

# Temporal lobe epilepsy: clinical semiology and age at onset

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Received April 23, 2003; Accepted January 20, 2005

**ABSTRACT** – The objective of this study was to define the clinical semiology of seizures in temporal lobe epilepsy according to the age at onset. We analyzed 180 seizures from 50 patients with medial or neocortical temporal lobe epilepsy who underwent epilepsy surgery between 1997-2002, and achieved an Engel class I or II outcome. We classified the patients into two groups according to the age at the first seizure: at or before 17 years of age and 18 years of age or older. All patients underwent intensive video-EEG monitoring. We reviewed at least three seizures from each patient and analyzed the following clinical data: presence of aura, duration of aura, ictal and post-ictal period, clinical semiology of aura, ictal and post-ictal period. We also analyzed the following data from the clinical history prior to surgery: presence of isolated auras, frequency of secondary generalized seizures, and frequency of complex partial seizures. Non-parametric, chi-square tests and odds ratios were used for the statistical analysis.

There were 41 patients in the “early onset” group and 9 patients in the “later onset” group. A relationship was found between early onset and mesial temporal lobe epilepsy and between later onset and neocortical temporal lobe epilepsy ( $p = 0.04$ ). The later onset group presented a higher incidence of blinking during seizures ( $p = 0.03$ ), a longer duration of the post-ictal period ( $p = 0.07$ ) and a lower number of presurgical complex partial seizures ( $p = 0.03$ ). The other parameters analyzed showed no significant differences between the two groups. We conclude that clinical and semiological differences exist between patients with temporal lobe epilepsy according to the age at onset. [*Published with video sequences*]

**Key words:** temporal epilepsy, semiology, video-EEG, age, evolution of semiology



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Clinical semiology of seizures constitutes one of the main areas of study in patients with epilepsy (Jackson 1889, Golub *et al.* 1951, Gastaut 1970, Escueta *et al.* 1982). Most studies have been performed in temporal lobe epilepsy as this is the most common form of epilepsy referred for epilepsy surgery (Engel 1993). Most patients referred for temporal lobe epilepsy surgery have a video-EEG recording with a

detailed study of the electroclinical features and subsequently become seizure-free, confirming the diagnosis of temporal lobe epilepsy.

Many of these studies are based on a global analysis of the semiology of the temporal lobe seizures (Serafetinides and Falconer 1963, Escueta *et al.* 1977, Theodore *et al.* 1983). Some of them sought differences according to the localization (mesial or neocorti-

cal) (Saygi *et al.* 1994, Gil-Nagel *et al.* 1997, Foldvary *et al.* 1997, Pfander *et al.* 2002) and lateralization (dominant or non-dominant) of the epileptic focus (Fakhoury *et al.* 1994, Williamson *et al.* 1998, Marks and Laxer 1998). Although there are several reports on the influence of age on epilepsy (Jallon P *et al.* 1981, Hauser 1992), few studies have analyzed temporal lobe seizure semiology according to age. Some studies in children have analyzed changes in temporal lobe seizure semiology with age (Brockhaus and Elger 1995, Fogarasi *et al.* 2002) and other studies have analyzed changes in ictal semiology in elderly patients (Tinuper *et al.* 1996). However, to our knowledge, there are no clinical studies defining the clinical semiology of seizures in temporal lobe epilepsy according to the age at onset.

The objective of the present study was to analyze the clinical semiology of temporal lobe seizures according to the age at onset and to determine a possible relationship between the age at onset and the clinical features.

## Methods

We analyzed 50 patients with mesial or neocortical temporal lobe epilepsy who underwent epilepsy surgery between 1997 and 2002 and obtained an Engel class I or II outcome. There were 46 patients (92%) with an Engel I, and 4 patients (8%) with an Engel II outcome.

Four patients with an Engel class II outcome were included because they had experienced a marked improvement in seizure frequency after surgery, presenting only infrequent seizures. Furthermore, the presurgical evaluation (video-EEG monitoring and MRI) in these 4 patients was suggestive of a temporal origin.

The patients were divided into two groups according to the age at the first seizure: the "early onset" group (EOG), with an onset at or before 17 years of age, and the "later onset group" (LOG), with an age at onset of 18 years or older.

Video-EEG recordings were reviewed by two epileptologists. A total of 180 complex partial seizures (CPS) were studied. The median number of seizures analyzed per patient was 3.6, with a range of 3 to 5. We analyzed seizures starting from the first recorded seizure until 3 typical, fully representative and technically adequate seizures had been observed. In most patients these were the first three seizures, but in other patients more seizures had to be analyzed. The first seizures were preferred because seizures recorded later during video-EEG monitoring can be influenced by factors such as medication withdrawal and may not be representative of the patient's habitual seizures. Patients with fewer than three seizures or with significantly different types of seizure were not included because surgery is not performed in these patients in our protocol.

The definition of semiological features was based on observation by experienced video-EEG reviewers who decided whether signs were present or absent. The following clinical data were analyzed in all the seizures:

1. Aura: the presence or absence of an aura was analyzed. If present, the semiology and duration was studied. The duration was defined as the time from when the patient pushed the alert button to the first change in the interaction with the environment;
2. Ictal period: the semiology and duration were studied. We analyzed the presence or absence of the following ictal symptoms: body shifting, arrest, staring, clonic movements, tonic or dystonic posturing, head turning, preserved speech, manual automatisms, oral automatisms, leg automatisms and eye blinking. The duration was measured by means of clinical and EEG data, from the first change in interaction with the environment to the cessation of ictal signs and resolution of the ictal EEG changes;
3. Postictal period: the semiology and duration were studied. We analyzed the presence or absence of dysphasia, aggressiveness, urinary disturbances, and the degree of confusion (none, mild, moderate, severe). The duration was measured as starting from the outset of the ictal period, defined above, and ending when the patient was fully orientated and able to speak with our trained Video-EEG Unit nurse.

The clinical history prior to surgery was studied in all patients, analyzing the following data:

1. Presence of isolated auras;
  2. Frequency of secondary generalized tonic-clonic seizures (SGTCS). The patients were classified into the following groups: no SGTCS, infrequent SGTCS (< 1/month) and frequent SGTCS (> 1/month);
  3. Frequency of complex partial seizures (CPS) defined as the number of seizures per month. Patients were grouped into the following categories: < 5 seizures/month, 5 to 20 seizures/month and > 20 seizures/month.
- Patients were classified as neocortical or mesial temporal lobe epilepsy based on MR and/or pathological findings. Surgical procedures performed in this series of patients included temporal neocortical lesionectomy (11 patients) and temporal lobectomy with amygdalohippocampectomy (39 patients).

## Statistical analysis

The statistical analysis was performed using the chi-squared and Fisher's exact tests for the analysis of qualitative variables: presence or absence of auras preceding CPS, presence or absence of isolated auras, frequency of SGTCS and CPS, and presence or absence of ictal and post-ictal signs. A Mann-Whitney test was used for the analysis of quantitative variables (duration of auras, duration of ictal period and duration of post-ictal period).

**Table 1.** Distribution of patients.

	EOG	LOG	P value
<b>Patients</b>	41 (82%)	9 (18%)	
<b>Age at onset</b>	7.5	24.4	
<b>Age at time of study</b>	35.9	43.8	
<b>Sex</b>			
M	19 (46.3%)	4 (44.4%)	
F	22 (53.7%)	5 (55.6%)	
<b>Localization</b>			0.04
Mesial	32 (78.0%)	4 (44.4%)	
Neocortical	9 (22.0%)	5 (55.6%)	
<b>Side of onset</b>			0.48
Non-dominant hemisphere	20 (48.7%)	3 (33.3%)	
Dominant hemisphere	21 (51.3%)	6 (66.9%)	

EOG: early onset group (onset at or before 17 years); LOG: later onset group (onset at or after 18 years).

Statistical significance:  $p < 0.05$  (chi-squared and Fisher's exact tests).

Finally, the odds ratio for the age at onset and the localization was calculated.

## Results

There were 41 patients (82%) in the EOG and 9 patients (18%) in the LOG. The mean age at onset was 7.5 years (range 1-17 years) in the EOG and 24.4 years (range 18-44 years) in the LOG. The mean age at the time of the video-EEG study was 35.9 years in the EOG and 43.8 years in the LOG. There were 19 males (46.3%) and 22 females (53.7%) in the EOG and 4 males (44.4%) and 5 females (55.6%) in the LOG.

Regarding the lateralization of seizure onset, 20 patients (48.7%) in the EOG had a non-dominant hemisphere onset and 21 patients (51.3%) had a dominant hemisphere onset. In the LOG, 3 patients (33.3%) had a non-dominant hemisphere onset and 6 patients (66.9%) had a dominant hemisphere onset. No statistically significant correlation was found between the hemisphere of onset and the age at onset, although a predominance of dominant hemisphere onset patients was found in the LOG. These data are summarized in *table 1*.

Patient follow-up was at least one year, with a median of 28.10 months and a range of 12-62 months. Surgical outcome according to Engel's classification for outcome included 46 patients (92%) in class I, with 35 patients (70%) in class IA (completely seizure-free), 8 patients (16%) in class IB (non-disabling, simple partial seizures after surgery), 2 patients (4%) in class IC (some disabling seizures after surgery, but free of disabling seizures for at least 2 years) and 1 patient (2%) in class ID (generalized convulsions only after withdrawal of antiepileptic medication). The remaining 4 patients (8%) were in class IIB (infrequent, disabling seizures after surgery).

Pathological findings included 35 patients (70%) with hippocampal sclerosis, 11 patients (22%) with benign tumours (3 dysembryoplastic neuroepithelial tumours and 8 gangliogliomas), 2 patients (4%) with neocortical temporal gliosis, 1 patient (2%) with a cavernoma, and 1 patient (2%) with no lesion (although MR spectroscopy showed mesial neuronal loss). These data are summarized in *table 2*.

The localization of the lesion was studied in the two groups. In the EOG, 32 patients (78.0%) had mesial temporal lesions (including mesial temporal sclerosis) and 9 patients (22.0%) had neocortical temporal lesions. In the LOG, 4 patients (44.4%) had mesial temporal lesions and 5 patients (55.6%) had neocortical temporal lesions. A statistically significant correlation ( $p = 0.04$ ) was observed between early onset of epilepsy and mesial temporal lesions and between later onset of epilepsy and neocortical temporal lesions. The odds ratio for early onset and mesial temporal lesion was 4.44 (range 0.80-26.12) compared to patients with later onset and mesial temporal lesion.

**Table 2.** Pathological findings.

	EOG	LOG
<b>Hippocampal sclerosis</b>	31	4
<b>Benign tumours</b>	8	3
Ganglioglioma	6	2
DNET	2	1
<b>Other</b>	2	2
Cavernoma	0	1
Gliosis	1	1
No lesion	1	0

EOG: early onset group; LOG: later onset group.  
DNET: dysembryoplastic neuroepithelial tumor.

Auras preceding seizures were present in 23 patients (56.1%) in the EOG and in 4 patients (44.4%) in the LOG. This predominance of auras in the EOG appeared both in patients with mesial lesions as well as in those with neocortical lesions, although the association of auras with an early onset was not statistically significant in either of these groups. Epigastric auras were predominant in the EOG (13/23, 56.5%), whereas no specific type of aura was predominant in the LOG. The duration of the aura was longer (13.7 seconds) in the LOG than in the EOG (7.2 seconds), but the difference was not statistically significant. These data are summarized in *table 3*.

Analysis of the semiology during the ictal period showed only small differences between the EOG and the LOG. Only the presence of blinking reached a statistically significant difference ( $p = 0.03$ ), with a predominance in the

LOG. The mean duration of the ictal period was very similar in both groups, 65.0 seconds for the EOG and 67.7 seconds for the LOG. These data are summarized in *table 4*.

The mean duration of the post-ictal period was longer in the LOG (288.9 seconds) than in the EOG (184.6 seconds). This difference was close to statistical significance ( $p = 0.07$ ). The longer duration in the LOG was observed in the non-dominant hemisphere onset as well as in the dominant hemisphere onset patients. These data are presented in *table 5*.

The clinical history prior to surgery showed a higher frequency of isolated auras in the EOG 20/41 (48.8%) compared to the LOG 1/9 (11.1%); this difference was statistically significant ( $p = 0.03$ ). The higher frequency of auras was observed both in patients with mesial lesions

**Table 3.** Characteristics of auras.

	EOG	LOG	P value
<b>Aura</b>	23/41 (56.1%)	4/9 (44.4%)	0.52
Mesial	19/32 (59.3%)	2/4 (50%)	0.72
Neocortical	5/9 (55.5%)	2/5 (40%)	0.87
<b>Type</b>			
Abdominal	13 (56.5%)	1 (25%)	0.25
Psychic	3 (13.0%)	0 (0%)	
Cephalic	5 (21.8%)	1 (25%)	
Autonomic	0 (0%)	1 (25%)	
Fear	2 (8.7%)	0 (0%)	
Somatosensory	0 (0%)	1 (25%)	
<b>Duration</b> (seconds)	7.2	13.7	0.12

EOG: early onset group (onset at or before 17 years); LOG: later onset group (onset at or after 18 years).

Statistical significance:  $p < 0.05$  (chi-squared, Fisher's exact and Mann-Whitney tests).

**Table 4.** Characteristics of ictal period.

	EOG	LOG	P value
Body shifting	3 (7.3%)	0 (0%)	0.40
Arrest	15 (36.5%)	1 (11.1%)	0.66
Staring	39 (95.1%)	8 (88.8%)	0.47
Clonic movements	5 (12.1%)	2 (22.2%)	0.61
Dystonic posturing	16 (39.0%)	3 (33.3%)	0.75
Head turning	9 (21.9%)	0 (0%)	0.12
Speech	8 (19.5%)	1 (11.1%)	0.55
Manual automatisms	17 (41.4%)	3 (33.3%)	0.65
Oral automatisms	25 (60.9%)	7 (77.7%)	0.34
Leg automatisms	3 (7.3%)	0 (0%)	0.40
Blinking	3 (7.3%)	3 (33.3%)	0.03
Tonic posturing	4 (9.7%)	0 (0%)	0.32
<b>Duration</b> (seconds)	65.0	67.7	0.24

EOG: early onset group (onset at or before 17 years); LOG: later onset group (onset at or after 18 years).

Statistical significance:  $p < 0.05$  (chi-squared, Fisher's exact and Mann-Whitney tests).

**Table 5.** Characteristics of post-ictal period.

	EOG	LOG	P value
Dysphasia	15 (36.5%)	4 (44%)	0.66
Confusion			0.65
None	0 (0%)	1 (11.1%)	
Mild	12 (29.3%)	2 (22.2%)	
Moderate	22 (53.6%)	5 (55.5%)	
Severe	7 (17.1%)	1 (11.1%)	
Aggressiveness	1 (4.9%)	1 (11.1%)	0.50
Urinary disturbances	1 (4.9%)	1 (11.1%)	0.50
<b>Duration</b> (seconds)	184.6	288.9	0.07
Non-dominant hemisphere	119	176	0.21
Dominant hemisphere	246	345	0.29

EOG: early onset group (onset at or before 17 years); LOG: later onset group (onset at or after 18 years).

Statistical significance:  $p < 0.05$  (chi-squared, Fisher's exact and Mann-Whitney tests).

**Table 6.** Characteristics of seizures.

	EOG	LOG	P value
<b>Isolated SPS</b>	20 (48.8%)	1 (11.1%)	0.03
Mesial	17/32 (53.1%)	1/4 (25%)	0.28
Neocortical	3/9 (33.3%)	0/5 (0%)	0.14
<b>CPS/ month</b>			0.80
5	15 (36.6%)	5 (55.5%)	
5-20	21 (51.3%)	4 (44.4%)	
> 20	5 (12.1%)	0 (0%)	
<b>SGS</b>			
None	20 (48.8%)	6 (66.6%)	1.18
Rare	17 (41.5%)	2 (22.2%)	
Frequent (> 1/month)	4 (9.7%)	1 (11.1%)	

EOG: early onset group (onset at or before 17 years); LOG: later onset group (onset at or after 18 years); SPS: simple partial seizures; CPS: complex partial seizures; SGS: secondary generalized seizures.

Statistical significance:  $p < 0.05$  (chi-squared and Fisher's exact tests).

and in patients with neocortical lesions. No differences were observed between the EOG and the LOG in the analysis of the frequency of CPS and SGTCs. These data are summarized in *table 6*.

## Discussion

Changes in the semiology of temporal seizures related to the age have been reported in previous studies (Yamamoto *et al.* 1987, Brockhaus and Elger 1995, Tinuper *et al.* 1996, Fogarasi *et al.* 2002). Tinuper *et al.* reported that seizures became less elaborate and briefer in a subgroup of patients aged > 60 years than in younger patients. These data suggest that seizure semiology is determined not only by the age at onset but also by the age of the patients at the time of the study.

A relationship has been found in our series between the EOG and mesial lesions and the LOG and neocortical

lesions. Previously, Foldvary *et al.* (1997) reported a mean age at seizure onset of 8.4 years in a group of patients with mesial temporal lobe epilepsy (MTLE) and 18.5 years in a group of patients with neocortical temporal lobe epilepsy (NTLE). In a series of 67 patients with MTLE, the authors found that seizures began at or before 16 years of age in 88% of patients, the mean age at seizure onset being 9 years (French *et al.* 1993). However, another study found no differences in the age at onset in MTLE and NTLE (Burgerman *et al.* 1995). Overall, as was previously suggested, it appears that mesial temporal structures are more susceptible to an earlier development of epileptogenesis.

It may be possible to explain the predominance of auras in the EOG by the presence in this group, of more patients with mesial lesions. According to some studies (Saygi *et al.* 1994, Gil-Nagel *et al.* 1997, Foldvary *et al.* 1997), auras are more common in mesial temporal lobe epilepsy, although this association has not been confirmed in other



studies (O'Brien *et al.* 1996). Separate analyses of auras in patients with mesial lesions and in patients with neocortical lesions showed a predominance of auras in the patients with an early onset, in each of these groups. Based on previous studies of the clinical course of the epilepsy, we hypothesize that seizures in patients with an early onset, who had a longer clinical course at the time of the study than those with a later onset, could have damaged the brain and extended the epileptic focus to symptomatic areas capable of producing auras, however this point has not been demonstrated (Hughes 1985, Mathern *et al.* 1996, Pitkanen 2002, Engel 2002). With respect to the semiology of auras, epigastric auras are more frequently observed in some studies of temporal lobe epilepsy (Gupta *et al.* 1983). The association of epigastric auras with mesial lesions could explain the predominance of this semiology in the EOG (Saygi *et al.* 1994, Gil-Nagel *et al.* 1997, Foldvary *et al.* 1997, Pfander *et al.* 2002).

The analysis of the semiology during the ictal period did not show marked differences between the groups analyzed, observing only a statistically significant predominance of blinking in the LOG. In previous papers, the semiology of temporal seizures has been analyzed with regard to the localization (mesial or neocortical) (Saygi *et al.* 1994, Gil-Nagel *et al.* 1997, Foldvary *et al.* 1997, Pfander *et al.* 2002), and lateralization (dominant or non-dominant) of the epileptic focus (Fakhoury *et al.* 1994, Williamson *et al.* 1998, Marks and Laxer 1998). Several associations were described in these studies: oral automatisms were associated with MTLE (Gil-Nagel *et al.* 1997, Foldvary *et al.* 1997), manual automatisms were associated with MTLE in some reports (Foldvary *et al.* 1997, Pfander *et al.* 2002), and with NTLE in other reports (Gil-Nagel *et al.* 1997), and ictal language was typically associated with a non-dominant hemisphere onset (Gabr *et al.* 1989, Yen *et al.* 1996). With respect to ictal blinking, an ipsilateral onset has been associated with unilateral blinking (Benbadis *et al.* 1996). Nevertheless, there is little information about the mechanisms and pathways involved in the production of blinking. For this reason, we consider that the association found in our work between blinking and the later onset group is only an observational feature and so far there is no explanation for it. In previous studies, the duration of seizures has been found to be similar in MTLE and NTLE (Saygi *et al.* 1994) or longer in MTLE (Foldvary *et al.* 1997). As the present study is the first, to our knowledge, which attempts to find a correlation between the semiology of seizures and the age at onset, there are no previous studies with which to perform comparisons. No significant differences between the two groups compared were observed during the ictal period, but further studies with larger series of patients are necessary in order to determine the influence of the age at onset on the ictal period.

A longer duration of the post-ictal period in the LOG was observed in our series. This point could be explained by

### Legends for video sequences

Two typical seizures in representative patients from the two groups analysed.

**Patient 1.** Representative patient from the early onset group.

This **patient** was 22 years old. He had his first seizure when he was 2 years old. He had right mesial temporal lobe epilepsy secondary to hippocampal sclerosis. At the present time, following surgery, he has been seizure-free for 5 years.

In this **seizure**, the patient had a prolonged epigastric aura. We observed an ictal period with right arm dystonia and left hemifacial clonic movements. The seizure ended with nose wiping. The post-ictal period was brief (< 1 minute) and with no language disturbances.

**Patient 2.** Representative patient from the later onset group.

This **patient** was 44 years old. He had his first seizure when he was 30 years old. He had left neocortical temporal lobe epilepsy secondary to a traumatic lesion. At the present time, following surgery, he has been seizure-free for 2 years.

In this **seizure**, the patient had no aura. During the ictal period he had oral automatisms (sucking), body turning to the right and, finally, manual automatisms with his left hand. The post-ictal period was prolonged (> 10 minutes) and associated with severe confusion and language disturbances.

the presence of more dominant hemisphere-onset patients, a characteristic which, as suggested by some authors, is associated with a longer post-ictal period (Dantas *et al.* 1998, Williamson *et al.* 1998, Marks and Laxer 1998). However, the independent analysis of dominant hemisphere- and non-dominant hemisphere-onset patients according to the age at onset, showed a longer post-ictal period in the LOG of dominant hemisphere-onset and non-dominant hemisphere-onset patients, although differences were not significant in this case. Further explanations are therefore required; we think that the LOG includes older patients and these patients may have a larger epileptogenic area due to their longer clinical course, thus leading to a longer recovery period. Despite the different duration of the recovery periods, no differences were observed regarding the level of confusion or the presence of dysphasia. In previous studies, post-ictal dysphasia has been associated with amygdalar atrophy (Guerreiro *et al.* 1999) or with seizure onset in the dominant hemisphere (Fakhoury *et al.* 1994, Gabr *et al.* 1989). However, as suggested by some authors, few studies have been performed on post-ictal signs and it is difficult to establish comparisons with our results (Leutmezer and Baumgartner 2002).

Finally, an association was found between the EOG and the presence of more isolated auras, and the same explanation as that for auras preceding CPS can be postulated. In previous studies, a decrease in SGS was observed in patients over 60 years of age (Tinuper *et al.* 1996) and in children compared to adolescents (Olbrich *et al.* 2002). However, no differences were observed in our analysis in this respect.

In conclusion, according to the results of this study, the age at onset of seizures in patients with temporal lobe epilepsy may condition some clinical and semiological characteristics. We observed an EOG made up of younger patients, with a predominance of mesial lesions and more commonly associated with auras, and a LOG made up of older patients, with neocortical lesions and longer post-ictal periods. However, there are two problems which have affected this study: 1. the definition of the groups and the difficulty in defining the appropriate age interval to classify the patients. 2. The small number of patients and their heterogeneity, including some factors which can influence semiology and affect the results: age of the patients at the time of the study, localization of the epileptic focus (mesial or neocortical), hemisphere of onset (dominant or non-dominant), and different pathology. We believe that further studies with larger numbers of patients and more homogeneous groups are necessary. □

**Acknowledgements.** This work received the Epileptic Disorders and John Libbey Eurotext award as best communication on clinical semeiology at the 5<sup>th</sup> European Congress on Epileptology held in Madrid, 2002.

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