REVIEW ARTICLE

Temporal Lobe Epilepsy Surgery in Children Versus Adults:
From Etiologies to Outcomes

Yun-Jin Lee, MD¹, Joon Soo Lee, MD²

¹Department of Pediatrics, Pusan National University Children’s Hospital,
Pusan National University School of Medicine, Yangsan-si, Korea,
²Department of Pediatrics, Pediatric Epilepsy Clinics, Severance Children’s Hospital,
Brain Research Institute, Yonsei University College of Medicine, Seoul, Korea

RUNNING TITLE: Temporal lobe epilepsy in children versus adults

Corresponding author:
Joon Soo Lee, MD, PhD
Department of Pediatrics, Severance Children’s Hospital,
Yonsei University College of Medicine,
134, Shinchon-dong, Seodaemum-gu, Seoul, 120-752, Korea
Tel: +82-2-2228-2063
Fax: +82-2-393-9118
E-mail: joonsl96@yuhs.ac
Abstract

Temporal lobe epilepsy (TLE) is the most common type of medically intractable epilepsy in adults and children, and hippocampal sclerosis is the most common underlying cause of TLE. TLE in infants and young children is often due to etiologies other than hippocampal sclerosis, including tumors, cortical dysplasia, trauma, or vascular malformations. Differences in seizure semiology have also been reported. In infants and young children, motor manifestations are prominent; however, these become less obvious with increasing age. Automatisms tend to become increasingly complex with age. In childhood and especially in adolescence, the clinical manifestations are similar to those of the adult population. Selective amygdalohippocampectomy can lead to excellent postoperative seizure outcome in adults, but favorable results have been seen in children. Anterior temporal lobectomy may prove to be a more successful surgery than amygdalohippocampectomy in children with intractable TLE. The presence of a focal brain lesion on MRI is one of the most reliable independent predictors of a postoperative good seizure outcome. Seizure-free is the most important predictor of improved psychosocial outcome with advanced quality-of-life and a lower proportion of patients with disabilities in adults and children. The brain is more plastic during infancy and early childhood, which promotes greater recovery, while longer epilepsy duration is an important risk factor for surgically refractory seizures. Therefore, surgery for patients with medically intractable TLE should be performed as early as possible.

Key words: Temporal lobe epilepsy, Child, Adult, Temporal lobectomy

Abbreviations: TLE; temporal lobe epilepsy, MTS; mesial temporal sclerosis, HS; hippocampal sclerosis, AED; antiepileptic drug, MCD; malformation of cortical development,
CPS; complex partial seizures, ATL; anterior temporal lobectomy, SAH; selective amygdalohippocampectomy,
Introduction

Temporal lobe epilepsy (TLE) is the most common sort of medically intractable epilepsy in adults, while about 20% of patients in the pediatric population have epilepsy of temporal lobe origin. TLE is known to be remediable by surgery, and mesial temporal sclerosis (MTS, also called hippocampal sclerosis, HS) is the most common underlying cause of TLE (about 81%)\(^1\).

TLE associated with MTS frequently manifests between 6 and 10 years of age, but cases presenting in infancy and up to age 32 years have been reported\(^2\). Clinically, MTS appears to be a progressive disorder. Indeed, although seizures can initially be controlled with antiepileptic drugs (AEDs), they reemerge and become medically intractable in 60 to 90% of patients\(^2\).

Previous studies have revealed favorable surgical outcomes in children and adolescents with intractable seizures following temporal lobectomy\(^3,4\). These results appear to encourage the epilepsy surgery, but conducting presurgical evaluations of young children is much more difficult than evaluations of older patients. Additionally, studies concentrating on the postoperative cognitive and/or memory outcomes in children are relatively rare, because of measurement scale limitations, low frequencies of complaints about memory problems and the relatively recent development of early epilepsy surgery\(^4\).

For these reasons, comparing clinical characteristics including histopathology, seizure semiology, EEG findings, and postoperative seizure and neuropsychological outcomes between children and adults undergoing temporal lobe surgery may yield important findings.
Etiologies

Pathologic examination of MTS reveals neuronal loss in the hippocampus, predominantly involving the hilar region, CA1, CA3, CA4, and dentate gyrus. MRI findings are correlated with pathologic results, demonstrating hippocampal atrophy and abnormal T2 signal intensity in the hippocampus, best seen on thin (2 mm) coronal sections through the hippocampus. Bilateral MRI abnormalities are observed in about 20% of patients.

Although there are many similarities between children and adults with temporal seizures, there are significant differences due to unique characteristic of the pediatric brain. HS is relatively less frequent in infants and children. Specifically, 60% of adults with TLE have MTS, while only 20% of children have HS. A large number of children have other etiologies including tumors, malformation of cortical development (MCD), trauma or non-specific gliosis, vascular malformations, etc. It is often difficult to recognize diverse pathologies using neuro-imaging.
Clinical features

Complex partial seizures (CPS) are the most common manifestation of mesial TLE\textsuperscript{2}. About one-third of patients have secondarily generalized tonic-clonic seizures in addition to CPS or as the primary seizure type. Distinct characteristics of mesial TLE seizures include the following:

- Aura or simple partial seizure with sensory symptoms occurs in most patients, including a rising epigastric sensation, and psychic phenomena such as deja vu, jamais vu, or fear\textsuperscript{9}. Auras of taste and smell are less common, but relatively specific for TLE.

- CPS usually manifests with a behavioral arrest and staring that lasts between 30 and 120 seconds. The patients are usually unaware and unresponsive during this period. Occasionally, more detailed observation reveals the presence of olfactory hallucinations, or ictal automatisms\textsuperscript{9}.

- Automatisms are common, occurring in about 60% of CPS associated with mesial TLE\textsuperscript{2}. These are repetitive, stereotyped, purposeless movements that are typically mild, involving the hands (picking, fidgeting, fumbling) and mouth (chewing, lip smacking).

- Lateralizing features can occur during or after a partial or secondary generalized seizure\textsuperscript{9}. Unilateral automatisms are usually ipsilateral to the seizure focus, while dystonic posturing almost always occurs on the contralateral side. Head deviation at onset is usually ipsilateral to the seizure; however, when it occurs later as a more forceful appearance (so-called “versive”), it is contralateral\textsuperscript{10}. Contralateral ictal paresis has been documented as a reliable lateralizing sign. Ictal vomiting has been connected to right-sided onset, and unilateral eye blinking usually occurs on the ipsilateral side. Both ictal aphasia and ictal speech arrest have been regarded as seizure onset in the language-
dominant lobe, whereas verbalization is related to seizure onset in the non-dominant lobe\textsuperscript{(11)}. The lateralizing or localizing signs in MTS are presented in Table 1.

- Less common behaviors include ictal speech, affective behaviors (laughing, crying or fear), hypermotor behaviors usually associated with frontal lobe seizures, and so-called "leaving behavior" (walking or running away)\textsuperscript{(12)}.

- Postictal confusion usually lasts minutes. Postictal hemiparesis can occur contralateral to the seizure focus, and postictal aphasia can occur with a seizure from the dominant hemisphere. Nose-wiping is performed by the hand ipsilateral to the ictal focus\textsuperscript{(13)}.

Children with TLE have diverse ictal semiology\textsuperscript{(11)}. Prominent motor signs are usual manifestations in early life\textsuperscript{(7)}, and children less than 6 years of age show ictal semiology more similar to frontal lobe seizures, such as bilateral tonic posture and head drop. Convulsive motor signs tend to decrease with increasing age. Differences of semiology are strongly related to brain maturation and neuropsychological development. Aura is rarely observed in very young children, probably because they cannot describe their subjective feelings.

Brockhaus and Elger\textsuperscript{(14)} studied 29 children with TLE, aged 18 months to 16 years. They reported that seizure semiology in children > 6 years was similar to that in adults and included auras, staring or behavioral arrest, automatisms, versive and dystonic posturing. However, children < 6 years of age showed different semiology, such as symmetric motor signs of the limbs (up to 80%), which are less common (about 40%) in older children. Complex automatisms increased with age. While simple automatisms (e.g., oro-alimentary or gestural) were noted in preschool children, more complex automatisms such as clapping, beating hands or shuffling were only observed in children older than eight. A summary of characteristics seen in these subtypes of TLE is shown in table 2.
EEG findings

Interictal EEG typically shows temporal sharp waves, with the maximum values being observed at the anterior or mid temporal electrodes (F7/F8, T1/T2, T3/T4) (Fig. 1). Bitemporal independent discharges are observed in 30 to 40% of patients with mesial TLE[1]. The ictal EEG shows well-defined rhythmic and evolving discharges with a buildup. Lateralized postictal slowing is often observed. Sphenoidal electrodes sometimes have an advantage at detecting inferiorly directed mesial temporal discharges not seen with scalp electrodes, and may provide valuable localization findings in patients with TLE[1].

Epileptiform abnormalities in younger children with TLE may have limited localizing value due to their widespread distribution. Interictal and ictal EEG findings in younger children with TLE usually show more diffuse and irregular discharges and suggest extra-difficulties in the determination of temporal lobe seizure onset[3]. Specifically, children with neoplasms frequently have unusual EEG features, including multifocal epileptiform discharges and poorly localized or lateralized ictal activities[11].
**Decision for Temporal Lobe Surgery**

Most epileptologists view MTS as a progressive disorder characterized by medically intractable seizures, memory loss, and variable behavioral changes. Because temporal lobectomy in such cases is a much better treatment than continued AEDs, there is no reason to defer presurgical evaluation, once medical intractability has been established. Additionally, because children with intractable seizure show an intellectual decline over time, it is thought that early surgery could reduce the severity of cognitive impairment\(^{(5)}\).

The algorithm\(^{(6)}\) of epileptic surgery in patients with TLE is given in Figure 2. Optimal selection of surgical candidates requires a comprehensive evaluation of the clinical, electrophysiological, neuroimaging, and neuropsychological data by a multidisciplinary team that includes pediatric epileptologists, neuroradiologists, neurosurgeons, and neuropsychologists. If a focal lesion in a unilateral temporal lobe is suspected on MRI, such patients are subjected to further evaluation, such as video/EEG monitoring, neuropsychological testing, and functional MRI for language and memory hemisphere dominance. Language localization studies (Wada) and other functional studies are considered in cooperative patients. Invasive evaluation is performed when discordant findings are identified among noninvasive tests. The surgical approach is selected according to the preoperative diagnosis, EEG findings, and anatomic characteristics on MRI. Multimodal imaging techniques have recently been shown to lead to greatly improved surgical outcomes in temporal lobectomies (Fig. 3).

1. **Seizure-related outcomes**

Temporal lobe surgery for intractable seizures has been demonstrated to be safe and
effective for adults and children\textsuperscript{17-19}. Wiebe et al\textsuperscript{17} confirmed the effectiveness of anterior temporal lobectomy (ATL) in adults with intractable seizures of TLE in a randomized controlled trial. They found that 58% of patients in the surgical group became seizure-free, compared to only 8% in the medical group. Duchowny et al\textsuperscript{7} reported that 75% of children were seizure-free after temporal lobectomy prior to 12 years of age. The Cleveland Clinic Foundation revealed similar results with 74% of pre-adolescents and 80% of adolescents becoming seizure-free after temporal lobe surgery\textsuperscript{15}.

To determine the net-benefit of surgery, a systematic review and meta-analysis\textsuperscript{20} was performed. The results suggested that the efficacy of surgery was four times as likely as medication alone to result in a seizure-free outcome of intractable epilepsy. Nevertheless, a seizure-free outcome was achieved in 12% of similar patients who did not undergo surgery by AED alone.

Selective amygdalohippocampectomy (SAH) is a preferred technique in many centers, because it spares tissue by preserving the lateral temporal neocortex with a similar seizure outcome to ATL. Patients with SAH achieved the same degree of seizure control and more favorable neuropsychological profile\textsuperscript{21}. Similarities and differences following SAH exist between children and adults with intractable TLE. A retrospective study in 9 children and 14 adults with intractable TLE\textsuperscript{18} revealed that SAH could lead to excellent postoperative seizure outcome in adults, while less favorable results were seen in children. Most adults had MTS, whereas children had a wide range of different pathologies. Accordingly, ATL may prove to be a more successful operation than SAH in children with intractable TLE.

In one study, postoperative outcomes of 52 children and adults with medically intractable TLE were compared\textsuperscript{19}. Seizure-free outcomes were achieved in 63.2% (12/19) of children and 72.7% (24/33) of adults. The mean extent of surgical resection was significantly
broader in children than in adults (5.0 cm vs 4.1 cm). Additionally, HS was the most common pathologic finding in both groups (57.9% in children, 78.8% in adults), while MCD and dual pathology were significantly more frequent in children than in adults.

Long-term follow-up studies in adults and children demonstrated a decline in seizure-free rates as postoperative time increased\(^\text{22,23}\). Decrease from 61% seizure-free rate at 1 year to 41% at 10 years was noted in a large retrospective review of 325 adults and pediatric patients with temporal lobectomy\(^\text{22}\). Among children with temporal lobe surgery, 67% were seizure-free during the 10 to 20 year follow-up\(^\text{23}\). Patients with tumors or cavernous angioma had better outcomes than those with other histopathologies.

2. Cognitive and memory outcomes

There are some risks to cognitive functioning following temporal lobectomy. Left-sided resections have been associated with a decrease in verbal memory, while spatial memory and learning may be affected by right-sided surgery. Approximately 30-60% of patients who undergo left-sided (speech dominant) resection experience a substantial decline in verbal memory following surgery\(^\text{24}\). In contrast, right-sided surgery patients generally show postoperative improvement in verbal memory, although some exhibit a decline. Patients with higher presurgical abilities are at greater risk for postoperative memory decline\(^\text{24}\).

One study evaluating children after temporal lobe surgery reported stable verbal memory scores six months after left-sided surgery and improved scores after right-sided resection\(^8\). Children also appear to recover lost cognitive function more quickly and completely than adults\(^\text{25}\). Post-operative verbal memory declines in children were found three months after surgery, but recoveries were obvious just one year after surgery\(^\text{25}\). The data
generated in a 1-year follow-up suggested greater plasticity and compensational capacity in childhood during 1-year follow-up. Another study with a follow-up duration of less than two years did not find improvements in intellectual functioning\textsuperscript{26} suggesting that a prolonged period was required for cognitive recovery.

Skirrow et al\textsuperscript{27} reported the results of long-term follow-up of 42 children who underwent temporal lobe surgery after an average postoperative period of nine years. A significant increased in IQ was found in the surgical group after follow-up period of \(> 5\) years, that was not observed in the nonsurgical control group. The surgical group also reported better psychosocial outcome including quality of life. Better postsurgical cognitive improvements in children with lower preoperative IQs have been noted in previous studies\textsuperscript{27,28}. 
**Preoperative predictors of surgical outcomes**

The presence of a focal brain lesion on MRI is one of the most reliable independent predictors of a good outcome following temporal lobe surgery\(^22\). McIntosh et al\(^22\) indicated that the lack of an obvious abnormality or the presence of diffuse pathology is a risk factor for recurrence after surgery. Neoplastic lesions may be completely removed using intraoperative navigation with MRI in addition to lesionectomy. Conversely, the entire epileptogenic zone of MTS and MCDs is not always revealed on MRI, which may limit the effective surgical resections.

Longer epilepsy duration is an important risk factor for surgically refractory seizures and surgery for patients with medically intractable TLE should be performed as early as possible\(^15\). The effect of low IQ has been confirmed to be associated with poor postoperative seizure outcomes as it implies bilateral and potentially diffuse rather than focal brain pathology\(^20\). Early febrile seizures, early postoperative seizures, AEDs withdrawal, and duration of epilepsy have also been reported to contribute to late relapses\(^22\).

Previous studies have reported various predictors related to postoperative memory outcome, including side of resection, preoperative memory level, duration of epilepsy, extent of HS, and Wada test\(^28,30\). Binder et al\(^30\) used a multivariate approach to predict the variables of postoperative verbal memory outcome. Good preoperative performance, late age at onset of epilepsy, and left dominance on the Wada test were all predictive factors of memory decline.
Conclusions

Patients undergoing temporal lobectomy during childhood had distinctly different clinical features, interictal EEG, and pathologic findings than those who underwent the procedure during adulthood; however, both showed favorable surgical outcomes. Although there are many similarities between children and adults with TLE, there are significant differences due to features that are unique to the pediatric brain. One of the reasons for this marked difference is likely the different pathology between groups.

Temporal lobe resections for intractable epilepsy in children are safe and effective procedures that have a favorable impact on seizure control. The success in children may reflect the shorter epilepsy duration and greater plasticity of the brain. It should be noted that there is a risk of language deficits when the procedure is performed in the dominant hemisphere. The disruptive effects of frequent seizures and numerous AEDs on the developing brain in children can result in brain damage and progressive mental handicap. Therefore, early diagnosis of intractable epilepsy and referral for surgical treatment will be paramount if we wish to improve long-term prognoses.
References


Figure 1. Left temporal sharp waves are seen in a patient with left temporal lobe epilepsy. The sharp waves clearly stand out from the background activity.

Figure 2. Algorithm of epileptic surgery in a patient with temporal lobe epilepsy\textsuperscript{16} (TLE; temporal lobe epilepsy, CD; cortical dysplasia, MTS; mesial temporal sclerosis, AH; amygdalohippocampectomy).

Figure 3. Multimodal neuroimages of a patient with left temporal lobe epilepsy of ganglioglioma. (A) MRI showed increased signals on left uncus and hippocampus. (B) FDG-PET revealed decreased glucose metabolism in the same areas. SPM (statistical parametric mapping) analysis also indicated decreased glucose metabolism on the same areas when compared to normal controls with a $p < 0.001$. (C) SISCOM (Subtraction ictal SPECT coregistered to the MRI) analysis also pointed to the same areas. (D) Coregistered surface marked FDG-PET images with a 10\% asymmetric threshold to the MRI showed the red zones on the left temporal areas with various views.
Table 1. Lateralizing or localizing signs in temporal lobe epilepsy

<table>
<thead>
<tr>
<th>Motor manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head deviation, eye deviation, or both</td>
</tr>
<tr>
<td>Unilateral tonic or dystonic posturing</td>
</tr>
<tr>
<td>Contralateral ictal paresis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Language signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ictal aphasia</td>
</tr>
<tr>
<td>Ictal speech arrest</td>
</tr>
<tr>
<td>Verbalization of coherent speech</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Postictal findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postictal aphasia</td>
</tr>
<tr>
<td>Deficit motor postictal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Others signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ictal vomiting</td>
</tr>
<tr>
<td>Unilateral eye blinking</td>
</tr>
<tr>
<td>Ictal automatisms with preserved consciousness (non-dominant hemisphere)</td>
</tr>
<tr>
<td>Nose wiping at the end of mesial temporal seizures (ipsilateral)</td>
</tr>
</tbody>
</table>
Table 2. Characteristics of temporal lobe epilepsy in different age-groups\(^{1(1)}\)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Infants and toddlers (0-3 years)</th>
<th>Pre-school and early school (3-6 years)</th>
<th>Older children, adolescents and adults (&gt; 6 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Etiology</strong></td>
<td>CD, low grade neoplasm, tuberous sclerosis, etc.; HS uncommon</td>
<td>CD, low grade neoplasm; HS less common</td>
<td>HS is most common; CD, low grade neoplasm, or vascular malformation</td>
</tr>
<tr>
<td><strong>Semiology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Auras</strong></td>
<td>Rare or difficult to recognize</td>
<td>May be present</td>
<td>Common, especially abdominal aura</td>
</tr>
<tr>
<td><strong>Motor signs</strong></td>
<td>Prominent motor signs; tonic, clonic, myoclonic which may be bilateral and symmetric</td>
<td>Less prominent motor signs; may show dystonic posturing or version</td>
<td>Less motor signs; contralateral dystonic posturing is common</td>
</tr>
<tr>
<td><strong>Automatisms</strong></td>
<td>Common; simple in character; usually oro-alimentary</td>
<td>Common; more complex with increasing age; hand automatism in addition to oro-alimentary</td>
<td>Common; complex and more discrete; oral, hand and verbal automatism</td>
</tr>
<tr>
<td><strong>EEG</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Interictal</strong></td>
<td>Extratemporal and generalized sharp waves commonly seen in addition to temporal spikes, especially in patients with tumors</td>
<td>Anterior temporal sharp waves; extratemporal or contralateral temporal sharp waves are often seen</td>
<td>Unilateral sharp waves maximum at the sphenoidal or anterior temporal electrodes</td>
</tr>
<tr>
<td><strong>Inctal</strong></td>
<td>Poorly localized/falsey lateralized (occasionally generalized) seizure patterns especially in patients with tumors</td>
<td>Usually lateralized and maximum in the temporal electrodes</td>
<td>Usually localized seizure patterns from ipsilateral temporal lobes with maximum at sphenoidal or anterior/inferior temporal electrodes</td>
</tr>
<tr>
<td><strong>Imaging</strong></td>
<td>Tumor, CD</td>
<td>Tumor, CD, less common</td>
<td>Increased FLAIR signal, with hippocampal atrophy</td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td>CD, low grade tumor etc</td>
<td>Low grade tumor, CD, HS</td>
<td>HS</td>
</tr>
</tbody>
</table>

CD; cortical dysplasia, HS; hippocampal sclerosis