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Temporal lobe epilepsy surgery in children and adolescents: Clinical characteristics and post-surgical outcome

Vera Cristina Terra-Bustamante*, Luciana M. Inuzuca, Regina M.F. Fernandes, Sandra Funayama, Sara Escorsi-Rosset, Lauro Wichert-Ana, Antonio C. Santos, David Araujo, Helio R. Machado, Americo C. Sakamoto

Department of Neurology, Hospital das Clinicas, Av Bandeirantes, 3900 Monte Alegre, Brazil

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Summary

Background and purpose: Temporal lobe epilepsy (TLE) encompasses 10—20% of the cases of intractable epilepsy in pediatric patients. Mesial temporal sclerosis (MTS) can still be encountered in adolescent patients, but is rare in children under 5 years of age. In this paper we report on the surgical outcome of a series of TLE patients ranging in age from 1 to 18 years at the time of operation.
Patients and methods: Thirty-five patients (37 surgeries) with medically intractable TLE were operated upon between January 1996 and December 2002. The following variables were analyzed: age at surgery, age at epilepsy onset, history of an initial precipitating injury, etiology, seizure semiology, interictal and ictal EEG findings, surgical complications, and post-surgical seizure outcome.
Results: There were 68.6% females and 31.3% males, and complex partial seizures (CPS) occurred in 86.5%. The most common etiology was MTS (40%) followed by isolated cortical developmental abnormalities (22.9%). In the age group up to 5 years, cortical development abnormalities predominated, and 71% of these children had multifocal interictal EEG. Patients older than 10 years had more frequently MTS (78.6%) and focal temporal interictal EEG abnormalities. Post-surgical seizure outcome showed that 88.5% of patients were in Engel classes I and II.
Conclusions: Adolescents with TLE had clinical features, electrographic findings, and seizure outcome similar to those observed in adult patients. However, younger children up to 5 years of age had distinct ictal semiology and different etiological, electrophysiological and outcome profiles, clearly suggesting that they behave as a special subgroup within the TLE.

* Corresponding author. Tel.: +55 16 6022613; fax: +55 16 6330760.
E-mail address: vctbusta@rnp.fmrp.usp.br (V.C. Terra-Bustamante).

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Introduction

Temporal lobe epilepsy (TLE) is the most common type of medically intractable epilepsy in adults, and hippocampal sclerosis (HS) its major pathological substrate. Extratemporal and multilobar epilepsies predominate in children, but temporal lobe cases are still encountered, usually occurring associated with neocortical lesions.[1] In a community-based cohort of children with new-onset TLE, it was previously observed that approximately 81.0% of them had monthly seizures before starting antiepileptic drug (AED) treatment, and that only 22.0% of them had mesial temporal sclerosis (MTS).[2] Although MTS has been reported in children as young as four months,[3] it is not frequently seen in children younger than 5 years.[4] Spontaneous remission can occur in 10—18% of the patients with early-onset complex partial seizures (CPS),[5] but at present the long-term outcome cannot be clearly predicted.

In children some questions still remain unresolved, including how to predict prognosis and whether precocious AED treatment can prevent intractability. These questions need to be considered when dealing with TLE in the pediatric population. On the other hand, several studies have shown an excellent surgical outcome of temporal lobectomy in younger patients,[6] with figures similar to those observed in adult patients. These findings obviously encourage early surgery, but the presurgical investigation of this age group is much more complex and difficult in comparison to older patients. Whenever invasive electrodes are needed to precisely localize the epileptogenic zone it is known that they carry higher risks in the pediatric group.

The presence of more diffuse neocortical pathologies, including cortical developmental abnormalities (CDA), tumors and hypoxic lesions, in association with incomplete CNS myelinization may predispose to the occurrence of atypical seizure types in pediatric TLE, including infantile spasms, tonic seizures and tonic-clonic seizures.[7] Interictal and ictal EEG findings are usually more diffuse and show more complex electrographic patterns, including hypsarrhythmia, thus posing additional difficulties for the determination of temporal lobe seizure onset.[6] The association of temporal lobe lesions and seizures with clinical semiology suggestive of temporal lobe origin, and the convergence with other diagnostic methodologies, such as positron emission tomography (PET) or ictal single photon emission computerized tomography (SPECT) may suffice for topographic localization. However, electrocorticography (ECoG) and chronic invasive recordings may eventually be necessary in more complex clinical scenarios, potentially leading to more precisely tailored resections and consequently to better surgical outcome.[8]

As is the case for adults, TLE surgery in children and adolescents may also carry cognitive morbidity, especially when performed in the dominant side.[9] On the other hand, in patients with mental retardation and behavioral problems there is good correlation between seizure control or reduction and improvement of these symptoms.[10]

The objective of the present study is to report on the experience of the Ribeirão Preto Pediatric Epilepsy Surgery Program in the surgical treatment of medically intractable TLE in children and adolescents.

Patients and methods

Patient selection

We included all 35 children and adolescents (18 years of age or less) who had been submitted to TLE surgery at our center, from January 1996 to December 2002. Patients were evaluated at the Ribeirão Preto Pediatric Epilepsy Surgery Program (CIREP) using previously published standardized protocols approved by the Ethics Committee of our institution. All had medically intractable epilepsy.

Methodology

Presurgical evaluation included a detailed clinical history and neurological examination, interictal scalp EEG, interictal and ictal Video-EEG monitoring, structural and functional imaging, and neuropsychological testing. The Video-EEG monitoring of all patients were recorded on a Vangard digital EEG system. EEG samples were saved either manually by a trained EEG technician, or automatically, at a rate of 5 min samples/h of monitoring. Interictal spike counts were visually performed considering exclusively these automatically saved EEG samples. Electrocorticography and subdural chronic evaluation were eventually performed to better identify the localization and limits of the epileptogenic area. Neuroimaging workup included high resolution 1.5 T Siemens Vision MRI and multiple ictal and interictal SPECT scans. Neuropsychological testing was performed whenever possible (all cases, except for those patients with profound mental retardation or severe behavioral problems).

The following variables were analyzed: (1) sex; (2) age at surgery; (3) presence of an initial precipitating injury (IPI); (4) age at epilepsy onset; (5) seizure semiology; (6) seizure frequency; (7) interictal and ictal EEG findings; (8) etiology; (9) surgical

Table 1 Demographic data in 35 patients submitted to temporal lobe surgeries.

N	Sex	Age of IPI	Febrile seizure	Age at epilepsy onset	Age at surgery	Duration of epilepsy	Seizures types	Seizure frequency	Neurological examination	EEG interictal	EEG ictal 1	Number of seizures	ECoG Subdural strips	Pathology	Engel Classif	Follow-up (years)
1	M	3 mo	Yes	3 y	9 y	6 y	aura-CPS	Weekly	Normal	Bilateral temporal	Ipsilateral temporal	4	—	MTS	I	1
2	F	12 mo	No	10 y	17 y	7 y	aura-CPS	Weekly	Normal	Bilateral temporal	Bilateral temporal	12	—	MTS	I	5
3	F	—	No	10 y	11 y	1 y	aura-CPS	Monthly	Normal	Ipsilateral temporal	Ipsilateral temporal	2	—	AVM	I	1
4	M	3 mo	No	3 y	14 y	11 y	aura-CPS	Weekly	Normal	Ipsilateral temporal	Bilateral temporal	6	—	MTS	I	4
5	F	—	No	15 y	17 y	2 y	CPS	Weekly	Normal	Bilateral temporal	Bilateral temporal	3	—	DNET	I	2
6	F	—	No	1 y	11 y	10 y	aura-CPS	Sporadic	Normal	Ipsilateral temporal	Not registered	0	—	CDA	I	3
7	F	9 mo	Yes	5 y	9 y	4 y	aura-CPS	Weekly	Normal	Multifocal	Contralateral temporal	6	ECoG	OLIGODENDR.	I	4
8	M	—	No	4 mo	5 y	4 y 8 mo	CPS	Daily	Normal	Ipsilateral temporal	Hemispheric	5	ECoG	CDA	I	3
9	F	15 days	No	8 y	18 y	10 y	aura-CPS	Weekly	Developmental delay	Bilateral temporal	Ipsilateral temporal	3	—	MTS	I	2
10	F	1 mo	Yes	8 y	17 y	9 y	aura-CPS	Weekly	Normal	Ipsilateral temporal	Ipsilateral temporal	3	—	MTS	I	5
11	F	—	No	7 y	18 y	11 y	aura-CPS	Weekly	Normal	Ipsilateral temporal	Ipsilateral temporal	11	—	DNET	I	4
12	F	—	No	3 y	18 y	15 y	aura-CPS	Monthly	Normal	Ipsilateral temporal	Ipsilateral temporal	3	—	MTS PORENC. CIST	I	2
13	F	—	No	3 y	18 y	15 y	aura-CPS	Monthly	Normal	Ipsilateral temporal	Ipsilateral temporal	3	—	MTS	II	3
14	F	—	No	5 y	6 y	1 y	aura-CPS	Sporadic	Normal	Ipsilateral temporal	Ipsilateral temporal	1	ECoG	DNET	I	5
15	F	2 mo	Yes	6 y	14 y	8 y	aura-CPS	Daily	Developmental delay	Ipsilateral temporal	Multifocal	6	—	MTS	III	7
16	F	—	No	1 y	14 y	13 y	aura-CPS	Weekly	Normal	Ipsilateral temporal	Ipsilateral temporal	4	ECoG	CDA MTS	I	1
17	M	—	No	2 y	12 y	10 y	aura-CPS	Weekly	Normal	Multifocal	Ipsilateral temporal	5	ECoG	CDA DNET	I	3
18	M	—	No	1 mo	1 y	11 mo	CPS tonic seizures	Daily	Developmental delay, left hemiparesis	Multifocal	Ipsilateral temporal	11	ECoG	CDA	IV	6
19	F	2 mo	No	4 mo	12 y	11 y 8 mo	Tonic seizures	Daily	Developmental delay	Multifocal	Multifocal	Status epilepticus	—	CDA	I	1
20	F	—	No	6 y	9 y	3 y	aura-CPS non epileptic seizures	Daily	Normal	Ipsilateral temporal	Ipsilateral temporal	1	ECoG	DNET	I	1

21*	M	—	No	4 y	14 y	10 y	aura-CPS	Weekly	Normal	Ipsilateral temporal	Ipsilateral temporal	9	—	MTS	II	3
22	F	16 mo	No	3 y	8 y	5 y	aura-CPS	Daily	Developmental delay	Multifocal	Ipsilateral temporal	57	ECoG	MTS	I	3
23	F	6 mo	No	1 y	4 y	3 y	Infantilie spasm tonic seizures	Daily	Developmental delay	Multifocal	Multifocal	14	ECoG	CDA	I	6
24	F	2 mo	Yes	9 y	11 y	2 y	CPS	Monthly	Normal	Multifocal	Ipsilateral temporal	14	ECoG	CDA	I	3
25	F	—	No	1 y	5 y	4 y	aura-CPS	Weekly	Developmental delay Right palpebral ptosis	Ipsilateral temporal	Ipsilateral temporal	9	—	MTS	III	6
26	M	—	No	2 y	5 y	3 y	CPS	Sporadic	Normal	Multifocal	Multifocal	12	—	CDA MTS	I	4
27	M	—	No	1 y	17 y	16 y	aura-CPS	Monthly	Developmental delay right hemiparesis	Ipsilateral temporal	Hemispheric	11	—	MTS	I	4
28	F	—	No	2 mo	4 y	3 y 10 mo	Infantile spasm focal motor seizures	Daily	Developmental delay	Multifocal	Multifocal	24	ECoG	CDA	III	6
29	F	2 mo	Yes	6 y	17 y	11 y	aura-CPS	Weekly	Normal	Ipsilateral temporal	Ipsilateral temporal	19	—	MTS	I	6
30	F	1 mo	Yes	5 y	16 y	11 y	aura-CPS	Weekly	Normal	Ipsilateral temporal	Ipsilateral temporal	11	—	MTS	I	3
31	M	1 mo	No	7 y	17 y	10 y	aura-CPS	Weekly	Normal	Bilateral temporal	Ipsilateral temporal	10	ECoG + subdural strips	MTS	I	6
32*	F	—	No	7 y	16 y	11 y	aura-CPS	Weekly	Developmental delay	Multifocal	Hemispheric	11	ECoG + subdural strips	CDA MTS GLIOSIS	II	3
33	F	—	No	2 y	3 y	1 y	CPS	Weekly	Developmental delay	Multifocal	Ipsilateral temporal	7	ECoG	CDA	II	5
34	M	—	No	4 y	9 y	5 y	CPS	Weekly	Normal	Not registered	Ipsilateral temporal	2	—	CDA MTS	I	3
35	M	—	No	1 y	17 y	16 y	Infantile spasms tonic seizures	Daily	Developmental delay	Multifocal	Multifocal	6	ECoG	CDA OLIGODEND	I	5

Sporadic = <1 month^{-1}; monthly = 1—3 months^{-1}; weekly = 4—29 months^{-1}; daily = $\geq$30 months^{-1}, y: years, mo: months.

* Patients reoperated on.

complications; (10) duration of follow-up, and (11) post-surgical outcome. Postoperative seizure status was obtained on the occasion of follow-up visits with the medical staff. Whenever this information was not available or was considered unclear, the patient or a close relative was contacted by telephone. Seizure outcome was classified according to Engel's scheme[11] as follows: class I (seizure free or non-disabling simple partial seizures only, or occasional generalized convulsion with AED withdrawal); class II (initially free of disabling seizures followed by rare seizures, or rare disabling seizures, or disabling seizures after surgery but rare for at least 2 years, or nocturnal seizures only); class III (worthwhile improvement with at least 75% reduction in seizure frequency); and class IV (no worthwhile improvement or no appreciable change). Post-surgical AED therapy was kept unchanged for at least 2 years in patients with monotherapy, and for those with polytherapy dosages were reduced or converted to monotherapy whenever possible. For this analysis, patients were divided into three subgroups according to their age at surgery: 0—5, 6—10 and 11—18 years.

Statistical analysis

Fisher's exact test and Mann—Whitney test were applied for statistical analysis, with level of significance set at $p < 0.05$. For analysis of age at the onset of epilepsy median and non-parametric statistics (Kruskal—Wallis *H*-test) were used. Mann—Whitney *U*-tests were employed for pairwise comparisons.

Results

We analyzed 35 patients with medically intractable TLE who were submitted to a total of 37 surgeries within the age range of 1—18 years. The main characteristics of this group of children and adolescents are shown in Table 1. Twenty-four patients (68.6%) were females and 11 males (31.4%). Twenty-three patients (65.7%) had normal neurological development while 12 (34.3%) had discrete to moderate developmental delay, and two of them additional hemiparesis. The youngest child in the entire group was only 1 year old, the oldest was 18 years old (mean: 11.9 years; median: 12 years), and 13 (37.1%) were under 10 years of age at surgery. Fourteen patients (40.0%) had an IPI and seven of them (20.0% of the total population, and 50.0% of those with IPI) had febrile seizures in the first year of life.

The mean age at epilepsy onset was 4.3 years (median: 3 years), the onset of epilepsy occurred in the first 5 years of life in 23 (65.7%) children, from 6 to 10 years in 11 (31.4%), and from 11 to 18 years in only one (2.9%). Mean duration of epilepsy was 7.5 years. The most frequent seizure type was CPS with or without aura (26 and 6 patients, respectively). All those who had aura reported it at anamnesis. Auras were epigastric (13 patients), vegetative (6), *jamais vu* (2), indescribable sensation (2), auditory (1), *deja vu* (1), forced thinking (1), and dizziness (1). Other seizure types included tonic seizures (four patients) and infantile spasms (3). Most of the patients had daily (25.7%) or weekly (51.4%) seizures at the time of surgery.

Table 2 shows interictal and ictal Video-EEG findings according to age subgroups. Patients aged 5 years or less more frequently had multifocal interictal or ictal EEG (71.0 and 43.0%, respectively), while patients aged more than 10 years predominantly had focal temporal interictal and ictal EEG findings (62.3 and 58.3%, respectively). During video-EEG monitoring we recorded a mean of nine seizures per patient (zero to 57 seizures), excluding from this calculation one patient who had *status epilepticus* and innumerable seizures during monitoring. Ictal SPECT was obtained in 57.0% of the patients and contributed to the diagnosis in 71.5% of these cases.

Table 2 Interictal and ictal findings on Video-EEG monitoring, per age subgroup.

Topography/age	Interictal EEG				Ictal EEG			
	0—5 years	6—10 years	11—18 years	Subtotal 1	0—5 years	6—10 years	11—18 years	Subtotal 2
Temporal ipsilateral	2	2	15	19	3	4	14	21
Temporal contralateral	—	—	—	—	—	1	1	2
Temporal bilateral	—	1	4	5	1	—	2	3
Multifocal	5	2	5	12	3	1	5	9
Hemispheric	—	—	—	—	—	—	1	1
Not registered	—	1	—	1	—	—	1	1

Table 3 Pathological data of the surgical *specimens* of the 35 patients at surgery age.

Pathology	0—5 years	6—10 years	11—18 years	Total
MTS	1	2	11	14
CDA	5	—	3	8
DNET	—	2	2	4
CDA + MTS	1	1	1	3
CDA + gliosis	—	—	1	1
CDA + oligodendroglioma	—	—	1	1
CDA + DNET	—	—	1	1
MTS + porencephalic lesion	—	—	1	1
AVM	—	—	1	1
Oligodendroglioma	—	1	—	1

MTS: mesial temporal sclerosis; CDA: cortical development abnormalities; DNET: desembrioplastic neuroepitelial tumors; AVM: arterio-venous malformation.

In 46.0% of the surgeries, additional EEG data were required. Intraoperative ECoG was performed in 43.0% of the cases, while acute ECoG plus chronic subdural recordings were used in 5.0% of the cases. One patient had foramen oval implantation.

Temporal lobe resections were performed in 35 patients (37 surgeries), and only one of them had selective amygdalo-hippocampectomy. In patients with ECoG or subdural electrode implantation, surgeries were tailored based on interictal and ictal findings. Two MTS patients needed to be re-operated and underwent extension of their previous anterior mesial temporal lobe resections, due to persistence of disabling seizures.

The surgical specimens revealed multiple etiologic factors that are shown in Table 3, with a wide predominance of MTS (40.0% of surgeries) and isolated CDA (22.9% of surgeries). Four patients had both MTS and CDA. Other pathologies included dysembryoplastic neuroepithelial tumors (8 cases = 11.5% of surgeries), oligodendroglioma (2 cases), porencephalic lesions (1 case), gliosis (1 case), and arteriovenous malformations (1 case). Dual pathology was present in 24.3% of the cases (eight patients), usually consisting of CDA associated with other lesions.

There were three major etiologies, namely, MTS (19 patients: 14 isolated MTS + 5 MTS plus other etiologies), CDA (14 patients: 8 isolated CDA + 6 CDA plus other etiologies), and tumors (six patients). Statistically significant differences were observed when comparing median age at epilepsy onset and epilepsy etiology: CDA (median: 1.0 year), MTS (median: 4.5 years) and DNET (median: 6.5 years). Differences were observed when comparing CDA and MTS ($p = 0.007$), and CDA and DNET ($p = 0.015$). There was no difference between MTS and DNET ($p = 0.16$). Comparison of the two major etiologies (comparison restricted to isolated MTS versus isolated CDA) revealed that the MTS subjects were older at the time of surgery ($p = 0.02$), but had similar duration of epilepsy ($p = 0.14$). Invasive recordings were more frequently employed in the CDA subgroup ($p = 0.001$).

A trend towards a differential distribution of etiologies was observed when age at surgery was included in the analysis, with children up to 5 years of age more frequently having CDA (85.7%) while patients above 10 years had mainly MTS (62.5%). However, this difference was not significant ($p = 0.08$).

Table 4 shows the postoperative seizure outcome. Seventy-seven percent of the patients were classified as Engel I, 11.5% as Engel II, 8.7% as Engel III, and 2.8% as Engel IV. Patients classified as Engels I and II corresponded to 88.5% of the cases. A good outcome was observed in 76.8% of the youngest subjects (Engel classes I and II), and in 95.5% of the patients older than 11 years. This difference was not significant. Mean follow-up was 3.8 years, ranging from 1 to 7 years (median: 5 years). No outcome difference was observed between the MTS and CDA subgroups.

New postoperative neurological deficits occurred in one patient (2.9%) who developed hemianopsia after resection extending to part of the occipital lobe. In this series there was only one patient with remission of both epileptic and non-epileptic seizures after surgery.

Table 4 Seizure outcome and age subgroup.

Engel	0—5 years	6—10 years	11—18 years	Total (%)
Class I	3	6	18	27 (77.0)
Class II	1	—	3	4 (11.5)
Class III	2	—	1	3 (8.7)
Class IV	1	—	—	1 (2.8)
Total	7	6	22	35

Discussion

Temporal lobe epilepsy in some series corresponds to less than 10% of the epilepsy surgeries in the pediatric population.[12,13] A predominance of neocortical lesions has been previously reported.[1] In our series, we operated on 35 children and adolescents between 1 and 18 years of age and found prevalence of 40.0% of MTS and 22.9% of CDA. This etiologic profile varies when distinct age subgroups are considered. Among children aged 5 years or less, 85.7% had CDA, while 62.5% of the patients older than 10 years had MTS as the main etiology of epilepsy. Also, patients with CDA had an earlier epilepsy onset than patients with MTS or DNET. Dual pathology was observed in 24.3% of the patients, with almost all of them having CDA plus MTS. Although 96.8% of the patients had epilepsy onset before 10 years and had weekly seizures, 65.0% of them were operated upon after 11 years of age. Complex partial seizures were present in 86.5% of the patients, preceded by auras in 70.0% of the cases. This rate is higher than previously described in the literature,[14] and we speculate whether this could be explained by the fact that 64.8% of our patients were adolescents with normal neurological status.

Video-EEG monitoring additionally showed other differences between distinct age subgroups, with 71.0% of multifocal interictal spikes occurring in children under 6 years, and 62.0% of focal temporal interictal spikes seen in patients above 10 years. Ictal patterns had focal onset in approximately 58.0% of the patients, with no differences between age groups. Other authors previously showed more focal interictal EEG abnormalities in adolescents than in children.[6] These data may suggest that patients operated upon at younger ages have more diffused abnormalities.

Seizure outcome was similar to figures previously reported for adult TLE patients, with 88.5% of the patients being in Engel classes I or II.[15] When considering age subgroups we observed a more favorable outcome in older patients (95.4% of subjects above 10 years) compared to children aged 1—5 years (76.9%). Differences in etiological profile may probably explain these results. MTS is more commonly seen in older patients and usually carries a better prognosis than CDA. Additionally, patients operated upon early more frequently have catastrophic epilepsy than those operated upon during adolescence. Complications are more frequently observed in children than in adult series, but we had only one patient with major postoperative neurological morbidity (hemianopsis).

The delay in the indication of surgical treatment in patients with TLE was also reported by other authors.[16] Since up to 42.0% of children and adolescents who do not control epileptic seizures with the first AED remit spontaneously, factors predicting intractability would certainly help to indicate surgical treatment more precociously.[17] Our results are consistent with literature data.

In conclusion, seizure outcome and overall clinical and electrographic findings in pediatric TLE are similar to those observed in adult patients. However, TLE in patients under 5 years of age has different features, clearly suggesting that this is a special subgroup of TLE.

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