

Pre-Surgical Evaluation of Intractable Epilepsy in Children

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Abstract

Objective

This review summarizes some patterns of pre-surgical evaluation of epilepsy in children with medically refractory seizures. Epilepsy surgery is a valuable therapeutic option for many children with intractable epilepsy. The most effective treatment for intractable partial epilepsy is a focal cortical resection with excision of the area of ictal onset and initial seizure propagation (the epileptogenic zone). EEG monitoring continues to prove indispensable in pre-surgical planning of refractory epileptic patients by defining the epileptogenic zone. Technological progresses in both structural and functional neuroimaging techniques have led many medical centers to consider surgical treatment of epilepsy. In children undergoing pre-surgical evaluation, the goals of neuroimaging studies include the identification of structural abnormalities in the brain, eloquent regions of the brain including language, memory, and sensorimotor functions, and the relation of these regions to the potential epileptogenic region. Neuropsychological testing plays a crucial role in assessing the potential impact of surgery on cognitive function of the patients and helps in lateralizing the cerebral hemisphere dominant for verbal and nonverbal function in older children. The Wada test is an invasive procedure to determine language dominance and can be used to assess the risk of postoperative memory deficits in children with temporal lobe epilepsy. Some children scheduled for resection still need to undergo further precise localization of the epileptogenic zone and functional mapping with invasive EEG monitoring through intracranial subdural grid and/or depth electrodes. Epilepsy surgery has the potential of changing the life quality of children by improving or eliminating seizures in carefully selected patients.

Key Words: Rrefractory epilepsy; seizure; neuroimaging; EEG monitoring.

Introduction

Epilepsy is a paroxysmal neurological disorder due to sudden synchronous high voltage discharges arising from a number of hyperexcitable neurons. Approximately 0.5–3% of the world population suffers from epilepsy. In most patients with epilepsy, the prognosis for seizure control is good. However, about 20–30% of epileptic patients, that is, some 10–15 million people worldwide, develop difficult-to-treat or intractable epilepsies despite the advent of new antiepileptic drugs and intensive monitoring (1, 2).

Pediatric epilepsy is a common, chronic, and challenging physical illness for children and their families. Childhood epilepsies are the most frequent neurological

problems that occur in children. Epilepsy is the most common neurological disorder of childhood with an annual incidence of 5–7 per 10 000 in the age group of 0–15 (3). Data from a variety of epidemiological investigations have indicated that recurrent seizures occur in 1–2% of children, with the highest incidence rate in the first year of life (4, 5). Approximately 10–40% of children with epilepsy will continue to have seizures despite optimal medical management with antiepileptic drugs (AEDs, 6, 7, 8). Children who are candidates for epilepsy surgery have medically refractory epilepsy which may be defined as inadequate seizure control in spite of appropriate medical therapy with AEDs or adequate seizure control, but with unacceptable drug-related side effects. Definitions of intractability must be individualised to the patient. However, the commonest definition for intractable epilepsy is when seizures continue in a child despite maximally tolerated doses of more than two AEDs, occurrence of an average of one seizure per month for ≥ 18 months with no more than a 3 month seizure free period during these 18 months (9). When two AEDs for the correct seizure type and in adequate doses fail, there is only a 5–10% probability of achieving seizure control with a third drug (10, 11). There are several factors to be considered in a definition of medical intractability, including the number of AEDs failures, minimum frequency at which seizures must occur to be considered intractable, duration of unresponsiveness to AEDs, epilepsy syndrome involved, cause of seizures in the absence of a clear epilepsy syndrome, and patient age at the onset of seizure attacks. In addition to pharmacoresistance, children with disabling AED's side-effects may be surgical candidates. Infants and children, whose seizures have a focal onset are refractory to AEDs and are prolonged, tend to have the worst cognitive outcome (12). Recurrent seizures themselves affect early developing brain, learning, and memory and contribute to an adverse neurological outcome (13). Furthermore, children with intractable epilepsy may benefit from early surgical intervention to avoid the prolonged use of AEDs and its effect on cognitive and psychosocial development. Early surgical treatment of epilepsy in children also increases the chances of postoperative neurological reorganization due to the inherent functional plasticity of the brain.

Therefore, during treatment of children with medically refractory epilepsy, it is crucial to consider seizure control and to give allowance for normal cognitive development. Aggressive diagnosis and surgical treatment can prevent altering of neuroplasticity in young patients with refractory epilepsy (14).

Certain epilepsy etiologies are more commonly observed in the children population, which have been recognized as contributing to the medical intractability, including cortical malformation due to abnormal neuronal and/or glial proliferation or apoptosis (for example, congenital microcephalies and megalencephaly, cortical hamartomas of tuberous sclerosis, cortical dysplasia with balloon cells, dysembryoplastic neuroepithelial tumor), abnormal neuronal migration (lissencephalies, cobblestone complex syndromes, heterotopias), abnormal cortical organization (polymicrogyrias, schizencephalies), and malformations of neocortical development not otherwise specified. In addition, some children with refractory epilepsy may suffer from inborn errors of metabolism (pyruvate metabolic, paroxysmal and mitochondrial disorders). Other origins associated with medical intractability include mesial temporal sclerosis, different forms of genetic conditions, CNS infections, head trauma, and brain tumours (1,16,17).

Epilepsy surgery is a valuable therapeutic option for the approximately 7-15% of pediatric intractable epilepsy patients (18, 5). Some other reports indicate to a higher percentage even as high as twenty five percent of patients with intractable epilepsy have surgically remediable epilepsy syndromes (19).

Epilepsy surgery for children could be divided into curative and palliative types. Extratemporal cortical resection is the most common curative epilepsy surgery in infants and children. Palliative epilepsy surgery include multiple subpial resections when the epileptogenic zone is localized to eloquent cortex and corpus callosotomy for drop attacks in children with multiple seizure types. Epilepsy surgery is a radical treatment of epilepsy and is not without risk. Absence of prohibitive adverse consequences from the surgery, and preserved ability of the remaining brain to carry on normal functions should be considered. Potential deficits should be weighed against the anticipated benefits. The definitive successful outcome of epilepsy surgery is a seizure-free state

without significant neurological impairments. The pre-surgical evaluation aims at searching for, and defining the boundaries of the abnormal area at the origin of the seizures, specifically the area necessary and sufficient for the generation of focal seizures. Precise localization of the epileptogenic zone is crucial to enhance the seizure outcome after resection of the involved region especially in focal cortical resection. Furthermore, this prevents any unnecessary brain tissue resection and subsequent neurological deficits. Multiple tests are needed to lateralize and localize the epileptogenic zone and function in the brain and thus ascertain the candidacy of a child with medically refractory seizures for surgery. The pre-surgical studies are designed from non-invasive tests including patient semiology and physical examination, scalp EEG and video-EEG monitoring, neuroimaging, and neuropsychological tests to the invasive test including Wada test and intracranial EEG, and the data are discussed by a multidisciplinary epilepsy surgery team on a regular basis to formulate a decision of whether to proceed to the next stage of testing.

History, Semiology and Physical Examination

A detailed history, including seizure onset and evolution over time, may offer certain pathology. A history of previous febrile seizures suggests medial temporal lobe epilepsy rather than neocortical temporal lobe epilepsy (20). It is also important to obtain a family history to rule on the possibility of genetic syndromes. History of patients can determine pharmacokinetic anomalies, the wrong drugs, non-epileptic events, or poor compliance. Description of seizure semiological features of seizure attacks, the AEDs applied, and a comprehensive neurological examination are very helpful in determining whether seizure attacks are indeed medically intractable. Based on ictal semiology and clinical signs and symptoms the localization of epileptic zone should be hypothesized. A clinical history to determine the seizure semiology and to ascertain the earliest symptom in the clinical progression of the seizure semiology is crucial, but may be limited by the fact that the ictal neuronal discharge may commence in a silent area and only secondarily involve cortex responsible for the initial overt clinical manifestation of the seizure attack. Although

auras are less common in children than in adolescents and adults, occurrence of aura may help to localize the symptomatogenic zone. The symptomatogenic zone refers to the area of neocortex that generates the clinical semiology of habitual clinical seizures when activated. As stated previously, the epileptogenic zone is responsible for the epilepsy, it is the “current generator” that should be surgically resected, as opposed to the symptomatogenic zone, the “symptom generator” responsible for the “seizure”, or clinical symptoms. A symptomatogenic zone may be either overlapping with, or completely distinct from the epileptogenic zone. Dividing the seizure into its elementary sequential ictal components with attention to lateralizing and localizing signs allows the precise definition of the different symptomatogenic zones and possibly the associated epileptogenic zone. For instance, the probability that an abdominal aura is caused by a temporal epileptogenic zone rises from 73.6% to 98.3% when the aura evolves into an automotor seizure (21).

Thorough general and neurological examination with a special attention to dysmorphic features, focal signs, distinctive skin findings suggestive of neurocutaneous syndromes such as Tuberous sclerosis, Sturge Weber syndrome, Epidermal nevus syndrome, Neurofibromatosis Type I, are needed mainly to rule out a general neurological disorder as the origin of medically refractory epilepsy.

Scalp EEG and Video-EEG Monitoring

Video-EEG monitoring is important in documenting ictal events, lateralizing and localizing the electrographic onset of seizures, and defining the seizure semiological factors. This method is important to rule out non-epileptic seizures, and localize the symptomatogenic and epileptogenic zones. Admission to an epilepsy monitoring unit for prolonged video-EEG monitoring also has the advantage of allowing prolonged evaluation of interictal EEG activity during wakefulness and sleep, adjustment of AEDs to obtain adequate seizures, and monitoring the effect of medications if new ones are added. Newer methods of EEG analysis, such as EEG dipole analysis and EEG source imaging, provide excellent localizing information in pediatric patients, especially in cases of extratemporal lobe epilepsy.

Activating procedures such as hyperventilation and light stimulation are useful in some patients. Sleep deprivation and reduction of AEDs often increase the probability of occurrence of interictal and ictal epileptiform activity. AEDs reduction, however, may alter the electrographic and clinical features of habitual seizures.

Non-epileptiform abnormalities, which may help localize the epileptogenic zone, include slowing and suppression of normal activity. Focal slowing indicates dysfunction in a particular region, which may support the case for identifying the epileptogenic zone (22). Persistent slowing supports an underlying structural abnormality. Rhythmic temporal theta activity supports a temporal focus. As well, focal background attenuation is suggestive of an epileptogenic focus (23). Distortions of normal EEG rhythms by interictal activities can also aid in localizing or lateralizing abnormalities. This may include asymmetry or poor architecture of the posterior dominant alpha rhythm in waking or asymmetric spindles or vertex waves in sleep. Epileptiform abnormalities such as spikes, sharp waves, and spike-wave complexes during the interictal record are supportive of epilepsy, and help to localize the irritative zone. The irritative zone refers to the cortical region generating interictal epileptiform discharges. The irritative zone further defines the extent of the epileptogenic zone. This zone may be defined by surface or intracranial EEG. Magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI) may also define this zone of interictal activity in deeper cortical or subcortical areas.

The exact number of seizure attacks required by video-EEG monitoring is unclear, and appears to vary dependent upon location and seizure type. However, recording at least three and preferably five seizures has been advocated (24). It was suggested that ictal EEG localization is helpful when more than 75% of the recordings reveal the same ictal onset region (25). Focal rhythmic bursts of high frequency discharges with evolution to increasing amplitude and slowing is the most commonly observed pattern in focal seizure onset (26). Focal rhythmic fast activity is more common in extratemporal than temporal epilepsy, and is associated with seizures of frontal dorsolateral origin, whereas focal temporal theta at ictal onset characterizes temporal lobe epilepsy (27).

Though video-EEG monitoring remains fundamental in the pre-surgical investigation, it has several limitations in its ability to define the epileptogenic zone. The sensitivity of detecting an epileptic potential by surface EEG is dependent upon the depth, size, orientation, and duration of a discharge. Scalp EEG has the potential to localize poorly, or even falsely, the epileptogenic zone in some children because the majority of children with medically refractory localization-related epilepsy have an extratemporal focus which is difficult to localize, or even lateralize, with scalp EEG. Deeper cortical and subcortical seizure onset and propagation may not have a surface EEG correlate. Small areas of seizure activity, even if on the surface, may not have a surface correlate until larger regions of cortex are involved (28).

Neuroimaging

The introduction of contemporary imaging modalities has been pivotal in the care and management of patients with partial epilepsies. Structural and functional neuroimaging studies are essential in the evaluation of individuals with partial epilepsy syndromes. Approximately one-third of patients with partial epilepsy have structural lesions underlying the epileptic brain tissue (29). Structural neuroimaging techniques, such as computed axial tomography (CT) and magnetic resonance imaging (MRI), were important initial steps in the diagnostic evaluation of patients with partial or localisation-related epilepsy (30).

Functional neuroimaging methods permit three-dimensional visualisation of localised dynamic changes within the brain. Several different imaging techniques such as single photon emission computed tomography (SPECT), positron emission tomography (PET), and functional fMRI have been developed to identify the anatomic localisation of disturbances not necessarily accompanied by structural alterations. These techniques complement neurophysiological and clinical data for identifying the site of seizure onset and initial propagation, that is, the epileptogenic zone, and also regions of potential epileptogenicity (31). Both structural and functional neuroimaging techniques play important roles in diagnosis, classification, and operative outcome of epilepsy surgery.

A lesion detected in imaging is not necessarily the

epileptogenic lesion. The significance of any lesion should be interpreted in the context of the findings from other testing modalities. When MRI is concordant with EEG recordings, in the proper clinical setting, surgery can be performed without necessitating further investigations (e.g. tumor). However, when MRI is discordant with EEG studies, fails to detect a lesion, or reveals certain abnormalities like cortical dysplasia, further studies with functional imaging, and possibly intracranial EEG recordings may be needed to a better delineation the borders of the epileptogenic zone (32).

Structural Imaging

The performance of MRI, and continuous technical improvements within the past three decades, is allowing the detection of subtle structural abnormalities in patients previously considered as non-lesion epilepsy. Subtle lesions are better visualized on MRI compared with CT, although CT may be indicated in special circumstances such searching for intracranial calcifications. Structural imagings especially MRI can also confirm complete resection (33). T1-weighted, T2-weighted, gadolinium contrast, FLAIR, coronal and axial images are different protocols of MRI that can identify lesions in epileptic patients. Magnetic resonance spectroscopy is another modality that helps in lateralization of epileptogenic zone, and relies on neuronal loss quantification; the lower the ratio of N-acetyl aspartate peak to choline and creatine peaks, the more the neuronal loss (34).

Structural neuroimaging is recommended for all children with recently diagnosed localization-related or generalized epilepsy who do not have the clinical and EEG features characteristic of classical idiopathic focal or generalized epilepsy and for all children younger than 2 years of age. Nearly 50% of individual imaging studies in children with localization-related new-onset seizures were found to be abnormal; 15–20% of imaging studies provided useful information on etiology or/and seizure focus, and 2–4% provided information that potentially altered immediate medical management (35). It is rare to find a significant imaging abnormality in the absence of a history of a localization-related seizure, abnormal neurologic examination, or focal EEG. Infants are more likely to have focal malformation of cortical development as a cause of seizures than older children (36).

CT scan identifies clinically relevant lesions in 7–24% of children with epilepsy. However, CT scan only changes the medical management in very small group of the patients. Children older than 2 years, with generalized seizures, normal examination, and either generalized EEG abnormalities or normal EEG are unlikely to benefit from CT imaging (37). MRI is considered the structural imaging modality of choice because of superior anatomic resolution and characterization of pathologic processes. CT scan is more available than MRI, is less expensive, and is less likely to require sedation for younger children. However, CT scan can not identify focal cortical dysplasia, mesial temporal sclerosis, small tumors, and vascular malformations. For these lesions MRI should be performed (35).

Imaging early in the course of epilepsy is directed at identifying an etiology for seizures that requires medical or surgical attention. Structural neuroimaging can be used to identify a remote lesion such as porencephaly, to find a focal lesion responsible for the seizures that do not require immediate surgery but would be potentially amenable to surgical intervention such as mesial temporal sclerosis, to find a chronic process that has therapeutic implication such as brain tumor, to identify an acute process that requires immediate surgery such as hemorrhage or hydrocephalus, and to establish an non-specific abnormality such as periventricular leukomalacia (35). Any child younger than the 2 years of age requires different MR imaging sequences because of the affect of developmental myelination on the ability to detect certain lesions such as cortical dysplasia.

Non-structural Imaging

Functional MRI

During the past 15 years, functional MRI (fMRI) has become an increasingly popular means by which to study localization of specific brain functions. fMRI seems an ideal method for brain mapping, as it is non-invasive, safe, and devoid of radiation exposure. There have been many challenges in applying data and protocols from the adult fMRI literature to children. The smaller head size and neck length of young children, structural immaturity and continuous brain growth and development in early childhood, and lack the ability to active participation and cooperation during evaluation are challenges to perform

fMRI in children. In an attempt to include younger and less cooperative children, studies also have begun to incorporate the use of passive language and motor tasks, which can be accomplished successfully in sleeping or sedated infants and children (38, 39). Using fMRI reduces the need for the more invasive options. 63% of patients were able to avoid further diagnostic or more invasive studies after fMRI was completed (40).

The most used clinical application for fMRI in children has been in the pre-surgical evaluation of patients undergoing epilepsy and tumour surgery. It is crucial to localize language and motor function in the preoperative state to help the surgeon to determine the surgical approach, extent of resection, and risk of post-surgical neurological deficits. Epileptic patients have a higher percentage of atypical language development than do healthy controls. Early studies in adults showed that 94% of healthy controls had left lateralized language dominance, compared with only 78% of epilepsy patients (41). This finding makes it even more relevant to ensure confidence in the knowledge of primary language control before surgery. fMRI has been shown to have a high sensitivity (81%–100%) for identifying critical language sites (42). Absence of an MRI lesion not only discourages consideration of a patient for surgical candidacy, but is also associated with poor surgical outcome (43). In addition to delineate the boundaries of language cortex, fMRI can be used to improve our understanding of how chronic diseases such as epilepsy affect language networks and functional reorganization. Non-lesional epilepsy, history of stroke, earlier age of seizure onset, and atypical handedness also appeared to increase the prevalence of atypical language.

Another clinical use for fMRI in children is to define the area of preoperative motor mapping. This can help surgical team to determine the feasibility of surgical resection and guide them in establishing a risk-benefit ratio when there is a high risk of motor compromise during surgery (44).

PET and SPECT

PET represents a useful diagnostic tool for pre-surgical evaluation of epileptic patients, particularly when fMRI fails to detect epileptic zone. PET is widely accepted as an essential part of the diagnosis and evaluation of

neoplastic and non-neoplastic disease processes. PET imaging is based on the detection of photons that arise from the decay of injected radiotracers. A number of PET tracers make it possible to visualize different aspects of brain function such as blood flow, glucose metabolism, protein synthesis, and neurotransmission. F-18 FDG is the most widely used PET tracer for evaluating brain glucose metabolism for localizing epileptogenic focus in clinical practice. Because of its long uptake period (40–60 min), FDG-PET is more suitable for capturing the interictal state of epilepsy rather than the ictal state. The pattern of glucose metabolism in a PET scan is hypometabolism of the ipsilateral temporal lobe with or without less severe hypometabolism in the extratemporal structures such as frontal, parietal, and contralateral temporal lobes. If lesions are associated with epilepsy, the extent of hypometabolism is greater than the size of the structural lesion (45). It has been reported that interictal PET is more sensitive than MRI in localizing epileptogenic focus in both temporal and extra-temporal epilepsy (46). Furthermore, it has been shown 18F-FDG-PET to have 63–100% sensitivity in lateralizing temporal lobe epilepsy and to provide complementary information to MRI (47). PET is a valuable tool for diagnosis of epileptic children suffering from focal cortical dysplasia and Tuberous sclerosis complex. PET has been reported to be 75–100% sensitive in localizing areas with focal cortical dysplasia (48). A multimodality imaging approach using MRI and PET registration as well as DTI has been demonstrated to be useful in pre-surgical evaluation to localize epileptogenic tubers (49). Alpha-[11C] methyl-l-tryptophan is a PET-trace used in children with tuberous sclerosis for epilepsy surgery evaluation.

The unique characteristic of regional cerebral blood flow tracers is their capacity to identify the epileptogenic focus during a seizure by showing a focal area of significantly increased perfusion, which corresponds to the epileptogenic zone. As these tracers are trapped within the brain, the SPECT image represents the regional cerebral blood flow during the seizure, though the image is acquired after the seizure. With an injection at the onset of a seizure, there is an increased probability of visualizing an epileptogenic focus seen as a focal area of increased uptake. Long duration of a seizure

attack is also important factor to delineate epileptic zone by SPECT. The epileptogenic focus is observed as an area of hyperperfusion on the ictal SPECT scan. This area is often surrounded by a zone of hypoperfusion that becomes more prominent at the end of the ictal period (50). The tracer injection for the interictal scan is administered when the patient has not had a seizure for at least 30 minutes. If required a properly trained nurse sedates the child as a preparation for the acquisition of the SPECT scan in the nuclear medicine unit. The principal role of the interictal SPECT is to aid the localization of the seizure focus by comparison to the ictal scan, either visually or with subtraction of the interictal from the ictal images. During the interictal period, the epileptogenic zone usually shows decreased cerebral blood flow and is observed as an area of hypoperfusion on the interictal SPECT scan (51).

Neuropsychological Testing

Neuropsychological assessment remains a critical investigation in the pre-surgical evaluation of epilepsy surgery patients. Neuropsychological assessment is included in the protocols for evaluation of epilepsy surgery candidates, providing information about the patient's cognitive dysfunctions, allowing for prediction of possible cognitive deficits derived from surgery and yielding objective measures of any post-surgical changes. These test helps in lateralizing the cerebral hemisphere dominancy for both verbal and non-verbal function in older children. Data provided by neuropsychological testing is essential in interpreting other pre-surgical diagnostic tests in terms of lateralizing and localizing of seizure zone. Detailed neuropsychological feedback enables the patient to make an informed decision, and forms the basis of the rehabilitation programs that can be implemented before the surgery (52), thus minimizing the most significant morbidity associated with epilepsy surgery today (53).

Wada Test

In many adult patients with medically refractory epilepsy for whom surgical resection of a seizure focus is considered, the Wada test (named after Dr. John Wada, who developed the test), also known as the intracarotid amobarbital procedure, is an integral part of the

preoperative evaluation (38). During the Wada test, the physician puts one side of the brain of patient to sleep by injecting an anesthetic medication into the right or left internal carotid artery for few minutes. The suppressed hemisphere of the brain cannot communicate with the other side. In order to confirm that the activity of injected side of the brain is suppressed, EEG recordings are performed during the test. The ability to speak and the memory are tested for both hemispheres.

Wada testing is used for lateralization of language and memory; it may also help to lateralize the seizure focus. This test is also helpful in pre-surgical evaluation of children with medically intractable epilepsy. However, performing angiography presents special challenges in these children. Many of these children have IQs in the cognitively impaired to borderline intelligence frange (54). Children may become agitated or combative, and the procedure may have to be abandoned (55). In such circumstance, not only is no diagnostic information obtained but there is also a risk of femoral artery spasm or injury. For this reason, Wada test is not as widely used in children, especially in children younger than 10 years (56). Therefore, non-invasive tests like fMRI are used initially in children, although there may be a role for Wada test if those tests are equivocal or there is contraindication for MRI. However, some methods such as using propofol anesthesia facilitate controlled cerebral angiography in pediatric patients without compromising the results of Wada testing (57). Selective middle cerebral artery Wada test can be done to assess the risk of post-surgical neurological deficits before functional hemispherectomy (58).

Intracranial EEG

When a standard pre-surgical evaluation (consisting of video- EEG, MRI, functional neuroimaging and neuropsychological assessment), cannot identify the epileptogenic focus, invasive intracranial electrodes are often required to help with localization. The main purpose of intracranial recording is to further delineate the area of onset and early propagation of a seizure. For these purposes, coverage of large areas of the brain placed through a craniotomy or bilateral craniotomies is required. In non-temporal epilepsy, invasive recordings are frequently required when

epileptogenesis from a region distant to surface EEG electrodes is suspected, such as an inferior or mesial frontal or occipital surface (59). The greatest benefit of invasive monitoring may be achieved among children who their brain development is intact and who have a restricted epileptogenic zone, as defined by scalp EEG and imaging. Patients with clinical evidence of a diffuse encephalopathy or multifocal and diffuse epileptogenic patterns on scalp EEG and multifocal neuroimaging lesions are unlikely to benefit. These invasive studies are especially important in cases of extratemporal lobe epilepsy, which is common in the children, and in cases of temporal lobe epilepsy when lateralization cannot be adequately done by scalp EEG (60, 25, 14) Invasive monitoring helpful when studies suggest epileptogenic zone in the posterior temporal occipital region encroaching upon language cortex, and when distinction between anterior temporal and orbital frontal epilepsy is not clear (61). If the epilepsy is lesional but the data are discordant for localization of the epileptogenic zone, if patient suffers from non-lesional seizure, or if the epileptogenic zone appears to reside wholly or partially in eloquent cortex, then intracranial monitoring by depth and/or subdural (grid) electrodes during a seizure attack is necessary to map out regions of epileptogenicity in the brain prior to epilepsy surgery.

The use of intracranial recordings does not lack potential complications, even though invasive recordings provide much more sensitive information than scalp recordings. The chronic implantation of electrodes carries the risk of mass effect, hemorrhage, and infection. It is desirable, then, to limit the number of studies and electrodes possible without compromising the ability to gain sufficient information for subsequent surgery.

In conclusion, The primary aim of epilepsy surgery is to stop seizures in children with medically intractable epilepsy. The data indicate that this goal is achieved in a majority of carefully selected patients in whom surgery is undertaken. Early epilepsy surgery has been advised because of the view that refractory, ongoing, multiple repetitive seizure attacks are harmful from a neurobiological, psychosocial, and learning perspective. There are several factors associated with and affecting pharmacological resistance and such factors should

be taken into consideration when a patient is being investigated as a potential candidate for epilepsy surgery.

References

1. Lowenstein DH. Seizures and epilepsy. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL (eds) *Harrison's Principles of Internal Medicine*, 14th edn. McGraw-Hill, New York. 1998. P.2311-2325.
2. Leppik IE. Intractable epilepsy in adults. *Epilepsy Res Suppl* 1992; 5:7-11.
3. Nettekoven S, Strohle A, Trunz B, Wolters M, Hoffmann S, Horn R, et al. Effects of antiepileptic drug therapy on vitamin D status and biochemical markers of bone turnover in children with epilepsy. *Eur J Pediatr* 2008; 167:1369-1377.
4. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. *Epilepsia* 1993; 34:453-468.
5. Camfield CS, Camfield PR, Gordon K, Wirrell E, Dooley JM. Incidence of epilepsy in childhood and adolescence: a population-based study in Nova Scotia from 1977 to 1985. *Epilepsia* 1996; 37:19-23.
6. Sillanpää M, Jalava M, Kaleva O, Shinnar S. Long-term prognosis of seizures with onset in childhood. *N Engl J Med* 1998; 338:1715-1722.
7. Dlugos DJ, Samuel MD, Strom BL, Farrar JT. Response to first drug trial predicts outcome in childhood temporal lobe epilepsy. *Neurology* 2001; 57:2259-2264.
8. Berg AT, Shinnar S, Levy SR, Testa FM, Smith Rapaport S, Beckerman B. Early development of intractable epilepsy in children: a prospective study. *Neurology* 2001; 56:1445-1452.
9. Berg AT, Vickrey BG, Testa FM, Levy SR, Shinnar S, Di Mario F, et al. How long does it take for epilepsy to become intractable? A prospective investigation. *Ann Neurol* 2006; 60:73-9.
10. Kwan RP, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med* 2000; 342:314-319.
11. Farrell K, Wirrell E, Whiting S. The definition and prediction of intractable epilepsy in children. *Adv Neurol* 2006; 97:435-442.
12. Meador KJ. Cognitive outcomes and predictive factors in epilepsy. *Neurology* 2002; 58(S5):S21-6.
13. Holmes GL. Effects of seizures on brain

- development: lessons from the laboratory. *Pediatr Neurol* 2005; 33:1-11.
14. Cross JH, Jayakar P, Nordli D, Delalande O, Duchowny M, Wieser HG. Proposed criteria for referral and evaluation of children for epilepsy surgery: recommendations of the Subcommission for Pediatric Epilepsy Surgery. *Epilepsia* 2006; 47:952-959.
 15. Barkovich AJ, Kuzniecky RI, Jackson GD, Guerrini R, Dobyns WB. Classification system for malformations of cortical development: update 2001. *Neurology* 2001; 57:2168-2178.
 16. Nolan MA, Sakuta R, Chuang N, Otsubo H, Rutka JT, Snead OC III. Dysembryoplastic neuroepithelial tumors in childhood: long-term outcome and prognostic features. *Neurology* 2004; 62:2270-2276.
 17. Whiting S, Farrell K, Wirrell E. Diseases and syndromes associated with intractable epilepsy. *Adv Neurol* 2006; 97:443-462.
 18. Morris HH 3rd, Dinner DS, Lüders H, Wyllie E, Kramer R. Supplementary motor seizures: clinical and electroencephalographic findings. *Neurology* 1988;38:1075-82.
 19. Berg AT. Defining intractable epilepsy. *Adv Neurol* 2006; 97:5-10.
 20. Gil-Nagel A, Risinger MW. Ictal semiology in hippocampal versus extrahippocampal temporal lobe epilepsy. *Brain (Pt 1)* 1997; 120:183-192.
 21. Henkel A, Noachtar S, Pfander M, Lüders HO. The localizing value of the abdominal aura and its evolution: a study in focal epilepsies. *Neurology* 2002; 58:271-276.
 22. Blume WT. Clinical profile of partial seizures beginning at less than four years. *Epilepsia* 1989; 30:813-819.
 23. Quesney LF, Gloor P. Localization of epileptic foci. *Electroencephalogr Clin Neurophysiol* 1985; S37:165-200.
 24. Spitzer AR, Cohen LG, Fabrikant J, Hallett MA. Method for determining optimal interelectrode spacing for cerebral topographic mapping. *Electroencephalogr Clin Neurophysiol* 1989; 72:355-361.
 25. Yoshinaga H, Ohtsuka Y, Abiru K, Nakan K, Oka E. Utility of scalp-recorded ictal electroencephalograms in childhood epilepsy with complex partial seizures. *Pediatr Int* 2004; 46:342-345.
 26. Geiger LR, Harner RN. EEG patterns at the time of a focal seizure onset. *Arch Neurol* 1988; 35:276-286.
 27. Foldvary N, Klem G, Hammel J, Bingaman W, Najm I, Lüders H. The localizing value of ictal EEG in focal epilepsy. *Neurology* 2001;57:2022-2028.
 28. Sarco DP, Burke JF, Madsen JR. Electroencephalography in epilepsy surgery planning. *Childs Nerv Syst* 2006;22:760-5.
 29. Cascino GD. Epilepsy: contemporary perspectives on evaluation and treatment. *Mayo Clin Proc* 1994; 69:1199-1211.
 30. Schauble B, Cascino GD. Advances in neuroimaging: management of partial epileptic syndromes. *Neurosurg Rev* 2003; 26:233-246.
 31. Engel J Jr. Overview of functional neuroimaging in epilepsy. *Adv Neurol* 2000; 83:1-9.
 32. Hirsch E, Arzimanoglou A. Children with drug-resistant partial epilepsy: criteria for the identification of surgical candidates. *Rev Neurol (Paris)* 2004; 160:5S210-9.
 33. Hader WJ, Mackay M, Otsubo H, Chitoku S, Weiss S, Becker L. Cortical dysplastic lesions in children with intractable epilepsy: role of complete resection. *J Neurosurg Spine* 2004; 100:110-117.
 34. Chuang NA, Otsubo H, Chuang SH. Magnetic resonance imaging in pediatric epilepsy. *Top Magn Reson Imaging* 2002; 13:39-60.
 35. Gaillard WD, Chiron C, Cross JH, Harvey AS, Kuzniecky R, Hertz-Pannier L, et al. ILAE, Committee for Neuroimaging, Subcommittee for Pediatric. Guidelines for imaging infants and children with recent-onset epilepsy. *Epilepsia* 2009; 50: 2147-53.
 36. Vanderver A, Chang T, Kennedy C, Acosta M, Conry JA, Pearl PL, et al. MR Imaging for the diagnosis of cerebral dysplasia in new onset seizures in children. *Ann Neurol* 2003; 54:S114.
 37. Sharma S, Riviello JJ, Harper MB, Baskin MN. The role of emergent neuroimaging in children with new-onset afebrile seizures. *Pediatrics* 2003; 111:1-5.
 38. Redcay E, Kennedy DP, Courchesne E. fMRI during natural sleep as a method to study brain function during early childhood. *Neuroimage* 2007; 38:696-707.
 39. Freilich ER, Gaillard WD. Utility of functional MRI in pediatric neurology. *Curr Neurol Neurosci Rep* 2010;10:40-6.
 40. Medina LS, Berna B, Dunoyer C, Cervantes L, Rodriguez M, Pacheco E, et al. Seizure disorders: functional MR imaging for diagnostic evaluation and surgical treatment-

- prospective study. *Radiology* 2005;236:247–253.
41. Fitzgerald DB, Cosgrove GR, Ronner S, Jiang H, Buchbinder BR, Belliveau JW. Location of language in the cortex: a comparison between functional MR imaging and electrocortical stimulation. *Am J Neuroradiol* 1997; 18:1529–1539.
 42. Bizzi A, Blasi V, Falini A, Ferroli P, Cadioli M, Danesi U, et al. Presurgical functional MR imaging of language and motor functions: validation with intraoperative electrocortical mapping. *Radiology* 2008; 248:579–589.
 43. Seo JH, Holland K, Rose D, Rozhkov L, Fujiwara H, Byars A, et al. Multimodality imaging in the surgical treatment of children with nonlesional epilepsy. *Neurology* 2011; 76:41-8.
 44. DeTiege X, Connelly A, Liegeois F. Influence of motor functional magnetic resonance imaging on the surgical management of children and adolescents with symptomatic focal epilepsy. *Neurosurgery* 2009; 64:856–864.
 45. Koepp MJ, Woermann FG. Imaging structure and function in refractory focal epilepsy. *Lancet Neurol* 2005; 4:42–53.
 46. Spencer S. The relative contributions of MRI, SPECT, and PET imaging in epilepsy. *Epilepsia* 1994; 35(S6):S72–S89.
 47. O'Brien TJ, Hicks RJ, Ware R, Binns DS, Murphy M, Cook MJ. The utility of a 3-D, large-field-of-view, PENN-PET scanner in the presurgical evaluation of partial epilepsy. *J Nucl Med* 2001; 42:1158–1165.
 48. Olson DM, Chugani HT, Shewmon DA, Phelps ME, Peacock WJ. Electrocorticographic confirmation of focal positronemission tomographic abnormalities in children with intractable epilepsy. *Epilepsia* 1990; 31:731–739.
 49. Chandra PS, Salamon N, Huang J, Wu JY, Koh S, Vinters HV. FDG-PET/MRI coregistration and diffusion-tensor imaging distinguish epileptogenic tubers and cortex in patients with tuberous sclerosis complex: a preliminary report. *Epilepsia* 2006;47:1543–1549.
 50. Prince DA, Wilder BJ. Control mechanisms in cortical epileptogenic foci. "Surround" inhibition. *Arch Neurol* 1967; 16:194–202.
 51. Patil S, Biassoni L, Borgwardt L. Nuclear medicine in pediatric neurology and neurosurgery: epilepsy and brain tumors. *Semin Nucl Med* 2007; 37:357-81.
 52. Thompson PJ, Korenhof L, Kapur N. Memory rehabilitation in people with epilepsy. In Zeman A, Kapur N, Jones-Gotman M (eds). *Epilepsy and memory*. Oxford University Press: Oxford; 2010.P.2225-2230.
 53. Demase DF, Gruenthal M, Balint J. The national temporal lobectomy survey. *Seizure* 2009; 18:702–710.
 54. Szabo C, Wyllie E. Intracarotid amobarbital testing for language and memory dominance in children. *Epilepsy Res* 1993; 15:239-246.
 55. Jones-Gotman M. Presurgical psychological assessment in children: special tests. *J Epilepsy* 1990; 3S:93-102.
 56. Riviello JJ Jr, Helmers SL, Mikati M, Holmes GL. The preoperative evaluation of the child with epilepsy. *Neurosurg Clin N Am* 1995; 6:431-442.
 57. Masters LT, Perrine K, Devinsky O, Nelson PK. Wada testing in pediatric patients by use of propofol anesthesia. *AJNR Am J Neuroradiol* 2000; 21:1302-5.
 58. Urbach H, Von Oertzen J, Klemm E, Koenig R, Linke DB, Kurthen M, et al. Selective middle cerebral artery Wada tests as a part of presurgical evaluation in patients with drug-resistant epilepsies. *Epilepsia* 2002;43(10):1217-23.
 59. Zumsteg D, Wieser HG. Presurgical evaluation: current role of invasive EEG. *Epilepsia* 2000; 41(S3):S55-S60.
 60. Benbadis SR, Wyllie E, Bingaman W. Intracranial EEG and localization studies. Wyllie E: *The Treatment of Epilepsy: Principles and Practice* ed 3 New York, Lippincott Williams & Wilkins 2001; 1067–1075.
 61. Jayakar P. Invasive EEG monitoring in children: when, where, and what? *J Clin Neurophysiol* 1999; 16:408-418.