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Corpus Callosotomy in Pediatric Intractable Epilepsy: Microsurgical Technique Implication and Variation

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1. Introduction

Medically intractable epilepsy is considered for surgical intervention first for resection of localized area of brain in which cases seizure control is expected generally. Nevertheless, those with non-localizing lesions in the imaging studies as well as multifocal spikes in electroencephalography (EEG) are not candidates for the resective surgery. For palliative intervention, corpus callosotomy may be considered for these patients. Early detection of proper candidates for surgical intervention in pediatric patients with medically intractable seizures may give a better chance of recovering their developmental potential by protecting the brain from further epileptic discharges.

2. Back ground with historical development

The cerebral hemispheres are connected by six midline commissural structures: the anterior commissure, posterior commissure, corpus callosum, hippocampal commissure, the massa intermedia of the thalamus, and the fornix. Corpus callosum is the largest commissure and represents large areas of cortex in bilateral cerebral hemispheres. The concept behind the callosotomy is the hypothesis that the corpus callosum is the most important pathways for the spread of epileptic activity between the hemispheres especially in the secondarily generalized seizures. As to support the hypothesis, more than 60% of the 300 million fibers in the corpus callosum are fast conduction myelinated fibers. (Aboitiz, Scheibel et al. 1992; Tomasch 1954).

The first callosotomy was done by Dandy during a brain tumor operation in 1992, however, Van Wagenen and Herren were the first to apply the procedure to undertake the procedure for epilepsy patients in 1940. (Van Wagenen and Herren 1940) The first operations were consisted of right frontal craniotomy with the sagittal sinus and anterior falx divided. The lateral and third ventricles were entered during callosotomy and the one side of fornix or anterior commissure was disconnected. In 1960's, Bogen and colleagues developed the two types of commissurotomy, complete vs. partial. Partial commissurotomy consisted of anterior 1/3 of callosotomy, anterior commissure, and one fornix for the patients with epileptic discharges from frontal and temporal areas. (Wyler 1993) In 1970, Lussenhop first

reported their application of corpus callosotomy in children with intractable epilepsy. (Luessenhop 1970; Crowell and Ajmone Marson 1972) In 1970's, surgical microscope was first used for callosotomy by Wilson and his extraventricular approach prevented postoperative hydrocephalus. (Wilson, Reeves et al. 1978) Wyler further refined microsurgical technique in callosotomy entering the cavum septum pellucidum between the two pericallosal arteries in 1990's. (Wyler 1993) Currently, endoscopic anterior callosotomy and radiosurgical callosotomy are some new approaches attempted by some investigators. (Pendl, Eder et al. 1999; Tubbs, Smyth et al. 2004; Eder, Feichtinger et al. 2006)

Along with clinical application of callosotomy, experimental data has accumulated as well over the years. Erickson's work established the major role of corpus callosum as the seizure propagation pathway in the monkeys. (Pendl, Eder et al. 1999) Effect of the callosotomy in the seizure generalization has also been demonstrated in animal studies. (Crowell and Ajmone Marson 1972; Marcus and Watson 1966)

3. Indication

The common indication for callosotomy is those types of seizures of generalized or partial seizures with rapid secondary generalized patterns and without localizing lesions. Most effective seizures that are controlled with callosotomy are the atonic or tonic seizures characterized by sudden drop attacks that result in catastrophic events of self inflicting trauma to the patients as well as major burden to the parents. Many investigators have reported the elimination or reduction of frequency as well as the severity of the drop attacks most effectively compared to any other seizure types. (Gates, Leppik et al. 1984; Purves, Wada et al. 1988; Nordgren, Reeves et al. 1991; Spencer, Spencer et al. 1993)

Majority of patients with medically intractable seizures without localizing lesions undergoing callosotomy usually comprise of many different types of seizures. Infantile spasm, Lennox-Gastaut Syndrome, and West syndrome are the well known syndromic epilepsy with multiple seizure types that are good candidates for the callosotomy. Primary generalized seizures with tonic or tonic-clonic seizures are also found to respond well.

In our institute, the followings are the criteria for callosotomy candidates. 1) Medically intractable seizures that are treated over two years with use of all standard anticonvulsant medications in adequate serum level. 2) Types of seizures that are potentially amenable to callosotomy as mentioned above. 3) There is no identifiable single localizing lesion for resection. 4) Seizures that could be localized to one hemisphere or single foci after the callosotomy. Mental retardation is not contraindication for the surgery

4. The debate on extent of callosotomy

Debate still exists on extent of callosotomy and the indication for the completion of the callosotomy. Historically, callosotomy was tailored to the seizure types and location of seizure discharge by the extent of disconnection and completion of disconnection is done in staged fashion in order to circumvent the possible complication of callosotomy such as split-brain syndrome and posterior disconnection syndrome. Therefore, most epilepsy centers undertake 2-stage operation. (Spencer, Spencer et al. 1988; Andersen, áRogvi-Hansen et al. 1996) After 6-months from partial section, persistent generalizing seizures may benefit from completion of commissurotomy and second surgery is undertaken in most cases. Purves et al supported the anterior callosotomy alone is sufficient for some patients controlling

seizure. (Purves, Wada et al. 1988) However, the seizure outcome is far better in total callosotomy compared to partial callosotomy in many series especially in pediatric patients without concerned neuropsychological complications. (Rathore, Abraham et al. 2007) We had the same 2-stage callosotomy principle previously as well. With retrospective review of our series, patients with total callosotomy had better seizure outcome than partial callosotomy without neuropsychological deficits. (Kim, Yang et al. 2004) The results of Lassonde and Sauerwein, Lassonde et al and Maehara and Shimizu have similar outcome supporting our data. (Lassonde, Sauerwein et al. 1991; Lassonde and Sauerwein 1997; Maehara and Shimizu 2001) Therefore, in our institute, young patients before puberty with drop attacks and intractable generalized tonic clonic seizures are selected for the one stage total callosotomy with less complications related to surgeries with change in paradigm of treatment policy. (Shim, Lee et al. 2008)

5. Surgical procedure in Severance Children's Hospital Epilepsy Clinic

Presurgical evaluation is done by a multidisciplinary team of pediatric neurologists, neurosurgeons, neuroradiologists, clinical psychologists and the neuromodulation technicians. It includes detailed medical history of patients with physical and neurological examination. Continuous EEG with video monitoring is undertaken to identify the seizure types. Magnetic resonance imaging include diffusion tensor imaging is routinely done and ictal and interictal SPECT, and PET scan are done in most cases. Neuropsychological evaluation is routinely done to check the cognitive function as well as the social behavior adaptation using Korean Wechsler Intelligent Scale for children. EEG, MRI and neuropsychological testing and repeated postoperatively as well.

General anesthesia is used and intraoperative electrocorticography is used in selected cases for investigation only. Patients are positioned supine on operating table and head fixating pin is not used. Patient's head is rested on gel donut pillow and fixed to the table with plastic tapes around the donut pillow and the head. Currently, for one stage operation, we have developed no shaving with absorbable skin suture policy. Patients' hair is parted at the incision line and separated with rubber band or iodine oint for the short hair. Bicoronal skin incision is used over the coronal suture centered more to right except in cases where the dominant pathology is on the left side or other causes difficulty in entering the non dominant hemisphere. Craniotomy is made one centimeter crossing the sagittal suture with 6 centimeter total width and 4 centimeter anterior and 3 centimeter posterior to coronal suture in most cases. Special care should be taken making the craniotomy across the sagittal sinus. Dura is opened in curvilinear fashion based on the sagittal sinus and parasagittal draining veins are dissected and protected during interhemispheric dissection. Initial interhemispheric dissection is aided by self retaining retractor holding the brain on both sides. Surgical microscope is installed. Exposed cortex is protected with cottonoids. Interhemispheric dissection is aided by bipolar cautery and cottonoids used as the retractor on anterior and posterior ends of dissection. Meticulous dissection of arachnoid attachments leads to CSF leakage and brain relaxation is achieved without using mannitol or lumbar drainage of CSF preoperatively. Care should be paid to take enough time for brain relaxation before hemispheric retraction to avoid retraction injury. Adequate dissection exposes the paired pericallosal arteries on whitish background of corpus callosum. Dissection should continue until the genu and isthmus are exposed.

Callosal disconnection is done using microdissector and microsuction at the body level between the pericallosal arteries. Under microscope, the midline can be easily identified by the small arteries supplying the callosum itself entering perpendicularly into the midline. In addition, midline dissection will expose the midline cleft formed by the wall of lateral ventricles (Figure 1).

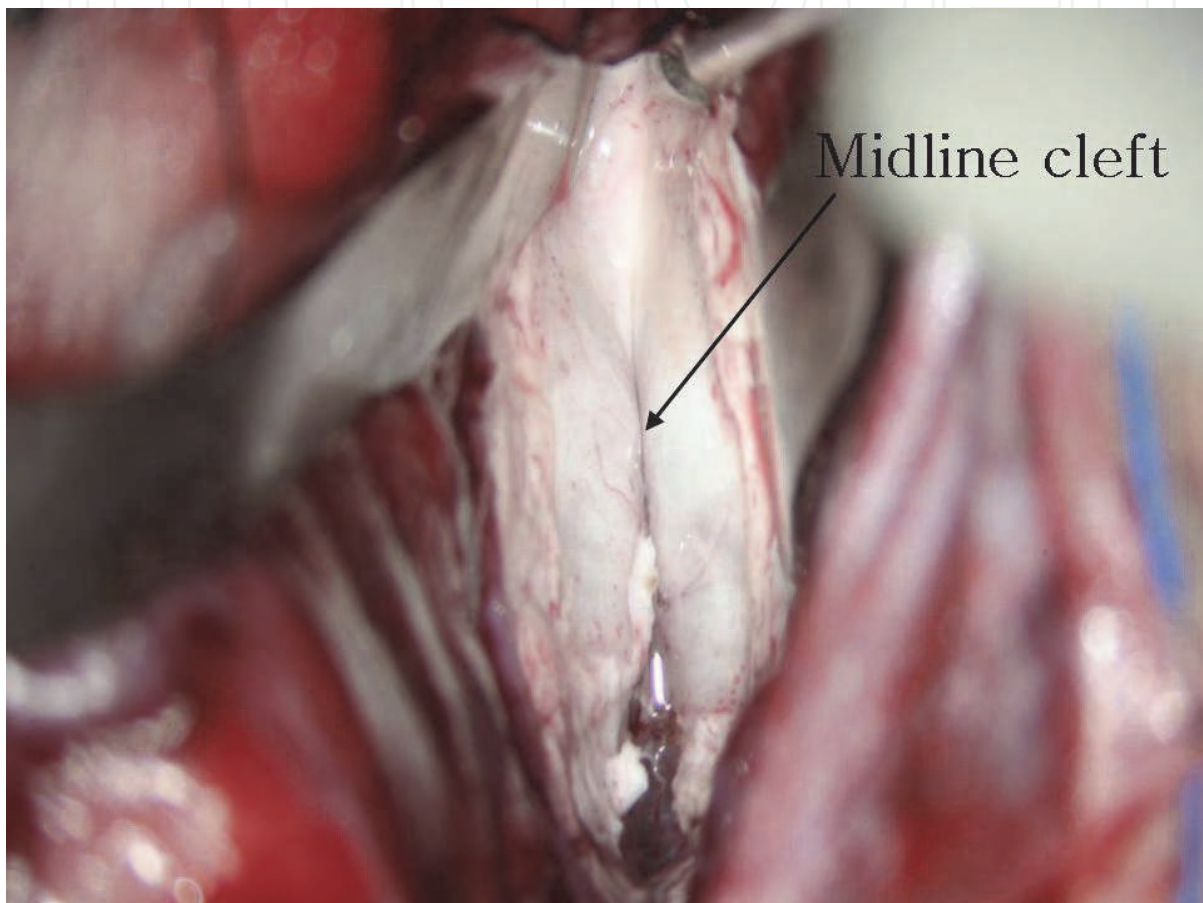


Fig. 1. Callosotomy following midline cleft

The midline cleft is followed down to the roof of third ventricle and anterior callosotomy is carried out. Anterior commisurotomy is carried out until the arachnoid membrane is exposed until the dorsum of anterior cerebral artery is exposed. For better view, head elevation may be required during anterior callosotomy. After completion of anterior callosotomy, the midline cleft is followed posteriorly with lowering the patient head position. Posterior callosotomy is completed when dissection is followed until the arachnoid membrane covering the vein of Galen and the internal cerebral vein. (Figure 2) Complete hemostasis is achieved using bipolar cautery.

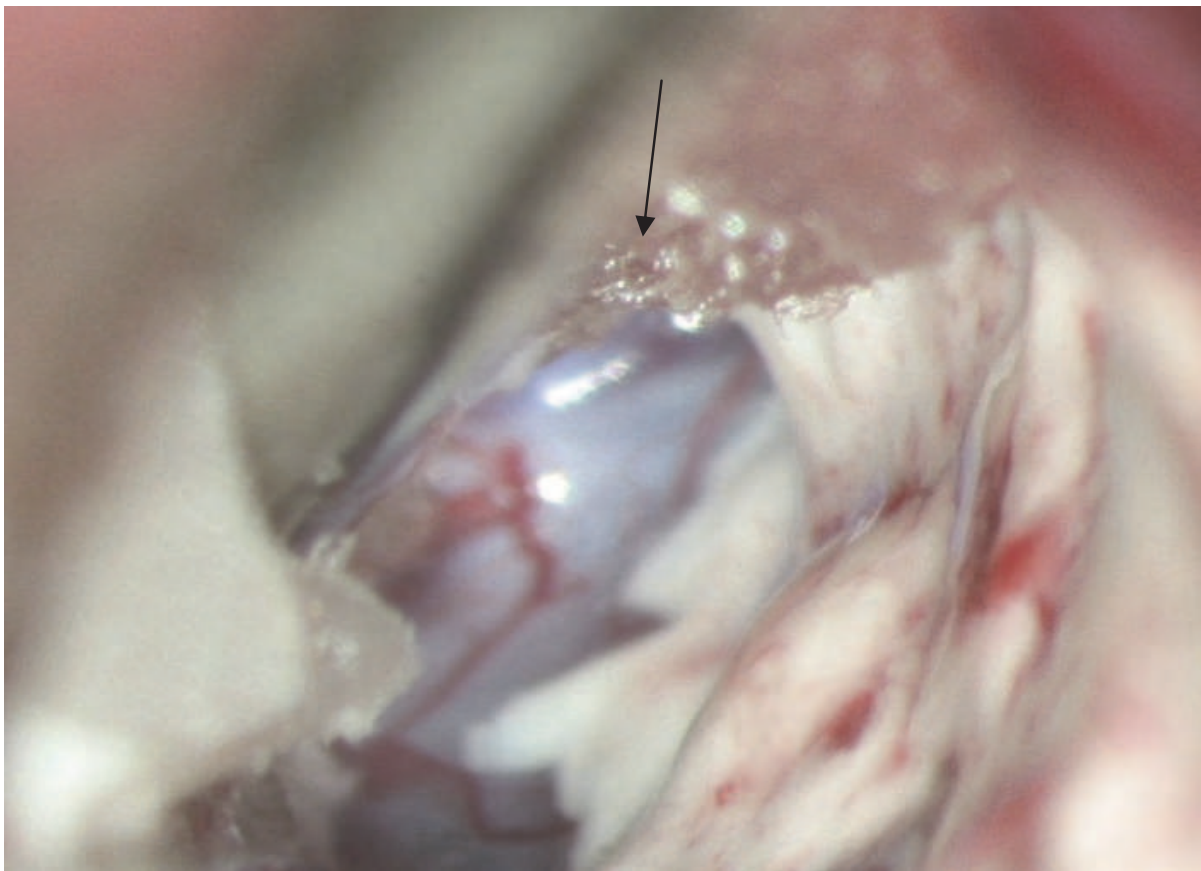


Fig. 2. Boundary of posterior callosotomy

Black arrow indicates arachnoid membrane covering the vein of Galen and internal cerebral vein is exposed indicating the completion of posterior callosotomy.

Navigation system is not an essential part of the surgery but it may assist the midline section and confirm the length or selectiveness of callosotomy in special cases where length of commisurotomy is tailored. (Jea, Vachhrajani et al. 2008) Intraoperative ECOG is not used routinely unless specific area of interest existed.

After saline irrigation confirming complete hemostasis, dura is closed with nonabsorbable monofilament sutures in water-tight fashion. Bone flap was fixated with metal craniofix buttons or absorbable buttons. Galea and subcutaneous suture is done using absorbable multifilament sutures with a subgaleal drainage tube inserted. Skin is closed with rapid vicryl 3-0. A drain is removed on postoperative day 2 and wound care is done with regular shampoo and topical antibiotic oint until the sutures are dissolved. Patients are monitoring in neurosurgical intensive care unit for overnight and transferred to the general ward the next day. Patients are usually discharge in a week after postoperative MRI taken.

Postoperative MRI is taken with DTI images to confirm the extent of callosotomy before patient's discharge. (Figure 3a, b, c) Patients are followed closely at the epilepsy outpatient clinic for seizure progression and control. Neuropsychological testing is followed after surgery at the outpatient clinic.

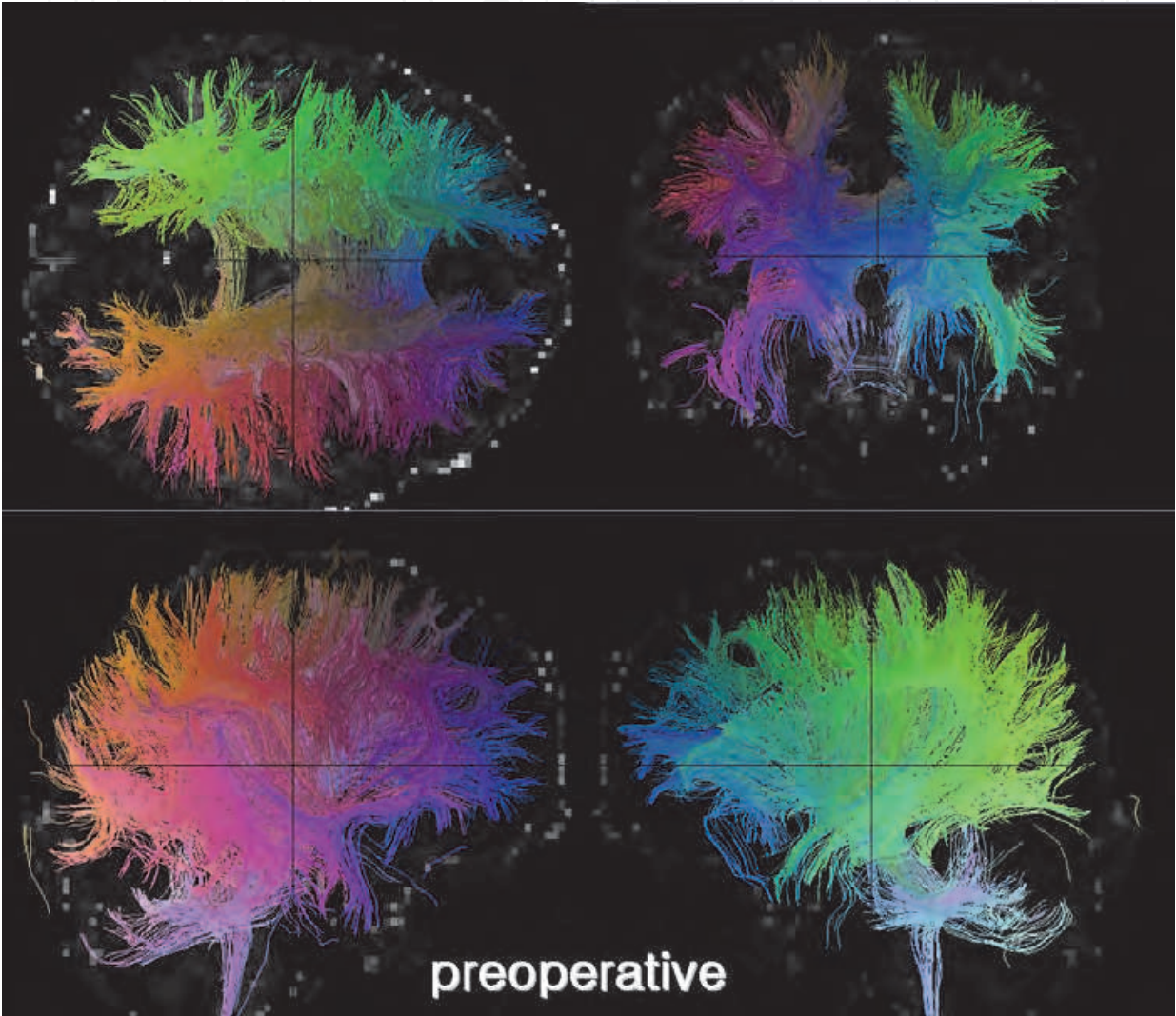


Fig. 3a. Preoperative DTI

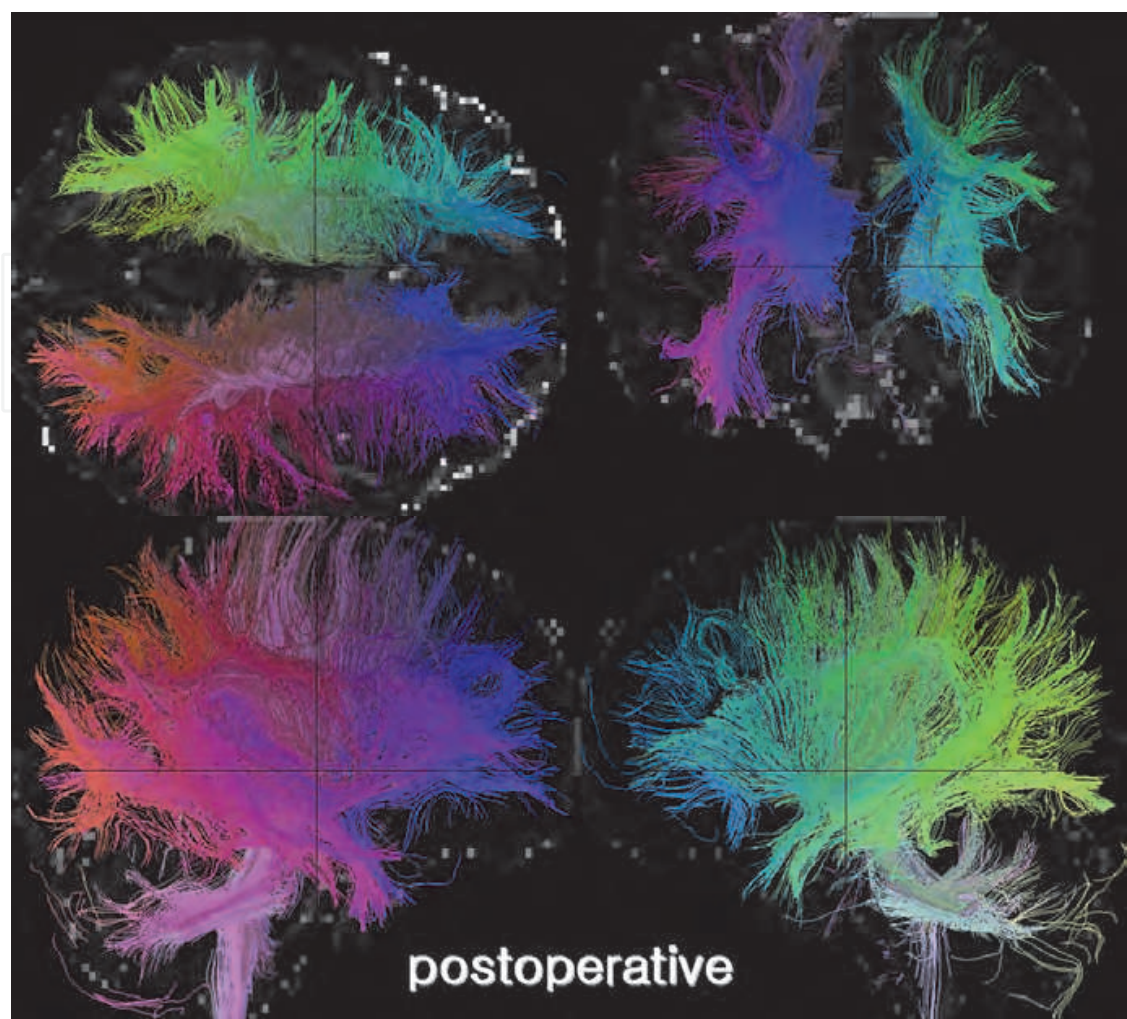


Fig. 3b. Postoperative DTI

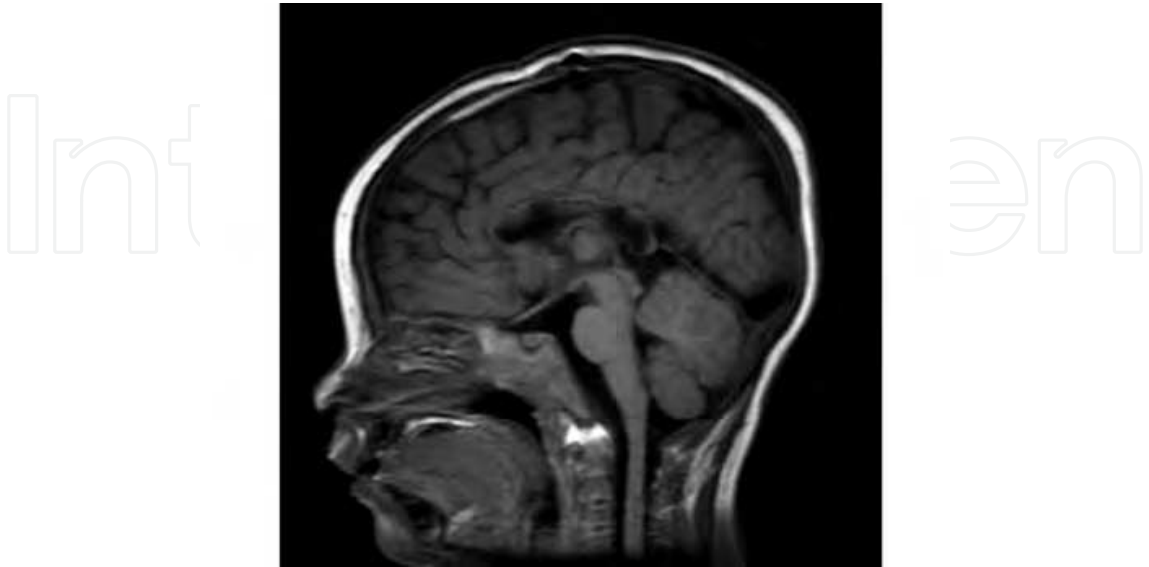


Fig. 3c Midsagittal section of MRI Postoperative DTI shows total disconnection of callosal fibers in Fig 3b and misagittal section of MRI confirming total callosotomy.

6. Outcome

Seizure outcome after callosotomy varies with investigators. In 1993, analysis of multicenter results was reported by Engel Jr. et al. Among 563 patients, 7.6% became seizure free and 60.9% improved. (Engel Jr., Van Ness et al. 1993) Recent long term follow-up results by Sunaga shows drop attack seizure free rate of 90% with total callosotomy and 54% with partial callosotomy with mean follow up of 7 years. Relapse rate of drop attack was 36% after 6 years from surgery. Total callosotomy patients had less relapse rate (7%) compared to partial callosotomy cases (31%) (Sunaga, Shimizu et al. 2009). Tanriverdi et al also reported the seizure outcome of 95 patients who was undergone callosotomy for seizure control. Generalized tonic clonic seizure types and drop attacks were the most well responding seizure types. Two third of their patients had favorable outcome with those seizure types. The seizure outcome was related to the extent of callosal section in their report. (Tanriverdi, Olivier et al. 2009) Pinard et al showed better outcome with total callosotomy in drop attacks among pediatric West syndrome cases. (Pinard, Delalande et al. 1999)

Most patients being candidates of callosotomy experience multitude of seizure types. Therefore, it is feasible to analyze the outcome by the seizure types. Favorable outcome as more than 50% reduction in seizures was noted in generalized tonic-clonic seizures (38-86%), generalized tonic seizures (43-60%), atonic seizures (60-83%) and complex partial seizures (50-51%). (Fuiks, Wyler et al. 1991; Oguni, Olivier et al. 1991; Reutens, Bye et al. 1993) Our data shows 35% seizure free rates in total. 76.4 % showed significant improvement after surgery and drop attacks was the seizure type with most effective result (91.2%). Generalized tonic-clonic seizures were also well controlled with total callosotomy (83.3%). Complex partial seizures, myoclonic seizures show less favorable outcome compared to drop attacks and GTC seizures. (Shim, Lee et al. 2008) Absence seizures are also well respond to the procedure according to Roberts and Siegel even though the procedure was not targeting the seizure type (Roberts and Siegel 2006).

Drop attacks are one of the most difficult seizures types for the patients as well as the caregivers. After the callosotomy, reduction of drop attacks is dramatic and the quality of life for the patient as well as the family has improved. Yang and his co-workers investigated the overall satisfaction and quality of life in 25 families. Mean reduction of severity of seizure activity was 64%. 76% of parents were satisfied with the surgical result and 72% described good level of satisfaction for family's quality of life. The key life domains showing improvement after surgery were level of self-care, family life and school performance. They reported significant improvement in hyperactivity, attention span, and social skills in 11 patients. (Yang, Wong et al. 1996) Similar results were produced by Gilliam and colleagues with improvements in alertness and responsiveness in children and 85% of families were satisfied with the operation. (Gilliam, Wyllie et al. 1996) Our results show 64.7% of parents reported improvement in overall daily function and 73.5% of parents show some satisfaction with the surgical result. Parents with younger patients expressed better satisfaction than parents of older children. These correlate with better functional outcome in younger patients with seizure control. These may indicate younger patients have better chance of recovering the neuropsychological and functional loss due to pervasive epileptic discharges.

Cognitive function is affected as well. Some reported improvement in cognitive function resulted from diminished seizure activity as well as the reduction of seizure medication. (Nordgren, Reeves et al. 1991) For our experience, with improved seizure

control, most patients' alertness and response to the surrounding have improved especially in the younger children. Majority of our patients had severe or profound mental retardation preoperatively and those with mental retardation showed better outcome. It may be due the fact the younger patient group has much retardation and may gain more from the surgery. Lassonde et al reported some benefit for all children regardless of their age with marked improvement in social adjustment and higher IQ associated with better outcome in patients younger than 13. (Lassonde and Sauerwein 1997) Shimizu and colleagues reported 77% improvement in overall behavior and 60% improved in expansion of vocabulary. No worsening of cognitive function was detected in this study. (Shimizu and Maehara 2000)

7. Morbidity

Hydrocephalus was common surgery related morbidity for callosotomy especially with surgical techniques entering the lateral and third ventricles in old days. With improvement in microsurgical techniques, hydrocephalus became rare complication. Aseptic meningitis, septic meningitis or ventriculitis, frontal lobe swelling and infarction and postoperative hematoma (subdural and epidural) are possible complications. Sagittal sinus tearing with bleeding and wound infection are some of the surgery related complication. In our experience, with no hair shaving and absorbable skin suture, wound complication or infection has not occurred. Aseptic meningitis occurs with continued fever for a week and subsides spontaneously or with use of short term steroids.

Neuropsychological complications well studied in the callosotomy are acute disconnection syndrome, posterior disconnection syndrome, split-brain syndrome, and deficit reinstatement. Acute disconnection syndrome includes mutism, difficulty in speech initiation, left side hemiparesis and urgency incontinence. There are debates on the effect of acute disconnection vs. surgical retraction on the parasagittal cortex on these symptoms. These phenomena usually disappear in a week after surgery. In our series, two patients showed mutism and apraxia which recovered shortly.

Posterior callosal section is well known for disconnection syndrome characterized by interhemispheric sensory dissociation. Sensory input from the non dominant hemisphere has no connection to the language dominant hemisphere. Incomplete section is known to preserve the dominant hemispheric access to the contralateral brain. Split brain syndrome is present in patients with near total or total callosotomy. Language impairment, hemisphere competition and disordered attention-memory sequencing are the signs of the split brain syndrome. These usually resolve itself with time. Deficit reinstatement usually occurs to patients with mixed cerebral dominance or transcallosal compensation due to early hemispheric injury. The preoperative lateral deficit may exacerbated or newly appear after callosotomy.

Some patients especially younger than 10 years of age do not experience these disconnection syndromes after total callosotomy. (Lassonde, Sauerwein et al. 1991; Lassonde and Sauerwein 1997; Rougier, Claverie et al. 1997; Sauerwein and Lassonde 1997; Pinard, Delalande et al. 1999; Rathore, Abraham et al. 2007) The callosal connection and bihemispheric connection are known to be completed at the age of 10 or 11 years. Therefore, early functional absence of callosal connections may lead to development alteration and selective reinforcement of the connection that are normally reinforced in usual

circumstances. In addition, due to long term effect of intractable seizures, language and motor function may be dominant in both hemispheres.(Mamelak, Barbaro et al. 1993) These may explain the absence of disconnection syndrome in young patients with total callosotomy and better functional outcome in these patients after surgery.

8. Conclusion and future modification

Callosotomy in pediatric epilepsy is a valuable tool to control seizure early on in order to protect the developing brain from further damage and to give chance to recover neuropsychological function from damage done by seizure itself as well as seizure medication. We advocate one stage total callosotomy in young patients with medically intractable epilepsy without localizing lesions especially effective in drop attacks and secondary generalized epilepsy. With improvement in microsurgical techniques, excellent seizure outcome as well as functional outcome may be reached without previously known high rate of morbidity and mortality. Early detection of patients required for surgical intervention is very important to increase the benefit of early seizure control in recovering lost neuropsychological functions. Patient selection, tailoring of the surgery and excellent surgical skill are mandatory in order to deliver the promised results for intractable epilepsy patients as well as for their family.

Currently with development of surgical aides such as neuronavigation and intraoperative MRI, more selected callosotomy may be attempted in older patients with higher functional baselines. Using diffusion tensor imaging overlaid on the navigation system prior to surgery may be used to depict the tracts from area of interest during operation and can help tailor the extent of resection. In addition, callosotomy may be used as localizing tool for epilepsy with suspicion of localizing lesion, nevertheless cannot be delineated due to fast generalization of epileptic discharge. After disconnection of the callosal fibers, the hidden epileptogenic focus may reveal itself and the seizure may be controlled with further resective surgery. Some of rare intractable seizures such as startle epilepsy may be benefitted from callosotomy as well.

9. Acknowledgement

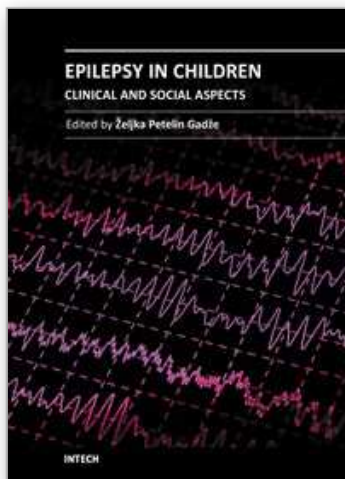
We acknowledge the great success of our epilepsy clinic to the well-coordinated multidisciplinary team work.

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Epilepsy in Children - Clinical and Social Aspects

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Epilepsy is a neurological condition that accompanies mankind probably since its inception. About 400 years before Christ, the disease was already known by Hippocrates, who wrote the book “On The Sacred Disease”. Classically, epilepsy has been defined as a chronic condition characterized by an enduring propensity to generate seizures, which are paroxysmal occurring episodes of abnormal excessive or synchronous neuronal activity in the brain. Out of all brain disorders, epilepsy is the one that offers a unique opportunity to understand normal brain functions as derived from excessive dysfunction of neuronal circuits, because the symptoms of epileptic seizures are not the result of usual loss of function that accompanies many disease that affect the brain. I am therefore extremely honoured to present this book. The 15 very interesting chapters of the book cover various fields in epileptology – they encompass the etiology and pathogenesis of the disease, clinical presentation with special attention to the epileptic syndromes of childhood, principles of medical management, surgical approaches, as well as social aspects of the disease.

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