Journal of Epilepsy and Clinical Neurophysiology

J Epilepsy Clin Neurophysiol 2006; 12(1 suppl. 1):26-31

# Temporal Lobe Epilepsy in Childhood: Review Article

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#### **ABSTRACT**

Introduction: The authors present a review article on temporal lobe epilepsy in childhood. Methods: We performed a search in the literature. Results: The main etiologies of temporal lobe epilepsy in childhood are developmental tumors and focal cortical displasia, besides temporal medial sclerosis. The clinical features may be variable particularly in children younger than six years of age. Epilepsy may present with generalized seizures. Electroencephalographic findings are also variable and show a functional dysfunction of several brain areas besides temporal lobes, especially frontal lobes. Conclusion: Recent advances demonstrate that temporal lobe epilepsy in childhood present with great etiologic, clinical and electroencephalographic diversity.

Key words: Temporal lobe epilepsy, childhood, etiology, clinical features, electroencephalogram.

#### RESUMO

Epilepsia de lobo temporal na infância: artigo de revisão

Introdução: As autoras apresentam um artigo de revisão sobre epilepsia de lobo temporal na infância. Material e métodos: Realizou-se levantamento bibliográfico sobre o assunto, acrescido de contribuições pessoais. Resultados: As principais etiologias da epilepsia de lobo temporal na infância são tumores do desenvolvimento e displasias corticais focais, além de esclerose mesial temporal. O quadro clínico é florido em crianças menores de seis anos e pode cursar com crises generalizadas. Os achados eletrencefalográficos também são variáveis e apontam para o comprometimento funcional de outras áreas cerebrais além dos lobos temporais, particularmente os lobos frontais. Conclusão: Avanços recentes mostram que a epilepsia de lobo temporal na infância apresenta grande diversidade etiológica, clínica e eletrencefalográfica.

Palavras-chave: epilepsia de lobo temporal, infância, etiologia, clínica, eletrencefalograma.

# HISTORICAL DATA

Clinico-electroencephalographical studies on temporal lobe epilepsy (TLE) in children have been performed since  $1960^{(1)}$ .

In the previous decade, the expression "psychomotor seizures" was introduced in the literature<sup>(2)</sup>. This expression included benign childhood epileptic syndromes, which were subsequently separated into idiopathic and symptomatic, that is, benign childhood epilepsy and TLE<sup>(3)</sup>.

The syndrome of "Benign Psychomotor Epilepsy" of childhood, proposed by Dalla Bernardina<sup>(4)</sup>, was not universally accepted as it included clinical findings of benign epilepsy with centro-temporal paroxysms, symptomatic TLE and nocturnal terror. The authors have concluded recently that this syndrome was an atypical presentation of benign epilepsy with centro-temporal paroxysms<sup>(5)</sup>.

Harvey et al.<sup>(6)</sup> studying clinical, electroencephalographic (EEG) and neuroimaging features of 63 children with recently diagnosed TLE, classified it in three

Received Oct. 30, 2005; accepted Nov. 25, 2005.

subgroups, according to the etiology: TLE with developmental malformations (cortical dysgenesis, arachnoid cyst or low grade tumor), TLE with mesial temporal sclerosis (MTS) and significant antecedents (complex febrile seizure, traumatic brain injury or meningoencephalitis), and cryptogenic TLE. This latter group had a better seizure and psychological prognosis and may represent a benign syndrome of TLE.

Major advances occurred, mostly in the last decade, resulting from several studies with long term video-EEG monitoring in children<sup>(7-10)</sup>.

# **ETIOLOGY**

In children, the most frequent etiologies of TLE are low-grade tumors, cortical dysplasia, MTS and dual pathology (presence of an extra-hippocampal lesion as well as MTS). Although MTS is the most frequent cause of TLE in adults, there is no consensus about its real incidence in children.

A recent study<sup>(11)</sup>, which tried to determine the incidence and etiology of TLE in 30 recently diagnosed children, found developmental malformation in eight children, TLE with MTS/significant antecedents in seven and cryptogenic TLE in 15 of them (50%).

Mesial temporal sclerosis affects 10 to 20% of children undergoing surgical treatment of TLE in the second half of the first decade of life and is considered rare in children younger than five years of age <sup>(8,9,12)</sup>; it is, however, the most frequent etiology in some studies, reaching 70% of the cases of TLE<sup>(13)</sup>. Magnetic resonance imaging (MRI) detected MTS in 57% of 53 children, two to 17 years of age (mean age of 10 years), which led the authors to claim that this is the most common lesion in children with refractory TLE and that it is underdiagnosed in that age range, delaying surgical procedures<sup>(14)</sup>.

Mesial temporal sclerosis has been correlated with previous antecedents of complex febrile seizures(15) occurring in about 43% of patients with MTS<sup>(16)</sup>. In spite of a high incidence of complex febrile seizures in patients with MTS, it is not well determined whether the febrile seizures are a causal factor or just an epiphenomenon of MTS<sup>(17,18)</sup>. Temporal lobe epilepsy due to MTS may present with different forms of epilepsy onset(19). In a group of patients with epilepsy onset in adolescence (mean age: 15,34 years) a family history of epilepsy was frequently found and complex febrile seizures occurred earlier than in the group of patients with epilepsy onset in childhood (mean age: 5,4 years) (19). Other authors (20) found that MTS after complex febrile seizure an uncommon event, which would confirm the favorable outcome of those with febrile seizures.

The low grade tumors most frequently found in TLE in childhood are neuronal or glioneural tumors

[ganglioglioma, gangliocytoma, dysembryoplastic neuroepithelial tumors (DNET)] and low grade astrocytomas. Gangliogliomas and gangliocytomas are mixed glial lesions, the latter having a predominance of the neuronal component. Gangliogliomas are the main tumors responsible for refractory epilepsy with onset below 15 years of age<sup>(21)</sup>. They present a highly variable morphology on MRI(22). A complete lesionectomy is considered curative(23). Their growth and histological findings suggest that these tumors, especially the gangliogliomas and DNET, could originate from a cortical malformation or they might be the final end of the spectrum of cortical dysplasias<sup>(24-26)</sup>. The DNET occur chiefly in the mesial structures of the temporal lobe. They are intracortical, well-circumscribed, multinodular tumors and, histologically, there is no consensus whether the neurons are neoplastic, malformed or dysplastic. They are characterized clinically by refractory complex partial seizures (CPS) with onset in childhood(16). Pleomorphic xanthoastrocytoma is rare and affects adolescents and young adults(6). Oligodendrogliomas are infiltrative tumors, which affect children with an incidence of 7-14%(8,9).

Focal cortical dysplasia was originally described in the temporal lobe <sup>(27)</sup> and is considered by some authors as the most frequent cause of refractory TLE in children <sup>(7,28,29)</sup>. It is now known that the temporal lobe is not its preferential location <sup>(30)</sup>. Neuropathological findings indicative of cortical dysplasias were present in 21 of 33 (64%) surgical specimens from children with refractory TLE<sup>(31)</sup>.

Dual pathology has been considered in recent studies of children with TLE who underwent surgical procedures. Mohamed et al. (32) studied 17 children and 17 adolescents with TLE and found abnormalities in the temporal neocortex ipsilateral to MTS in all the children and in 60% of the adolescents. The histopathological confirmation of dual pathology with findings of mild to moderate cortical dysplasia occurred in 79% of the patients. Bocti et al. (29) found cortical dysplasia in the temporal neocortex associated with MTS in 67% (eight out of 12) children who underwent anterior temporal lobectomy as treatment for refractory TLE in a 20-year neuropathological review. The neocortical lesions in the temporal lobe ipsilateral to MTS may not necessarily be cortical malformations but may simply be indicative of mesial TLE.

Other lesions may also be associated with TLE such as vascular malformations, neurocysticercosis and meningoencephalitis such as herpetic encephalitis.

### **CLINICAL FEATURES**

The knowledge of the clinical picture of TLE in children has greatly improved since 1990, from studies of

series of patients undergoing video-EEG monitoring and advanced neuroimaging evaluation as part of the presurgical assessment. Those series have shown enormous clinico-electroencephalographical diversity.

Problems with the clinical diagnosis of TLE in children were approached by Davidson & Falconer<sup>(33)</sup>, who described some main aspects: difficulty in describing the auras which frequently were incorrectly interpreted by the family, variable clinical severity in different stages of life, loss of follow-up in adolescence, and the difficulty of interpreting the EEG in children. These factors obscure the diagnosis in younger children<sup>(34)</sup>.

In infants, the identification of loss of consciousness and, therefore, the definition of CPS, is more difficult. Findings in infants suggestive of CPS are: arrested activity with possible alteration of consciousness, undetected aura, mild but specific orofacial automatisms, a greater number of secondary generalized tonic-clonic seizures and prolonged seizures (duration more than one minute)<sup>(12)</sup>. Infantile spasms and generalized myoclonic seizures also occur frequently<sup>(35,36)</sup>.

Among the main series of studies, Duchowny et al. (7) described a classical triad in 16 children younger than 12 years of age who underwent early surgery. This included a staring gaze with behavioral arrest, tonic motor phenomena and stereotyped automatisms. The group was divided according to age range and it was noted that coarse motor manifestations (tonic or clonic movements) were more common in infants and preschool-aged children and that stereotyped behavioral automatisms became progressively more complex with advancing chronological age. The authors found that attention deficit disorder with or without hyperactivity was the most evident clinical finding (75% of cases) associated with epilepsy.

Wyllie et al.<sup>(8)</sup> studied 14 children younger than 12 years of age and found almost all of them presented with auras. Abdominal or gustative sensations were encountered in the patients who had MTS; oromandibular automatisms occurred in all of the patients; less complex gestural automatisms in the younger subjects; and dystonic posturing was found in half of the patients with MTS. Some subjects also presented with gagging, retching, rhythmic groaning, head nodding and bilateral tonic extension of the limbs.

Brockhaus & Elger<sup>(9)</sup> described the cases of 29 children younger than 16 years of age, who were grouped into preschool (from 18 months to six years of age), school (from seven to 12 years of age) and adolescents (from 13 to 16 years of age). In the preschool children the most frequent initial ictal symptom was an awakening reaction with conspicuous motor alterations with variable presentation: tonic or clonic symmetrical movements, atonic phenomena such as head nodding, infantile spasms, simple

automatisms followed by versive movements and dystonic posturing. Hypermotricity and posturing similar to that of frontal lobe seizures in adults were also present. The authors used the expression "complex partial" in a group of young children in whom it is difficult to determine the level of consciousness. In the other groups, the findings were similar to that of adults, the automatisms becoming progressively more complex with increasing age and the motor alterations being predominantly asymmetrical, unilateral or bilateral, with tonic and/or clonic movements and dystonic posturing. The increasing complexity of automatisms reflect the developing abilities of the child.

Blume et al.<sup>(37)</sup>, studying 14 children ranging in age from two to 12 years, found aura in almost all of them (fear, abdominal sensations or cephalic aura) and automatisms in 12 of them (oroalimentary, gestural and ambulatorial). Tonic or clonic motor phenomena were seen in 12 children. The mean age of onset was two years and six months and the mean age of the presurgical evaluation was six years.

Pedreira<sup>(16)</sup> studied 34 children younger than 16 years of age with TLE and arranged them in three groups according to etiology: neocortical lesions (16 patients), MTS (16 patients) and dual pathology (two patients). The auras, chiefly ascendant epigastric sensation, were reported by 61,76% of the patients but only in 38,10% of them during video-EEG recordings. The group with MTS experienced epigastric aura in 77% of cases, which is statistically significant when compared to the group with neocortical lesions (18%). Patients with CPS presented with a prolonged duration of aura (statistically significant) in the group with MTS (78,2 seconds), these values being lower than those found in adults.

Nordli et al. (38) studied the ontogeny of partial seizures in 123 patients (infants and young children) and observed relevant differences in the clinical pictures of epileptic seizures between children and adults. Myoclonic seizures, asymmetric clonus and symmetric tonic posture diminished with age. On the other hand, the non-responsiveness increased in children over two years of age and auras, dystonic posture and secondary generalization increased in those over the age of six.

Fogarasi et al.<sup>(39)</sup> also showed an inverted linear correlation of behavioral and motor manifestations with advancing age through video-EEG monitoring of 15 children aged 11 to 70 months old. All patients under 42 months old presented with tonic and myoclonic behaviors as well as epileptic spasms. Hypomotor (sudden arrest of activity) and /or automotor (behavioral arrest with oral and manual automatisms) seizures occurred in almost half the patients over 42 months of age (five out of 11). The term "hypomotor" is most descriptive of the loss of consciousness in children<sup>(34)</sup>.

Nordli et al.<sup>(38)</sup> and Fogarasi et al.<sup>(39)</sup> conducted a longterm follow-up of their patients and demonstrated the importance, and the influence, of brain maturation in clinical and EEG manifestations.

## INTERICTAL AND ICTAL EEG FEATURES

Among the main series of surgical studies, Duchowny et al. (7) studied children under the age of 12, using sphenoidal electrodes, but did not find differences in interictal and ictal EEGs within the various age groups. Therefore, they concluded that sphenoidal electrodes are less useful in children than in adults for localizing temporal lobe seizure origin. The authors believe that the lesions of TLE in childhood rarely occur only in the mesial area, and the EEG data is indicative of this poorly circumscribed pattern.

Wyllie et al. (8) also studied 14 children under the age of 12 and subdivided them according to their etiology. In the MTS and cortical dysplasia group, the interictal and ictal findings were similar to those of adolescents and adults. The patients with tumoral lesions had clinical characteristics similar to those of adults, as well as polymorphic EEG findings. All children presented with atypical interictal EEG findings such as extratemporal epileptiform or contralateral temporal activity. The ictal activity showed poorly localized or falsely lateralized electroencephalographic patterns. Since these children progressed well after surgical intervention the authors concluded that, in tumors, this EEG pattern could be correlated with age and etiology. The results suggest that invasive electrodes seem to be ineffectual in the preoperative assessment of children with temporal lobe tumors; however, they are recommended when extratemporal functional localization studies are needed.

Other authors<sup>(9)</sup> found, the pattern of the EEG in TLE in children was age-related and the EEG findings were subdivided according to age. In the preschool children group (under six years old) generalized discharges predominate while ictal and electrocorticographic registers of children aged over six presented acute or focal rhythmic theta waves predominantly over the temporal regions. Patients with tonic or clonic movements had a propagation of ictal activity to extratemporal regions and to the contralateral hemisphere. This finding implies that younger children still presenting typical clinical ictal patterns should undergo a pre-operative assessment. Clinical and EEG findings, which are nonlocalizing, do not necessarily imply a poor prognosis when there is a structural lesion detected by neuroimaging.

Blume et al.<sup>(10)</sup> analyzed the results of temporal lobectomy in 14 children under 12 with clinically typical partial seizures and found active interictal spikes in the

epileptogenic temporal lobe in 13 patients (93%) and no false lateralizing signs. These results suggested that invasive monitoring is unnecessary. In addition, generalized epileptiform paroxysms were present in six patients (43%) and persistent polymorphic delta activity over the epileptogenic temporal lobe in nine patients (64%). These findings seem to be similar to those found in adults except for the high percentage of generalized epileptiform activity. The predominance of neocortical lesions (tumoral and dual pathology) could contribute to EEG diversity (generalized/multifocal pattern).

The ictal register of 21 patients who underwent long-term invasive monitoring showed an initial pattern of intracranial low amplitude beta activity followed by slower theta rhythm registered simultaneously in the initial site and adjacent areas. The propagation tended to occur firstly in the ipsilateral frontal lobe and then in the contralateral temporal lobe via the hippocampal commissura. The only difference between the group under 14 years old (eight patients) and the over 18-year-old group (13 patients) was a higher tendency of the latter to have seizures restricted to the temporal lobe and a lower tendency of the former to present with secondary generalized seizures<sup>(40)</sup>.

Pedreira<sup>(16)</sup> demonstrated that the interictal register of 34 symptomatic TLE patients allowed for the localization of the lesion in 41,75% of the patients with neocortical lesion and about twice as many (81,25%) of MTS patients. The ictal EEG alterations lateralized the lesion in both groups equally (66,67% and 68,75% respectively). The localization in the ipsilateral temporal lobe, however, was higher in the MTS group (43,75%) than in the neocortical lesions group (14,28%). The 30-second ictal rhythmic activity allowed for the localization of the epileptogenic lesion in 71,42% and 92,80% of patients with neocortical lesions and MTS groups respectively and thus presented a higher localizing value than the initial ictal alterations.

Ebner<sup>(41)</sup>, comparing EEG findings of 16 children versus 50 adults with MTS, noticed that the children (100%) showed intermittent slow waves ipsilaterally to MTS, while only 68% of adults presented with them exclusively or predominantly in the ipsilateral temporal lobe. The epileptiform discharges in adults were most frequent over the temporal lobe whereas 37,5% of children had maximal activity in extratemporal electrodes (31,25% ipsilateral and 6,25% contralateral) as well as generalized activity (12,5%). Ictal discharges were localized and restricted to temporal lobe in adults more (58%) than in children (18,75%) who showed predominantly extratemporal discharges (81,35%) associated with regional temporal seizures. No seizure was registered in the contralateral hemisphere in the pediatric group. In

children there is easy lateralization but difficult localization of the epileptogenic area.

# **SURGICAL FEATURES**

Epilepsy surgery in children has gained great impulse in the last decade and has been considered the best, if not the only, therapeutic option for many forms of refractory epilepsy<sup>(13,42,43)</sup>. This procedure allows for the control of epileptic seizures and reduces medication and undesirable effects of antiepileptic drugs, which can affect behavior as well as cognition<sup>(44,45)</sup>. Surgical treatment has even been suggested for children with mental impairment or behavioral disorders since the partial control, or changes in the form of seizures, allow the patient to have a better quality of the life<sup>(46)</sup>.

Temporal lobectomy in children with refractory TLE has been reported in the literature<sup>(28,47-51)</sup>.

Blume et al.<sup>(37)</sup>, reviewing several studies in the literature totaling 309 children and adolescents with a one-year postoperative follow-up concluded that the efficacy in eliminating or reducing seizures ranged from 73 to 100% of cases. Davidson & Falconer<sup>(33)</sup> described a series of 40 children who underwent surgery for TLE and found the best results were achieved in seizure control and behavior when MTS was the lesion found during surgery. Early temporal lobectomy may prevent the patient from behavioral disorders in adulthood, impaired family and social life as well as cognitive disorders.

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