RENATA CRISTINA FRANZON BONATTI

ASPECTOS CLÍNICOS, NEUROFISIOLÓGICOS E COMPORTAMENTAIS EM CRIANÇAS COM EPILEPSIAS DO LOBO TEMPORAL

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Tese de Doutorado apresentada à Pós-Graduação da Faculdade de Ciências Médicas da Universidade Estadual de Campinas, para obtenção do título de Doutor em Ciências Médicas, área de concentração Neurologia.

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"Todo nosso conhecimento se inicia dos sentimentos".

“Ogni nostra cognizione principia da sentimenti”.

(Leonardo da Vinci)

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AH	Atrofia Hipocampal
CPC	Crise Parcial Complexa
CPS	Crise Parcial Simples
CTCG	Crise Tônico-Clônica Generalizada
CTCGS	Crise Tônico-Clônica Secundariamente Generalizada
DAE(s)	Droga(s) Antiepiléptica(s)
DNET	Tumor(es) Neuroepitelial(is) Disembrioplástico(s)
ELT	Epilepsia(s) do Lobo Temporal
EMT	Esclerose Mesial Temporal
EEG	Eletrencefalograma(s), Eletrencefalográficos(a)
PET	Tomografia por Emissão de Pósitron
RM	Ressonância Magnética
SPECT	Tomografia Computadorizada por Emissão de Fóton Único
TC	Tomografia Computadorizada
TCE	Traumatismo crânio-encefálico
TIPDA	Atividade Delta Polimórfica Intermitente Temporal
TIRDA	Atividade Delta Rítmica Intermitente Temporal
Vídeo-EEG	Vídeo-Eletrencefalograma ou Vídeo-Eletrencefalográfico(a)

RESUMO

O conhecimento sobre as epilepsias do lobo temporal (ELT) na infância teve seu grande impulso com os dados clínico-eletrencefalográficos obtidos nos estudos de monitorização com vídeo-EEG em pacientes com epilepsia refratária submetidos à investigação pré-cirúrgica (Artigo 1). Os objetivos do presente estudo foram determinar os aspectos clínicos, comportamentais e neurofisiológicos (EEG) de crianças com ELT. A etiologia mais freqüente em nosso estudo foi atrofia hipocampal, seguida, ora por dupla-patologia, ora por lesões tumorais (Artigos 2 e 6, respectivamente). No Artigo 2 subdividimos os 36 pacientes estudados de acordo com a faixa etária: grupo A (≤ 6 anos) composto por seis pacientes e grupo B (> 6 anos) com 30 pacientes. Observamos que a presença de componentes motores, crises mioclônicas, distúrbios comportamentais e atraso de fala ocorreram mais freqüentemente no grupo A. Presença de postura distônica e de automatismos predominaram nos pacientes do grupo B. A aura epigástrica, muitas vezes relatada pelas crianças com ELT como sensação de "dor abdominal", pode ser mal interpretada, inclusive por médicos, dificultando o diagnóstico precoce da ELT sintomática (Artigo 3). Em relação às crises mioclônicas, nossos dados reforçam a idéia de que essas podem ser manifestações generalizadas de um insulto focal ao sistema nervoso central, ou seja, um padrão de resposta idade-dependente (Artigo 4). Duas crianças com lesão tumoral (ganglioglioma) no lobo temporal esquerdo apresentavam distúrbios de comportamento como agressividade e hiperatividade, os quais pioraram após o procedimento cirúrgico, provavelmente pelo fenômeno da "normalização forçada" (Artigo 5). Atividade epileptiforme temporal foi evidenciada em todos os estudos (Artigos 2, 6 e 7). Entretanto, ocorreu grande porcentagem de atividade epileptiforme extratemporal e generalizada, predominantemente nas crianças mais jovens (Artigo 2). No Artigo 6, comparamos 53 crianças com ELT de diferentes etiologias com 53 adultos com esclerose mesial temporal e o resultado foi maior freqüência de descargas extratemporais nas crianças. Ao compararmos exclusivamente as crianças com esclerose mesial (30 pacientes), com os mesmos pacientes adultos, o resultado foi semelhante, ou seja, presença de maior número de EEG com descargas extratemporais no grupo pediátrico nas áreas frontais, parietais e occipitais. Portanto, crianças com ELT, inclusive quando a etiologia é a esclerose mesial temporal, apresentam maior freqüência de descargas extratemporais interictais do que adultos. Ao compararmos os achados interictais de crianças (16 pacientes) e adultos (12

pacientes) com ELT devido a lesões tumorais, observamos que os dois grupos apresentaram descargas epileptiformes extratemporais, além das descargas temporais, sem relevante diferença estatística. Esse resultado parece estar relacionado com a própria etiologia, já que estudos prévios mostram achados neurofisiológicos pouco localizatórios e falsamente lateralizatórios, tanto em crianças quanto em adultos (Artigo 7). No artigo 8 foram avaliadas 149 crises de 25 pacientes com ELT de difícil controle submetidos à monitorização por vídeo-EEG. Os aspectos analisados foram padrão ictal inicial, atividade ictal rítmica persistente e padrão pós-ictal. A lateralização mostrou-se superior à localização. Entretanto, esses valores foram inferiores aos encontrados na literatura em adultos com ELT mesial.

ABSTRACT

The knowledge of temporal lobe epilepsy (TLE) in childhood has had a great improvement with the clinico-electroencephalographic data obtained in studies with video-EEG monitoring of patients with refractory epilepsy undergoing pre-surgical investigation (Article 1). The objectives of the present study were to determine the clinical, behavioral and neurophysiological (EEG) features of TLE in children. The most frequent etiology in our study was hippocampal atrophy, followed either by dual-pathology or by tumoral lesions (Articles 2 and 6, respectively). In Article 2, we divided the 36 patients studied in groups according to the age range: group A (≤ 6 years) with six patients and group B (> 6 years) with 30 patients. We observed that motor components, myoclonic seizures, behavioral disorders, and delayed speech occurred most frequently in group A. Dystonic posturing and automatisms predominated in patients of group B. Epigastric aura, frequently described by children with TLE as a sensation of "abdominal pain", may be misinterpreted, even by physicians, which make difficult the early diagnosis of symptomatic TLE (Article 3). Regarding myoclonic seizures, our data support the idea that they may be generalized manifestations of a focal insult to the central nervous system and also an age-dependent pattern (Article 4). Two children with tumoral lesions (ganglioglioma) in the left temporal lobe had aggressiveness and hyperactivity wich worsened after the surgical procedure, probably due to the phenomenon of "forced normalization"(Article 5). Temporal epileptiform activity was detected in all the studies (Articles 2, 6 and 7). However, there was a great frequency of extratemporal and generalized epileptiform activity, mainly in younger children (Article 2). In the Article 6, we compared 53 children with TLE of varied etiologies with 53 adults with temporal mesial sclerosis and the result was more frequent extratemporal discharges in children. When we compared children with exclusively mesial sclerosis (30 patients) with the same adult patients, the result was similar, that is, there was a greater number of EEGs with extratemporal discharges in the pediatric group on the frontal, parietal and occipital areas. Therefore, children with TLE, including those with mesial temporal sclerosis as the etiology, present more frequent interictal extratemporal discharges than adults. Comparing the interictal EEG findings of children (16 patients) and adults (12 patients) with TLE caused by tumoral lesions, we observed that both groups presented with extratemporal epileptiform discharges, besides temporal discharges, without statistically significant difference. This result seems to be related to the etiology itself, since

previous studies have shown neurophysiologic findings which were little localizing and falsely lateralizing both in children and in adults (Article 7). In article 8, 149 seizures from 25 patients with medically refractory TLE, which underwent video-EEG monitoring, were analyzed. We analyzed intial ictal pattern, persistent rhythmical ictal activity and post-ictal pattern. The lateralization was superior to the localization. However, our data showed values inferior to those reported in the literature about adults with mesial TLE.

1- INTRODUÇÃO

1.1- Apresentação

As epilepsias do lobo temporal (ELT) em adultos (Blume et al., 2001; Engel, 2001; Fisher et al., 2005), particularmente a ELT mesial, apresentam aspectos clínicos e eletrencefalográficos bem definidos.

Na infância, o assunto começou a ser mais detalhadamente abordado nas séries cirúrgicas nas quais os pacientes eram submetidos à monitorização vídeo-eletrencefalográfica (vídeo-EEG).

Nestes estudos, envolvendo pacientes com diferentes etiologias, principalmente lesões tumorais, malformações do desenvolvimento cortical, esclerose mesial temporal e dupla-patologia, há uma grande diversidade nos aspectos clínicos, com tendência a se encontrarem manifestações clínicas atípicas nas crianças mais jovens, especialmente lactentes, e achados típicos de ELT nas crianças maiores.

Também os aspectos eletrencefalográficos exigem que mais estudos sejam desenvolvidos nessa área e propiciam um amplo campo para pesquisa.

Este trabalho visa o esclarecimento das peculiaridades clínicas e do papel desempenhado pelos registros eletrencefalográficos interictais e ictais na ELT na infância.

1.2- Revisão da Literatura

1.2.1- Epilepsias do Lobo Temporal no Adulto

Definição

ELT é a forma mais comum de epilepsia parcial em adultos, acometendo cerca de 40% dos adultos jovens com epilepsia.

ELT pode ser classificada em três subsíndromes: ELT mesial (medial), ELT lateral (neocortical) (Walczak, 1995; Berkovic et al, 1996) e ELT familiar (Cendes et al., 1998; Kobayashi et al., 2000). A ELT mesial, cuja etiologia mais freqüente é a esclerose

mesial temporal (EMT), apresenta alta prevalência e características clínicas e eletrencefalográficas próprias bem definidas (Gloor, 1991; Engel, 1992; French et al., 1993). A EMT é encontrada em 60 a 70% das autópsias e séries cirúrgicas e é, há décadas, a entidade responsável pela maioria dos procedimentos cirúrgicos (Falconer, 1974). Os pacientes com ELT mesial apresentam, com freqüência, refratariedade às drogas antiepilépticas (DAEs) e têm um bom prognóstico com o tratamento cirúrgico (Jack et al.,1992; Engel et al.,1993b).

A classificação internacional de epilepsia e síndromes epilépticas proposta pela Comissão de Classificação e Terminologia da ILAE (*Comission on Classification and Terminology of the International League Against Epilepsy*, 1989) propõe que o diagnóstico de ELT obedeça aos seguintes critérios:

Características clínicas - crises parciais simples caracterizadas por sintomas autonômicos e/ou psíquicos e certos fenômenos sensoriais, como sintomas olfatórios e auditivos; crises parciais complexas freqüentemente começando com parada da atividade seguida por automatismos oroalimentares e por outros automatismos; os ataques têm duração geralmente superior a um minuto, com confusão pós-ictal, seguidos por amnésia e recuperação gradual.

Características eletrencefalográficas (EEG) – o EEG interictal pode ser normal ou mostrar leve ou acentuada assimetria da atividade de base; espículas, ondas agudas e/ou ondas lentas temporais podem ser uni ou bilaterais, síncronas ou assíncronas. Estes achados nem sempre estão apenas na região temporal. Registros intracranianos podem definir melhor as anormalidades.

Especialistas, segundo encontro promovido pela ILAE (Engel et al., 2002), definiram alguns critérios diagnósticos para a ELT mesial associada a EMT, entre os quais temos que a semiologia das crises é essencial, mas não específica; EEG ictal/interictal com distúrbio epileptiforme localizado na região temporal média ou anterior médio-basal não é essencial e não é específico; além disso, há vários outros critérios que não são essenciais: história de insulto precipitante inicial, história familiar, período latente, período silente, idade de início das crises, alteração de memória, alteração predominantemente unilateral à

tomografia por emissão de pósitron (PET), resistência às DAEs, bom prognóstico pós-operatório e evolução progressiva (pode ser específica); esclerose hipocampal predominantemente unilateral é específica, mas não é essencial.

Exclui-se ELT mesial em adultos quando há aura primariamente sensitiva ou focal motora, atividade epileptiforme extratemporal, alteração cerebral difusa e déficits neurológicos focais (Engel et al., 2002).

ELT lateral com lesão estrutural envolvendo áreas associativas do lobo temporal pode se caracterizar por ilusões/alucinações auditivas ou um bloqueio súbito e precoce da fala ou afasia ictal (lesões na região temporal lateral e superior), alucinações visuais complexas associadas a movimentos (lesões na região temporal posterior e inferior). Quando as crises se propagam rapidamente para a porção medial do lobo temporal, a semiologia pode ser semelhante à da ELT mesial.

Antecedente familiar de crises epilépticas ou de crises febris é fator relevante e bem estabelecido na literatura (Fernandez et al.,1998; Jackson et al.,1998; Engel et al., 2001).

ELT pode ocorrer de forma esporádica (isolada) ou familiar, esta geralmente apresentando modo de herança autossômica dominante com penetrância incompleta (Cendes et al.,1998; Kobayashi et al., 2000).

ELT familiar é uma síndrome descrita recentemente, sendo considerada quando dois ou mais familiares (parentes em primeiro ou segundo graus), preenchem os critérios para ELT. Há duas formas distintas: ELT mesial familiar e ELT lateral familiar (ou epilepsia parcial autossômica dominante com auras auditivas) (Kobayashi et al., 2000). ELT mesial familiar tem características clínicas e EEG semelhantes às dos pacientes sem história familiar de epilepsia. ELT lateral familiar, ligada ao cromossomo 10q, apresenta sintomas como zumbidos e ruídos, alteração da percepção de sons ou linguagem (afasia ictal), EEG com descargas epileptiformes na região temporal posterior e ressonância magnética (RM) normal (Poza et al.,1999; Winawer et al., 2000).

Analisando anormalidades hipocampais em crianças com familiares com ELT familiar, foram encontradas atrofia hipocampal, hipersinal em T2 e outras anormalidades naquelas que tiveram apenas algumas crises ou crise febril única. Estes achados sugerem que estas crianças possam estar num "período silente" da história natural da EMT e que mecanismos genéticos desconhecidos levariam ao desenvolvimento das características patológicas da EMT precocemente, com diferentes graus de expressão (Kobayashi et al., 2001).

ELT noturna corresponde a um grupo de pacientes com baixa freqüência de crises parciais complexas (CPC) que ocorrem exclusiva ou predominantemente durante o sono, ausência de crises agrupadas, raro antecedente familiar de epilepsia, baixa prevalência de crise febril e melhor prognóstico cirúrgico quando comparada às outras formas de ELT (Bernasconi et al., 1998).

Aspectos Clínicos no Adulto

ELT mesial apresenta características específicas que obedecem a uma ordem seqüencial: crises parciais simples (CPS), algumas vezes seguidas por CPC. Ocorrem também crises tônico-clônicas secundariamente generalizadas (CTCGS) que são facilmente controladas na vida adulta. O evento ictal inicial pode ser CPC ou crise tônico-clônica generalizada (CTCG), geralmente febril prolongada, que após um "período silente" durante a puberdade e adolescência reaparece no início da vida adulta (Engel, 1992; Engel, 1993a; French et al., 1993).

Na ELT, as CPS ou auras são referidas pela maioria dos pacientes. A mais freqüente delas é a aura epigástrica, que se caracteriza por sensações abdominais ou no tórax inferior, sugerindo origem nas estruturas mesiais (Henkel et al., 2002). As auras psíquicas são fenômenos experienciais, dismnésicos (*déjà vu e entendu vecu, jamais vu e entendu vecu*), ilusórios, alucinatórios e cognitivos (como despersonalização), por estimulação de estruturas límbicas e neocorticais do lobo temporal. Aura emocional, como a sensação de medo, pode preceder, acompanhar ou seguir outros fenômenos e sugere envolvimento amigdaliano. As auras citadas acima apresentam valor localizatório no lobo temporal (Dantas & Yacubian, 2001).

Auras cefálicas, somatossensitivas, auditivas, vertiginosas, olfativas, gustativas e sexuais também podem estar presentes em pacientes com ELT (Dantas & Yacubian, 2001). As auras auditivas e vertiginosas são sugestivas de ELT neocortical (Walczak, 1995).

Um número reduzido de pacientes (apenas 14%) refere auras precedendo as CPC durante o registro vídeo-EEG, provavelmente devido à redução nas doses das DAEs (Dantas & Yacubian, 2001).

As CPC caracterizam-se por reação de parada de atividade, automatismos oroalimentares e manuais simples ou complexos, com duração superior a um minuto (Kotagal et al., 1989; Steinhoff et al., 1998). Os automatismos manuais são, geralmente, ipsilaterais à zona epileptogênica e, às vezes, bilaterais. A postura distônica do membro contralateral tem importante valor lateralizatório, decorrendo do envolvimento dos gânglios da base e da área motora suplementar. Paresia ictal contralateral também tem sido relatada em CPC (Oistreich et al., 1995). O ato de “esfregar o nariz com a mão” foi detectado em pacientes com ELT, geralmente como manifestação pós-ictal, e tem valor lateralizatório ipsilateral (Leutmezer et al., 1998). Versão cefálica contralateral não é considerada lateralizatória.

Crises do lobo temporal esquerdo (quando hemisfério cerebral esquerdo é dominante para linquagem) apresentam disfasia e dislexia pós-ictais mais prolongadas e do lobo temporal direito podem cursar com fala ictal (Steinhoff et al., 1998). Pode haver exacerbação das crises após estresse emocional, privação de sono e próximo ao período menstrual (French et al., 1993; Jorge, 1999). Ao exame neurológico podemos encontrar assimetria de expressão facial espontânea contralateral e déficit de memória (Jones-Gotman et al., 1991; Cascino et al., 1993).

Têm sido descritas algumas manifestações não usuais em adultos com ELT mesial com comprometimento do hemisfério não-dominante (direito), tais como: automatismos de “beijo afetivo” (Mikati et al., 2005) e um novo sinal clínico denominado “*hush sign*” que é a movimentação repetitiva do índex direito na boca enquanto enruga os lábios durante CPC (Kutlu et al., 2005).

Adultos com ELT, especialmente a EMT, apresentam uma série de distúrbios comportamentais e neuropsicológicos próprios da síndrome e, muitas vezes, agravados pela refratariedade medicamentosa (elevado número de crises e politerapia). São classicamente descritos e comprovados pelos testes neuropsicológicos os comprometimentos seletivos das funções de memória (Hermann et al., 1997). Ocorrem também depressão, agressividade e pseudocrise.

Segundo o modelo de memória material específica, déficit de memória verbal se correlaciona com comprometimento do hipocampo de lobo temporal do hemisfério dominante para a linguagem (geralmente o esquerdo) e o de memória vísuo-espacial com lesão no lobo temporal do hemisfério não-dominante (geralmente o direito) (Novelly et al., 1984). Estudos mais recentes sobre cirurgia de epilepsia demonstraram que a relação entre EMT e as funções de memória são mais evidentes quando a lesão ocorre no hemisfério cerebral esquerdo (memória verbal comprometida) do que no direito (Novelly et al., 1990; Hermann et al., 1997; Alessio et al., 2004).

Os pacientes com epilepsia de difícil controle freqüentemente apresentam comorbidades psiquiátricas, tais como surtos psicóticos, antecedentes de psicose pós-ictal e efeitos adversos com as DAEs, beneficiando-se com suporte psiquiátrico adequado antes da realização do tratamento cirúrgico (Savard & Manchanda, 2000).

Aspectos EEG no Adulto

As anormalidades eletrencefalográficas interictais e ictais definem a localização da zona epileptogênica.

Pacientes com EMT têm EEGs interictais e ictais típicos, que são expressão da localização do foco epileptogênico na região temporal mesial. EEGs com registro de superfície mostram atividade epileptiforme (espículas e ondas agudas) na região temporal anterior-médio-basal (F_7/F_8, T_3/T_4), principalmente nos eletrodos zigomáticos (Z_1/Z_2), esfenoidais ou nasofaríngeos.

A lateralização da atividade epileptiforme interictal é considerada quando há um predomínio de 90% das descargas em um lobo temporal (Chung et al., 1991; Gambardella et al., 1995a; Gilliam et al., 1997a). Na ELT, EEGs interictais que apresentam

anormalidades epileptiformes, atividade delta rítmica intermitente e trens de atividade delta polimórfica máxima nos eletrodos F7/F8 ou T3/T4, são considerados adequados para a localização (Gambardella et al., 1995b; Gilliam et al., 1997a).

Williamson et al. (1993) encontraram anormalidades paroxísticas em 96% de uma série de 64 pacientes com ELT mesial durante monitorização prolongada, sendo a localização na região temporal anterior em 94%. Atividade paroxística interictal bilateral independente ocorreu em 42% dos pacientes com predomínio no sítio de origem da crise em metade deles.

Atividade interictal não epileptiforme (ondas delta) na região temporal tem sido descrita em 30 a 90% dos pacientes com ELT, podendo apresentar-se como atividade delta rítmica intermitente temporal (TIRDA) ou atividade delta polimórfica intermitente temporal (TIPDA). A presença de TIPDA foi encontrada em 20% dos pacientes com epilepsia extratemporal sugerindo cautela no seu uso como valor localizatório na avaliação pré-cirúrgica de ELT, sendo considerada porém, como um bom indicador lateralizatório. A presença de TIRDA é altamente específica e indicativa de crises no lobo temporal, podendo ser usada como valor lateralizatório na ELT (Gambardella et al., 1995b; Geyer et al., 1999). A presença de atividade epileptiforme (espículas e ondas agudas) e não epileptiforme (ondas delta) sugere que a região do cérebro responsável pelas descargas epilépticas também possa produzir ondas lentas patológicas no EEG de superfície.

A presença de bissincronia secundária (surtos de espícula-onda generalizados) relaciona-se à idade e o significado clínico é a tendência em haver crises generalizadas em idade precoce, não diminuindo a eficácia da lobectomia temporal no controle das crises (Sadler & Blume, 1989).

Em adultos com ELT, a realização de EEGs interictais seriados é necessária para lateralização do foco epileptogênico. Se o paciente tem EEGs interictais com descargas epileptiformes unilaterais concordantes com dados clínicos e de neuroimagem, a monitorização vídeo-EEG para registro de crises pode ser desnecessária (Barry et al., 1992; Holmes et al., 1996; Pataraia et al., 1998; Cendes et al., 2000). A sensibilidade do EEG interictal tem variado de 25 a 95% (Steinhoff et al.,1998).

Um estudo correlacionando padrões eletrencefalográficos pré-cirúrgicos e o seguimento após lobectomia temporal anterior demonstrou que os melhores resultados foram obtidos nos pacientes com espículas temporais unilaterais em EEG interictal de superfície. O grupo com EEGs interictais com espículas temporais bilaterais também obteve melhora com tratamento cirúrgico (76% de melhora). Porém, os pacientes com espículas interictais com propagação extratemporal, mesmo que unilateralmente, tiveram uma pior resposta, sendo que só um terço dos pacientes melhoraram, mesmo com monitorização intracraniana prévia (Barry et al., 1992).

Estudo recente realizado por Cendes et al. (2000), envolvendo 170 pacientes com EMT, demonstrou concordância relevante entre EEGs interictais e ictais. Houve apenas 3% de discordância entre o EEG interictal e o ictal quanto à lateralização. Em 92% dos pacientes o EEG interictal e ictal concordaram na lateralização, demonstrando então a importância da realização de EEGs interictais seriados (neste estudo, foram realizados, em média, 5 exames por paciente).

O método neurofisiológico mais seguro para localização e lateralização do foco epileptogênico é o registro ictal. A análise do EEG ictal na ELT envolve vários aspectos, tais como a morfologia da descarga ictal, seu padrão inicial, duração, localização e lateralização. O padrão ictal inicial mais freqüente é a atividade teta rítmica, sendo observada também atividade delta ou alfa rítmica, ou ainda espículas rítmicas. Alteração do padrão inicial com duração $\geq$ 3s foi definido como primeira mudança ictal inequívoca (Pataraia et al., 1998). A atividade teta rítmica muitas vezes ocorre 10 a 20 segundos após o início ictal (Walczak et al., 1992).

A localização pode ser temporal, regional, hemisférica, bilateral lateralizada ou não. Atividade rítmica ictal e ondas lentas pós-ictais são consideradas lateralizatórias quando apresentam uma amplitude duas vezes maior em um hemisfério em relação ao outro. A atenuação pré- e/ou pós-ictal também precisa ter metade da amplitude do registro do hemisfério contralateral para ser considerada lateralizatória (Walczack et al., 1992).

O início eletrográfico focal de uma crise tipicamente evolui da seguinte maneira: (I) atenuação focal da atividade do EEG; (II) descarga rítmica rápida focal e de baixa-amplitude; e (III) aumento progressivo da amplitude com lentificação, que se propaga para uma distribuição anatômica regional (Chabolla & Cascino, 2001).

1.2.2- Epilepsias do Lobo Temporal na Infância

Histórico

Estudos clínico-eletrencefalográficos sobre ELT em crianças vêm sendo realizados desde 1960 (Chao et al., 1962).

Na década anterior, havia sido relatada a presença de "crises psicomotoras" na infância (Glaser & Dixon, 1956). Este termo englobava síndromes epilépticas benignas da infância, as quais foram posteriormente separadas em idiopáticas e sintomáticas, isto é, epilepsia benigna da infância e ELT (Ounsted et al., 1966).

A síndrome da "Epilepsia Psicomotora Benigna" da infância proposta por Dalla Bernardina et al. (1985) não foi universalmente aceita porque incluía achados clínicos de epilepsia benigna com paroxismos centro-temporais, ELT sintomática e terror noturno. Recentemente, os autores concluíram que se tratava de apresentação atípica da epilepsia benigna com paroxismos centro-temporais (Dalla Bernardina et al., 1992).

Harvey et al. (1997) estudando aspectos clínicos, EEG e de neuroimagem de 63 crianças com ELT recém-diagnosticada, classificaram de acordo com a etiologia em três grupos: ELT com alterações do desenvolvimento (disgenesia cortical, cisto aracnóide ou tumor de baixo grau), ELT com EMT/antecedentes significantes (crise febril complicada, trauma crânio-encefálico ou meningoencefalite) e ELT criptogênica. Este último grupo apresentou melhor prognóstico das crises e dos problemas psicológicos (comportamentais), podendo representar uma síndrome benigna da ELT.

Embora, desde a década de 1960, haja descrições sobre os aspectos clínicos, eletrencefalográficos e anátomo-patológicos da ELT na infância decorrentes de séries de pacientes submetidos à investigação pré-cirúrgica, foi na década de 1990 que apareceram

os grandes avanços devido à monitorização vídeo-EEG prolongada (Duchowny et al.,1992; Wyllie et al.,1993; Brockhaus & Elger,1995; Blume et al.,1997b).

Etiologia

Os exames de neuroimagem, especialmente RM são fundamentais para o diagnóstico etiológico da ELT. A introdução de novas técnicas para avaliação da causa e origem da epilepsia, tais como RM, vídeo-EEG com monitorização prolongada, técnicas funcionais de imagem como tomografia por emissão de fóton único (SPECT), RM com espectroscopia e volumetria e RM funcional vem aumentando progressivamente a capacidade de investigação neurológica e ajudando a localizar a origem da epilepsia em casos lesionais (Cendes et al.,1993a; Cendes et al.,1993b; Cendes et al.,1993d; Harvey, 1993; Harvey et al., 1999) e principalmente "não lesionais" (Berkovick et al.,1991; Kuzniecky et al.,1993). Tais técnicas têm permitido a definição precisa de lesões epileptogênicas e têm revelado a presença de anormalidades não reconhecidas previamente, tais como displasias corticais e tumores do desenvolvimento. Têm também permitido a visualização e apreciação do papel da atrofia hipocampal (AH) como causa de ELT, a qual é facilmente reconhecida e de excelente prognóstico cirúrgico (Cendes et al.,1993c; Cendes et al.,1997). Todas essas descobertas têm aumentado consideravelmente o diagnóstico etiológico preciso e o domínio da terapêutica cirúrgica para epilepsia na infância.

Em crianças, as causas mais freqüentes de ELT são os tumores de baixo grau de desenvolvimento, as malformações do desenvolvimento cortical, a EMT e dupla-patologia (presença de uma lesão extrahipocampal além da EMT). Embora a EMT seja a causa mais freqüente de ELT no adulto, na infância não há consenso sobre sua verdadeira incidência.

Estudo recente (Sztriha et al., 2002), procurando caracterizar a incidência e a etiologia da ELT em 30 crianças recém-diagnosticadas, encontrou ELT com alteração do desenvolvimento em oito crianças, ELT com EMT/antecedentes significantes em sete e ELT criptogênica em 15 delas (50%).

A EMT apresenta incidência de 10 a 20% em crianças submetidas ao tratamento cirúrgico na segunda metade da primeira década de vida e é considerada rara em crianças menores de cinco anos (Wyllie et al.,1993; Brockhaus & Elger, 1995; Bourgeois,

1998). Por outro lado, é a etiologia mais freqüente em alguns estudos, chegando a 70% dos casos de ELT (Mizrahi et al., 1990). Num trabalho com 53 crianças de dois a 17 anos (média de 10 anos), a RM mostrou a presença de EMT em 57% da casuística levando os autores a afirmarem ser a EMT a lesão mais comum em crianças com ELT refratária e que esta é subdiagnosticada nesta faixa etária, retardando o procedimento cirúrgico (Grattan-Smith et al., 1993).

A EMT tem sido correlacionada com antecedentes pregressos de crise febril complicada (Kuks et al., 1993). Entende-se por crise febril complicada uma crise prolongada (com duração superior a 15 minutos), ou que se repita em 24 horas, ou que seja focal (lateralizada) (Van Landingham et al., 1998). Pode estar presente em cerca de 43% dos pacientes com EMT (Pedreira, 1998). Apesar da elevada incidência de crises febris complicadas (ou complexas) em pacientes com EMT, não está bem definido se a crise febril é um fator causal ou um epifenômeno da EMT (Berg et al., 2001; Cendes, 2004). ELT devido a EMT pode apresentar pico trimodal de início da epilepsia (Janszky et al., 2004). No grupo com idade de início da epilepsia na adolescência (idade média: 15,34 anos), história familiar de epilepsia foi mais freqüente e as crises febris complexas ocorreram mais precocemente que no grupo cuja idade de início das crises foi na infância (idade média: 5,43 anos) (Janszky et al.,2004). Para outros autores (Tarkka et al., 2003), EMT após crise febril complicada é um evento incomum, confirmando a boa evolução de crise febril.

Os tumores de baixo grau mais freqüentemente encontrados na ELT na infância são os tumores neuronais ou glioneurais [ganglioneuroma, ganglioglioma, gangliocitoma, tumores neuroepiteliais disembrioplásticos (DNET)], os oligodendrogliomas e os astrocitomas de baixo grau. Os gangliogliomas e gangliocitomas são lesões gliais mistas, tendo este último predomínio do componente neuronal. Os gangliogliomas são os principais tumores responsáveis por epilepsia de difícil controle medicamentoso que se iniciam antes dos 15 anos de idade (Sutton et al., 1983). Apresentam morfologias bastante variáveis à RM (Tampieri et al., 1991). A lesionectomia completa é considerada curativa (Johannsson et al., 1981). O crescimento e os achados histológicos sugerem que estes tumores, principalmente os gangliogliomas e DNET, poderiam se originar de uma

malformação cortical ou ser o espectro final das displasias corticais (Prayson et al., 1993; Shimbo et al., 1997; Coimbra, 2002). Os DNET ocorrem principalmente nas estruturas mesiais do lobo temporal. São intracorticais, bem circunscritos, multinodulares e histologicamente não há consenso se os neurônios que o constituem são neoplásicos, malformados ou displásicos. Caracterizam-se, clinicamente, por CPC refratárias de início na infância (Pedreira,1998). O xantoastrocitoma pleomórfico é raro e acomete adolescentes e adultos jovens (Harvey et al., 1997). Os oligodendrogliomas são tumores infiltrativos que, em crianças, tem uma incidência de 7 a 14% (Wyllie et al., 1993; Brockhaus & Elger, 1995).

A displasia cortical focal foi primeiramente descrita no lobo temporal (Taylor et al., 1971) e é considerada por alguns autores como a causa mais freqüente de ELT refratária em crianças (Duchowny et al., 1992; Duchowny et al., 1995; Bocti et al., 2003). Atualmente, sabe-se que o lobo temporal não é seu local preferencial (Palmini et al., 1991). Achados neuropatológicos compatíveis com displasia cortical foram encontrados em 21 (64%) de 33 dos espécimes cirúrgicos de crianças com ELT refratária (Porter et al., 2003).

Patologia dupla (*dual pathology*) tem se destacado em estudos recentes de crianças com ELT submetidas ao procedimento cirúrgico. Mohamed et al. (2001) estudaram 17 crianças e 17 adolescentes com ELT, encontrando anormalidades no neocórtex temporal ipsilateral à EMT em todas as crianças e em 60% dos adolescentes. A comprovação histopatológica de dupla-patologia com achados de displasia cortical leve a moderada ocorreu em 79% dos pacientes. Bocti et al. (2003) encontraram displasia cortical no neocórtex temporal associada à EMT em sete de 12 hipocampos analisados, de 22 crianças submetidas à lobectomia temporal anterior para tratamento de ELT refratária, numa revisão anátomo-patológica de 20 anos.

Outras lesões ainda podem estar associadas à ELT como as malformações vasculares (MAV e angioma cavernoso), neurocisticercose e meningoencefalites, como a encefalite herpética.

Aspectos Clínicos da ELT na Infância

O conhecimento do quadro clínico da ELT em crianças teve grande impulso a partir de 1990, em estudos de séries de pacientes submetidos à monitorização vídeo-EEG e avanços de neuroimagem para tratamento cirúrgico. Estas séries mostraram enorme diversidade clínico-eletrencefalográfica.

Problemas no diagnóstico clínico da ELT em crianças foram levantados por Davidson & Falconer (1975), que descreveram três aspectos principais: dificuldade em descrever as auras (muitas vezes mal interpretadas pela família), gravidade clínica variável em diferentes estágios da vida, perda do seguimento na adolescência e a difícil interpretação do EEG da criança. Tais questões até recentemente permaneciam obscuras em crianças menores (Wyllie, 1995).

Em lactentes, a identificação da perda da consciência e, portanto, a definição de CPC é mais difícil. Achados sugestivos de CPC em lactentes são: parada da atividade com possível comprometimento da consciência, aura não detectada, automatismos discretos e principalmente orofaciais, maior quantidade de CTCGS e crises mais prolongadas (mais de um minuto de duração). Também ocorrem freqüentemente espasmos infantis e crises generalizadas, tipo mioclônicas (Bourgeois, 1998; Franzon et al., 2004; Franzon et al, 2005).

Dentre as principais séries, Duchowny et al. (1992) analisaram 16 crianças menores de 12 anos operadas precocemente e descreveram uma tríade clássica: olhar fixo com parada de atividade, fenômenos motores e automatismos comportamentais.

Wyllie et al. (1993) estudaram 14 crianças, também menores de 12 anos, encontrando auras em quase todas. A sensação abdominal ou gustativa foi vista nos pacientes com EMT, automatismos oromandibulares em todos e gestuais menos complexos nos mais jovens, e postura distônica em metade dos pacientes com EMT. Alguns apresentaram náusea, esforço para vomitar, gemido rítmico e extensão tônica bilateral dos membros.

Brockhaus & Elger (1995) descreveram 29 crianças menores de 16 anos, subdivididas em pré-escolares (18 meses a seis anos), escolares (7 a 12 anos) e adolescentes (13 a 16 anos). Nos pré-escolares (seis pacientes), o sintoma ictal inicial mais freqüente foi reação de despertar e as alterações motoras se destacaram com apresentação variável: movimentos tônicos ou clônicos simétricos, fenômenos atônicos como queda da cabeça, espasmos infantis, automatismos simples seguidos por movimentos versivos e postura distônica. Hipermotricidade e posturas similares às das crises do lobo frontal em adultos também estiveram presentes. Nos demais grupos, os achados foram semelhantes aos de adultos, sendo os automatismos progressivamente mais complexos de acordo com a faixa etária, as alterações motoras sendo predominantemente assimétricas, unilaterais ou bilaterais, com movimentos tônicos e/ou clônicos, postura distônica e CTCGS.

Blume et al. (1997a), estudando 14 crianças de dois a 12 anos, encontraram CPS em quase todas (medo, sensação abdominal ou aura cefálica) e automatismos em 12 delas (oroalimentares, gestuais e ambulatoriais). Fenômenos motores tônicos ou clônicos foram vistos em 12 crianças e CTCG em seis delas. A idade média de início foi de dois anos e seis meses e da avaliação pré-operatória foi de seis anos. As CPC também em crianças raramente cedem espontaneamente e freqüentemente são refratárias ao tratamento clínico.

Em nosso meio, foram estudadas 34 crianças menores de 16 anos com ELT (Pedreira,1998), subdivididas em três grupos segundo a etiologia: lesões neocorticais (16 pacientes), EMT (16 pacientes) e dupla-patologia (dois pacientes). As auras (CPS), predominantemente sensação epigástrica ascendente, foram referidas por 61,76% dos pacientes e em apenas 38,10% durante registros vídeo-EEG. O grupo com EMT apresentou aura epigástrica em 77% da casuística, valor estatisticamente significativo em relação ao grupo com lesões neocorticais (18%). As CPC apresentaram duração mais prolongada (estatisticamente significante) no grupo com EMT (78,2 segundos), sendo os valores inferiores aos encontrados em adultos.

Nordli et al. (2001) estudaram a ontogenia de crises parciais em 123 pacientes (lactentes e crianças jovens) e concluíram que existem diferenças importantes na expressão clínica de crises epilépticas entre crianças e adultos. As crises mioclônicas, clônus

assimétrico e postura tônica simétrica diminuíram com o avançar da idade. Por outro lado, a não-responsividade aumentou após os dois anos e auras, postura distônica e generalização secundária aumentaram após os seis anos de idade.

Fogarasi et al. (2002) também demonstraram uma correlação linear inversa das manifestações motoras e comportamentais com a idade, através da monitorização vídeo-EEG de 15 crianças de 11 a 70 meses. Todos os pacientes menores de 42 meses de idade apresentaram componentes tônicos e mioclônicos e espasmos epilépticos. Crises hipomotoras (parada súbita da atividade) e/ou automotoras (alteração do comportamento com automatismos orais ou manuais) ocorreram em quase metade dos pacientes com mais de 42 meses (cinco de 11).

Epilepsia tem freqüentemente impacto negativo sobre as funções cognitivas e comportamentais na vida diária da criança (Camfield & Camfield, 1994). O comprometimento cognitivo é uma comorbidade psicossocial importante em crianças com epilepsia, dependendo de vários fatores como idade de início das crises, tempo de evolução da epilepsia, síndrome epiléptica, freqüência de crises e politerapia medicamentosa (Nolan et al., 2003). Pacientes com início das crises epilépticas na infância têm, a longo prazo, maior risco de problemas sociais e educacionais (Sillanpää et al.,1998).

Lindsay et al. (1979) citaram alguns fatores adversos que comprometem o desempenho social da criança com ELT como QI menor que 90, necessidade de escola especial, início das crises antes dos dois anos, CPC diárias, cinco ou mais CTCG e síndrome hipercinética. Wyllie et al., em 1993, encontraram deficiência mental leve ou inteligência limítrofe em um terço dos pacientes. Dentre as principais séries cirúrgicas, Duchowny et al. (1992) encontraram que o distúrbio do déficit de atenção com ou sem hiperatividade foi o mais evidente problema clínico (75% dos casos) associado à epilepsia.

Transtornos globais do desenvolvimento que consistem em comprometimento na linguagem, do contato social e do comportamento, como estereotipias e restrito foco de interesse, foram encontrados em crianças com ELT após cirurgia (Szabó et al., 1998; Szabó et al., 1999).

Psicose e piora de distúrbios comportamentais após a ressecção de ganglioglioma ou DNET também têm sido relatadas na literatura em adultos e em crianças e os autores propuseram que este fato possa decorrer de "normalização forçada" (Andermann et al., 1999; Guimarães et al., 2004).

Devido ao comprometimento do sistema límbico, as crianças com ELT estão suscetíveis a desordens comportamentais específicas como déficit de atenção com ou sem hiperatividade e alterações de linguagem. A atenção é uma função neurológica complexa que depende de estruturas anatômicas envolvendo o tronco cerebral, córtex e sistema límbico, além de neurotransmissores como a dopamina e noradrenalina. A capacidade de atenção é idade-dependente de acordo com a maturidade e os interesses, ou seja, de acordo com a atenção e intenção seletivas diferentes (Kandel et al., 1997).

Em crianças com ELT, durante a avaliação pré-operatória, neuropsicólogos têm descrito desordens comportamentais específicas como déficit de atenção, com ou sem hiperatividade, e alterações de linguagem (Franzon et al., 2004; Guimarães et al., 2004).

Em relação às funções neuropsicológicas em crianças com ELT, déficits de memória também são relatados. Alguns reportaram prejuízos específicos de acordo com a especialização hemisférica (Cohen, 1992; Jambaquè et al., 1993; Schoenfeld et al., 1999). Essas alterações correspondem ao padrão clássico de memória material específica relatado em adultos, ou seja, que a memória verbal está comprometida em crianças com ELT esquerda e a memória visual naquelas com ELT direita.

Outros estudos não encontraram déficits de memória material específica (Camfield et al., 1984; Adams et al., 1990; Hershey et al., 1998; Bigel e Smith, 2001). Lendt et al (1990) não identificaram déficits de memória, mas prejuízos da atenção e linguagem, principalmente em ELT à esquerda. A relação entre a lateralização da lesão e o desempenho nos testes de memória permanece não definida (Lendt et al., 1999; Gleissner et al., 2002).

Os efeitos de variáveis como freqüência de crises, neuropatologia, idade de início e duração da epilepsia nas funções neuropsicológicas também não estão estabelecidos (Camfield et al., 1984; Jambaquè et al., 1993; Lendt et al., 1999).

Estudo correlacionando neuropatologia (EMT, tumor e dupla patologia) mostrou pior desempenho nos testes de memória no grupo com dupla patologia e sem diferenças significativas entre os grupos com EMT e tumor (Bigel e Smith, 2001).

Entre os estudos existe maior concordância quanto à influência negativa da duração da epilepsia nas funções cognitivas (Jambaquè et al., 1993; Lendt et al., 1999; Nolan et al., 2004).

Em relação ao procedimento cirúrgico, dois estudos atuais relataram que três meses após, há associação entre diminuição da memória verbal e ressecção à esquerda. Porém após um ano da cirurgia, o declínio da memória verbal mostrou uma recuperação significativa, inclusive quando comparado com os resultados em adultos (Gleissner et al. 2002; Gleissner et al., 2005). Para os autores, esses achados podem estar relacionados à plasticidade neuronal do cérebro imaturo.

O campo das funções neuropsicológicas em ELT na infância precisa ser melhor esclarecido (Szabó et al., 1998).

EEG Interictal e Ictal na Infância

O registro eletrográfico associado a crises clinicamente típicas é a melhor maneira de se detectar o foco epileptogênico em ELT (Blume & Kaibara, 1991).

Crises parciais refratárias são, na maioria das vezes, causadas por anormalidade estrutural do cérebro. A área epileptogênica, porém, pode estar na vizinhança da lesão, não sendo a sua distribuição anatômica necessariamente congruente com a anormalidade estrutural (Blume & Kaibara, 1991).

Atividade epileptiforme focal (espículas e ondas agudas) é o achado eletrencefalográfico específico mais comumente correlacionado a crises parciais em registros pré-cirúrgicos seriados de EEGs de superfície. Espículas focais são apenas indicadores presuntivos de origem das crises e para confirmação do valor estes dados devem ser corroborados pela descrição clínica, registro ictal, anormalidades da atividade de base (delta) e achados de neuroimagem (Blume & Kaibara, 1991).

Atividade delta polimórfica focal persistente sugere uma associação com lesão cortical destrutiva também em crianças e corresponde freqüentemente ao sítio cirúrgico (Blume & Kaibara, 1991).

Duchowny et al. (1992), estudando crianças menores de 12 anos com uso rotineiro de eletrodos esfenoidais, não demonstraram diferenças na capacidade de localização da origem das crises nesta faixa etária.

Wyllie et al. (1993), estudando 14 crianças também menores de 12 anos, subdividiram-nas de acordo com a etiologia. Nos grupos com EMT e displasia cortical os achados EEGs interictais e ictais foram semelhantes aos de adolescentes e adultos, com exceção de um paciente de seis anos de idade, que teve algumas descargas epileptiformes generalizadas. No grupo com lesão tumoral, entretanto, todas as crianças apresentaram achados EEGs interictais atípicos como atividade epileptiforme extratemporal ou temporal contralateral. A atividade ictal, portanto, apresentou padrão eletrencefalográfico pobremente localizatório ou falsamente lateralizatório no início das crises. Como estas crianças apresentaram boa evolução pós-operatória concluiu-se que este padrão EEG em tumores possa ser correlacionado com idade e etiologia. Os resultados sugerem que eletrodos invasivos parecem não ser importantes na avaliação pré-operatória de crianças com tumores do lobo temporal, sendo o uso indicado apenas quando estudos da localização funcional extratemporal são necessários.

Para outros autores (Brockhaus & Elger, 1995), no entanto, a expressão EEG da ELT em crianças foi idade-dependente e os achados de EEGs foram subdivididos de acordo com a faixa etária. No grupo de pré-escolares (menores de seis anos), predominaram descargas generalizadas e, em crianças maiores de seis anos, os registros ictais e eletrocorticográficos mostraram ondas agudas ou teta rítmicas, focais, predominantemente sobre a região temporal. Nos pacientes com movimentos tônicos ou clônicos, houve propagação da atividade ictal para regiões extratemporais e para o hemisfério contralateral. Concluindo, crianças menores, mesmo tendo comportamentos ictais atípicos, devem ir para a avaliação pré-cirúrgica.

Blume et al. (1997a) analisaram os resultados de lobectomia temporal em 14 crianças menores de 12 anos com crises parciais clinicamente típicas, e encontraram espículas ativas interictais no lobo temporal epileptogênico em 13 pacientes (93%), não havendo sinais falsamente lateralizatórios. Tais resultados sugeriram não haver necessidade de monitorização invasiva. Foram encontrados também paroxismos epileptiformes generalizados em seis pacientes (43%) e atividade delta polimórfica persistente sobre o lobo temporal epileptogênico em nove pacientes (64%). Estes achados, portanto, parecem ser semelhantes aos encontrados em adultos, exceto pela grande porcentagem de atividade epileptiforme generalizada.

O registro ictal de 21 pacientes submetidos à monitorização invasiva a longo prazo mostrou como padrão inicial mais freqüente, a presença de atividade beta de baixa amplitude intracraniana seguida por ritmo teta mais lento, registrado simultaneamente no local de início e áreas adjacentes. A propagação tendeu a ocorrer para o lobo frontal ipsilateral primeiramente e depois para o lobo temporal contralateral via comissura hipocampal. A única diferença entre o grupo menor de 14 anos (oito pacientes) e o maior de 18 anos (13 pacientes) foi a maior tendência das crises ficarem restritas ao lobo temporal e a menor tendência à generalização secundária, no primeiro grupo (Kramer et al., 1998).

No estudo de Pedreira (1998), envolvendo 34 pacientes com ELT sintomática, verificou-se que o registro interictal permitiu a localização da lesão em 41,75% dos pacientes do grupo com lesão neocortical e em praticamente o dobro (81,25%) dos pacientes com EMT. As alterações EEGs ictais lateralizaram a lesão nos dois grupos de forma equivalente (66,67% e 68,75%, respectivamente). A localização no lobo temporal ipsilateral, porém, foi maior no grupo com EMT (43,75%) do que no grupo com lesões neocorticais (14,28%). A atividade rítmica ictal por 30 segundos permitiu a localização da lesão epileptogênica em 71,42% e 92,80% dos pacientes dos grupos com lesões neocorticais e EMT, respectivamente, tendo, portanto, maior valor localizatório do que as alterações ictais iniciais.

Ebner (1999), ao comparar os achados de EEGs de 16 crianças versus 50 adultos com EMT, notou que todas as crianças (100%) apresentaram ondas lentas intermitentes ipsilaterais à EMT, enquanto 68% dos adultos as apresentaram exclusiva ou

predominantemente no lobo temporal ipsilateral. As descargas epileptiformes nos adultos foram máximas sobre o lobo temporal enquanto 37,5% das crianças tiveram atividade máxima nos eletrodos extratemporais (31,25% ipsilateral e 6,25% contralateral), além de atividade generalizada (12,5%). As descargas ictais foram bem mais localizadas e restritas no lobo temporal de adultos (58%) do que no grupo pediátrico (18,75%), havendo predomínio de descargas extratemporais (81,25%) associadas às crises temporais regionais no último grupo. Nenhuma crise na população pediátrica foi registrada no hemisfério contralateral.

Cirurgia

A cirurgia de epilepsia na infância, que tem tido grande impulso na última década, é para muitas formas de epilepsias refratárias a melhor, se não a única, opção terapêutica (Davidson et al.,1972; Mizrahi et al.,1990; Wyllie et al.,1998). Este procedimento permite o controle das crises epilépticas e conseqüentemente a redução medicamentosa, reduzindo os efeitos indesejáveis das DAEs que podem também afetar o comportamento e a cognição (Bourgeois,1988; Britton et al.,1994; O'Brien et al.,1996). O tratamento cirúrgico tem indicação em crianças mesmo com deficiência mental ou distúrbio de comportamento, pois o controle parcial ou modificação do tipo de crise pode melhorar a qualidade de vida (Adams et al.,1990; Guerreiro et al.,1994; Da Costa & Guerreiro, 2000).

Lobectomia temporal em crianças com ELT refratária vem sendo especificamente relatada na literatura (Falconer,1972; Meyer et al.,1986; Adelson et al., 1992; Fish et al.,1993; Duchowny et al.,1995; Goldstein et al.,1996; Hopkins et al.,1997).

Blume et al. (1997b) revisaram vários estudos da literatura totalizando 309 crianças e adolescentes com seguimento por um ano no pós-operatório e concluíram que a eficácia em eliminar ou reduzir as crises variou de 73 a 100% dos casos.

Na série de 40 crianças submetidas à cirurgia por ELT e descritas por Davidson & Falconer (1975), os melhores resultados cirúrgicos quanto ao controle das crises e também o comportamento, foram obtidos quando EMT era a lesão encontrada à cirurgia. A lobectomia temporal realizada mais precocemente evita que o paciente apresente distúrbios comportamentais na idade adulta, com repercussões na vida familiar e social, além de distúrbio cognitivo.

2- OBJETIVOS

Geral

Determinar os aspectos clínicos, comportamentais e neurofisiológicos (EEGs) em crianças com ELT.

Específicos de cada Artigo (Capítulos)

Artigo 1: Revisar a literatura sobre ELT na infância.

Artigo 2: Avaliar as características clínicas e EEGs da ELT na infância.

Artigo 3: Apresentar um caso clínico de dor abdominal (aura) devido à síndrome epiléptica parcial.

Artigo 4: Relatar dois pacientes com crises mioclônicas e ELT.

Artigo 5: Descrever os distúrbios comportamentais em duas crianças com ELT devido a ganglioglioma.

Artigo 6: Interpretar os achados do EEG interictal em crianças com ELT e verificar a presença de descargas epileptiformes extratemporais.

Artigo 7: Avaliar e comparar o padrão de EEG interictal em crianças e adultos com ELT devido às lesões tumorais.

Artigo 8: Avaliar os achados ictais em crianças com ELT.

3- MÉTODOS

ASPECTOS ÉTICOS DA PESQUISA

Este estudo foi aprovado pelo Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da Unicamp (Anexo 1).

O estudo oferece riscos mínimos aos pacientes e a maioria dos exames contribui de maneira absoluta na investigação diagnóstica, algumas vezes para instituição da terapêutica cirúrgica.

Todos os indivíduos participantes e seus pais ou responsáveis foram devidamente esclarecidos quanto às finalidades da pesquisa e assinaram formulário de consentimento informado (Anexo 2).

SUJEITOS (PACIENTES)

O presente estudo envolveu os pacientes com ELT acompanhados nos ambulatórios de Epilepsia Infantil do Hospital das Clínicas – Unicamp, entre janeiro de 2000 a abril de 2005.

Critérios de Inclusão

1. Pacientes de até 18 anos de idade com ELT;
2. Diagnóstico clínico, eletrencefalográfico e/ou de neuroimagem (RM) compatível com ELT;
3. Pacientes cujos pais concordassem em participar da pesquisa e assinassem o termo de consentimento pós-informação.

Critérios de Exclusão

1. Suspeita ou confirmação de doença progressiva metabólica;
2. Pacientes que, durante o extenso processo de avaliação, apresentassem exames complementares sugestivos de epilepsia extra-temporal;

3. Não realização dos exames complementares necessários ou perda do seguimento;

4. Não assinatura do termo de consentimento pós-informação.

MÉTODOS

1. ELT foi definida baseando-se nos critérios clínicos e EEG propostos pela Sub-Comissão da ILAE (1989) ou segundo a definição estabelecida por alterações estruturais de exames de neuroimagem: tomografia computadorizada (TC) ou RM.

2. Considerando-se que crianças possam apresentar menos freqüentemente quadro clínico típico do que adultos, o preenchimento de formulário com dados clínicos mais abrangentes foi necessário (Anexo 3).

3. Realização de EEGs interictais seriados (Anexo 4).

4. Os EEGs foram realizados obedecendo-se às normas internacionais para colocação de eletrodos "Sistema 10-20". Os aparelhos utilizados foram de 14 canais, analógico e de 32 canais, digital, ambos da marca Nihon Kohden. As montagens estão em conformidade com as recomendações da AMERICAN EEG SOCIETY ASSOCIATION, usando a montagem com eletrodo zigomático além das montagens referencial com vértex e a média, bipolares longitudinais e transversais. A duração mínima dos traçados foi de 20 minutos, sendo a velocidade do papel de 30 mm por segundo. Os exames foram realizados sob sono e vigília, na maioria dos pacientes. Métodos de estimulação (hiperpnéia – 3 minutos, e fotoestimulação intermitente com flashes de 1,2,3,9,18,20,30 Hz de frequência) foram rotineiramente utilizados. Nas crianças menores e naquelas pouco colaborativas, a fase de sono pôde ser induzida por hidrato de cloral.

5. Monitorização vídeo-EEG ambulatorial ou com paciente internado até o registro de crises. O aparelho utilizado foi digital Nihon Kohden de 64 canais. Os laudos foram elaborados pela autora e a orientadora. Foram submetidos ao exame todos os pacientes com epilepsia refratária com necessidade de avaliação pré-cirúrgica.

6. Avaliamos os resultados cirúrgicos segundo a classificação de Engel (Anexo 5) daqueles pacientes submetidos ao tratamento cirúrgico (amigdalohipocampectomia seletiva, lobectomia temporal anterior ou lesionectomia).

7. Os aspectos comportamentais foram avaliados clinicamente com o suporte de profissional especializado da área da psicologia.

8. A análise estatística utilizada foi especificada em cada artigo (Capítulos).

4- RESULTADOS (Capítulos)

ARTIGO 1

Review Article: Temporal Lobe Epilepsy in Childhood

Renata C. Franzon, Marilisa M. Guerreiro

Review Article: Temporal Lobe Epilepsy in Childhood

Submetido ao *Journal of Epilepsy and Clinical Neurophysiology*

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[2]. This expression included benign childhood epileptic syndromes, which were subsequently separated into idiopathic and symptomatic, that is, benign childhood epilepsy and TLE[3].

The syndrome of "Benign Psychomotor Epilepsy" of childhood, proposed by Dalla Bernardina[4], 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[5].

Harvey et al.[6] studying clinical, electroencephalographic (EEG) and neuroimaging features of 63 children with recently diagnosed TLE, classified it in three 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[7-10].

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[11], 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[8,9,12]; it is, however, the most frequent etiology in some studies, reaching 70% of the cases of TLE[13]. 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[14].

Mesial temporal sclerosis has been correlated with previous antecedents of complex febrile seizures[15] occurring in about 43% of patients with MTS[16]. 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[17,18]. 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[21]. 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[24-26]. 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[27] and is considered by some authors as the most frequent cause of refractory TLE in children[7,28,29]. It is now known that the temporal lobe is not its preferential location[30]. Neuropathological findings indicative of cortical dysplasias were present in 21 of 33 (64%) surgical specimens from children with refractory TLE[31].

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[33], 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[34].

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)[12]. Infantile spasms and generalized myoclonic seizures also occur frequently[35,36].

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.[8] 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[9] 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.[37], 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[16] 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 nonresponsiveness

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.[39] 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[34].

Nordli et al.[38] and Fogarasi et al.[39] conducted a long-term 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 pre-operative assessment of children with temporal lobe tumors; however, they are recommended when extratemporal functional localization studies are needed.

Other authors[9] 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.[10] 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[40].

Pedreira[16] 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[41], 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[13,42,43]. 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[44,45]. 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[46].

Temporal lobectomy in children with refractory TLE has been reported in the literature[28,47-51].

Blume et al.[37], 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[33] 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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ARTIGO 2

Clinical, Electroencephalographic and Behavioral Features of Temporal Lobe Epilepsy in Childhood

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Original Article

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ABSTRACT

This study describes the clinical, electroencephalographic, and behavioral features of 36 children with temporal lobe epilepsy. Patients were divided into two groups: group A, with 6 patients (< 6 years), and group B, with 30 patients (6–18 years). Statistical analysis was performed considering the significance level of .05. Regarding the clinical features of the focal seizures, motor components were more frequently seen in children younger than 6 years of age ($P < .01$), whereas automatisms were more frequently seen in patients older than 6 years of age ($P < .05$). Associated myoclonic seizures were more frequent in the younger age group ($P < .01$). Behavioral disorders such as hyperactivity and aggressiveness and speech delay were more common in the younger age group ($P < .05$). Temporal lobe epilepsy in children younger than 6 years of age is more frequently associated with motor components, myoclonic seizures, behavioral disorders, and speech delay. Conversely, temporal lobe epilepsy in older patients has frequent automatisms. (*J Child Neurol* 2004;19:418–423).

Temporal lobe epilepsy in childhood presents clinical, etiologic, and electroencephalographic (EEG) peculiarities.[1-7] Its diagnosis is frequently difficult because the clinical characteristics classically present in adult temporal lobe epilepsy might not be evident, particularly in young children (infants and preschool-aged children). In addition, the EEG findings can be diverse and can even show generalized epileptiform abnormalities.[1-3,5,7]

In the clinical evaluation of adults with temporal lobe epilepsy, we usually notice the presence of partial seizures with autonomic symptoms, such as epigastric aura, psychic phenomena, auditory or olfactory symptoms, arrest of activity, oroalimentary and gestural automatisms, and dystonic posturing. Seizure duration is usually greater than 1 minute, secondary generalization can occur, and postictal confusion is a frequent finding.[8-10] Interictal EEG can be normal or show baseline or epileptiform abnormalities, either unilaterally or bilaterally, in the temporal regions.[8]

Davidson and Falconer pointed to the difficulties of clinical diagnosis of temporal lobe epilepsy in childhood and emphasized the following points: the auras usually have a poor description and are misinterpreted by family members; there is a variable severity of the condition at different stages of life; there is frequent interruption of follow-up in adolescence; and the interpretation of the EEG is usually even more difficult in children than it is in adults.[11] These issues still remain troublesome today, particularly in younger children.[12]

In the last decade, video-EEG monitoring performed as part of the presurgical evaluation of children with temporal lobe epilepsy enabled a better understanding of the clinical and EEG features of temporal lobe epilepsy in children.[1-3,5,7] More recently, the clinical, EEG, and etiologic features of temporal lobe epilepsy in childhood are being even more clearly delineated.[4-6,13]

The aim of our study was to evaluate the clinical and EEG characteristics of temporal lobe epilepsy in childhood.

MATERIALS AND METHODS

From January 1999 to February 2002, we evaluated 36 consecutive patients with temporal lobe epilepsy seen at the pediatric epilepsy clinic of a tertiary hospital.

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The diagnosis of temporal lobe epilepsy was based on clinical and EEG findings.[8] Moreover, neuroimaging findings were also assessed to corroborate the diagnosis. Clinical criteria were a history of simple partial seizures, complex partial seizures, or both, with characteristics compatible with mesial temporal lobe origin (in general, rising epigastric sensation, fear, experiential phenomena, and autonomic signs and symptoms[14]) and no suggestion of another partial epilepsy syndrome. EEG criteria were the presence of interictal epileptiform discharges over midinferiomesial temporal regions or consistent intermittent slow-wave abnormalities with episodes of rhythmic delta activity localized over the temporal areas.

The clinical data were gathered from the history given by the parents and also from the video-EEG monitoring performed in 11 patients. Seizure evaluation consisted of (1) aura, when the initial manifestation was fear, abdominal discomfort, gustative sensation, or other less frequent symptoms (auditive, vertiginous, or psychic phenomena); (2) motor component, which was considered present if the patient had tonic or clonic movements or hypermotor manifestations (wide, violent, stereotyped, and purposeless movements of the trunk and limbs); (3) dystonic posturing, for its localization value,[9,15,16] considered separately; and (4) gestural and oroalimentary automatisms. In addition, the presence of myoclonic or generalized tonic-clonic seizures was considered.

Each patient had 4 to15 interictal EEG records (mean 6.3). All EEG recordings were performed following the International 10-20 system.[17] Interictal EEGs had a minimum duration of 20 minutes, and awake and sleep samples were obtained. Hyperventilation and intermittent photic stimulation were performed. Chloral hydrate was used to induce sleep when needed.

We used the referential montages with vertex and average, longitudinal and transverse bipolars, and transverse bipolar montages using zygomatic electrodes (anterior temporal electrodes T_1 and T_2). The findings were categorized into (1) normal during wakefulness, drowsiness, and/or sleep; (2) abnormal with nonepileptiform disturbance: focal or generalized slow waves in the theta or delta range; (3) abnormal with epileptiform discharges: spikes or focal sharp waves, multifocal, generalized, or spike and slow wave; and (4) abnormal with both epileptiform and nonepileptiform disturbances.

Video-EEG monitoring was usually performed on an outpatient basis, 8 hours per day, in an average period of two to three days until seizures were captured. When taper of antiepilepsy drugs was needed, it was performed on an inpatient basis. We used a digital device with 32 channels for that purpose.

Magnetic resonance imaging was performed in a 2.0-Tesla scanner using our epilepsy protocol: (1) sagittal T_1-weighted spin echo, 6 mm thick (TR = 430, TE = 12), for optimal orientation of the subsequent images; (2) coronal T_1-weighted inversion recovery, 3 mm thick (flip angle = 200 degrees; TR = 2800–3000, TE = 14, inversion time T_1 = 840, matrix = 130 × 256, field of view = 16 × 18 cm); (3) coronal T_2-weighted fast spin echo, 3 to 4 mm thick (flip angle = 120 degrees; TR = 4800, TE = 129, matrix = 252 × 320, field of view = 18 × 18 cm), (4) axial images parallel to the long axis of the hippocampi; T_1-weighted gradient echo, 3 mm thick (flip angle = 70 degrees, TR = 200, TE = 5, matrix = 180 × 232, field of view = 22 × 22 cm); (5) axial T_2-weighted fast spin echo, 4 mm thick, (tip angle [TA] 120 degrees, TR = 6800, TE = 129, matrix 252 × 328, field of view = 21 × 23 cm); and (6) volumetric (three-dimensional) T_1-weighted gradient echo, acquired in the sagittal plane for multiplanar reconstruction, 1 to 1.5 mm thick (TA = 35 degrees, TR = 22, TE = 9, matrix = 256 × 220, field of view = 23 × 25 cm).

The patients were divided into two groups for clinical and neurophysiologic analysis: group A (up to 6 years of age) and group B (> 6 years of age). Statistical analysis was performed using the chi-square test, considering the level of significance of .05.

RESULTS

There were 20 girls and 16 boys, ranging in age from 2 to 18 years (mean 11.5 years). Six patients were younger than 6 years old (group A), and 30 were older than 6 years (group B). Demographic data (identification, chronologic age, age at onset of epilepsy, and neurologic examination), relevant previous history, and neuroimaging data are displayed in Table 1.

Table 2 shows the clinical characteristics of the patients' epileptic seizures. The most frequent auras were epigastric discomfort and feelings of fear. Motor components were noticed in 83.3% (5/6) of the patients of group A and in 16.6% (5/30) of the patients of group B ($P < .01$). Automatisms occurred in 33.3% (2/6) of the subjects of group A and in 93.3% (28/30) of the subjects of group B ($P < .01$).

Generalized tonic-clonic and myoclonic seizures occurred in 50% (3/6) of the subjects in group A and in 34.5% (10/30) of the patients of group B ($P > .05$). Myoclonic seizures were clearly more common in the younger patients, occurring in 50% (3/6) of the subjects in group A and in 3% (1/30) of the subjects in group B ($P < .01$).

Interictal EEG findings are summarized in Table 3. Table 4 shows data concerning behavioral features. Speech delay, hyperactivity, and aggressiveness were more frequent in the patients of group A ($P < .05$). In this group, two patients (subjects 1 and 3) presented with marked aggressiveness after the surgical treatment of epilepsy; in one of them, there was worsening of a preexisting aggressiveness, whereas, in the other patient, it occurred only after surgery. It is interesting to note that although behavioral abnormalities were less frequent in older patients, two patients from group B (subjects 11 and 12) presented an acute psychotic event.

DISCUSSION

In this study, we found that temporal lobe epilepsy presents semiologic differences according to the patient's chronologic age. In young children (< 6 years old), seizures originating in the temporal lobe often present with motor components. Myoclonic seizures are also frequent at this age. Conversely, temporal lobe seizures in older patients resemble those of adults, with frequent automatisms.

Dystonic posturing, a classic feature of temporal lobe epilepsy in adults, was more frequent in older children with temporal lobe epilepsy, although it did not reach statistical

Table 1. Demographic and Neuroimaging Data of 36 Patients With Temporal Lobe Epilepsy

Patient	Group	AgeI (yr)	Gender	AgS (yr)	FS	PNE	FH	HT	SE	CT	MRI
1	A	2	F	1	N	Normal	N	N	Y	Hypodense cystic lesion in left TL	Tumor in left TL
2	A	2	M	0	N	NDR; Left hemiparesis	N	N	Y	Mass lesion in right TL	Tumor in right TL and in right thalamic region
3	A	6	F	4	N	Normal	N	N	N	Hypodensity in left TL	Tumor in left TL
4	A	5	F	2	N	Normal	N	N	Y	Subependymal lesions + hamartoma in left FL	Tuberous sclerosis (multiple hamartomas in left FL and in both temporal lobes)
5	A	6	F	2	N	Normal	Y	N	N	Arachnoid cyst of right TL	Arachnoid cyst of right TL
6	A	6	F	4	N	Choreoathetosis movement on the left side of the body	N	N	Y	Normal	Dual pathology (right HA + cortical dysplasia in the right TL)
7	B	16	F	4	N	Normal	Y	N	N	Normal	Dual pathology (right HA + cortical dysplasia in the right TL)
8	B	17	F	2	N	Normal	Y	N	N	Normal	Right HA
9	B	14	M	8	N	Right hemiparesis	N	N	N	Normal	Dual pathology (left HA + atrophy of left TL and adjacent areas)
10	B	15	M	13	N	Normal	N	N	N	Normal	Dual pathology (left HA + tumor in left TL)
11	B	8	M	3	N	Normal	Y	Y	Y	Normal	Dual pathology (left HA + hyperintense signal of the left TL—gliosis?)
12	B	10	M	5	N	Normal	Y	N	N	Normal	Dual pathology (right HA + hyperintense signal in the right TL)
13	B	15	M	3	N	Normal	N	N	N	Normal	Right HA
14	B	17	F	11	N	Normal	N	N	Y	Normal	Right HA
15	B	16	M	2	Y	Normal	Y	N	N	Normal	Left HA
16	B	13	F	2	N	NDR	N	N	Y	Assymmetry of lateral ventricles and right periventricular gray matter (heterotopia?)	Dual pathology (left HA + periventricular heterotopia)
17	B	16	F	3	N	Normal	Y	N	N	Normal	Left HA
18	B	7	M	4	Y	Normal	N	N	Y	Normal	Alteration in the form and in the signal of the right hippocampus
19	B	15	M	5	N	Facial angiofibroma	Y	N	N	Calcification in the left TL; tuberous sclerosis	—
20	B	9	F	1	N	Normal	N	N	N	Hypodense lesion in the right TL—tumor?	Tuberous sclerosis (lesion in the left TL, right TL, and right precentral region)
21	B	13	M	4	Y	Normal	Y	N	N	Normal	Right HA
22	B	14	M	4	Y	Normal	N	N	Y	Normal	Left HA
23	B	11	M	7	N	Normal	Y	N	Y	Normal	Right HA
24	B	11	F	1	N	NDR	Y	N	N	LTL atrophy	—
25	B	11	M	10	N	Normal	N	N	Y	—	Right HA
26	B	18	F	4	N	Normal	Y	N	N	Normal	Left HA
27	B	11	F	4	N	Normal	Y	N	Y	Normal	—
28	B	12	M	9	N	Normal	N	N	N	—	Gliosis at uncus of right TL and at right parahippocampal gyrus
29	B	16	F	1	N	Normal	Y	N	Y	—	Left HA
30	B	9	F	7	N	Normal	N	N	Y	Hypodense, cystic, and captating lesion of 0.2–0.3 cm in the LT region	Arachnoid cyst (left TL)
31	B	14	F	1	N	Normal	N	Y	Y	—	Left HA
32	B	17	M	2	N	Normal	Y	N	N	—	Right HA
33	B	15	F	1	N	Mental deficiency		N	N	Normal	Bilateral HA
34	B	14	F	12	N	Normal	N	N	N	Normal	Tumor in right TL
35	B	16	F	2	N	Left hemiparesis	N	N	N	Right VPD	Left HA
36	B	16	M	4	Y	Normal	N	N	N	Normal	Right HA

AgeI = age of investigation; AgS = Age of onset of the symptoms; CT = computed tomography; FH = familial history of epilepsy; FL = frontal lobe; FS = febrile seizure; HA = hippocampal atrophy; HT = previous head trauma; MRI = magnetic resonance imaging; N = no; NDR = neuropsychomotor development retardation; PNE = physical and neurologic examination; SE = status epilepticus; TL = temporal lobe; VPD = ventriculoperitoneal derivation; Y = yes.

Table 2. Clinical Features of Epileptic Seizures in 36 Patients With Temporal Lobe Epilepsy

Seizures Clinical Characteristics	*Group A (n = 6)*	*Group B (n = 30)*	*Statistics, χ^2*
Auras*	3	23	23
Fear	2	7	7
Abdominal	2	11	11
Others	0	6	6
Arrest of activity	6	25	25
Motor components	5	6	6
Dystonic Posturing	1	18	18
Automatisms	2	28	28
Myoclonic seizures	3	1	1
GTCS	2	10	10
SGTCS	5	17	17

GTCS = generalized tonic-clonic seizure; SGTCS = secondary generalized tonic-clonic seizure.
*Some patients presented with more than one type of aura.

significance. This clinical manifestation has occurred in 8.5 to 71% of children with temporal lobe epilepsy.[4,13,16,18]

In our study, myoclonic seizures occurred mainly in patients younger than 2 years of age, preceding the onset of focal seizures. Our finding supports the assumption that the developing brain is more prone to present generalized seizure as a consequence of a focal lesion. This idea was first introduced after focal cortical dysplasia was found in patients with infantile spasms evaluated by positron emission tomography.[19] Because the type of epileptic manifestation is age dependent and not only lesion dependent, childhood epilepsy shows a wide range of symptomatology. Therefore, temporal lobe epilepsy in infants can have great clinical variability, including generalized seizures, such as myoclonus. Because generalized epileptic syndromes can be secondary to a focal lesion, neuroimaging assessment is mandatory in childhood epilepsy. The coexistence of myoclonic and focal seizures seems to occur rarely in adults.[20,21]

Our findings are in accordance with a recent study on the ontogeny of focal seizures in infants and young children, which concluded that there are important differences between children and adults in the clinical expression of epileptic seizures.[18] Myoclonic seizures, for instance, usually become less frequent as the children grow older, whereas secondary generalized seizures and the classic manifestations of focal seizures, such as dystonic posturing, commonly increase in frequency with increasing age.

Table 3. Features of the Interictal EEG in 36 Patients With Temporal Lobe Epilepsy

EEG	*Group A*	*Group B*	*P*
Normal	2	16	.371
Nonepileptiform activity			
TNEA	4	26	.230
ET/GNEA	3	15	1.000
Epileptiform activity			
TEA	5	26	.829
CLTEA	3	5	.073
BTEA	0	7	.187
ETEA	3	12	.650
GEA	2	4	.230

BLTEA = bilateral temporal epileptiform activity; CLTEA = contralateral temporal epileptiform activity; EEG = electroencephalogram; ET/GNEA = extratemporal/generalized nonepileptiform activity; GEA = generalized epileptiform activity; TNEA = temporal nonepileptiform activity.

Table 4. Behavioral Features of 36 Patients With Temporal Lobe Epilepsy

Behavior	*Group A*	*Group B*	*P*
Hyperactivity	4	5	.009
Attention-deficit disorder	1	1	.193
Aggressiveness	4	7	.035
Mental deficiency/autism	2	2	.057
Speech delay	2	1	.015
Learning disabilities	—	5	.281
Pseudoseizures	—	3	.418
Depression	—	3	.418

Although our data showed that there is a clear-cut difference in the clinical and EEG characteristics of temporal lobe epilepsy in adults and children, it should be emphasized that some findings, such as myoclonic seizures, can be seen in other forms of focal epilepsy.

It is interesting to note that febrile seizures occurred in only five patients of group B, and most of them had hippocampal atrophy. This brings to mind the frequent relationship between febrile seizures and temporal lobe epilepsy.[22-24]

Two patients with a previous history of head trauma also presented with hippocampal atrophy. The trauma occurred at 18 months of age in both patients. At the time of the accident, the children presented with convulsive seizures and required intensive care treatment. Early head trauma (before the age of 5 years) has been associated with hippocampal atrophy.[25,26] The occurrence of severe and significant head trauma seems to impair seizure outcome after anterior temporal lobectomy.[27]

The interictal EEG in children with temporal lobe epilepsy is quite variable and difficult to interpret. One should consider the patient's age, the sleep/awake cycle, and the classic patterns of the benign epilepsies of childhood. In adult patients with temporal lobe epilepsy, EEG abnormalities are seen mostly over the temporal regions.[28] In children, although there is also a predominance of temporal abnormalities, bilateral, contralateral, extratemporal, or generalized abnormalities—epileptiform or not—are present as well. In our study, although not statistically significant, generalized extratemporal epileptiform activities were more frequently found in the younger age group.

The finding that EEGs in children can be less localizable than in adults can be explained by several factors: a peculiar reaction of the developing brain; a great variety of etiologic factors in the pediatric age range, such as focal cortical dysplasia, low-grade gliomas, tuberous sclerosis complex, and meningoencephalitis versus hippocampal atrophy in adults; and, the presence of different etiologic factors leading to dual pathology.[29] Moreover, even when only patients with hippocampal atrophy are evaluated, extratemporal and generalized epileptiform activities are frequent in

children, suggesting that the EEG findings of temporal lobe epilepsy vary according to the patient's age.

A question that remains to be answered is whether temporal lobe epilepsy in childhood would result from a more severe initial precipitating event, leading to more extensive brain damage and, therefore, more diffuse EEG abnormalities. Conversely, the differences in the neurophysiology of temporal lobe epilepsy in adults and children could be the result of different stages of brain maturation. The most prevalent etiology of temporal lobe epilepsy in our study was hippocampal atrophy, followed by dual pathology and tumor. In the younger age group, there was no patient with isolated hippocampal atrophy. This agrees with studies on younger children in whom tumors and cortical dysplasias were more frequent than was hippocampal atrophy.[3,5,7] Thus, although studies of adults with temporal lobe epilepsy show that hippocampal atrophy is the most frequently associated condition,[23,24] in younger children, conditions such as tumors and dual pathology are usually more frequently found.

Children with early onset of temporal lobe epilepsy can have global impairment of cognitive functions, including intelligence, speech, visuospatial perception, executive function, and memory.[30] These findings are in accordance with the more diffuse clinical and EEG alterations found in younger patients with temporal lobe epilepsy.

Behavioral disorders can be associated with temporal lobe epilepsy in childhood.[31] Two of our patients presented with reversible psychotic events before surgery (subjects 11 and 12). The surgical treatment of temporal lobe epilepsy in children, even when successful, does not seem to improve the patient's behavior.[32,33] Temporal lobectomy in adults, on the other hand, seems to improve the behavioral abnormalities.[34]

Two of our patients became very aggressive and agitated after surgical resection of tumor (ganglioglioma and oligoastrocytoma) in the left temporal lobe (subjects 1 and 3). Psychosis occurring after resection of ganglioglioma or dysembrioplastic neuroepithelial tumor in temporal lobe epilepsy has already been reported,[35] and the authors suggested that the event might result from "forced normalization." In the present study, behavioral disorders, such as hyperactivity and aggressiveness, as well as cognitive dysfunction, such as speech delay, were significantly more frequent in children younger than 6 years of age. The assumption that those manifestations are more prevalent in younger patients with temporal lobe epilepsy has not been previously reported and requires further confirmation.

We conclude that temporal lobe epilepsy in early childhood has peculiar characteristics, which are quite different from the classic clinical picture observed in adolescents and adults. Temporal lobe epilepsy in children younger than 6 years of age is more frequently associated with motor components. Moreover, myoclonic seizures, behavioral disturbances, and speech delay are also more frequent in this age range.

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ARTIGO 3

Recurrent Abdominal Pain: When an Epileptic Seizure Should be Suspected?

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Recurrent Abdominal Pain: When an Epileptic Seizure Should be Suspected?

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RECURRENT ABDOMINAL PAIN

When an epileptic seizure should be suspected?

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ABSTRACT - Recurrent episodes of abdominal pain are common in childhood. Among the diagnostic possibilities are migraine and abdominal epilepsy (AE). AE is an infrequent syndrome with paroxystic episodes of abdominal pain, awareness disturbance, EEG abnormalities and positive results with the introduction of antiepileptic drugs. We present one 6 year-old girl who had short episodes of abdominal pain since the age of 4. The pain was followed by cry, fear and occasionally secondary generalization. MRI showed tumor in the left temporal region. As a differential diagnosis, we report a 10 year-old boy who had long episodes of abdominal pain accompanied by blurring of vision, vertigo, gait ataxia, dysarthria, acroparesthesias and vomiting. He received the diagnosis of basilar migraine. In our opinion, AE is part of a large group (partial epilepsies) and does not require a special classification. Pediatric neurologists must be aware of these two entities that may cause abdominal pain.

KEY WORDS: partial seizures, temporal lobe tumor, basilar migraine, abdominal pain, symptomatic epilepsy.

Dor abdominal recorrente: quando suspeitar de crise epiléptica?

RESUMO - Episódios recorrentes de dor abdominal são freqüentes na infância e entre as causas neurológicas há migrânea e epilepsia abdominal (EA). EA é uma síndrome que consiste de episódios paroxísticos de dor abdominal associada à alteração de consciência, anormalidades eletrencefalográficas e boa resposta à terapia anticonvulsivante. Apresentamos uma menina de 6 anos que tinha desde os 4 anos episódios de curta duração de dor abdominal, seguidos por choro, medo e ocasional generalização secundária. A RM mostrou a presença de um tumor em região temporal esquerda. Como diagnóstico diferencial, apresentamos um menino de 10 anos que há 12 meses referia episódios de dor abdominal de longa duração acompanhados por turvação visual, vertigem, marcha atáxica, disartria, acroparestesia e vômito, recebendo posteriormente o diagnóstico de migrânia basilar. Em nossa opinião, EA faz parte de um grande grupo (epilepsias parciais) e não requer uma classificação especial. O neuropediatra deve estar alerta para essas duas entidades que podem cursar com dor abdominal.

PALAVRAS-CHAVE: crises parciais, tumor do lobo temporal, migrânea basilar, dor abdominal e epilepsia sintomática.

Recurrent episodes of abdominal pain are common in childhood. In a minority of patients in which an abdominal pathology is excluded a neurologic cause should be considered. Among the diagnostic possibilities are migraine and abdominal epilepsy (AE). AE is an infrequent syndrome with paroxystic episodes of abdominal or visceral pain, with awareness disturbance, EEG abnormalities and good results with the introduction of antiepileptic drugs (AED)[1-4].

Migraine is more frequent than AE and may occur in a classical form or as a distinct subentity, such as basilar migraine[3]. The latter consists of sudden, transitory episodes of visual blurring, vertigo, gait ataxia, dysarthria, acroparesthesias and a pulsatile occipital headache with vomiting[5].

Our objective is to present two patients with recurrent abdominal pain and different diagnosis.

CASOS

We report two children with recurrent abdominal pain having had unremarkable pediatric evaluation. Both pa-

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tients had detailed clinical histories, neurologic examinations and complementary exams (EEG, CT, MRI). The final diagnosis was different in the two patients. The follow-up is 18 months for both children.

Patient 1. A six year-old girl has had recurrent abdominal pain since 4 year- old, which she sometimes described as "my belly is dreaming". The duration of the episodes ranged from seconds to few minutes and crying and a "facies" of fear followed the pain. The frequency was initially once a day and progressively increased to six a day. Some of them were followed by awareness disturbance and occasionally a tonic-clonic seizure. After a negative abdominal investigation (including stool exams for ova and parasites, abdominal ultra-sound and routine blood exams, such as, liver, pancreas and renal function tests), she was referred to a child neurologist who found behavior alterations (hyperactivity and impulsivity). The remaining of the neurologic examination was otherwise normal. After that, she had refractory seizures with secondary generalization. She underwent an EEG exam and cranium CT scan, which showed a hypodense area in left temporal area. She was then referred to a tertiary care center in order to undergo further exams. MRI revealed a tumor in the left temporal lobe (Fig 1). Interictal EEG showed spikes and slow waves over left temporal lobe. Mus-

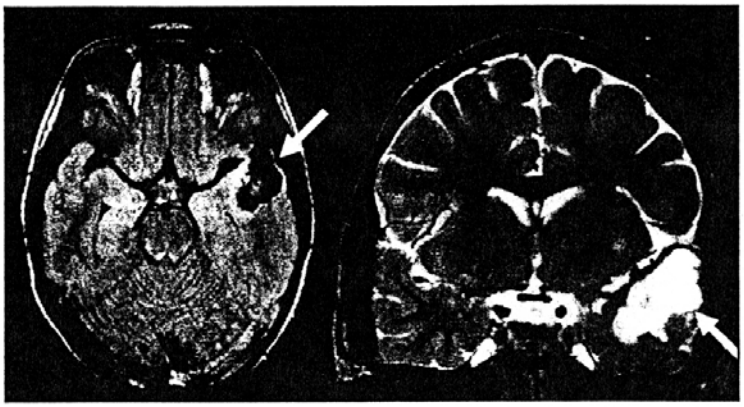

Fig 1. Patient 1. MRI. The figures show a cystic lesion with solid mural nodule on left temporal lobe.

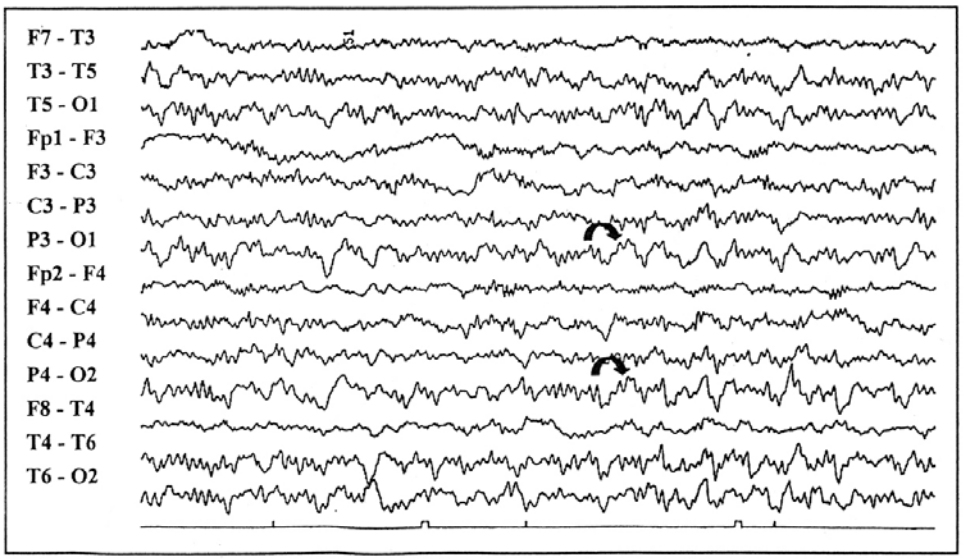

Fig 2. Patient 2. EEG. The figure shows intermittent slow waves (delta range) over occipital regions bilaterally, during an acute episode of basilar migraine.

cular artifacts contaminated ictal EEG. She had no other seizures after surgical resection. Histopathological exam showed an oligoastrocytoma grade II.

Patient 2. A ten year-old boy was having recurrent episodes of abdominal pain for the past 12 months. The duration of the episodes varied and ranged from hours to days. Blurring of vision, vertigo, ataxic gait, dysarthria, acroparesthesias, and vomiting accompanied them. He underwent an exhaustive abdominal investigation (including complete blood cell count, stool examinations for ova and parasites, abdominal ultra-sound and high digestive endoscopy). He did not improve after carbamazepine was introduced. He underwent an EEG examination during a typical episode of abdominal pain, which revealed lentification in the occipital region (Fig 2). A diagnosis of basilar migraine was proposed. He also underwent a MRI, which was normal. He did very well with specific treatment for migraine (Flunarizine).

DISCUSSION

These two cases show the importance and the difficulty of arriving at a correct diagnosis of the neurological causes of recurrent abdominal pain in childhood.

Patient 1 had the diagnosis of abdominal epilepsy. Two decades ago there were attempts to elaborate criteria for the definition of this entity, which are[6,7]: paroxystic abdominal pain; exclusion of visceral abdominal pathology; alteration of mental status during at least some episodes; clearly abnormal EEG; and, positive response to AED. Our patient fulfilled all those criteria, however, the presence of paroxysms of abdominal pain (followed or not by secondary generalization) made us believe that she had partial autonomic seizures.

The pathophysiology of abdominal epilepsy remains unknown. Some possible etiologies have been considered, such as prematurity, febrile seizures, and neuroendocrine dysfunction, but they are not convincing. There is a report of a case of abdominal epilepsy due to a cerebral tumor (astrocitoma) in the temporal area[8]. More recently, another case report showed cortical malformation, bilateral perisylvian polymicrogyria, at MRI associated with abdominal epilepsy[9]. When the abdominal pain presents as a short paroxysmal episode followed by either awareness disturbance or automatisms, an epileptic seizure is easily considered and, in those cases, temporal lobe is the most probable origin of the seizure[10]. Nevertheless, abdominal pain in childhood is not an easy symptom to characterize, particularly in young children, and other diagnosis should be considered.

Patient 2 had the diagnosis of basilar migraine. This condition may course with recurrent abdominal pain, which is usually gradual in the beginning, a positive familiar history of migraine, and a normal EEG or one revealing unspecific abnormalities[6]. Being migraine a frequent entity also in the pediatric population, this diagnostic hypothesis should enter the differential diagnosis of abdominal epilepsy.

Both abdominal epilepsy and basilar migraine can present with vomiting. In this case, Panayiotopoulos syndrome has to be considered. Ictal vomiting, deviation of the eyes, and occipital spikes characterize this syndrome. Peak age at onset is 5 years[11].

Another point to be considered is the EEG. Patients with abdominal epilepsy usually have specific EEG abnormalities, particularly of a temporal lobe seizure disorder[7], while patients with migraine have normal EEGs or present unspecific abnormalities, as was the case of our patient[5].

In our opinion, abdominal epilepsy is part of a larger group (partial epilepsies) and does not require a special classification because the abdominal pain is usually associated with other ictal manifestations compatible with the diagnosis of partial seizures[3]. However, it is not uncommon for pediatric neurologists to receive patients referred with this complaint. Therefore, one must be aware of the differential diagnosis of this condition, particularly considering migraine as a possibility because it is much more frequent than epilepsy.

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ARTIGO 4

Myoclonic Seizures in Symptomatic Temporal Lobe Epilepsy of Childhood

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Myoclonic Seizures in Symptomatic Temporal Lobe Epilepsy of Childhood

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ABSTRACT

Rationale and objective: Generalized epileptic manifestations may occur in symptomatic focal epilepsies in children, particularly in infants and pre-school children. Our aim here is to report two patients with myoclonic seizures associated with temporal lobe epilepsy. **Methodology:** Case report. **Results:** Two children with tumor in temporal lobe presented myoclonic seizures or spasms since infancy besides other types of seizures. **Conclusion:** Our findings support the idea that myoclonic seizures may be generalized manifestations of focal insults to the CNS, and this pattern may be an age-dependent specific response of a developing brain to a severe insult.

Key words: myoclonic seizures, infantile spasms, temporal lobe epilepsy, childhood.

RESUMO

Crises mioclônicas em epilepsia de lobo temporal da infância

Racional e objetivo: Manifestações epilépticas generalizadas podem ocorrer em epilepsias focais na infância, particularmente em lactentes e pré-escolares. Nosso objetivo é relatar dois pacientes que tiveram crises mioclônicas associadas a epilepsia de lobo temporal. **Método:** Descrição de caso. **Resultados:** Apresentamos duas crianças com tumor de lobo temporal que tinham crises mioclônicas além de outros tipos de crises epilépticas. **Conclusão:** Nossos dados reforçam a idéia de que crises mioclônicas podem ser manifestações generalizadas de insulto focal ao sistema nervoso central, e que este padrão pode ser uma resposta idade-dependente de um cérebro em desenvolvimento a um insulto grave.

Unitermos: crises mioclônicas, espasmos infantis, epilepsia de lobo temporal, infância.

INTRODUCTION

Myoclonus are sudden and brief muscular contractions and may be symmetric or asymmetric[1]. Myoclonus may be classified according to the etiology and pathophysiology in: epileptic in origin and non-epileptic[2]. Myoclonus of epileptic origin may be subclassified according to its pathophysiological mechanism in: reflex cortical myoclonus, reflex myoclonus of reticular origin, and myoclonic seizures of generalized epilepsies. It is suggested that reflex cortical myoclonus might be part of partial epilepsies through a mechanism of somatosensory activation followed by activation of cranial nerves and myotomes, the cortex beeing last to be activated[2].

The effect of age in the semiology of seizures in children with partial epilepsy is being more and more recognized. Seizures with motor components such as myoclonic seizures and infantile spasms, for example, occur preponderantly in the first years of life, whereas other semiologic manifestations such as manual automatisms and dystonic posturing predominate in older children and in adults[3-5]. The semiologic differences seen in children with

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temporal lobe epilepsy are due to the dynamic process of cerebral maturation, which affects the clinical manifestations in a consistent way.

The association of infantile spasms with focal structural lesions in the central nervous system is also well established[6-9].

Thus, generalized epileptic manifestations may occur in symptomatic focal epilepsies in children, particularly in infants and pre-school children. Our aim here is to report two patients with myoclonic seizures associated with temporal lobe epilepsy.

CASE REPORT

PATIENT 1:

This two years and four months old girl presented a generalized convulsive *status epilepticus* at seven months of age. At the age of 13 months she started having myoclonic seizures on awakening. Four months later partial seizures appeared characterized by staring, blinking and oroalimentary automatisms. Interictal EEG revealed multifocal epileptiform activity, maximal at left frontal and temporal areas. Ictal EEG showed seizure onset on the left mid-temporal area. Interictal SPECT (Single Photon Emission Computed Tomography) showed hypoperfusion of the left temporal lobe, maximally in the medial region, and the ictal SPECT revealed hyperperfusion of the left temporal lobe and hypoperfusion of the frontal lobes. Brain magnetic ressonance imaging (MRI) revealed a tumor in the left temporal lobe. She has been seizure free since surgery five years ago.

PATIENT 2:

This two year old boy had daily isolated extension spasms since birth until the age of six months, when he started having unilateral tonic seizures in the left arm and leg. Since age eight months he presented partial seizures, characterized by behavioral arrest, autonomic phenomena and oroalimentary automatisms. The interictal EEG revealed generalized epileptiform activity, mostly at the right hemisphere and focal activity on the right temporal area, and non-epileptiform right temporal activity. The ictal EEG showed seizure onset on the right anterior temporal area. SPECT was not performed. The brain MRI showed extensive tumor in the right temporal lobe, in the mesial region, and infiltrating thalamus, internal capsule and uncus. The tumor was not completely resected and he still has seizures four years after the surgical procedure.

DISCUSSION

The myoclonic seizures presented by our two patients seem to be generalized manifestations of focal insults to the CNS, and this pattern may be an age-dependent specific response of a developing brain to a severe insult. This idea was initially introduced by Chugani[10] who performed functional studies with PET (Positron Emission Tomography) in patients with infantile spasms and found that FDG-PET was more sensitive than MRI in the identification of focal abnormalities in those patients. The abnormalities appeared in the cortex as areas of decreased glucose-utilization interictaly or hypermetabolism on ictal periods or periods with epileptiform discharges on EEG. Neuropathological studies typically demonstrated cortical dysplasias. PET can effectively identify areas of unsuspected focal cortical dysplasia for which resective surgery offers improved prognosis[9].

Miyazaki et al.[11] performed SPECT in ten infants with infantile spasms and found cortical hypoperfusion in the temporal regions either unilaterally or bilaterally in seven of them (three had lesions shown on MRI), suggesting that the temporal lobes have relevant role in the pathophysiology of the myoclonic seizures. Furthermore, PET demonstrated bilateral temporal hypometabolism in a group of patients with infantile spasms, severe impairment of the neuropsychomotor development and autism who were not candidates for surgical intervention[12]. This finding offers further evidence of the implication of the temporal lobe in the pathophysiology of the myoclonic seizures.

Clusters of spasms immediately preceding partial seizures were registered in several patients[13-15]. The presence of partial seizures in children with spasms was associated with a poor prognosis regarding seizure control and the neuropsychomotor development. The EEG showed interictal background asymmetry in 85% of the cases.

Not only myoclonic seizures, but also features such as behavioral arrest, focal clonic seizures and ocular versive phenomena occurred in younger children with temporal lobe epilepsy and decreased with advancing age[3]. These clinical findings impair the diagnosis of TLE and delay surgical proposal. Early surgical treatment with complete resection of the focal structural lesion is important not only for the seizure control but also for the subsequent improvement of the neuropsychomotor development.

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ARTIGO 5

Abnormal Behavior in Children with Temporal Lobe Epilepsy and Ganglioglioma

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Case Report

Abnormal behavior in children with temporal lobe epilepsy and ganglioglioma

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Abstract

Temporal lobe epilepsy in childhood is characterized by great clinical, electroencephalographic, and etiological diversity. The prognosis after temporal lobe epilepsy surgery in childhood is usually good, with most patients achieving complete seizure control. However, in some children behavior deteriorates postoperatively. We report two girls (2 and 6 years of age) with refractory seizures due to temporal lobe ganglioglioma. They exhibited aggression and hyperactivity since the beginning of their epilepsy. In both patients, behavioral disturbances worsened postoperatively, despite complete seizure control. Patients and parents should be advised about possible behavioral disturbances after epilepsy surgery, especially in the presence of a temporal lobe developmental tumor, even when seizure control is achieved postoperatively.

Keywords: Temporal lobe epilepsy; Childhood; Behavior; Developmental tumor; Epilepsy surgery

1. Introduction

Temporal lobe epilepsy (TLE) in childhood presents great clinical, electroencephalographic, and etiological diversity. The main causes of TLE are low-grade tumors, mesial temporal sclerosis (MTS), and neoplastic and nonneoplastic malformations of cortical development [1–4]. In addition, the association of MTS and other lesions, that is, dual pathology, is frequently seen in childhood [5–7].

The most frequent low-grade tumors associated with TLE are astrocytomas and oligodendrogliomas and the neoplastic malformations of cortical development (or developmental tumors): ganglioglioma, dysembryoplastic neuroepithelial tumor, and gangliocytoma [2]. Patients usually have refractory seizures and epilepsy surgery is the treatment of choice [1–7].

Seizure control can improve quality of life, cognitive function, and behavior during daily activities [8]. Moreover, sick children often have special difficulties, which may lead to emotional and behavioral disturbances [9,10]. It is expected that after epilepsy surgery, patients experience an overall improvement in quality of life. Therefore, assessment of the impact of epilepsy in the child's life should include not only the frequency and type of seizure, but also behavioral, psychological, and social aspects [11].

The prognosis after TLE surgery in childhood is usually good, with most patients achieving complete seizure control. However, sometimes there is no behavioral improvement, and in some patients behavior may even worsen [12,13]. This issue has not yet been clarified.

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The objective of this study is to report two patients with TLE associated with developmental tumors who experienced worsening of behavioral disturbances after epilepsy surgery.

2. Methods

We evaluated two girls with TLE seen at the pediatric epilepsy clinic of our university hospital. The neuroimaging assessment of both patients showed a focal lesion at the left temporal lobe. They were evaluated before and 6 months after epilepsy surgery according to a quality-of-life questionnaire [14] and the Vineland Adaptative Behavior Scale [15].

Quality-of-life evaluation included items such as perception of seizures, general health, limitations in daily activities, adverse events of antiepileptic drugs, emotional aspects, cognition, memory, language, motor skills, and social relationships [14,16–18].

3. Results

3.1. Patient 1

This 2-year-old girl was born to unrelated parents after an uneventful pregnancy. She had myoclonic jerks since 7 months of age, and at 1 year, she developed complex partial seizures characterized by motor arrest and staring, lip protrusion, and oral automatisms, sometimes followed by secondary generalization. Neurological examination was normal. Interictal EEGs revealed epileptiform discharges and focal slowing over the left temporal lobe. Long-term video/EEG monitoring showed that the seizures started at the left medial temporal region. Seizures were refractory to several antiepileptic drugs. MRI revealed a focal lesion at the left temporal lobe (Fig. 1). Epilepsy surgery was performed and pathological examination revealed a ganglioglioma.

At the time of the surgery she was using vigabatrin, which was switched to carbamazepine 6 months after surgery. Carbamazepine was withdrawn without medical advice because she developed a skin rash, and she remained without medication.

She exhibited agitation and aggression since the first appointment. However, behavior disturbance worsened after surgery, despite seizure control and antiepileptic drug withdrawal. Her behavior improved only after the introduction of haloperidol.

3.2. Patient 2

This 6-year-old girl presented with partial seizures characterized by abdominal pain, automatisms, and facial expression of fear followed by secondary generalization since the age of 5 years. Neurological examination was normal. EEG showed independent epileptiform discharges over both temporal regions. Long term video/EEG monitoring indicated seizure onset at the left pos-

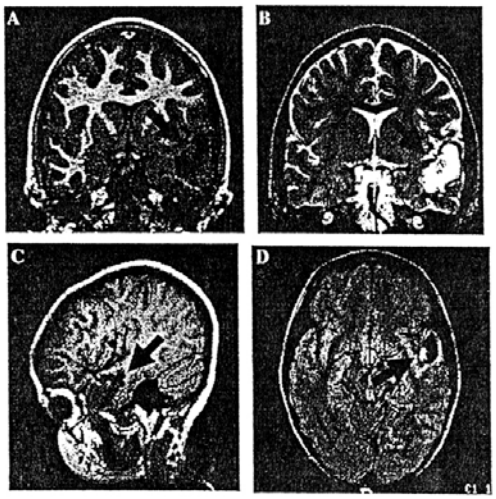

Fig. 2. Patient 2. (A) Coronal T1-IR image, (B) coronal T2 image, (C) sagittal T1 image, and (D) axial FLAIR image showing the left temporal lobe lesion (arrows).

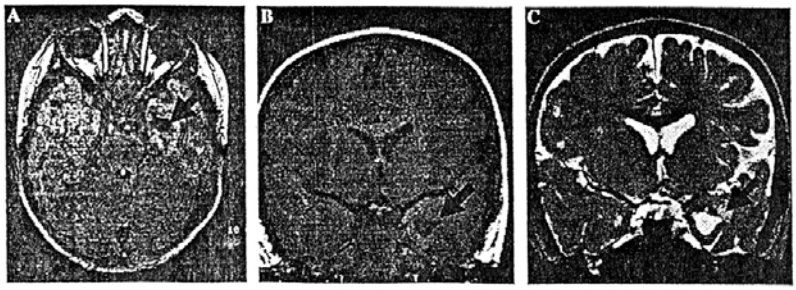

Fig. 1. Patient 1. (A) Axial T1 image, (B) coronal T1 image and, (C) coronal T2 image showing the left temporal lobe lesion (arrows).

Table 1
Results of the neuropsychological assessment pre- and postsurgery (VABS)

	Patient 1	Patient 2
Age at evaluation	2y/2y6m[a]	6y/6y6m
Communication		
Receptive language	1y10m/2y6m	4y7m/4y7m
Expressive language	1y4m/2y1m	3y11m/5y3m
Daily activities		
Personal	2y8m/2y10m	5y10m/6y5m
Domestic	2y3m/2y5m	5y8m/7y1m
Community	1y/1y9m	4y9m/5y4m
Socialization		
Personal relationship	2y2m/2y9m	5y3m/5y3m
Play leisure	2y4m/3y	4y3m/4y10m
Adaptation	11m/11m	4y1m/4y3m
Motor ability		
Global	2y7m/2y11m	>5y11m/>5y11m
Fine	2y6m/2y8m	5y11m/5y10m
SQ	2y6m/2y6m	4y6m/4y11m

[a] Presurgical age/postsurgical age. y, years; m, months; SQ, social quotient.

terior temporal lobe. Seizures were refractory to several antiepileptic drugs up to the maximum tolerated dose. MRI revealed a left temporal lobe lesion (Fig. 2). She underwent a lesionectomy, and the postoperative pathological examination revealed ganglioglioma.

She exhibited aggression and hyperactivity since the beginning of her epilepsy; however, postoperatively her behavior worsened.

Quality-of-life assessment is summarized in Tables 1 and 2.

4. Discussion

We found a postoperative improvement in most areas evaluated, including seizure perception and quality of life, which suggests that the surgery enabled positive changes in the child's life, as suggested by other reports [14,19]. However, behavioral and emotional aspects worsened after surgery.

Andermann et al. [12] showed that behavioral and psychiatric disturbances, as well as psychotic disturbances, delirium, depressive, paranoid, and schizophrenic symptoms may occur in children and adults after epilepsy surgery for ganglioglioma or dysembryoplastic neuroepithelial tumor. Our patients had ganglioglioma and exhibited exactly the same symptoms presented by the patients reported by Andermann et al. [12].

It is difficult to explain the physiopathology of these phenomena. Perhaps, seizure control after surgery leads to "forced normalization" [12]. This theory suggests that daily epileptiform discharges and frequent seizures make the patient more somnolent and calm, which may mask behavioral disturbances. In this setting, seizure control would trigger the appearance of behavioral disturbances. This type of postoperative complication has already been described by Taylor and Falconer [20,21].

Szabó et al. [13] reported that behavioral disturbances in children might worsen after temporal lobectomy. It is interesting to note that their patient had no tumor, but a focal cortical dysplasia in the temporal lobe. The association between developmental tumors and focal cortical dysplasia is well known [22–25], and it is believed that some forms of benign tumors may in fact represent dysplastic lesions with neoplastic transformation. Therefore, the findings of Szabó et al. [13] are in keeping with our observations.

Reversibility of the behavioral disturbances after temporal lobe resection was reported by Falconer and Davidson [26,27] both in adults and in children. He found a relationship between etiology and behavior outcome, as patients with mesial temporal sclerosis showed not only seizure relief but also behavior improvement after temporal lobectomy. The small number of his patients with tumors did not allow a correlation with behavior.

Although there are organic explanations for behavioral worsening after epilepsy surgery, the psychological aspects should not be neglected. Children with epilepsy often have low self-esteem, behavioral problems, and psychiatric disturbances [10]. Because a seizure is often a dramatic and frightening event, it is possible that after seizure control the family starts to pay more attention to behavior, which was not the most important concern before surgery. It is common for the family to expect that epilepsy surgery will not only control seizures, but also improve behavior. When this overall improvement does not occur, parents may have the perception that the patient's behavior is worsening.

Our findings indicate that patients and parents should be advised about possible behavioral disturbances after epilepsy surgery, especially when the lesion is a temporal

Table 2
Questionnaire of quality of life pre- and postsurgery

	Health	Physics	Drug effect	Behavior emotional	Cognitive	Social	School	Environment	Total
Patient 1	G/VG[a]	E/E	G/E	VG/B*	VG/E	E/E	E/VG[b]	VG/G[b]	VG/E
Patient 2	VG/VG	E/E	E/E	E/VG*	E/VG*	VG/E	E/E	VG/E	E/E

[a] Presurgery/postsurgery. E, excellent; VG, very good; G, good; B, bad.
[b] Aspects that worsened after surgery

lobe developmental tumor, despite improvement in seizure control.

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ARTIGO 6

Interictal EEG in Temporal Lobe Epilepsy in Childhood

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Running title: Interictal EEG in children with TLE.

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ABSTRACT

Purpose: To clarify the value of interictal discharges and verify which extratemporal regions may also show epileptiform activity in temporal lobe epilepsy (TLE) in childhood.

Methods: We studied 53 consecutive patients, from 2 to 18 years old (mean age = 11.32 years; 28 male) with TLE. Each patient had 1 to 15 interictal EEG recordings (mean: 5.6; total = 297 EEGs). Video-EEG monitoring was performed in 40 patients. All patients had MRI. The findings were compared with a control-group of 53 consecutive TLE adult outpatients with hippocampal atrophy. Each adult patient underwent 3 to 21 routine EEGs (mean: 10.67; total = 566).

Results: Our data showed that interictal EEGs of children with TLE present extratemporal epileptiform discharges more frequently than EEGs of adults with TLE. Although we found epileptiform discharges in all extratemporal cerebral regions, they occurred mostly in frontal and parietal areas. Twenty-five children and 10 adults had frontal epileptiform discharges (p=0.001). When only children with hippocampal atrophy (30) were compared with adults, we had similar findings (p=0.007). Our data showed variable findings concerning other extratemporal regions.

Conclusions: Our findings may suggest a close interaction between frontal and temporal lobes in children with epilepsy and provides further evidence of the existence of a medial temporal/limbic neural network.

Key words: epilepsy, childhood, temporal lobe, EEG, interictal discharges.

INTRODUCTION

In adults with temporal lobe epilepsy (TLE), the analysis of serial interictal EEG usually helps in the lateralization of the epileptogenic focus. When there are unilateral epileptiform discharges in interictal EEGs in accordance with clinical and neuroimaging

data, the need of video-EEG monitoring in order to register seizures may be questioned (Barry et al., 1992; Cendes et al., 2000; Holmes et al., 1980; Pataraia et al., 1998).

Reports of interictal EEGs in TLE in childhood are few and variable. The findings of interictal EEGs in mesial temporal sclerosis are similar among adolescents and adults (Mohamed et al., 2001; Wyllie et al., 1993). In children younger than 6 years of age, in addition to epileptiform activity in temporal lobe regions, generalized epileptiform discharges are also frequent (Blume and Kaibara, 1991; Brockhaus and Elger, 1995; Franzon et al., 2004), including maximal activity in extratemporal electrodes (Ebner, 1999). In patients with neoplastic lesions, interictal EEGs often present multifocal epileptiform activity (Wyllie et al., 1993). Therefore, interictal epileptiform discharges in children with TLE seems to predominate in temporal lobe but may also be seen in other brain regions (Blume, 1997; Blume et al., 1997; Franzon et al., 2004).

The aim of this study was to clarify the value of interictal discharges and verify which extratemporal regions may also show epileptiform activity in TLE in childhood.

METHODS

From January 1999 to February 2004 we evaluated 53 consecutive patients, from 2 to 18 years old (mean age = 11.32 years), 28 male and 25 female, with TLE seen at the Pediatric Epilepsy Clinics of two tertiary hospitals.

The diagnosis of TLE was based on clinical, electroencephalographic and neuroimaging findings. The clinical data were gathered from a detailed interview with the parents and from the video-EEG monitoring data. Seizures and epileptic syndromes were classified according to the ILAE classifications (Commission on Classification, 1981; Commission on Classification, 1989).

Each patient had 1 to 15 interictal EEG recordings (mean: 5.6). Patients with less than 4 routine EEG recordings were included in this study if they underwent telemetry as well. All EEG recordings were performed with electrodes placed according to the

international 10-20 System (Jasper, 1958). Interictal EEGs lasted for at least 20 minutes and were performed on awakeness and sleep. Hyperventilation and intermittent photic stimulation were obtained in cooperative patients. Chloral hydrate was used to induce sleep when necessary.

We used the referential montages with vertex and average, longitudinal and transverse bipolar montages, as well as transverse bipolar montages using zygomatic electrodes (anterior temporal electrodes- T_1 and T_2). The findings were categorized as follow: 1) normal during wakefulness, drowsiness and/or sleep; 2) abnormal with epileptiform discharges in temporal regions, such as spikes, sharp waves, spike-slow wave complexes or temporal intermittent rhythmic delta activity (TIRDA); 3) abnormal with epileptiform discharges in extratemporal regions such as frontal, parietal, central, occipital or generalized; 4) abnormal with non-epileptiform discharges such as intermittent and irregular slow waves in temporal or extratemporal regions.

Video-EEG monitoring was performed in 40 patients, with minimal duration of 48 hours. Whenever possible, patients underwent telemetry for five days or more. In order to capture the ictal phenomena, antiepileptic drugs were tapered down in some patients during the hospitalization. We used a digital device with 64 channels for telemetry.

MRI was performed in a 2.0T scanner, using our epilepsy protocol (Montenegro et al, 2002).

Our findings were compared with a control-group of 53 consecutive TLE adult outpatients followed in the Epilepsy Clinic of our University Hospital at Campinas. Each adult patient underwent 3 to 21 routine EEGs (mean: 10.67) following the same criteria described above.

Statistical analysis was performed using Fisher exact test, considering the level of significance of 0.05.

RESULTS

Fifty-three children had 297 EEGs analyzed. These data were compared with 566 EEGs of 53 adults (34 women) with TLE, ages ranged from 20 to 55 years-old (mean=35.83 years).

Twenty-four children had 76 normal EEGs, as opposed to 38 adults with 141 normal EEGs. Four children had only normal interictal EEGs and four children had only extratemporal discharges with no temporal discharge at all. All other children had discharges at least on temporal lobes. Table 1 shows temporal abnormalities and table 2 shows extratemporal abnormalities found in the EEGs of both children and adults. Frontal, parietal and occipital discharges were more frequently seen in children ($p<0.05$).

Table 3 shows the etiologies of the TLE of the children. All adult patients had hippocampal atrophy and other signs of mesial temporal sclerosis on MRI: 27 patients with right hippocampal atrophy, 20 with left hippocampal atrophy and 6 with bilateral hippocampal atrophy. The child with tuberous sclerosis and the child with meningoencephalitis were included in this study because we registered ictal seizures originating in temporal lobe. The patient with tuberous sclerosis had three tubers: one on each temporal lobe and the other on right parietal lobe. The patient who had meningoencephalitis showed on MRI hyperintense signal at the right temporal lobe. One child with dual pathology had right fronto-temporal atrophy predominating at the temporal and hippocampal region; she became seizure free after temporal lobectomy. All other children had focal neuroimaging abnormalities only in temporal lobes.

In another analysis, we separated the children according to the etiology and compared only children with hippocampal atrophy with adults, since every patient in the adult control-group had hippocampal atrophy on MRI. Table 4 shows our findings on epileptiform and non-epileptiform temporal activity in patients with hippocampal atrophy. Findings were similar for both groups. Table 5 shows our data on extratemporal epileptiform activity in patients with hippocampal atrophy. Frontal, parietal and occipital discharges were more frequent in children ($p<0.05$).

From a total of 53 patients, 23 children were operated on temporal lobe (selective amigdalo-hippocampectomy in five, temporal lobectomy in 10 and lesionectomy in eight patients). Pre-operative routine EEGs showed extra-temporal epileptiform discharges in 12 patients who underwent epilepsy surgery. Post-operative routine EEGs showed extra-temporal epileptiform discharges in only two patients, of whom one became seizure-free.

DISCUSSION

Our data showed that EEGs of children with TLE present extratemporal epileptiform discharges more frequently than EEGs of adults with TLE. Although we found epileptiform discharges in all extratemporal cerebral regions, they occurred mostly in frontal, parietal and occipital areas. This finding may suggest a close interaction particularly between frontal and temporal lobes, which is more evident in childhood. Studies using intracranial EEG recordings show that the propagation of the temporal epileptic discharges may follow two different routes and the spreading to frontal lobe might be faster and more frequent in younger children (Brockhaus and Elger, 1995; Kramer et al., 1998).

Evidence of neural networks supports the idea that the network structures are connected functionally and structurally (Spencer, 2002). One specific epilepsy network is the medial temporal/limbic network connecting hippocampi, amygdalae, entorhinal cortices, lateral temporal cortices, and extratemporal components of the medial thalamus and the inferior frontal lobes. Clinical observations, intracranial EEG, functional neuroimaging, anatomic observations, and the response of seizures to specific invasive treatments support the existence of the neural networks (Spencer, 2002). Scalp EEG studies are not mentioned because they usually do not contribute to elucidate the existence of this network. Besides, we cannot despise the fact that extratemporal spikes on the scalp EEG might come also from deep temporal focus and not necessarily suggest the existence of an extratemporal network (Hamer et al., 1999).

Extratemporal discharges presented by our patients disappeared after epilepsy surgery in most of them, which offers further evidence of the link between frontal and temporal regions based on routine EEGs of children with TLE.

Generalized epileptiform discharges were seen equally in both groups in our study as shown in table 2. Other authors found that generalized discharges may occur in children with TLE as well (Brockhaus and Elger, 1995; Ebner, 1999). The same finding may occur in approximately 10% of TLE adult patients probably due to secondary bilateral synchrony (Sadler and Blume, 1989). The coexistence of primarily generalized epilepsy and TLE is very rare (Diehl et al., 1998; Koutroumanidis et al., 1999).

In this study, every child had temporal lesion confirmed by MRI, despite the occurrence of non-localizing scalp EEG findings in most of them. This shows the importance of a multidisciplinary approach in this group of patients, with emphasis on neuroimaging studies. Therefore, neuroimaging assessment plays an important role in the diagnosis of TLE in childhood, because clinical presentation and neurophysiological data may not be as clear-cut as they are in adults (Franzon et al., 2004; Nordli et al., 2001). The most frequent finding was hippocampal atrophy followed by tumors. Mesial temporal sclerosis is considered rare in children with less than five years of age and relatively infrequent during the second decade (Mizrahi et al., 1990; Wyllie et al, 1993). Nevertheless, other studies find mesial temporal sclerosis to be the most frequent condition associated with childhood TLE (Grattan-Smith et al., 1993). Neocortical lesions, such as focal cortical dysplasia or tumors, occur frequently in childhood with TLE and may also be found in association with hippocampal atrophy (dual pathology). The association of mesial temporal sclerosis and focal cortical dysplasia may be found in neuropathological studies in 58% or 79% of the surgical specimens of children with refractory TLE (Bocti et al., 2003; Mohamed et al., 2001).

In patients with neoplastic lesions, interictal EEGs present multifocal epileptiform activity (Wyllie et al., 1993). This finding could indicate that large lesions may cause propagation of the discharge. Nevertheless, when we selected our children according to the etiology and compared only those with hippocampal atrophy with the control group, we still had similar results. In other words, even small and confined lesions such as

hippocampal atrophy may be associated with the spreading of temporal epileptiform discharges in children (Ebner, 1999).

The fact that TLE in childhood presents unique characteristics when compared with TLE in adults might suggest a different consequence of the initial precipitating injury in the developing brain.

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Table 1: Epileptiform and non-epileptiform temporal activity in patients with TLE

EEG	Children	Adults	p
Ipsilateral EA	44	48	0.39
Contralateral EA	9	10	1.0
Bilateral EA	13	16	0.66
Ipsilateral NEA	39	47	0.08
Contralateral NEA	6	11	0.29
Bilateral NEA	12	28	0.002
Total	53	53	

EA = epileptiform activity; NEA = non-epileptiform activity.

Table 2: Extratemporal epileptiform activity in patients with TLE

Areas	Children	Adults	p
Frontal	25	10	0.003
Parietal	16	2	0.0005
Occipital	10	0	0.001
Central	2	0	0.5
Generalized	10	5	0.2
Total	53	53	

Table 3: Etiologies in children with TLE

Etiology	Children
HA	30
Tumors	9
Dual-Pathology	6
HA + Tumor	2
HA + Dysplasia	4
Focal Cortical Dysplasia	3
Arachnoid cyst	2
Tuberous sclerosis	1
Meningoencephalitis	1
Cavernoma	1

HA = hyppocampal atrophy

Table 4. Epileptiform and non-epileptiform temporal activity in patients with HA

EEG	Children	Adults	p
Ipsilateral EA	24	48	0.19
Contralateral EA	3	10	0.36
Bilateral EA	5	16	0.2
Ipsilateral NEA	23	47	0.2
Contralateral NEA	2	11	0.1
Bilateral NEA	0	28	<0.0001
Total	30	53	

EA = epileptiform activity; HA = hyppocampal atrophy; NEA = non-epileptiform activity.

Table 5. Extratemporal epileptiform activity in patients with HA

Areas	Children	Adults	P
Frontal	14	10	0.01
Parietal	7	2	0.01
Occipital	5	0	0.005
Central	1	0	0.36
Generalized	4	5	0.6
Total	30	53	

ARTIGO 7

Interictal Electroencephalographic Findings in Children and Adults with Temporal Lobe Tumors

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Interictal Electroencephalographic Findings in Children and Adults with Temporal Lobe Tumors

Submetido a Arq. Neuropsiqr.

INTERICTAL ELECTROENCEPHALOGRAPHIC FINDINGS IN CHILDREN AND ADULTS WITH TEMPORAL LOBE TUMORS

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Running title: Interictal EEG in patients with TLE due to tumors.

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Abstract

Objective: To characterize clinical and interictal electroencephalographic aspects of children and adults with temporal lobe epilepsy (TLE) due to tumoral lesions.

Methods: We performed a retrospective analysis of the clinical and interictal electroencephalographic aspects of 16 children (64 exams) and 12 adults (78 exams) with lesions in the temporal lobe.

Results: The most frequent etiologies were gangliogliomas, DNETs, followed by astrocytomas. Auras occurred in both groups, mainly epigastric sensation. Other findings such as myoclonias, behavioral arrest and vomiting were more frequent in children. Temporal epileptiform and non-epileptiform activities, mostly unilateral, were found in both groups. Extratemporal epileptiform activities (frontal, parietal, central, occipital and generalized) were also found equally in both groups.

Conclusion: Our data showed that children and adults with TLE due to expansive lesions present with similar EEG findings.

Key Words: epilepsy, childhood, temporal lobe, EEG, tumors.

Neurodevelopmental tumors have been diagnosed with increasing frequency as a cause of refractory temporal lobe epilepsy (TLE), specially in children, due to a wider use of magnetic resonance imaging (MRI).

In some studies, they are considered the main cause of refractory TLE in children[1,2]. The tumors most frequently found are neuronal or glioneural tumors (gangliogliomas, ganglioglioma, ganglioneuroma, dysembryoplastic neuroepithelial tumor – DNET), oligodendrogliomas and astrocytomas, including pleomorphic xantoastrocytoma. Gangliogliomas are the main tumors responsible for the appearance of epileptic seizures of difficult control with medications with onset before the age of fifteen[3]. They are tumors of slow growth and there is absence of clinical signs of localization and also absence of signs of intracranial hypertension[4].

The growth of those tumors and their pathological findings suggest that they, specially gangliogliomas and DNET, might either originate from a cortical malformation or be the final end of the spectrum of the cortical dysplasias[5-9].

In children with TLE of different etiologies there is a wide clinico-electroencephalographic diversity[2,10-13] .

Knowing that tumoral lesions lead to a variable electroencephalographic pattern, particularly in children, we aimed to compare interictal EEG findings of children with those of adults with TLE due to tumoral lesions.

Patients and Methods

We performed a retrospective analysis of 16 patients younger than 17 years of age (mean age: 10 years), being 9 of the male gender, with expansive lesion in the temporal lobe followed at the ambulatory clinic of childhood epilepsy of the HC/Unicamp, from 1998 to 2005 (Group 1).

The interictal eletroencephalographic findings were compared to those of 12 adult patients, from 21 to 51 years of age, being 6 of the male gender, followed at the ambulatory clinic of epilepsy of difficult medical control of the HC/Unicamp (Group 2).

Two to 11 routine EEGs were recorded in each patient, following the international rules for electrodes placement: “system 10-20”. Two EEG devices were used, one with 14 channels (analogic) and another with 32 channels (digital), both from Nihon Kohden Company. The montages are in accordance with the American EEG Society Association, using montage with zygomatic electrode besides bipolar montages (longitudinal and transverse) and referential with vertex. The minimal duration of the tracings was 20 minutes. The examinations were performed during sleep, somnolence and while awaken. Methods of activation (hyperventilation and intermittent photic stimulation) were routinely used. In younger children and in those less collaborative, whenever necessary, the sleep phase was induced with chloral hydrate.

Telemetry was performed in nine children and six adults.

We used t-student and Fisher tests for statistical analysis.

Results

The mean age of onset of the epileptic seizures was 16,083 years in the adult patients and 6,437 years in the children, statistically significant data (p=0,010).

Simple partial seizures occurred in nine children and in 11 adults, being predominantly epigastric and visual aura. There were complex manual automatisms in nine patients of the groups 1 and 2 (56% and 75%, respectively). Other findings, such as myoclonias (two children), behavioral arrest at the beginning of the ictus (six children and two adults), and vomiting (four children and two adults), were more frequent in children and there was no significant difference between the two groups in signs and symptoms.

The neuropathological data of the patients who have already undergone surgery are on table 1 (12 children and six adults).

The most frequent etiologies were ganglioglioma, DNET, followed by astrocytoma. We found six lesions of temporal mesial topography in the children and also six lesions in the adults, there were 10 lateral lesions in the children and six in the adults. The lesions occurred most frequently in the right hemisphere: 10 children and eight adults.

Table 2 shows the temporal EEG findings of groups 1 and 2. The childhood group (Group 1) underwent 64 exams (mean: 4 exams per patient) and the adult group (Group 2) had 78 exams (mean: 6.5 exams per patient).

Table 3 shows the extratemporal EEG findings of groups 1 and 2.

Discussion

Our data showed that temporal interictal epileptiform and non epileptiform activity occur equally in all age ranges. Normal EEGs were significantly more frequent in the adults in this study. However, in the pediatric age range, 15.9% of the patients with TLE may have persistently normal EEGs[14].

Interictal extratemporal epileptiform activity was also found in both groups, which was unexpected, as TLE in childhood usually presents a greater clinico-electroencephalographic diversity[1].

Pre-operative studies performed in adults with temporal lobe tumors have demonstrated electrophysiological variability: temporal focal discharges, bilateral temporal activity, contralateral activity, extratemporal activity and presence of "mirror focus"[15-22].

Interictal EEGs of children with TLE may show extratemporal discharges, specially frontal, more frequently than in adults with mesial sclerosis[12]. We observed in the present study that the EEGs of adult patients with tumoral lesions also displayed extratemporal discharges. That suggests that this neurophysiological characteristic might be related to the etiology, independently of the age range. In other words, there was no significant difference between the extratemporal findings of children and adults because both age groups seem to have a similar neurophysiological behavior when the etiology is an expansive lesion of the temporal lobe. In patients with TLE caused by hippocampal sclerosis, however, there is a difference between the age ranges[12,23].

Our data showed that seizure onset was significantly earlier in children than in adults, despite same pathology and similar EEG findings. This may reinforce that EEG features in temporal lobe tumors are not age-dependent.

The clinical features of adults with tumoral lesions in the temporal lobe can be differentiated from those with mesial temporal sclerosis by the initial ictal pattern, by the behavioral sequence and by its time of appearance during the seizure[24]. Other authors found that seizures of neocortical origin are significantly shorter in duration[25]. In spite of those clinical differences, there is difficulty in evaluating each patient individually[26]. Our clinical findings were suggestive of mesial TLE with the presence of typical auras and automatisms, even in the lateral lesions. These findings may either reflect a rapid propagation to the mesial structures or simply occur by the activation of cortical areas distant from the epileptic focus. Few patients presented auras suggestive of neocortical involvement.

To conclude, this study suggests that interictal discharges in children and adults with TLE due to expansive lesions present with a polymorphic electroencephalographic pattern. Although children with TLE have frequent extratemporal epileptiform discharges, independently of the etiology, there is not significant difference when one compares children and adults with tumoral lesions. In TLE due to mesial sclerosis, there seems to be a difference between the two age groups.

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Table 1 – Etiology-Neuropathological Data

Neuropathological Findings	Children	Adults	p
Ganglioglioma	06	03	0,687
DNET	04	0	0,113
Astrocytoma	0	01	0,428
Pilocytic Astrocytoma	01	0	1
Cavernoma	01	01	1
Ruptured Epidermic Cyst	0	01	0,428
Without Definition	04	06	0,242

Table 2 – Interictal EEGs with Temporal Discharges (in numbers)

	Children	Adults	p
Temporal EA	15	09	0,285
Contralateral Temporal EA	03	05	0,230
Bilateral Temporal EA	06	04	1
Temporal NEA	13	07	0,230
Bilateral Temporal NEA	05	05	0,697
Contralateral Temporal NEA	0	03	0,114
Normals	04	09	**0,020**

EA: epileptiform activity; NEA: non-epileptiform activity

Table 3 – Interictal EEGs with Extratemporal Discharges (in numbers)

	Children	Adults	p
Frontal	04	02	0,673
Parietal	04	02	0,673
Occipital	02	0	0,492
Central	04	03	1
Generalized	03	0	0,238

ARTIGO 8

Aspectos Eletrencefalográficos Ictais da Epilepsia de Lobo Temporal na Infância

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Aspectos Eletrencefalográficos Ictais da Epilepsia de Lobo Temporal na Infância

ASPECTOS ELETRENCEFALOGRÁFICOS ICTAIS DA EPILEPSIA DE LOBO TEMPORAL NA INFÂNCIA

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Resumo

Objetivos: Avaliar os aspectos eletrencefalográficos ictais da ELT na infância. **Métodos**: monitorização vídeo-eletrencefalográfico de 25 crianças de 2 a 18 anos (média: 12,4 anos) com ELT sintomática. Monitorização ambulatorial ou com paciente internado. Os dados EEGs ictais foram subdivididos em padrão ictal inicial, atividade ictal rítmica persistente e padrão pós-ictal. **Resultados**: Foram analisadas 149 crises, de 1 a 22 crises por paciente (média: 5,96). A capacidade de localização da zona epileptogênica foi de 55,7% (83/149) na análise do padrão inicial, 55,7% (83/149) na atividade rítmica persistente e 32,8% (15/117) no padrão pós-ictal. A capacidade de lateralização foi de 77,1% (115/149) na análise do padrão inicial, 65,7% (98/149) na atividade rítmica persistente e 59,8% (70/117) no padrão pós-ictal. **Conclusões**: A capacidade de lateralização foi superior à localização da zona epileptogênica, entretanto, esses valores são inferiores aos observados em adultos com ELT associada à EMT.

Introdução

Os pacientes com epilepsia apresentam anormalidades eletrencefalográficas interictais e ictais que podem definir a localização da zona epileptogênica. Crises parciais refratárias são, na maioria das vezes, causadas por anormalidade estrutural do cérebro (Blume & Kaibara, 1991). O registro ictal tem seu uso indicado principalmente na avaliação pré-cirúrgica das epilepsias refratárias e a síndrome epiléptica mais detalhadamente estudada é a epilepsia do lobo temporal (ELT) mesial. A análise do eletrencefalograma (EEG) ictal na ELT envolve vários aspectos: a morfologia da descarga ictal, seu padrão inicial, duração, localização e lateralização. O padrão ictal inicial mais freqüente é a atividade rítmica teta, sendo observadas também atividades delta, alfa ou ainda espículas rítmicas (Risinger etal., 1989; Ebner e Hoppe, 1995; Pataraia et al., 1998). Alteração do padrão inicial com duração superior a três segundos foi definida como primeira mudança ictal inequívoca (Pataraia et al., 1998). A atividade teta rítmica muitas vezes ocorre 10 a 20 segundos após o início ictal (Walczak et al., 1992). A localização pode ser temporal, regional, hemisférica, bilateral lateralizada ou não. Atividade rítmica ictal e

ondas lentas pós-ictais são consideradas lateralizatórias quando apresentam uma amplitude duas vezes maior em um hemisfério em relação ao outro. A atenuação pré e/ou pós-ictal também precisa ter metade da amplitude do hemisfério contralateral para ser considerada lateralizatória (Walczak et al., 1992). O início eletrográfico focal de uma crise tipicamente evolui da seguinte maneira: (I) atenuação focal da atividade do EEG; (II) descarga rítmica rápida focal e de baixa-amplitude; e (III) aumento progressivo da amplitude com lentificação, que se propaga para uma distribuição anatômica regional (Chabolla & Cascino, 2001).

O objetivo deste trabalho foi avaliar os aspectos eletrencefalográficos ictais da ELT na infância.

Pacientes e Métodos

Foram estudados 25 pacientes de dois a 18 anos (15 meninas e 10 meninos), acompanhados no Ambulatório de Epilepsia Infantil do HC/UNICAMP, submetidos à monitorização vídeo-EEG de fevereiro de 2000 a agosto de 2005.

Todos os pacientes apresentavam ELT de difícil controle medicamentoso e foram submetidos à avaliação pré-cirúrgica.

Foram realizados dois a 11 EEGs de rotina, obedecendo-se às normas internacionais para colocação de eletrodos “sistema 10-20”. Os aparelhos utilizados foram de 14 canais (analógico) e de 32 canais (digital), ambos da marca Nihon Kohden. As montagens estão em conformidade com as recomendações da AMERICAN EEG SOCIETY ASSOCIATION, usando a montagem com eletrodo zigomático além das montagens bipolares (longitudinal e transversa) e referencial com vértex e average.

A monitorização vídeo-EEG foi realizada até o registro de no mínimo uma crise epiléptica, ambulatorialmente por cerca de seis a oito horas de registro por dia ou realização do exame com paciente internado, com redução medicamentosa. O aparelho utilizado para telemetria foi digital Nihon Kohden de 64 canais. Foram analisadas as alterações

eletrencefalográficas ictais iniciais, o padrão evolutivo e o pós-ictal imediato. Como achados ictais iniciais foram consideradas as primeiras modificações encontradas no EEG, sendo focais temporais (temporal, fronto-temporal, temporal médio, temporal médio-basal, temporal posterior, bilateral e contralateral) ou extratemporais, dessincronização da atividade elétrica (eletrodecremento focal temporal, hemisférico ou difuso) e artefatual. Padrão crítico (atividade rítmica persistente) foi considerada focal temporal, hemisférica, difusa ou ainda obscurecida por artefatos. Achados pós-críticos incluíram alentecimento ou atenuação focal temporal, hemisférica, hemisférica sendo máxima temporal, difusa e difusa máxima hemisférica. Os achados foram considerados lateralizatórios quando sua amplitude tinha pelo menos 50% de diferença.

Todos os pacientes apresentavam anormalidades estruturais do lobo temporal detectados nos exames de ressonância magnética (RM) de alta resolução. As imagens foram obtidas em um sistema de 2 T (Elscint Prestige®), usando protocolo para epilepsia.

Resultados

Foram analisadas 149 crises, de 1 a 22 crises por paciente (média: 5,96), de 25 pacientes, de dois a 18 anos (média: 12,4 anos), com epilepsia sintomática do lobo temporal.

Telemetria ambulatorial foi realizada em cinco pacientes por um a cinco dias (média: 2,4) e com paciente internado em 20 pacientes por um a oito dias (média: 4,5). A etiologia mais freqüente foi atrofia hipocampal (13 pacientes), seguida por lesões tumorais (sete pacientes) e dupla-patologia (cinco pacientes, sendo três com malformações corticais, um com lesão tumoral e outro com hamartoma no lobo temporal).

Os aspectos clínicos mais relevantes estão na Tabela 1. Em quatro eventos não foi possível fazer a correlação clínico-eletrencefalográfica e 26 eventos foram apenas auras (epigástrica em 11 e distúrbios autonômicos, como sensação de sede, em 15). Também foram encontradas auras olfativas (três crises), visual complexa (sete crises) e sensação de

medo (40 crises). Choro ou grito no início da crise foram vistos em 40 crises de seis pacientes.

Os dados EEGs ictais foram subdivididos em padrão ictal inicial (tabela 2), atividade ictal rítmica persistente (tabela 3) e padrão pós-ictal (tabela 4).O padrão ictal inicial foi eficaz em localizar (focalizar) a zona epileptogênica em 55,7% (83/149) das crises e lateralizá-la em 77,1% (115/149). Pela análise da atividade rítmica persistente, a localização foi possível em 57,7% (86/149) e a lateralização em 65,7% (98/149) das crises. Alteração do padrão pós-ictal foi observada em 117 crises, com localização em 12,8% (15/117) e lateralização em 59,8% (70/117). Em 32 crises (21,5%), não houve alteração pós-ictal evidente.

Discussão

Os estudos sobre EEG na infância são variáveis. Alguns deles (Duchowny et al., 1992) não demonstraram diferenças nos achados EEGs nas diferentes faixas etárias, outros encontraram diversidade de acordo com a etiologia (Wyllie et al.,1993). No entanto, para outros autores (Brockhaus & Elger, 1995), a expressão EEG da ELT em crianças foi idade-dependente e os achados de EEG foram subdivididos de acordo com a faixa etária: no grupo de pré-escolares (menores de seis anos) predominaram descargas ictais generalizadas e em crianças maiores de seis anos, os registros ictais e eletrocorticográficos mostraram ondas agudas ou teta rítmicas, focais, predominantemente sobre a região temporal. Isto nos sugere que crianças menores, mesmo tendo comportamentos ictais atípicos, devem ir para a avaliação pré-cirúrgica.

Auras foram detectadas em 76 crises (51%). A presença de automatismos exuberantes (realização de movimentos amplos e estereotipados) bem como movimentos de elevação e rotação do tronco foram vistos em seis pacientes (24%). Crises semelhantes às do lobo frontal em crianças com ELT já foram citadas na literatura (Brockhaus & Elger, 1995).

As crises parciais complexas em adultos caracterizam-se por reação de parada de atividade, automatismos oroalimentares e manuais simples ou complexos, com duração superior a um minuto (Kotagal et al., 1989; Steinhoff et al., 1998). A postura distônica do membro contralateral tem importante valor lateralizatório e foi encontrada em 11 pacientes (49 crises). O ato de esfregar o nariz com a mão foi detectado em pacientes com ELT, geralmente como manifestação pós-ictal, e tem valor lateralizatório ipsilateral (Leutmezer et al., 1998). Esse ato foi visto em nove dos nossos pacientes (16 crises). Aspectos clínicos semelhantes já foram descritos em crianças mais jovens (Fogarasi et al., 2002).

Quando as crises iniciaram ou mantiveram um padrão focal temporal, houve predomínio sobre a região anterior-médio-basal. Duchowny et al. (1994) descreveram a propagação de crises da região temporal posterior para córtex médio-basal, com padrão ictal clínico-EEG típicos de ELT mesial, sendo necessária a ressecção temporal ampliada nas crianças com refratariedade medicamentosa. Nordli et al. (2001) observaram que crises parciais de regiões anteriores do cérebro tenderam a aumentar com a idade, enquanto aquelas provenientes de regiões posteriores tenderam a diminuir com a idade (não estatisticamente significativo). São dados condizentes com a descrição de Gibbs (Gibbs, 1958) sobre a migração da descarga epileptiforme interictal das regiões posteriores para as anteriores com o decorrer do processo maturacional da criança. Apesar da pequena amostra de pacientes mais jovens (idade média: 12,4), crises envolvendo as regiões posteriores (têmporo-occipitais) ocorreram em nove pacientes (6%).

A localização (focalização) e a lateralização mostraram valores inferiores aos descritos na literatura em adultos com ELT mesial (Risinger et al., 1989; Williamson et al., 1993; Ebner e Hoppe, 1995). A capacidade de lateralização em adultos encontra-se em torno de 80%, atingindo valores superiores em alguns estudos (O'Brien et al., 1996; Foldvary et al., 2001). A lateralização mostrou-se superior à localização. Isto provavelmente se deve à proeminente propagação intra-hemisférica para o lobo frontal ipsilateral primeiramente e depois para o lobo temporal contralateral via comissura hipocampal apresentada em crianças e adolescentes com ELT (Kramer et al., 1998). O registro ictal de 21 pacientes submetidos a monitorização invasiva a longo prazo mostrou

como padrão inicial mais freqüente a presença de atividade beta de baixa amplitude intracraniana seguida por ritmo teta mais lento registrado simultaneamente no local de início e áreas adjacentes. A única diferença entre o grupo menor de 14 anos (oito pacientes) e maior de 18 anos (13 pacientes) foi a maior tendência das crises ficarem restritas ao lobo temporal e a menor tendência à generalização secundária no primeiro grupo (Kramer et al., 1998).

No estudo de Pedreira (1998), envolvendo 34 pacientes com ELT sintomática, lesões neocorticais, EMT e dupla-patologia, as alterações EEGs ictais lateralizaram a lesão nos dois primeiros grupos de forma equivalente (66,67% e 68,75%, respectivamente). A localização no lobo temporal ipsilateral, porém, foi maior no grupo com EMT (43,75%) do que no grupo com lesões neocorticais (14,28%). A atividade rítmica ictal por 30 segundos permitiu a localização da lesão epileptogênica em 71,42% e 92,80% dos pacientes dos grupos com lesões neocorticais e EMT, respectivamente, tendo, portanto, maior valor localizatório do que as alterações ictais iniciais.

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Tabela 1: Dados Clínicos de 25 pacientes (119 crises)

	No. Pacientes	No. Crises
Parada de atividade	14	44
Versão cefálica	9	37
Automatismos oromastigatórios	14	26
Automatismos manuais	13	30
Automatismos exuberantes	6	38
Elevação / rotação do tronco	6	31
Postura distônica	11	49
Coçar o nariz	9	16
Cuspir / vômitos	9	9
Postura tônica	2	19
CTCGS	5	16

CTCGS= crise tônico-clônica secundariamente generalizada

Tabela 2: Padrão Inicial Ictal

Número de crises	149
Temporal	7
Temporal médio	8
Temporal posterior	9
Fronto-temporal	5
Temporal médio-basal	32
Temporal médio-basal contralateral	6
Temporal bilateral	2
Eletrodecremento difuso	19
Eletrodecremento hemisférico	19
Eletrodecremento focal temporal	22
Artefatual	7
Frontal	13

Tabela 3: Atividade rítmica persistente

Número de crises	149
Temporal	6
Temporal médio	8
Temporal médio-basal	48
Temporal bilateral	9
Fronto-temporal	16
Temporal posterior	8
Hemisférica	12
Difusa	13
Artefatual	29

Tabela 4: Padrão pós-ictal – lentificação/atenuação do traçado

Número de crises	117
Temporal	4
Hemisférica, máxima temporal	11
Hemisférica	24
Difusa, máxima hemisférica	46
Difusa	32
Sem lentificação	31
Artefatual	1

5- DISCUSSÃO

O objetivo do trabalho de pesquisa foi determinar os aspectos clínico-eletrencefalográficos da ELT na infância. Cada um dos artigos apresentados contém discussão específica. Portanto, faremos agora uma breve discussão, além de discorrermos sobre outros aspectos relevantes.

ETIOLOGIA

Quanto à etiologia, a mais freqüente foi AH, encontrada em 44,44% (16/36) pacientes do primeiro estudo (artigo 2) e em 56,60% (30/53) do estudo do EEG interictal (artigo 6). O segundo grupo etiológico mais freqüente foi representado pelas lesões tumorais (artigo 6) e pela dupla-patologia (artigo 2). A análise por faixa etária mostrou que, nas crianças menores de seis anos (grupo A do artigo 2), a AH não foi encontrada isoladamente, corroborando os achados de séries de ELT na infância, nas quais a AH raramente é encontrada nas idades precoces (primeira década de vida) e perde em freqüência para tumores e displasias corticais (Duchowny et al., 1992; Wyllie et al., 1993; Pedreira, 1998).

A presença de dupla-patologia, principalmente a associação da AH com anormalidades no neocórtex temporal ipsilateral, tem sido apontada como etiologia mais freqüente em crianças (Mohamed et al., 2001; Bocti et al., 2003). Estes achados poderiam ajudar a explicar a maior variabilidade clínica-EEG nesta faixa etária.

Outras etiologias já citadas na literatura também foram encontradas na nossa casuística: esclerose tuberosa, cisto aracnóide, meningoencefalite, cavernoma e trauma crânio-encefálico.

Os dois pacientes que tiveram TCE aos 18 meses apresentam AH unilateral, um deles com lesão adicional no polo temporal ipsilateral sugestiva de gliose, não podendo ser afastada a possibilidade de displasia cortical. Estudos mostram que há associação entre TCE em idade precoce e EMT (Mathern et al., 1994; Marks et al., 1995).

O diagnóstico etiológico por RM não pôde ser feito em apenas dois pacientes (artigo 2), ambos com achados clínicos e EEGs típicos de ELT e alterações da imagem tomográfica (um deles com calcificação grosseira no LTE e outro com atrofia de LTE).

ASPECTOS CLÍNICOS

Em nosso estudo (artigo 2), encontramos a presença de aura na maioria dos pacientes (26/36 – 72,2%), sendo pouco freqüente nos mais jovens (apenas em 3/6 pacientes menores de seis anos). As auras mais observadas foram sensação de medo e sensação epigástrica ascendente. Esta última é a aura mais freqüentemente encontrada em adultos com ELT, especialmente em pacientes com EMT (O'Brien et al., 1998; Henkel et al., 2002). Esse dado também ocorreu em nossos pacientes, sendo já esperado pela grande porcentagem de EMT. Entretanto, foram também evidentes nos pacientes com ELT por lesões tumorais (artigo 7).

As crianças menores têm uma maneira peculiar de caracterizar as auras, usando expressões como "minha barriguinha está sonhando", "tem um bichinho na garganta", que precisam ser objetivamente questionadas e correlacionadas com os demais dados clínicos. Auras nas crianças menores, muitas vezes, não são detectáveis ou são mal interpretadas pelos familiares.

Outra peculiaridade interessante foi o fato de alguns pacientes terem passado por investigação clínica-laboratorial de dor abdominal durante semanas a meses antes do diagnóstico de epilepsia. Relatamos um caso (artigo 3) no qual houve atraso no diagnóstico até a paciente ser encaminhada a um neuropediatra e ao serviço terciário para ser submetida aos exames específicos e ao tratamento cirúrgico. Neste caso, a paciente apresentava inicialmente CPS, seguidas por episódios de CTCGS e distúrbio comportamental que na evolução mostrou-se compatível com ELT por lesão tumoral. O termo "epilepsia abdominal" é bastante controverso. Como dor abdominal é um sintoma muito freqüente em crianças, colocamos um exemplo de outra causa neurológica, a migrânea basilar. Os episódios migranosos foram interpretados como crises epilépticas, porém, não houve boa

resposta à DAE utilizada. Presença de anormalidades EEGs durante um evento migranoso, tais como lentificação posterior difusa, já foram descritas (Niedermeyer, 1999). Com o relato do paciente 1 procuramos alertar para que o diagnóstico de crises parciais seja realizado mais precocemente. Ao citar o paciente 2, procuramos deixar claro que nem sempre o diagnóstico de epilepsia é tão simples e deve-se ter muita cautela antes da confirmação diagnóstica.

Encontramos também (artigo 2) pacientes com crises generalizadas (13 crianças) e mioclônicas (três crianças). Esses achados foram mais freqüentes nas crianças menores de seis anos (3/6) mas a diferença entre os grupos não foi estatisticamente significante, talvez pelo pequeno tamanho da amostra do grupo A.

As mioclonias ocorreram em duas crianças lactentes (artigo 4), com tumor do lobo temporal. Posteriormente evoluíram com crises parciais compatíveis com ELT. Esses pacientes foram submetidos ao procedimento cirúrgico (lesionectomia) e permeneceram na classe I (caso 1) e classe III (caso 2) da classificação de Engel. Piores prognósticos em casos semelhantes, bem como a presença de mioclonias precedendo crises parciais, já foram relatados na literatura (Dalla Bernardina et al., 1984; Carrazana et al., 1993). A presença de espasmos infantis, principalmente assimétricos, ocorrendo ipsilateralmente à lesão estrutural do lobo temporal também já foi citada isoladamente na literatura (Fogarasi et al., 2002).

A terceira paciente com mioclonias era adolescente com EMT à direita. Após o procedimento cirúrgico aos 17 anos, suas crises parciais desapareceram, porém, permaneceram as crises mioclônicas e eventos não-epilépticos. Evoluiu com controle das crises, mas sem esclarecimento diagnóstico. A coexistência de mioclonias e crises parciais parece ser evento raro (Koutromanidis et al., 1999).

Nas crianças jovens (≤ 6 anos), crises com componentes motores (hipermotricidade, alguns componentes semelhantes às crises de lobo frontal) foram freqüentes. As manifestações motoras, tais como mioclonias, espasmos infantis, movimentos clônicos e posturas tônicas, foram analisadas em função da idade, sendo evidentes nos pacientes mais jovens, principalmente lactentes (Nordli et al., 2001;

Fogarasi et al., 2002). Analisando-se a porcentagem de componentes motores em função da idade, o resultado foi uma relação linear e inversa da taxa de componentes motores para o total de componentes das crises na idade da monitorização (Fogarasi et al., 2002). Crises secundariamente generalizadas estiveram presentes nos dois grupos, não havendo predomínio segundo a faixa etária (artigo 2). Nossos dados discordam da literatura que mostra uma menor tendência à generalização secundária no grupo mais jovem, inclusive adolescente (Kramer et al., 1998; Nordli et al., 2001). Esses achados podem ser justificados pelo pequeno tamanho amostral do grupo de lactentes e pré-escolares. Crises parciais estiveram presentes em todos os pacientes no decorrer de sua evolução. Presença de postura distônica e de automatismos manuais e complexos predominaram nos pacientes maiores de seis anos (grupo B do artigo 2).

Antecedentes de crises febris estiveram presentes em apenas cinco pacientes (13,88%) do grupo B, tendo a maioria EMT. Os nossos estudos não permitem conclusões a respeito da relação de crise febril com ELT. A literatura é controversa, havendo autores que apontam para a existência de estreita correlação entre ambos e que a crise febril precoce danifique o hipocampo, sendo uma causa de EMT (Abou-Khalil et al., 1993; Van Landingham et al., 1998). Outros acreditam que a causa da crise febril prolongada seja um hipocampo já lesado devido a uma injúria pré-natal ou perinatal, ou por predisposição genética (Fernandez et al., 1998; Cendes, 1995). Portanto, a questão se crises febris complexas são um epifenômeno ou um fator causal para EMT permanece para ser respondida.

Exame físico e neurológico foram predominantemente normais. Apagamento discreto do sulco nasogeniano contralateral à lesão estrutural (EMT) durante o riso espontâneo foi encontrado em nove pacientes (artigo 2).

ASPECTOS COMPORTAMENTAIS

Além do comprometimento da memória, outros distúrbios comportamentais foram encontrados nos nossos pacientes, tais como: hiperatividade, agressividade, distúrbio da fala e dificuldade escolar, além de deficiência mental e autismo (artigo 2).

Eventos não epilépticos (pseudocrises) e depressão ocorreram em três adolescentes do sexo feminino com AH (artigo 2).

Transtornos globais do desenvolvimento podem se associar com ELT na infância (Szabó et al., 1991). Presença de surtos psicóticos reversíveis ocorreram em dois pacientes. Um deles (paciente 12 da tabela 1 do artigo 2) foi submetido à lobectomia temporal anterior direita com melhora do comportamento (agressividade, hiperatividade, dificuldade escolar) após a cirurgia, mesmo permanecendo na classe II de Engel. Entretanto, há relato na literatura de que a cirurgia de ELT na infância parece não ter efeito sobre o comportamento, mesmo quando bem sucedida (Szabó et al., 1998; Szabó et al., 1999).

Duas outras crianças com lesão tumoral (ganglioglioma) no lobo temporal esquerdo apresentavam agressividade e hiperatividade antes da cirurgia, com nítida piora comportamental após a intervenção (artigo 5). Psicose ocorrendo após a ressecção de ganglioglioma ou DNET em ELT já foi relatada (Andermann et al., 1999) e os autores propuseram que este fato possa decorrer de "normalização forçada". Entretanto, uma delas, com acompanhamento a longo prazo após a cirurgia (48 meses), apresentou melhora do comportamento. Isso demonstra que em crianças o procedimento cirúrgico também pode contribuir para melhorar os distúrbios comportamentais e a qualidade de vida dos pacientes e de seus familiares.

ASPECTOS EEG

EEG Interictal

No adulto com ELT, há predomínio de atividade interictal nas regiões temporais (Williamson et al., 1993). No presente estudo, também houve predomínio de atividade epileptiforme temporal, apesar da considerável presença de atividade epileptiforme generalizada e extratemporal (artigos 2 e 6).

No artigo 2, ocorreu grande porcentagem de atividade epileptiforme extratemporal e generalizada, predominantemente nas crianças mais jovens. Porém, no artigo 6 comparamos a presença de descargas extratemporais envolvendo os vários lobos separadamente (frontal, parietal, central e occipital) e as descargas generalizadas de 53 crianças com ELT com 53 adultos com EMT e a atividade epileptiforme extratemporal foi mais freqüente nas crianças, principalmente nas áreas frontais.

Uma vez que o grupo de crianças com ELT tinha diferentes etiologias, selecionamos apenas as crianças com EMT (30 pacientes) para comparar com os adultos com EMT (53 pacientes) e encontramos também a presença de maior número de EEGs com descargas extratemporais (frontais, parietais, occipitais) no grupo pediátrico. Portanto, concluímos que crianças com ELT apresentam maior freqüência de descargas extratemporais interictais do que adultos, inclusive quando a etiologia é a EMT. Desconhecemos outros estudos que analisaram dados semelhantes aos nossos.

Esses achados justificam o acompanhamento de um maior número de pacientes com outros tipos de epilepsias, tais como epilepsias do lobo frontal e occipital, que eventualmente tiveram a suspeita de ELT. A investigação e monitorização vídeo-EEG demonstraram evidências clínicas e EEGs de outros diagnósticos, bem como a presença de lesões estruturais em outras regiões (frontais ou occipitais).

Em nossa casuística, tivemos dois pacientes com padrão EEG compatível com epilepsia rolândica (atividade epileptiforme envolvendo as regiões centrais). Há na literatura relatos de crianças com epilepsia rolândica e a presença de EMT à RM (Eeg-Olofsson et al., 2000; Morikawa, 2000).

Atividade epileptiforme e não epileptiforme temporal ocorreu nos dois grupos. Porém, atividade não epileptiforme bilateral foi mais freqüente nos adultos. Talvez isso possa se correlacionar com o longo tempo de evolução dos pacientes adultos com crises refratárias. Essa maior freqüência de descargas extratemporais em crianças pode ser reflexo da diferente manifestação da atividade elétrica no cérebro em desenvolvimento ou a presença de um evento inicial precipitante mais marcante levando a dano cerebral mais difuso, ou a um predomínio de diferentes fatores etiológicos levando à dupla-patologia.

Resolvemos comparar os achados dos EEGs interictais de 16 crianças versus 12 adultos com lesões tumorais (artigo 7). Os dois grupos apresentaram atividade epileptiforme temporal (ipsilateral à lesão estrutural), bem como descargas epileptiformes extratemporais, sem relevante diferença estatística. Esse resultado nos leva a acreditar que a semelhança dos dados tenha maior correlação com a etiologia (mecanismo neurofisiológico envolvendo as lesões tumorais) do que propriamente com a idade dos pacientes com ELT, já que os pacientes com ELT devido a lesões tumorais podem apresentar achados neurofisiológicos pouco localizatórios e até falsamente lateralizatórios, tanto em crianças (Wyllie et al., 1993) quanto em adultos (Foldvary et al., 1997; Labate et al., 2004).

EEG Ictal

No artigo 8 foram avaliadas 149 crises de 25 pacientes com ELT de difícil controle medicamentoso submetidos à monitorização vídeo-EEG. Os aspectos analisados foram: padrão ictal inicial, atividade ictal rítmica persistente e padrão pós-ictal. A localização e a lateralização da zona epileptogênica mostraram valores inferiores aos encontrados em adultos com ELT. Na literatura, a capacidade de lateralização encontra-se em torno de 80% (Risinger et al., 1989; Williamson et al., 1993; Ebner e Hoppe, 1995), atingindo valores superiores em alguns estudos (O'Brien et al., 1996; Foldvary et al., 2001). A lateralização mostrou-se superior à capacidade de localização. Isto provavelmente se deve à proeminente propagação intra-hemisférica apresentada em crianças e adolescentes com ELT (Kramer et al., 1998).

CONSIDERAÇÕES FINAIS

A apresentação clínica mais polimórfica, como a presença de mioclonias e hipermotricidade, em crianças mais jovens (menores de seis anos) com ELT, ou seja, em lactentes e pré-escolares, correlaciona-se com o processo maturacional da criança. Reforçar a sua relação com lesões focais do lobo temporal pode possibilitar o diagnóstico precoce da ELT na infância. O quadro clínico nas crianças maiores (escolares e adolescentes) pode

cursar com alguma variabilidade semiológica, mas na grande maioria das vezes é típico, ou seja, semelhante ao dos adultos.

"Epilepsia abdominal" é um termo bastante controverso e pouco aceito, e o nosso objetivo ao destacá-lo foi simplesmente salientar, entre as inúmeras causas de dores abdominais na infância, a presença das causas neurológicas, principalmente as crises parciais, além do diagnóstico diferencial com migrânea.

As alterações comportamentais observadas nas crianças com ELT são muito freqüentes e podem melhorar ou até mesmo desaparecer com o procedimento cirúrgico. Isso contribui para uma melhora da qualidade de vida desses pacientes e de seus familiares.

A realização de EEGs interictais seriados em crianças com ELT caracterizou-se pela presença de grande porcentagem de atividade epileptiforme extratemporal e generalizada, apesar do predomínio de atividade epileptiforme focal temporal unilateral. Esse padrão EEG característico foi encontrado nos pacientes com ELT de diferentes etiologias, inclusive a EMT. Esses achados foram confirmados ao compará-los com adultos com ELT associada à EMT.

A presença de descargas epileptiformes interictais em crianças com ELT associada a lesões tumorais mostrou-se semelhante aos achados de adultos com essa mesma etiologia. Neste caso, as descargas podem ser pouco localizatórias e até falsamente lateralizatórias. A revisão da literatura mostra que o padrão EEG mais difuso é encontrado em lesões tumorais, independentemente da faixa etária. O EEG, nestes casos, contribui de forma mais modesta para o diagnóstico, porém não necessariamente prejudica o prognóstico.

Ao analisarmos o padrão EEG ictal observamos que também nestes casos os achados foram menos localizatórios e lateralizatórios que nos descritos em adultos.

Os achados ictais e interictais em ELT na infância podem ser correlacionados à maior diversidade etiológica, inclusive com a presença de dupla-patologia ou lesões mais extensas, além da EMT.

Os nossos dados clínicos e eletrencefalográficos sobre ELT na infância nos permitem sugerir que a função do cérebro em desenvolvimento depende da integração de ampla rede neuronal, uma vez que diferentes áreas cerebrais podem ser recrutadas para realizar determinada função de forma menos compartimentalizada que a mesma função em adultos. Assim, a expressão de lesões focais também é funcionalmente mais difusa. Mais estudos são necessários para melhor esclarecer a base fisiopatológica e anatômica desses achados.

6- CONCLUSÕES

1. As manifestações clínicas da epilepsia de lobo temporal em escolares e adolescentes são semelhantes às dos adultos; e as das crianças mais jovens têm peculiaridades próprias da faixa etária.

2. Auras estão freqüentemente presentes nas crianças e, muitas vezes, são mal interpretadas.

3. Crises mioclônicas podem preceder as crises parciais em ELT.

4. Tumores do desenvolvimento em crianças também levam a distúrbios comportamentais específicos.

5. Crianças apresentam, de forma significativa, maior número de descargas epileptiformes extratemporais que adultos, independentemente da etiologia.

6. Descargas epileptiformes extratemporais são encontradas tanto em crianças quanto em adultos com lesões tumorais do lobo temporal.

7. A lateralização das descargas ictais mostrou-se superior à sua localização. Entretanto, esses dados são inferiores aos registrados em adultos.

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8- ANEXOS

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CEP, 19/04/05
(PARECER PROJETO 596/2002)

PARECER

I-IDENTIFICAÇÃO:

PROJETO: **"ASPECTOS COMPORTAMENTAIS EM CRIANÇAS E ADOLESCENTES COM EPILEPSIA DE LOBO TEMPORAL"**

PESQUISADOR RESPONSÁVEL: Renata Cristina Franzon

II - PARECER DO CEP

O Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da UNICAMP tomou ciência e aprovou a Emenda que altera a metodologia que contemplara a avaliação clínica e neurofisiológica dos pacientes, bem como o título para **"ASPECTOS CLÍNICOS, NEUROFISIOLÓGICOS E COMPORTAMENTAIS EM CRIANÇAS COM EPILEPSIA DE LOBO TEMPORAL"**, referente ao protocolo de pesquisa supracitado.

O conteúdo e as conclusões aqui apresentados são de responsabilidade exclusiva do CEP/FCM/UNICAMP e não representam a opinião da Universidade Estadual de Campinas nem a comprometem.

Profa. Dra. Carmen Silvia Bertuzzo
PRESIDENTE DO COMITÊ DE ÉTICA EM PESQUISA
FCM / UNICAMP

Termo de Consentimento

Eu, _____, responsável pelo menor _____, HC _____, afirmo pelo presente o meu consentimento para que o paciente acima seja submetido à avaliação clínica e eletrencefalográfica, comprometendo-me a responder ao questionário necessário e a realizar os exames necessários (EEGs de rotina pré e pós-operatório).

Autorizo a realização de exames de Ressonância Magnética necessários para o diagnóstico e seguimento pós-operatório.

O objetivo desta pesquisa é definir os aspectos clínicos e neurofisiológicos associados às descargas extratemporais (frontais) na ELT, podendo definir fatores prognósticos e antecipar os benefícios do tratamento cirúrgico.

Houve esclarecimento sobre os assuntos relacionados à pesquisa.

Campinas, _____ de _____ de _____

_____ _____

Assinatura do Responsável ***Assinatura do Pesquisador***

Dra. Renata Cristina Franzon

Telefone: (19) 3788-7933 ou 3788-7754

Obs: Em caso de dúvida ou reclamação favor entrar em contato com o Comitê de Ética em Pesquisa da FCM/Unicamp através do telefone (19) 3788-8936.

Formulário para Coleta de Dados

ANEXO 3
Formulário para Coleta de Dados
I. DADOS DEMOGRÁFICOS
1. Nome do paciente: 2. HC:
3. Idade de investigação: 4. Idade de início:
5. Sexo:
II. DADOS CLÍNICOS
1. Tipos de crises:
Aura ( ):
Tipos: Epigástrica( ) Dor Abdominal( ) Medo( ) Psíquica( ) Outras( )
Crise parcial complexa ( )
Parada da atividade( ) Postura distônica( ) Postura tônica( )
Automatismos: oromastigatórios( ) manuais( ) complexos( ) exuberantes( )
Versão cefálica( ) Hipermotricidade( )
Fenômenos atônicos( ) Fenômenos tônicos( ) Distúrbios autonômicos( )
Crise tônico-clônica generalizada( ) Crise mioclônica ( )
Crise tônico clônica secundariamente generalizada ( ) Crise febril ( )
Clusters ( )
2. Freqüência de crises diária ( ) semanal ( ) mensal ( )
3. Exame físico neurológico:
4. Distúrbio de comportamento:S ( ) N ( ) Se sim, qual?
5. Etilogia
( ) EMT ( ) Tumor ( ) Dupla-patologia ( ) Displasia cortical focal
( ) Outras ( ) Lobo temporal direito ( ) Lobo temporal esquerdo
6.Cirurgia: S( ) N( ) Técnica: Achado anátomo- patológico:

ANEXO 4
Dados Neurofisiológicos: EEG (números):
( ) normal
( ) Atividade epileptiforme temporal unilateral
( ) Atividade epileptiforme temporal bilateral ( ) síncrona ( ) independente
( ) Atividade não epileptiforme temporal unilateral
( ) Atividade não epileptiforme temporal bilateral ( ) síncrona ( ) independente
( ) Atividade epileptiforme generalizada
( ) Atividade epileptiforme multifocal
( ) Atividade não epileptiforme generalizada
( ) Atividade epileptiforme extratemporal ( ) Frontal ( ) Central
( ) Parietal ( ) Occipital ( ) Rolândica

Escala de Engel (Engel et al., 1993b)

Classe I – Livre de crises incapacitantes, exceto as crises ocorridas no pós-operatório precoce (duas 1as. semanas)

A - completamente sem crises desde a cirurgia

B - apenas crises parciais simples não íncapacitantes desde a cirurgia

C - algumas crises incapacitantes após a cirurgia, porém sem crises incapacitantes por no mínimo 2 anos

D - crises generalizadas apenas durante a retirada de drogas antiepilépticas

"crises não incapacitantes" - aura sem alteração da consciência ou crise parcial simples motora, sem conseqüências funcionais

Classe lI - Raras crises incapacitantes ("quase livres de crises")

A - inicialmente sem crises incapacitantes, porém agora tem raras crises

B - raras crises incapacitantes desde a cirurgia

C - algumas crises incapacitantes após a cirurgia, porém com raras crises por no mínimo 2 anos

D - crises exclusivamente noturnas

Classe III - Melhora significativa

A – redução significativa das crises

B - intervalos sem crises prolongadas, maiores que metade do período de seguimento, porém menores que 2 anos

"melhora significativa" - requer análise quantitativa do percentual de redução das crises, da função cognitiva e da qualidade de vida

Classe IV - Sem melhora significativa

A - redução significativa das crises

B - sem alteração observável

C – Piora das crises