Surgical Aspects in the Treatment of Pediatric Epilepsy

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Summary

Up to one third of children with epilepsy develop drug-resistant epilepsy, while in selected cases surgical treatment plays an important role. In this review we describe the indications for temporal lobe surgery and corpus callosotomy, the technical aspects of these surgeries, and morbidity and outcome following these procedures.

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Key words: Epilepsy surgery, refractory epilepsy, corpus callosotomy, pediatric epilepsy, selective amygdala-hippocampectomy

Aspects chirurgicaux du traitement de l'épilepsie chez l'enfant

Jusqu'à un tiers des enfants atteints d'épilepsie développent une épilepsie pharmacorésistante. Dans certains cas, le traitement chirurgical joue alors un rôle important. Dans cet article, nous passons en revue les indications de la chirurgie du lobe temporal et de la callosotomie, les aspects techniques de ces interventions, ainsi que la morbidité et les résultats obtenus avec ces procédures.

Mots clés : Chirurgie épileptique, épilepsie réfractaire, callosotomie, épilepsie pédiatrique, amygdalo-hippocampectomie sélective

Chirurgische Aspekte bei der Behandlung pädiatrischer Epilepsien

Bis zu einem Drittel der Kinder mit Epilepsie entwickelt eine pharmakorefraktäre Epilepsie, wobei in ausgewählten Fällen die chirurgische Behandlung eine wichtige Rolle spielt. In diesem Übersichtsartikel befassen wir uns mit den Indikationen für Temporallappenoperation und Korpus-Kallosotomie und erörtern die technischen Aspekte dieser Eingriffe sowie die Behandlungsergebnisse und die Morbidität nach diesen Verfahren.

Schlüsselwörter: Epilepsie-Chirurgie, refraktäre Epilepsie, Korpus-Kallosotomie, pädiatrische Epilepsien, selektive Amygdala-Hippokampektomie

Introduction

Incidence of epilepsy is correlated with age and in the pediatric population approximately 50 new cases a year are diagnosed per 100.000 children [1 - 3]. Of these children, up to one third will develop drug-resistant epilepsy [4]. Uncontrolled seizures carry higher mortality rates in children, along with poor neurocognitive and psychosocial outcome [5, 6]. Surgery plays an important role in the treatment of epilepsy caused by brain lesions, temporal lobe epilepsy, hippocampal sclerosis, drop attacks, and various congenital syndromes (e.g. Rasmussen syndrome, Lenaux-Gastaut syndrome). The different surgical techniques include amongst others, lesionectomy, hemispherotomy, temporal lobectomy, selective amygdala-hippocampectomy, and corpus callosotomy. In this article we describe two frequent surgical procedures for drug-resistant epilepsy, namely temporal lobe surgery and corpus callosotomy.

Temporal lobe surgery for drug-resistant epilepsy

Patients in whom the seizure onset will be identified in the temporal lobe are potential surgical candidates for resection and a population based study in childhood showed that up to 10% of these patients will harbor a lesion [7].

In epilepsy surgery, temporal lobectomy for refractory cases still stands out as the only level 1 evidence to support its use [8]. This study was carried out on adults but its evidence is strong enough to infer that it is equally valid in children.

The rate of drug-resistance is higher for children with new onset of seizure and presence of temporal lesion on MRI as opposed to those without lesions [4, 7, 9] hence early surgery has to be openly considered in such children where the workup is congruent with the lesion.

Assessment and indications

Along with the standard presurgical workup carried out in a multidisciplinary team [10], a pediatric epilepsy surgeon will give particular relevance to the magnetic resonance imaging (MRI) of the temporal lobe and its mesial structures. Of note, changes in the signal of mesiotemporal structures can be more subtle to identify in children as compared to adults; other pathologies than hippocampal sclerosis are more often encountered in children, such as dysplasia, tumors and post-ischemic changes [11, 12]. Temporal tumors are typically gangliogliomas, dysembryoplastic neuroepitelial tumors (DNET's), pilocytic tumors as well as the more aggressive primitive neuroectodermal tumors (PNETs).

The presence of a lesion should prompt the look for the so-called "dual pathology", where a neocortical lesion co-exists with a mesiotemporal lesion, raising the question of what came first and what is the consequence [13 - 15].

Considering their epileptogenicity, even lesions classically considered "oncologically" benign should be removed as they tend to confer an intractable trait to the epilepsy [9].

MRI can be "negative" when it does not show any structural abnormality within the temporal lobe in up to 50% of cases [11] but surgical treatment can still be successful in selected patients [16].

Technical aspects in pediatric temporal lobectomy

The surgery will depend on whether the resection involves only the lateral neocortex, the mesiotemporal cortex or both.

After adequate body and head positioning (pins head clamps are usually avoided below 2 years of age), neuronavigation is set up: it will prove useful in the planning of the skin incision, bone flap and in the orientation within the ventricle especially in redo cases but also when facing lesions difficult to distinguish from normal brain parenchyma.

Standard craniotomy is performed with obvious and particular care to hemostasis in each step, considering the low circulating blood volume in the pediatric population.

At this stage the extent of resection has to be determined:

- The lateral-to-medial extent of resection in the temporal lobe (and beyond, including non temporal cortex such as frontal and/or insular) is determined by presurgical workup and in discordant cases by electrocorticography (ECoG), done either intraoperatively (over minutes/hours) or preoperatively (over days). This could be particularly helpful to study adjacent tissue in cases where the lesion lays in the mesiotemporal structures.
- The anteroposterior extent of resection is classically based on the side of the "dominance". Dominance is usually referred to language function and is assessed in a variety of manners, with left dominance being much more common than right.

Crucial language areas usually lie more laterally and posteriorly in the dominant temporal lobe. When approaching lesions in these areas in adolescent or preadolescent patients, speech mapping can be performed either via an awake craniotomy in [17 - 19] or through an invasive monitoring prior to resection. Of note, a clinical series showed that speech representation on the cortex can be extremely variable and less represented in the perisylvian cortices in children younger than 8 years old [20].

Quadranopsia remains the typical visual impairment of temporal lobectomy. If the resection is taken further back to where fibers come off the geniculate (geniculocalcarine radiations) then the impairment can extend to hemianopsia either from direct disruption or from vascular injury.

The resection is carried out under microscope with the ultrasonic aspirator in a subpial fashion to respect sulci and normal parenchyma [21].

Anatomically, the inferior part of the circular sulcus of insula along with the limen insulae provides a crucial superior landmark to avoid entering the basal ganglia and deep perforators from the middle cerebral artery.

Once within the temporal horn of the lateral ventricle, in the anterior and inferior resections respecting the pia and following the tentorium will avoid injuries to the brain stem, major vessels and cranial nerves. Variably, and depending on the surgeon's previous experience in such cases, dysplastic brain or low grade tumors may be quite firm to palpation and to suction and may require the ultrasonic aspiration at lower settings.

How extensive the resection should be in mesiotemporal structures remains controversial in adults and children [22]. Also, a number of so called selective ap-

proaches to mesiotemporal structures, with variable sparing of the lateral neocortex, have been described especially in adults. Independently on the technical challenge of such approaches, some literature suggests though that these approaches can miss significant pathology in children with less favorable outcome [23, 24] especially in so called "negative" MRI.

In order to approach solely mesiotemporal structures, the ventricle can be entered via the middle temporal gyrus or the inferior temporal gyrus or through upward retraction and resection of the fusiform gyrus [25].

A "transylvian trancisternal" selective approach, also described in children, is the only one who does not require entering the ventricle [26] and should spare the superior visual field fibers and avoid consequent quadranopia.

Hippocampus, choroid plexus and amygdala are encountered in the ventricle: one should keep in mind that the amygdala lies anterior, medial and superior to the hippocampus and no pia exists at its superior border with the optic tract. The other surfaces of the amygdala (anterior, mesial and inferior) should be resected respecting the pia and should not go further back than the level of the middle cerebral artery.

The head of the hippocampus will be seen anterior to the inferior choroidal point (where the choroid plexus/fissure begins and where the anterior choroidal artery enters the lateral ventricle) and should be carefully aspirated subpially. The third nerve, the internal carotid artery and the posterior communicating artery can be seen. It is commonly recommended not to coagulate bleeding pial edges to avoid ischemic changes in the neighboring tissue but to use gentle compression and irrigation with cottonoids. The resection of the hippocampus is then carried out posterior to the choroidal point including the fimbria-fornix. The posterior limit will be determined preoperatively and will be guided by anatomy, neuronavigation and – in selected cases – electrocorticography. The posterior resection does not go further back than the level of the quadrigeminal cistern [27].

In non lesional cases, if the preoperative workup is congruent with a temporal onset, a standard lateral-mesiotemporal resection is carried out, according to anatomical landmarks. The use of ECoG, aiming at an end-of-resection clear off interictal activity, has been related to a better outcome, especially in negative-MRI temporal lobe epilepsies (TLE) [28, 29]. Conversely other studies in children have pointed out that an ECoG with persisting activity is not necessarily relevant for a good epileptologic outcome [30]. Obviously, its use has to be balanced with the potential postoperative functional deficit.

Complications and outcomes

Quadranopia is definitely frequent even in pediatric population after temporal lobectomies. Display of optic radiation within image-guidance during surgery seems to lower the risk of visual field deficit in temporal lobectomies [31, 32]. Implementation of intraoperative MRI and neuronavigation along with preoperative functional MRI and diffusion tensor imaging (DTI) maps should lower risks in visual, speech and memory functions, especially in dominant temporal lobe epilepsy [33]. Cranial nerves injuries, ischemic changes or brain stem lesion are much rarer.

Some studies in children have assessed memory deficits (namely verbal memory after left sided resections) and suggest that these are less frequent than in adult groups [34, 35]. Some studies showed that the overall seizure-free rate is higher in children less than 3 years old as compared to slightly older children, suggesting that the earlier the surgery is performed the better the epileptological outcome [36].

Overall epileptological outcome for TLE in children seems to be higher in lesionectomies as compared to Type I dysplasia and less well defined pathologies (where also the delimitation of resection margins would be more difficult) with a seizure freedom rate up to 70% at 5 years follow up [11].

When considering surgery for TLE in pediatric age, the benefits and its potential long term neurocognitive dysfunction (poorly understood) must be counterweighted by the neurocognitive deterioration that longstanding refractory epilepsy will cause in a child. It is certainly beneficial in what the old terminology called "catastrophic" epilepsy [37].

Corpus callosotomy

Corpus callosotomy was first described as a treatment of refractory epilepsy in 10 children by Van Wagenen and Herrin in 1940 [38]. Since then it has been a well-established surgical technique for refractory epilepsy, with a specific indication for drop attacks [39 - 41]. Over the years corpus callosotomy has shown to be effective in a wide range of refractory epilepsy such as tonic-clonic seizures, atonic seizures, drop attacks, recurrent status epilepticus, and Lenaux-Gastaut syndrome [39].

Through a corpus callosotomy the interhemispheric spread of seizures is disconnected. However, since apart from the corpus callosum other commissural pathways, such as the anterior, posterior, and hippocampal commissures are known, corpus callosotomy rarely results in a cure [39, 42]. Hence, the goal of the procedure is to decrease seizure frequency, and improve function and quality of life. In addition, most patients will remain on an antiepileptic regimen after the procedure. Although corpus callosotomy is generally well toler-

ated, transient or permanent neurological deficits such as disconnection syndromes (e.g. supplementary motor area syndrome and alien hand syndrome), hemiparesis, aphasia, mutism, and akinesia can occur. The recommended extent of callosotomy performed varies, while most recommended is a resection of the anterior half or two thirds callosotomy sparing the splenium, since it seems this leads to less neurological deficits [39, 41]. Children with failed anterior two thirds callosotomy might undergo a second procedure for complete callosotomy [41]. While children undergoing upfront complete callosotomy show better seizure control and improvement of a broader spectrum of seizure types than those who underwent two-stage complete callosotomy, the potential for postoperative neurological complications and possible unmasking of dormant seizures is higher [41, 43, 44]. Recently, some have advocated a selective posterior callosotomy for drop attacks sparing all frontal interconnectivities in patients with intellectual disability [45]. However, the specific indication and outcome for such procedures still needs to be determined through comparative studies with bigger cohorts. The extent of callosotomy remains a balance between achieving good seizure control and minimizing postoperative neurological complications. To date, in most cases a two-stage treatment is recommended, and the decision to perform an upfront complete callosotomy must be considered very carefully [41, 43, 44].

Preoperative assessments

A thorough preoperative epileptological workup to ascertain the intractability of the patient's seizures and the absence of indication for focal resection is performed. This includes medical history, physical examination, electroencephalography (EEG), video-monitoring EEG, magnetic resonance imaging of the brain in addition to structural and metabolic imaging studies, and neuropsychological evaluations.

Operative technique

The patient is positioned supine with the head secured in the 3-pin Mayfield clamp. The neck is moderately flexed and the torso is elevated 10 - 20 degrees above horizontal. Preoperative magnetic resonance imaging is co-registered to the scalp using the neuronavigation system. Frameless stereotactic navigation is helpful in assessing trajectories for the anterior and posterior limits of the callosotomy, planning the craniotomy accordingly, and avoiding large bridging cortical veins when approaching the corpus callosum. Either a small bi-coronal or U-shaped incision over the midline is planned, and the hair shaved accordingly.

A skip flap is raised and retained with sutures or clamps. Two to four burr-holes are completed, while a minimum of two burr-holes are placed over the superior sagittal sinus. The dura mater is separated from the bone and the craniotomy, one third anterior to the coronal suture, two thirds behind it, and crossing the midline, is fashioned. After elevation of the bone flap, bleeding over the superior sagittal sinus is usually controlled using Tachoseal, Tabotamp and cotton strips.

The dura is opened in a U-shaped fashion with a base toward the superior sagittal sinus. Small veins anterior to the coronal suture can be coagulated while larger veins and veins behind the coronal suture are spared. Tacking up the dura allows good visualization of the interhemispheric fissure, which is prepared by detachment of arachnoid adhesions.

Under microscopic visualization using the surgical microscope, the interhemispheric fissure is opened carefully, gently retracting the mesial frontal lobe until the pericallosal arteries are identified and separated to reach the glistening white corpus callosum in the midline. A retractor blade may be used to retract the mesial frontal lobe. Papaverine soaked cottonoids are used to cover the arteries which are retracted laterally. With help of the neuronavigation the midline and extent of the callosotomy (anterior two thirds or complete) is confirmed. The corpus callosum is exposed along the desired extent of the callosotomy. The callosotomy itself is traditionally done using suction and bipolar cautery until the midline cleft between the leaves of the septum pellucidum is exposed. Other techniques using carbon dioxide laser for callosotomy have been described as well [39]. The main advantages being preservation of the ependymal plane, creating a clean transection, minimal brain retraction, and minimizing surrounding thermal damage to brain tissue [39]. The transection is initially carried out to the ependymal surface of the ventricle, then completed anteriorly to the genu of the corpus callosum just shy of the anterior commissure. The patient is then repositioned by dropping the head and moving the retractors slightly more posteriorly to enable the resection of the splenium as far posteriorly as possible in a subpial fashion. In order to achieve a complete callosotomy the exposure of the midline pia over the vein of Galen posteriorly and inferiorly should be confirmed. After ample irrigation, control of hemostasis using bipolar cautery is achieved.

The dura is closed with a running suture in a water-tight fashion. The bone flap then secured to the skull with titanium plates and the skin closed in orderly fashion.

Endoscopic assisted corpus callosotomy, adapted from endoscopic transpenoidal surgery, was described and advocated by some authors [41, 46, 47]. The main aim of this technique is to minimize the size of incision and craniotomy. However, the field of surgery is larger than the view through the endoscope, and this can be frustrating at time, since it requires repeated repositioning of the endoscope. To date, no series demonstrate superiority of the endoscopic over microscopic

corpus callosotomy and vice versa, leaving the decision of the preferred technique with the treating neurosurgeon.

Outcome and complications

After corpus callosotomy good to excellent improvement of drop attacks is described in 60 - 80% of the patients, and in 40 - 80% of the patients with generalized tonic-clonic seizures and complex partial seizures [48, 49]. Long-term follow-up studies demonstrate also favorable long term affect for these patients [49]. In addition, positive change in behavior function, especially attention, but also overall daily cognitive functions were reported [48, 49]. Quality of life measures after corpus callosotomy exhibited better results, and parents and caregivers satisfaction was high. It seems that when surgery is performed early in childhood, greater chances of gaining behavioral improvements can be expected [48].

Neurological symptoms after partial callosotomy are typically mild and transient [49]. The classical disconnection syndrome is rarely seen and occurs more often after total callosotomy [49]. Mutism has been described after corpus callosotomy, while the occurrence of mutism is reduced when pial integrity of the cingulate gyri is preserved [50]. Further complications consist of swelling of the frontal lobe, cerebral infarction, hemiparesis, supplementary motor areal-syndrome, status epilepticus, and other craniotomy-related incidents [49]. However all reports describe complications as rare and mostly transient occurring in about 5% of the cases [49].

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