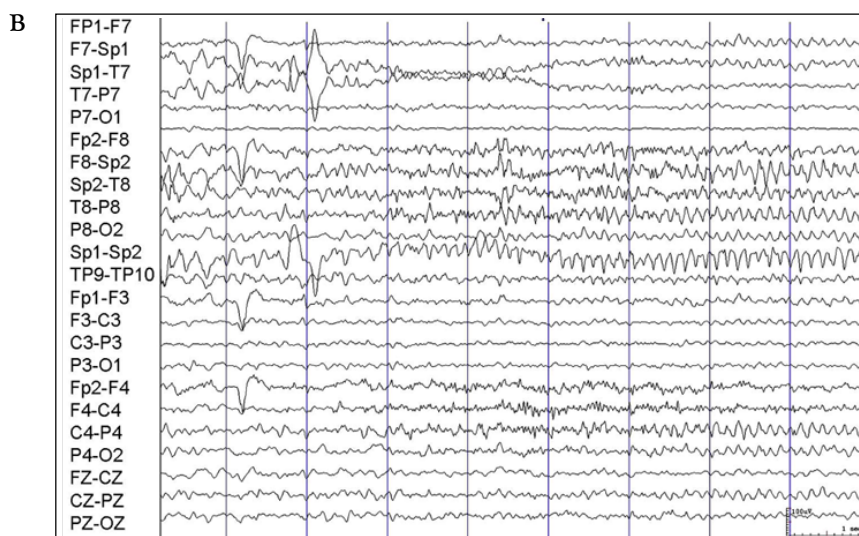
The patient underwent left anterior temporal lobectomy (ATL). Few months after surgery he had one seizure with equivocal loss of consciousness, related to skipping three doses of AED. Since then, he hasn't had any more seizures, with follow-up of 18 months.



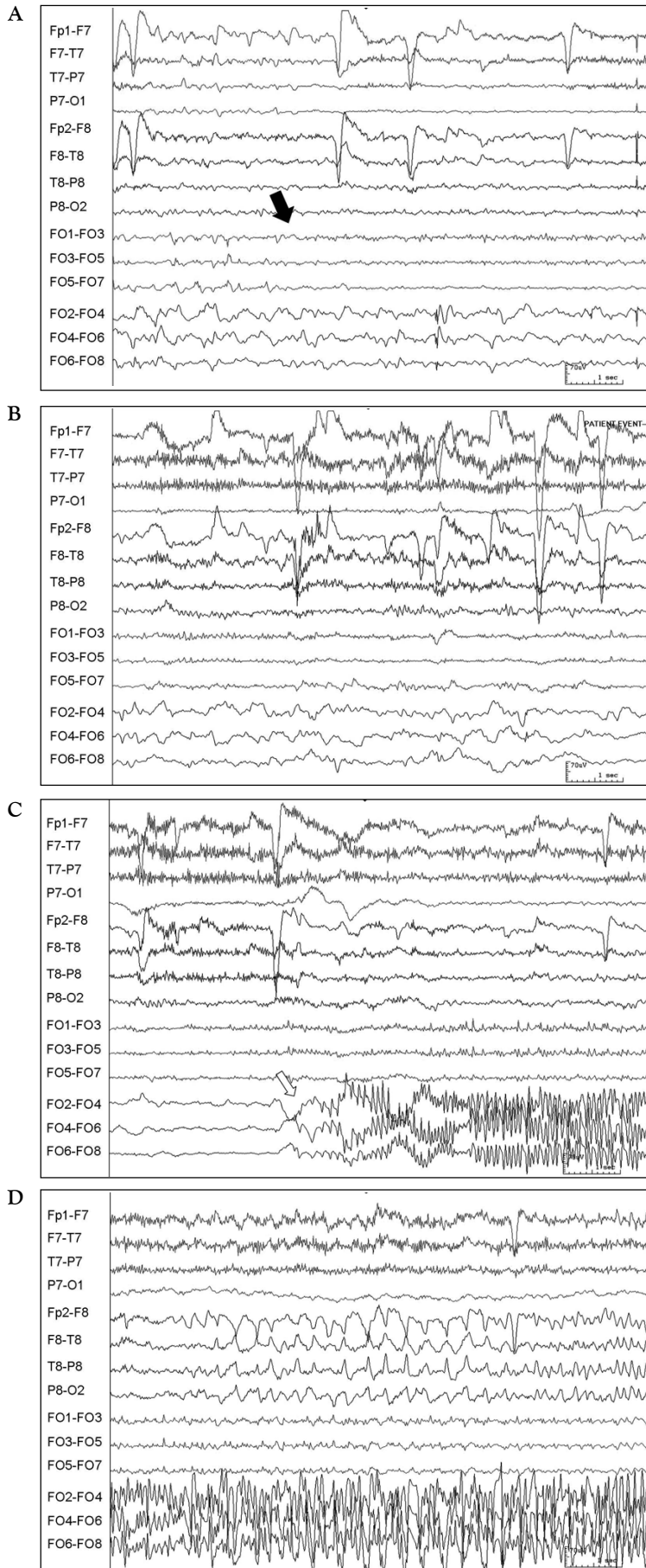
**Figure 1.** Patient 1: **A.** MRI, coronal FLAIR image, showing hyperintensity of the left hippocampus; **B.** MRI, coronal T1-weighted image, showing atrophic left hippocampus.



**Figure 2.** Patient 1:  
**A.** Scalp EEG, bipolar longitudinal montage. The arrow points the electrographic ictal onset over the right temporal region;



**B.** (continuation) Ictal rhythm clearly observed in the right temporal region.



**Figure 3. Patient 1:**

**A.** EEG with foramen ovale electrodes (FOE). The dark arrow points to the ictal onset, characterized by localized EEG attenuation in the left FOE contacts;

**B.** (continuation) Ictal rhythm of high frequency and low amplitude in the left FOE; no ictal activity is observed in the right FOE contacts;

**C.** (continuation) Twenty seconds after ictal onset in left FOE, the light arrow points to onset of ictal rhythm in the right FOE contacts;

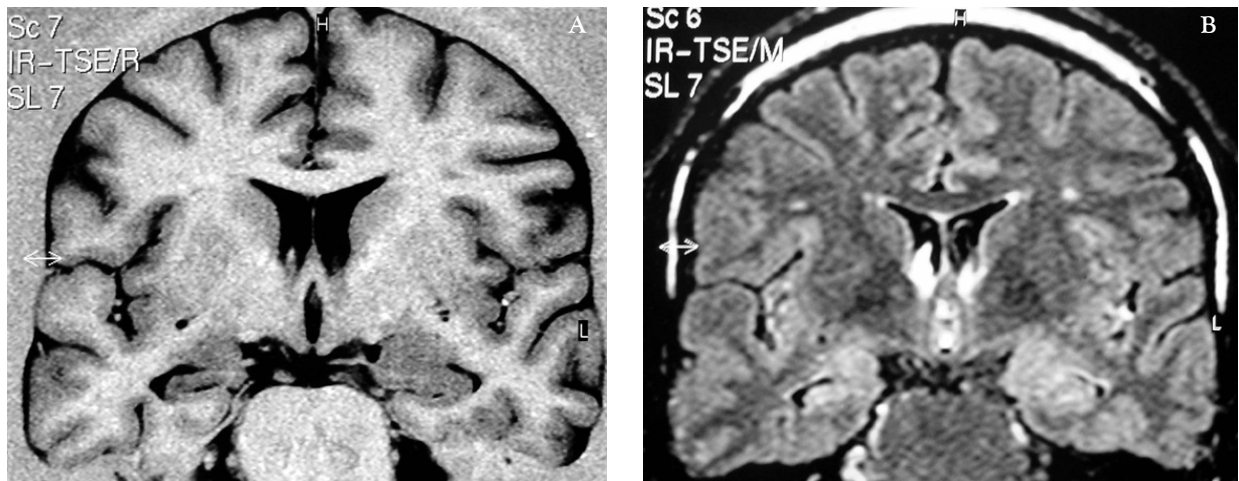
**D.** (continuation) Ictal rhythm in the right FOE contacts and over the right temporal region (scalp electrodes); no ictal activity is observed over the left temporal region (scalp electrodes).

# CASE 2:

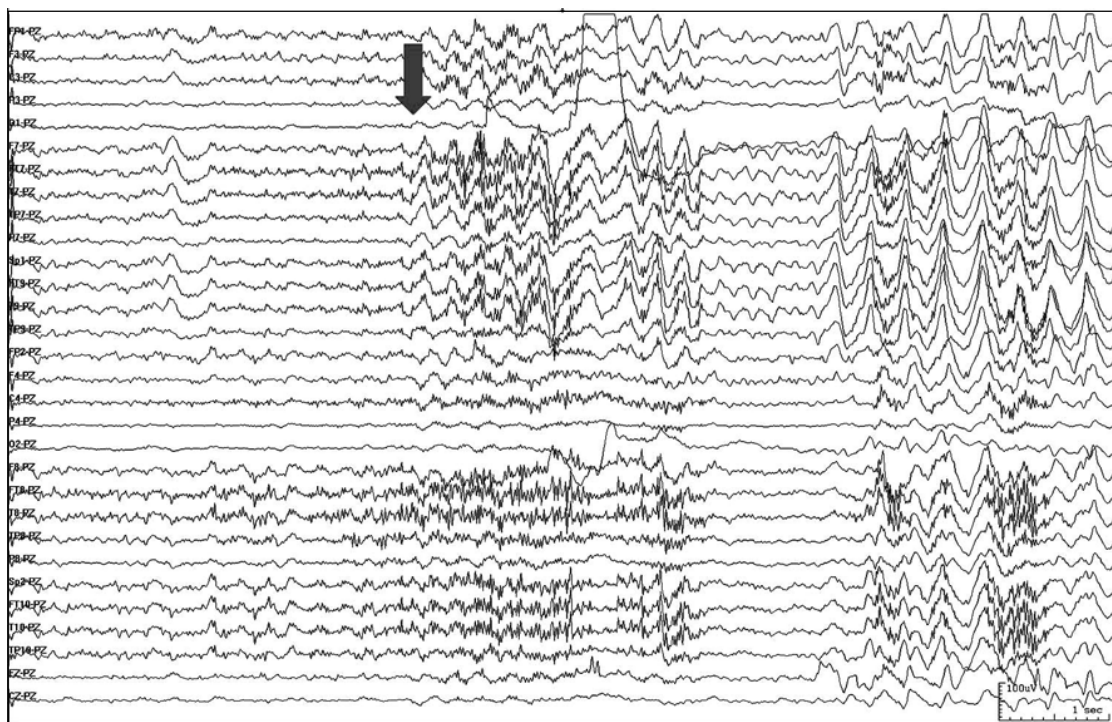
A 40-year-old right-handed man had a prolonged febrile seizure (over 30 minutes duration) at the age of 6 months. At 14 years he had a single generalized tonic-clonic (GTC) seizure and began to have recurrent spontaneous seizures. He described an epigastric aura, followed by staring, skin pallor and automatisms of the right hand; the left hand usually remained closed and immobile during seizures. In some of the seizures, comprehensible ictal speech was reported.

MRI demonstrated reduced volume and increased signal of the right hippocampus (Figure 4). Scalp-sphenoidal interictal EEG revealed bitemporal sharp waves. Seven seizures were registered. In four of these seizures it was possible to observe dystonic posturing of the left arm. In the other seizures no clear clinical lateralizing sign was observed. Ictal speech was not present in any of the seizures. In all seizures ictal onset was observed over the left temporal lobe or diffusely over the left hemisphere (Figure 5).

The patient is waiting for implantation of FO electrodes.



**Figure 4.** Patient 2: A. MRI, coronal IR image, showing markedly atrophic right hippocampus; B. MRI, coronal T2-weighted image, showing hyperintensity of the right hippocampus.



**Figure 5.** Patient 2: Scalp EEG, common reference montage (Pz). The arrow marks electrographic ictal onset over the left temporal region.



**CASE 3:**

A 36-year-old right handed woman had her first GTC seizure at the age of 17. Since then she has been presenting seizures that begin with an aura characterized by a “bad feeling” associated to tachycardia, followed by staring, oroalimentary and bimanual automatisms. The frequency of seizures was three to four per week.

MRI showed markedly atrophic left hippocampus, and normal right hippocampus. Interictal EEG revealed very frequent epileptiform discharges over the left temporal lobe and rare independent sharp waves over the right temporal lobe. She had six seizures recorded with scalp-sphenoidal EEG. In five of these seizures she presented dystonic posturing of the right arm and non forced deviation of the head to the left; the sixth seizure could not be clearly visualized. In five seizures ictal onset was observed in the right temporal lobe. Ictal onset could not be lateralized in the last seizure.

As in case 1, the patient had bilateral FO electrodes implanted. With these electrodes, baseline EEG showed frequent sharp waves in the left FO electrodes. She had three seizures, all of them with ictal onset captured by contacts in the left FO electrode, before the ictal activity could be visualized in the scalp-sphenoidal electrodes.

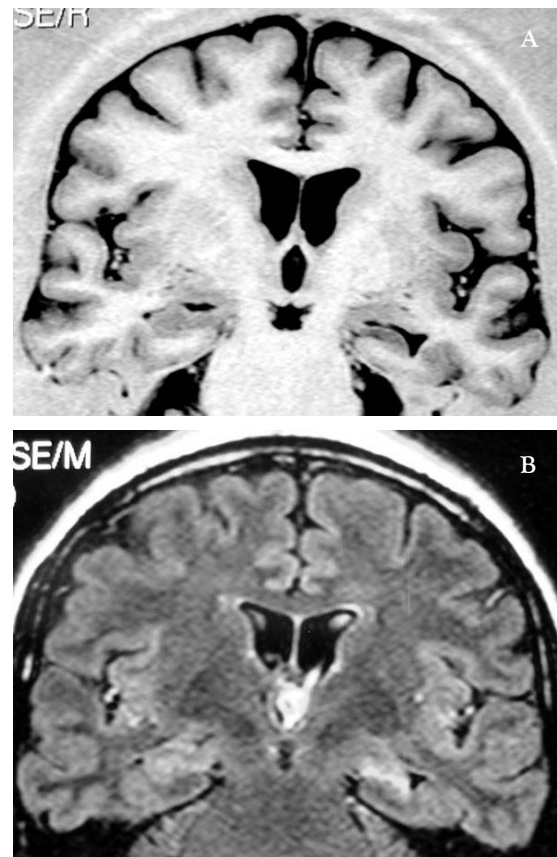
The patient was submitted to left ATL, and after 12 months of follow-up she is completely free of seizures and auras, still taking AED.

**CASE 4:**

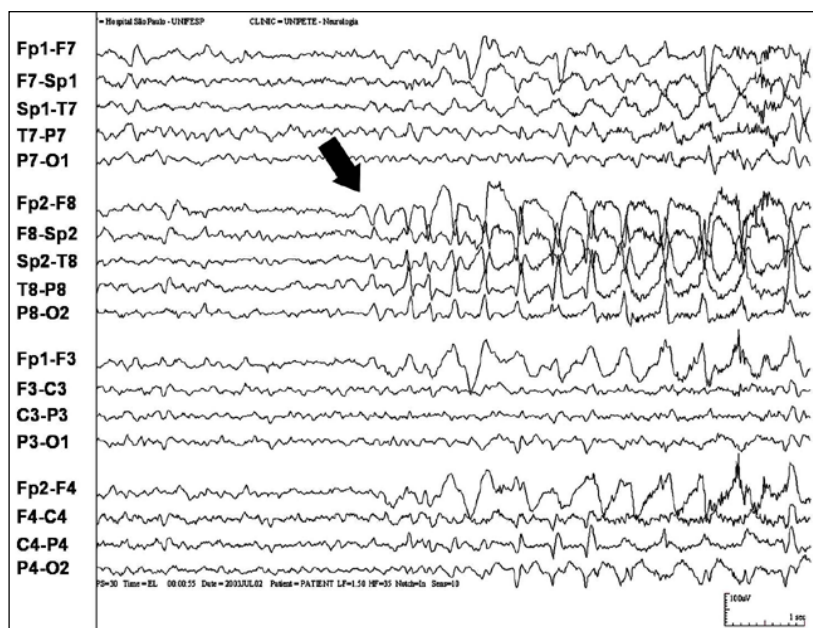
A 43-year-old right handed man had one single seizure when he was eight years old; this event could not be characterized. He had no further seizures until the age of 20, when he began to present GTC seizures occurring exclusively during sleep at night. A few years later he started to present seizures beginning with ill-defined aura, followed by staring and oroalimentary automatisms, with rare episodes of secondary generalization. The frequency of the seizures was two or three complex partial seizures per month.

MRI scan revealed marked hippocampal atrophy with abnormal signal on the left (Figure 6). The interictal EEG showed bitemporal epileptiform discharges. Prolonged video-EEG monitoring with scalp-sphenoidal EEG recorded five seizures. No clear lateralizing sign was seen in these seizures, but post-ictal aphasia was consistent in all. In all seizures ictal onset was markedly localized in the right temporal lobe (Figure 7). The patient had psychiatric complication after discharge from the video-EEG unit, with

severe post-ictal psychosis and suicidal attempt. He is currently awaiting implantation of FO electrodes.



**Figure 6.** Patient 4: **A.** MRI, coronal IR image, showing markedly atrophic left hippocampus; **B.** MRI, coronal T2-weighted image, showing hyperintensity of the left hippocampus.



**Figure 7.** Patient 4: Scalp EEG, bipolar longitudinal montage. The arrow points the electrographic ictal onset over the right temporal region.

## DISCUSSION

Prolonged video-EEG monitoring remains as one of the mainstays in pre-surgical evaluation of patients with refractory epilepsy. In patients with TLE, this evaluation usually begins with scalp and sphenoidal electrodes monitoring. This approach is sufficient in the majority of patients with TLE who are surgical candidates, as it is, in most cases, capable of localizing the epileptogenic zone, which in TLE corresponds to the epileptogenic temporal lobe. Invasive monitoring with depth or subdural electrodes is indicated in a selected group of patients<sup>(6)</sup>. Some authors, indeed, argue about the need for video-EEG monitoring in patients with TLE and all other data concordant in pointing to the same side as the epileptogenic temporal lobe<sup>(7)</sup>.

Indication of resective surgery in TLE depends of the finding of concordant radiological and neurophysiologic data. However, in several cases it is not possible to record seizures which are clearly lateralized, and in other cases there is discordance among the diagnostic data.

Patients with severe hippocampal sclerosis may present contralateral temporal scalp ictal onset, which has been called "burned-out hippocampus"<sup>(5)</sup>. This is considered to be an uncommon situation in epilepsy surgery centers. Mintzer et al.<sup>(5)</sup> reported five cases among 109 patients who had undergone depth electrode implantation for suspected TLE in two tertiary epilepsy centers. The authors restricted their search among patients submitted to invasive monitoring, as all patients had seizures with ictal onset ipsilateral to the HS confirmed by depth electrodes.

In this study, we searched for cases of "burned-out hippocampus" among all patients with TLE who were surgical candidates. Out of 72 patients with TLE and HS who underwent pre-surgical evaluation at our service, four had features of the so called "burned-out hippocampus." This is an incidence much higher than that reported by Mintzer et al.<sup>(5)</sup>. This is probably due to the fact that our population was biased toward the selection of patients with refractory TLE, who would probably benefit from surgery. Therefore, we had a homogeneous pool of patients with refractory TLE and unilateral HS.

It has been known for long that patients with gross temporal lesions may have seizures originating from the contralateral temporal lobe registered by scalp EEG<sup>(8)</sup>. Whether this applies to severe hippocampal atrophy is not known yet. Propagation of seizures generated in one atrophic hippocampus may occur primarily to the contralateral hippocampus, before spreading to the ipsilateral neocortex<sup>(9)</sup>. It is believed that severely injured hippocampi may be incapable of spreading ictal activity to the ipsilateral adjacent temporal neocortex. In such cases, ictal activity would spread, instead, to contralateral

mesial structures and neocortex, where it would be visualized by scalp electrodes<sup>(5)</sup>. This pattern of spread of the ictal activity would explain the false lateralization in scalp EEG.

Patients with "burned-out hippocampus" pose a particular challenge in the scenario of pre-surgical evaluation. Scalp-sphenoidal ictal onset contralateral to the side of HS raises the possibility of bilateral epileptogenicity, which might lead to denial of surgical treatment for these patients. However, in such patients one might as well be facing cases of false lateralization in scalp-sphenoidal EEG instead.

Clinical characteristics of seizures presented during scalp-sphenoidal EEG monitoring may not be of help in solving this problem, since patients may present features of involvement of one or the other temporal lobe. In case one, dystonic posturing of the arm ipsilateral to the HS was observed in four seizures, and comprehensible ictal speech in three, leading to the suspicion of involvement of the right temporal lobe. It is interesting to note that in one of the seizures the patient presented ictal spitting, usually considered to be a lateralizing sign pointing to the non-dominant temporal lobe<sup>(10)</sup>. In this case, clinical characteristics were discordant with the side of the HS. On the other hand, patient 3 presented dystonic posturing of her right arm in five out of six seizures, which was concordant with the side of the atrophic hippocampus.

Therefore, the resolution of this challenge usually depends on results of invasive monitoring. The implantation of depth electrodes, however, brings the risk of cerebral lesion. One alternative to the use of depth electrodes is the implantation, instead, of FO electrodes, inserted using the same technique utilized for therapeutic electrocoagulation of the third trigeminal branch within the gasserian ganglion. FO electrodes are capable of capturing interictal as well as ictal activity generated in mesial temporal lobe structures simultaneously with depth electrodes implanted in these structures, if anatomical volume involved is large enough, for instance, in the case of spikes occurring simultaneously in the amygdala and the hippocampus<sup>(11)</sup>. FO electrodes provide accurate register of mesial temporal seizures<sup>(12,13)</sup>, and are less invasive than other intracranial electrodes, thus reducing the risk to which patients are exposed to during invasive investigations<sup>(14)</sup>.

All five patients reported by Mintzer et al.<sup>(5)</sup> had confirmation of the epileptogenic temporal lobe by depth electrodes, which showed ictal onset ipsilateral to the atrophic hippocampus and therefore contralateral to the side of ictal onset as registered by scalp EEG. One of the limitations of this study was that simultaneous scalp and depth electrode recordings were not performed, raising the

question of whether a simple sampling error could have occurred, with seizures from one temporal lobe being registered on scalp study and seizures from the other temporal lobe being registered with depth electrodes. This was not a concern in our cases number 1 and 3, in whom simultaneous scalp and FO recordings were performed. All seizures captured by scalp electrodes, either alone or in conjunction with FO electrodes, showed emergence of a clear ictal rhythm over the temporal region contralateral to the atrophic hippocampus, visualized before this rhythm could be detected over the temporal region ipsilateral to the sclerotic hippocampus.

FO electrodes may therefore avoid the need for implantation of depth electrodes in patients with TLE and severe HS. This may not be the case in patients with MRI-negative TLE, in whom FO recordings have added no useful localizing information<sup>(15)</sup>.

Further studies will be necessary before one can affirm that patients with unilateral HS and scalp ictal EEG showing contralateral ictal onset may be operated without confirmation of the epileptogenic zone by invasive monitoring. In these patients, as we have shown in this article, semi-invasive monitoring with FO electrodes might be an interesting alternative.

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### Endereço para correspondência:

Luis Otávio S. F. Caboclo  
Av. Cons. Rodrigues Alves, 127/24A – Vila Mariana  
CEP 04014-010, São Paulo, SP, Brasil  
E-mail: locaboclo@ig.com.br

### Mande seu caso para:

JECN – A/c. de ANDRÉ PALMINI  
Av. Montenegro, 186 sala 505 – Petrópolis  
CEP 90460-160, Porto Alegre, RS, Brasil  
Fone/Fax: (51) 3331-0161