

PROGNOSTIC FACTORS IN MESIAL TEMPORAL LOBE EPILEPSY SURGERY

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ABSTRACT - Eighty-four patients submitted to anterior temporal lobectomy were evaluated retrospectively in order to correlate the different type of simple partial seizure (SPS) and their prognostic implications in patients with mesial temporal sclerosis. The patients were divided in two groups following the classification of Engel; Group 1 (53 patients) included patients Class I (without seizures or of good outcome) and Group 2 (31 patients) included Classes II, III and IV (with seizures or of bad outcome). The two groups were compared and results showed no statistical difference in relation to the demographic aspects as sex, side of surgery, age at onset of seizures and time of the patients' postoperative follow-up. Statistical analysis revealed no relationship between type of SPS and outcome. SPS did not show a statistical value in localizing the side of pathology. However, when the two groups were compared statistically in terms of patients' ages at the time of surgery, and the time elapsed from the onset of the seizures to the surgical intervention, it was observed that Group 1 (of good outcome) had seizures for smaller interval ($p < 0.05$) and was operated at an earlier age ($p < 0.02$) than Group 2 (of bad outcome). The presence or the type of SPS can not be used as a prognostic measure; surgical therapy must be considered as soon as clinical resistance is demonstrated.

KEY WORDS: simple partial seizure, hippocampal sclerosis, mesial temporal sclerosis, temporal epilepsy, epilepsy surgery.

Fatores prognósticos na cirurgia da epilepsia do lobo temporal mesial

RESUMO - Oitenta e quatro pacientes submetidos a lobectomia temporal anterior foram avaliados retrospectivamente com o intuito de correlacionar os diferentes tipos de crises parciais simples (CPS) e suas implicações prognósticas nos pacientes com esclerose mesial temporal. Os pacientes foram divididos em dois grupos de acordo com a classificação de Engel: o Grupo 1 (53 pacientes) englobando os pacientes Classe I (sem crises ou de boa evolução) e o Grupo 2 (31 pacientes) abrangendo as Classes II, III, IV (com crises ou de má evolução). Os grupos foram comparados e os resultados mostraram não haver diferença estatística, quanto aos aspectos demográficos como sexo, lado da cirurgia, idade de início das crises e tempo de acompanhamento pós-operatório dos pacientes. A análise estatística não mostrou relação entre evolução clínica e o tipo de CPS, assim como não mostraram as CPS ter um valor na localização do lado acometido. No entanto, quando os dois grupos foram comparados estatisticamente com relação às idades dos pacientes na ocasião da cirurgia e ao tempo decorrido a partir do início das crises até a intervenção cirúrgica, observou-se que o Grupo 1 (de melhor evolução) conviveu com as crises por intervalo de tempo menor ($p < 0,05$) e realizou as cirurgias em idades mais precoces ($p < 0,02$) do que as correspondentes do Grupo 2 (de pior evolução). A presença ou o tipo de CPS não pode ser um fator usado na determinação prognóstica; a cirurgia deve ser considerada tão breve seja demonstrada resistência ao tratamento clínico.

PALAVRAS-CHAVE: crise parcial simples, esclerose hipocampal, esclerose mesiotemporal, epilepsia temporal, cirurgia de epilepsia.

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The auras or simple partial seizures (SPS) are often the first symptoms that precede the complex partial seizure in temporal lobe epilepsy. They can have a duration of seconds up to one or two minutes before the partial or total loss of consciousness. Many studies have focused in characterizing their frequency¹⁻⁶ and value in localizing or lateralizing the onset of seizure^{3,7-12}, but there are few studies of surgical series trying to characterize their prognostic value^{10,13,14}. Many types of SPS have been described^{3,10,15-17}. Auras are frequent and typically occur also in isolation. In mesial temporal lobe epilepsies the SPS often consist of visceral ascending epigastric sensations¹⁰, fear, or both. Other vegetative autonomic symptoms and psychic phenomena, including memory flashbacks, déjà vu experiences, dreamy states, complex illusions, and multimodal hallucinations are less common¹⁸. It is at least very problematic, if not impossible, to describe ictal signs and symptoms in terms of their strict localization in the brain. An epileptic seizure remains a complex multidimensional dynamic event and the analysis of clinical signs and symptoms has to take into account the timing of a symptom within the seizure¹⁹.

Electrical stimulation has been used to study the functional organization of the brain, but virtually no symptoms can be considered pathognomonic for a specific brain region¹⁹. Studies have shown that seizures can begin in the amygdala, hippocampus or in both²⁰. Amygdalohippocampectomy or anterior temporal lobe resection were equally effective surgical treatments for mesial temporal lobe epilepsy²¹, with resulting freedom of seizures in 70 to 80% of the patients²².

Left hippocampal atrophy was associated with severe verbal memory deficits and there was no association between degree of right hippocampal atrophy and any of the memory tests²³. "Persisting auras" after resective surgery are still poorly understood. Since this phenomenon occurs not only with selective resections, but also with larger temporal lobectomies, it might indicate that the epileptogenic zone is often much more extensive than we tend to assume¹⁹. This fact suggests that SPS, like formed memories, are widely distributed and may eventually become consolidated in the neocortex^{10,14,24,25}. With the objective of correlating the different types of SPS and other factors with outcome, a retrospective analysis of patients with mesial temporal sclerosis submitted to temporal lobectomy was carried out.

METHOD

Eighty-four patients underwent anterior temporal lobectomy between June 1991 and March 1996 in the Epilepsie Zentrum Bethel (Bielefeld, Germany). They all had a histopathologic diagnosis of hippocampal sclerosis and at least one year of follow-up.

The patients were evaluated with regard to presenting or not simple partial seizures (auras), in agreement with the classification of epileptic seizures of the International League Against Epilepsy²⁷. Outcome was analyzed in the presence of each kind of SPS and in the presence of more than one type of SPS.

All patients were submitted to preoperative evaluation with interictal and ictal surface electroencephalogram with sphenoidal electrodes, neuropsychologic studies, psychosocial evaluation, PET, MRI and Wada test. Depth electrodes were used in six patients and semi-invasive evaluation with foramen ovale electrodes in other six.

All patients were submitted to standard cortico-amigdalohippocampectomy throughout an anterior temporal lobectomy under general anesthesia. Electrocorticography was not necessary in any case. All cases of dual pathology, including tumors and other diagnosis besides hippocampal sclerosis, as well as cases not well defined histopathologically, were excluded.

During the histopathologic analysis the hippocampus was always found preserved due to en-bloc resection, and, in many cases, only fragments of the amygdala and entorhinal cortex were present. Because of that fact the terms mesial temporal sclerosis and hippocampal sclerosis are used in this context in an interchangeable way. The first is related to neuronal loss and astrogliosis in the hippocampus, the adjacent entorhinal cortex and the amygdala. The second is related to hippocampal abnormalities, more specifically areas CA1 to CA4, dentate gyrus and subiculum.

Demographic data were evaluated with respect to sex, side of surgery, age of seizure onset, age at time of surgery, preoperative duration of epilepsy and length of follow-up. Patients were divided in two groups in agreement

Table 1. Distribution of 84 patients according to the Engel's classification for epilepsy surgery outcome.

Class of Engel's Classification	Number of Patients	Percentage of Patients
1A	35	41.7%
1B	14	16.7%
1C	1	1.2%
1D	3	3.6%
2A	3	3.6%
2B	5	6.0%
2C	0	0%
2D	4	4.8%
3A	8	9.5%
3B	1	1.2%
4A	4	4.8%
4B	6	7.1%
4C	0	0%

with Engel's classification²⁶. Group 1 included patients Class I (free of disabling seizures) and Group 2 embraced Classes II (rare disabling seizures), III (worthwhile improvement) and IV (no worthwhile improvement). Patients of group 1 were defined as of good outcome in this study.

For statistical analysis we performed the t-test for ages, duration of epilepsy, and duration of follow-up. We used the χ^2 -test to compare the two groups for sex, side of surgery, presence of SPS (epigastric, autonomic other than epigastric, somatosensory, psychic, unspecific) and the number of SPS the patients had before surgery. The χ^2 -test was also used to compare the distribution of SPS according to the side of the pathology.

RESULTS

There were 48 (57.1%) men and 36 (42,9%) women. Mean \pm SD age at onset of seizures was 9.3 \pm 6.9 years. The age at the time of surgery was 31,2 \pm 11,7 years. The duration of epilepsy was 21,8 \pm 11,7 years. There were 41 (48.8%) right temporal lobe and 43 (51,2%) left temporal lobe lobectomies. The length of follow-up was 30.7 \pm 14.8 months. The distribution of the patients according to Engel's classification is shown in Table 1.

Fifty-three patients had a good outcome and they were included in Group 1. Mean \pm SD age at the onset of seizures was 9.1 \pm 7.3 years; age at the time of surgery was 28.8 \pm 11.8 years; duration of epilepsy was 19.8 \pm 11.9 years; follow-up was 28.5 \pm 15.2 months. The 31 who had bad outcome were included in Group 2. Mean \pm SD age at the onset of seizures was 9.7 \pm 6.3 years; mean age at the time of surgery was 35.0 \pm 10.6 years; mean duration of epilepsy was 25.3 \pm 10.6 years; mean follow-up was 34.4 \pm 13.5 months.

There was no statistical difference between the two groups in terms of age at onset of seizures ($p>0.6$), length of follow-up ($p=0.08$), right or left temporal sclerosis ($p>0.3$) or frequency of males or females ($p>0.8$). However, there was statistical difference between the two groups in terms of age at the time of surgery ($p=0.02$) and duration of the epilepsy ($p=0.05$). Table 2 shows the data of the two groups and the "p" values.

There was no significant difference between the two groups in the presence of SPS. There were 56 (66.6%) patients presenting epigastric SPS. Thirty-seven (69.8%) patients of the Group 1

Table 2. Demographic aspects in groups with good (1) and bad (2) outcome after temporal lobectomy.

Demographics aspects	Group 1 n=(53)	Group 2 (n=31)	p value
Sex	30M (56.6%) 23F (43.4%)	18M (58.1%) 13F (41.9%)	p =0.9
Side of surgery	24 R (45.3%) 29 L (54.7%)	17 R (54.8%) 14 L (45.2%)	p=0.4
Age at onset of seizures (Mean \pm SD)	9.1 \pm 7.3	9.7 \pm 6.3	p=0.7
Age at the time of surgery (Mean \pm SD)	28.9 \pm 11.9	35.0 \pm 10.6	p=0.019
Duration of epilepsy (before surgery) (Mean \pm SD)	19.8 \pm 11.9	25.3 \pm 10.6	p=0.036
Length of follow-up (Mean \pm SD)	28.5 \pm 15.2	34.4 \pm 13.5	p=0.079

F, Female; M, male; R, right; L, left

and 19 (61.3%) in the Group 2 had epigastric SPS. Table 3 shows the sort of SPS the two groups presented and the p-values obtained by χ^2 -test.

We also evaluated the difference between the groups in the presence of more than one sort of simple partial seizure. The patients presented with none to four types of SPS. Two patients did not have SPS, 66 had one type, 11 had two types, 4 had three types, and one 4 types of SPS. There was no significant difference between the two groups in terms of numbers of SPS the patients had ($p>0.3$). The distribution of the patients, based on the numbers of simple partial seizures they had, is shown in Table 4.

We compared the frequency of the different SPS types in patients with left-side pathology to patients with right-side pathology. None of the SPS types was significantly associated with the side of pathology ($p\geq 0.09$).

Table 3. The distribution of simple partial seizure in groups with good (1) and bad (2) outcome after temporal lobectomy.

Simple partial seizures	Group 1 (n=53)	Group 2 (n=31)	p-value
Epigastric	37 (69.8%)	19 (61.3%)	0.42
Psychic	11 (20.8%)	9 (29.0%)	0.39
Unspecific	10 (18.9%)	6 (19.4%)	0.95
Somatosensory	5 (9.4%)	2 (6.5%)	0.63
Autonomic (other than epigastric)	1 (1.9%)	3 (9.7%)	0.11

Some patients had more than one type of simple partial seizure.

Table 4. Number of patients with different numbers of types of SPS in groups with good (1) and bad (2) outcome after temporal lobectomy.

	No SPS	1 SPS	2 SPS	3 SPS	4 SPS
Group 1 (n=53)	2 (3.77%)	41 (77.36%)	8 (15.09%)	2 (3.77%)	0 (0%)
Group 2 (n=31)	0 (0%)	25 (80.65%)	3 (9.68%)	2 (6.45%)	1 (3.23%)

SPS, simple partial seizure(s)

DISCUSSION

The frequency of SPS in temporal lobe epilepsy has been reported as between 20 and 90% in studies from several epilepsy centers¹⁻⁵. We detected only two patients free of SPS. Therefore, of the 84 studied patients, 82 (97.6%) presented with SPS.

Our series shows a much greater frequency of patients with SPS compared to the other studies¹⁻⁵. On the other hand, most studies included non-specific temporal lobe epilepsy, while the present study looked at temporal lobe epilepsy with hippocampal sclerosis only. This stress that mesial temporal lobe epilepsy is more related with the presence of SPS than epilepsies with other pathological basis¹³.

Many studies have tried to evaluate the value of SPS in localizing or lateralizing the onset of seizures^{1,3,7-12}. There are studies that have examined the localizing value of SPS in order to correlate the phenomenology of the aura with the presumed location of scalp EEG recordings^{7,12}, and the presumed location of intracranial EEG recordings^{11,14}. Furthermore, there is a study¹⁰ that correlated the phenomenology of auras with the structural pathology presumed to underlie the seizure disorder. That study¹⁰, and others studies using EEG to determine the localizing value of SPS^{9,28}, reported that epigastric SPS as well as gustatory and olfactory SPS are significantly more frequent in patients with hippocampal sclerosis than in those with other temporal or extratemporal lesions. As we studied patients with hippocampal sclerosis only, we can not compare the frequency of SPS among other epilepsies to analyze their localizing value. However, we found 66.6% of patients with epigastric SPS, significantly more than the 37.2% of Fried et al.¹⁰. Although the present study could not examine the localizing value, it supports studies that have reported that epigastric SPS are more frequent in patients with hippocampal sclerosis than in those with other temporal or extratemporal lesions^{9,10,28}.

In the present study the semiology of SPS did not correlate with the side of pathology in the brain. The lateralizing value of SPS has been controversial. In one study⁷, an association was observed between autonomic and psychic SPS with interictal abnormalities of the right temporal lobe. Another study²⁸, suggested an association of visceral SPS with right temporal lobe seizures. In other studies, the semiology of SPS was found to have value in localizing but not in lateralizing the onset of seizures^{10,11}. Furthermore, a study¹² using scalp EEG found no localizing or lateralizing significance of SPS.

Several predictive signs in terms of a better surgical outcome following selective amygdalohippocampectomy have been found in the Zurich amygdalohippocampectomy series¹⁸. The signs predicting better surgical outcome were presence of pathology in general, hippocampal sclerosis in particular; history of febrile seizures and presence of unilateral material-specific neuropsychological memory deficits; short length of preoperative years with recurrent seizures; absence of severe memory deficits; and low age at operation¹⁸.

In agreement with the Zurich results¹⁸, we found good correlation of outcome with shorter duration of epilepsy before surgery ($p < 0.05$) and the age of surgery accomplishment ($p < 0.02$). Patients who had seizures during a longer period and who had surgery later had a worse outcome. The importance of earlier surgery for epilepsy is emphasized in Danish²² and Japanese studies²⁹. We suggest that surgical therapy should be considered as soon as drug resistance is demonstrated.

A study evaluating the characteristics and prognostic meaning of the SPS showed that subclinical seizures and SPS were of favorable prognostic significance for patients undergoing temporal lobectomy¹³. Our study is the first in literature with a selected sample of patients, with temporal lobe epilepsy with hippocampal sclerosis only, and we showed no significant difference in presence of SPS between the group with good or bad outcome.

As previously established, the surgical outcome of mesial temporal lobe epilepsies is more favorable than other non-lesional cortical epilepsies that start in temporal neocortex and sometimes called cryptogenic^{22,30}. Even though some studies reported the same outcome for temporal sclerosis

and for lesions of temporal and extratemporal lobes^{10,22}, there is a study reporting that seizures outcomes were worse in tumor patients compared to hippocampal sclerosis patients³¹. Mesial temporal sclerosis offer freedom of seizures in 70-80% of the patients and in non-lesional cortical partial epilepsy only 30-40% of the patients will be free of seizures²². Furthermore, the presence of SPS is more common when the mesial area of the temporal lobe is injured^{4,13}.

Studies involving different pathologies of the temporal lobe could find better outcome in cases related with SPS, probably because they would be referring to cases of mesial temporal sclerosis.

We conclude that the presence or the type of SPS can not be used as a prognostic measure mainly if the diagnosis of mesial temporal lobe epilepsy has already been established.

Acknowledgement - We thank Prof. P R M de Bittencourt for linguistic revision of the manuscript and Prof. L G Caleffe, for statistical analysis.

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