Local cortical dysplasias are congenital MCDs frequently associated with refractory epilepsy in both children and adults. The prevalence of FCDs in patients with focal epilepsy may be as high as 25%. Successful resection and subsequent characterization of FCDs was first described by Taylor et al. in 1971 from pathological specimens obtained in patients treated for intractable temporal lobe epilepsy. Among pediatric patients treated surgically for intractable epilepsy, FCDs comprised the most common diagnostic category identified in surgical specimens from a multicenter survey of pediatric epilepsy surgery. Although FCDs present most commonly in childhood with epilepsy, developmental delays, or focal neurological deficits, they may also be a rare cause of epilepsy in adult patients. Surgical evaluation and treatment of FCDs requires an understanding of the underlying cytological and cortical architectural abnormalities associated with clinical, imaging, and EEG findings. In this review we discuss the histopathological classification of FCDs, the presurgical assessment of patients with FCDs and intractable epilepsy, describe the surgical approaches to FCDs, and outline our current knowledge of outcomes after surgery in these patients.

Histopathological Characteristics of FCD

The establishment of a uniform terminology and classification of histopathological findings associated with FCDs has recently been proposed by a consensus panel of neuropathologists, neuroepileptologists, and neuroradiologists. Many names including ‘malformations of cortical development,’ ‘neuronal migration disorders,’ and ‘Taylor-type’ or ‘balloon cell dyplasias,’ have been used to describe FCDs. This lesion is also often included with milder histopathological abnormalities referred to as microdysgenesis, the criteria for which is also not uniform among neuropathologists. Palmini and colleagues determined that several distinct histopathological features of the cortex must be present for a lesion to be considered a true FCD. These include architectural abnormalities, either dyslamination or columnar disorganization with or without dysmorphic neurons, giant cells, or balloon cells (Fig. 1). Palmini et al. described 2 major types and 4 subtypes of FCD: Type IA with isolated architectural abnormalities alone; Type IB, including giant neurons; Type IIA “Taylor-type” FCD with lamination abnormalities and dysmorphic neurons; and Type IIB, also with balloon cells (Fig. 2). The classification of histological abnormalities apart from those of true FCDs, which are characterized by heterotopic neurons only, under the category of mild MCDs was meant to replace findings erroneously described as microdysgenesis. Although strictly a pathological classification, an expected correlation with neuroimaging results was summarized within the classification system. Mild MCDs and Type IA and IB FCDs were not considered likely to have correlating characteristics on MR images, unlike Type II which
would probably exhibit changes including increased cortical thickness, blurring of grey–white junction, and extension of cortical tissue towards the ventricle (transmantle dysplasia).

Malformations of cortical development are thought to result from environmental or genetic influences in different stages of normal prenatal development affecting cellular proliferation, migration, or cortical organization. Advances in the molecular mechanisms underlying malformations of cortical development have demonstrated heterogeneity in gene dysfunction with strikingly similar phenotypic consequences on cortical mantle formation.

The epileptogenicity of FCDs is hypothesized to be caused by abnormal synaptogenesis and dysregulated γ-aminobutyric acid-mediated inhibitory signalling. Enhanced neuronal hyperexcitability may also play a role in the abnormal synchronization of neuronal populations, leading to prolonged trains of epileptic activity.

Preoperative Evaluation

The preoperative evaluation in a patient with medically refractory seizure starts with a detailed history and physical examination. Seizure semiology may provide information about the location of the epileptogenic zone, and can contribute to the prognosis of seizure control after resection. Neurological deficits identified on physical examination may point to the area of cortex most affected and provide clues as to the focal, multifocal, or diffuse nature of the underlying pathological entity.

Electroencephalography

Patients with medically intractable seizures should undergo preoperative evaluation with video-assisted scalp EEG to correlate ictal EEG graphic events with the seizure semiology. The ictal onset zone is defined as the region showing focal rhythmic activity, bursts of high-frequency discharges, repetitive spiking, or electrodecremental patterns. The disadvantage of scalp EEG is that in patients with FCDs there is a high incidence of widespread interictal spiking, which may obscure identification of the epileptogenic zone. Hamiwka and colleagues considered prominent interictal spiking to be significant if it showed consistent focality, had rhythmic features, occurred as trains of focal fast activity, or was associated with focal attenuation of background activity. Generalized tonic–clonic seizures were found to be the most common seizure type in a series of 120 patients found to have FCD after resection of an epileptogenic focus.

Magnetoencephalography

Magnetic source imaging can be used for noninvasive presurgical evaluation of epileptogenic foci with the potential for more accurate EEG localization. Magnetoencephalographic activity is recorded to identify the location of interictal spike foci. Magnetoencephalography signals are principally generated by intraneuronal currents from sources with tangential orientation such as pyramidal neurons in the basal or fissural cortex. The dipole clusters generated from magnetic source imaging studies have been shown to be located in the area of FCD that shows signal prolongation on T2-weighted MR images.

Magnetic Resonance Imaging

Patients with medically intractable epilepsy should un-
dergo MR imaging in 3 planes for best characterization of the potential underlying FCD. If a temporal lobe lesion is suspected, preoperative MR imaging should include T1-weighted sagittal studies, coronal MPRAGE, coronal FLAIR, and fast T2-weighted coronal sequences. Preoperative MR images obtained in patients with a suspected extratemporal lesion consists of axial fast FLAIR, fast T2-weighted axial, T1-weighted sagittal, and coronal MPRAGE MR imaging sequences. Typical features of FCDs on MR imaging include cortical thickening, abnormal gyral and sulcal contours, an indistinct gray–white matter junction, and abnormal signal intensity in the subcortical white matter (Fig. 3). Findings suggestive of Type II FCDs include focal cortical thickening, blurring of the gray–white matter junction, and T2-weighted hyperintensity of subcortical white matter often tapering toward the ventricle (Fig. 2). In a small proportion of patients (2.9–17%) no abnormality is identified on MR imaging sequences. When an FCD is suspected but is not apparent on standard MR imaging sequences, additional phase array coil MR imaging can be used to identify subtle surface changes not seen with a regular coil. Epileptic foci evaluated on MR spectroscopy demonstrate decreased N-acetyl aspartate/choline and N-acetyl aspartate/creatine ratios, and increased pH, increased inorganic phosphate, and decreased phosphate monoester levels.

Functional Neuroimaging

Indications for the use of ictal SPECT or FDG-PET include intractable epilepsy with normal MR imaging findings, multilobar lesions, and discordant findings on electroencephalographic, clinical, and MR imaging evaluations. On ictal SPECT imaging studies, seizures arising from MCDs demonstrate an area of hyperperfusion. Gupta et al. have reported the usefulness of ictal SPECT as an adjunct in the evaluation of children with focal cortical dysplasias. Ictal SPECT and FDG-PET are concordant with scalp EEG localization of the epileptogenic zone in 39 and 50% of cases respectively when preoperative MR images are nondiagnostic. Although SPECT may be enhanced with the use of computerized subtraction and MR imaging coregistration techniques, discordant results with standard MR images and localizing EEG make SPECT a complementary method for defining the epileptogenic zone. Some authors have suggested that FDG-PET may be more useful for revealing mild or cryptogenic lesions in children than MR images because the extent of the cortical abnormality is usually larger on FDG-PET. Areas of severe hypometabolism on interictal FDG-PET or hypermetabolism on ictal FDG-PET in children with FCDs have been correlated with the frequent occurrence of cytomegalic neurons and balloon cells on histopathological studies and more abnormal intraoperative electrocorticographic scores.

Cognitive Assessment

The degree of cognitive impairment depends on the timing, nature, and severity of neurological insults: early global insults may be associated with severe, generalized cognitive deficits and focal insults occurring later with milder, more localized cognitive problems. Disruptions in specific aspects of cortical development leading to the presence of FCDs may result in specific abnormalities in cognitive development. Cognitive and developmental problems asso-

Fig. 2. A and B: Axial and coronal T2-weighted MR images obtained in a 13-year-old patient with occipital lobe epilepsy. A hyperintense lesion in left mesial occipital pole is demonstrated. C: Photomicrograph demonstrating abundant balloon cells of Taylor-type dysplasia (FCD IIB). H & E, original magnification × 200.
Associated with FCDs in children have been reported to be common by some while other authors report a low prevalence of cognitive problems associated with these focal malformations. Correlation of pathological substrates with cognitive function examined after resection in patients with intractable epilepsy have suggested that the less severe forms of FCD (FCD Type I) in fact have worse associated cognitive problems than the histologically more severe subtypes (FCD Type II). Alternatively, cognitive dysfunction with MCDs may be a function of the location of focal disturbance rather than related to distinct subtypes of MCDs. However, cognitive profiles in studies of FCDs have not been well described in the literature. A spectrum of cognitive dysfunction in patients undergoing surgical intervention for intractable epilepsy exists, however, and a low IQ level should not exclude patients from surgical intervention. High IQ has been demonstrated as an independent predictor of reduced seizure freedom at 2 years postoperatively. The severity of mental retardation associated with FCDs may correlate more with the presence of epilepsy and its age of onset than with the nature of the histopathological subtype. This suggests that early diagnosis and treatment of intractable seizures in children may improve clinical outcomes. When language or memory could be affected by the surgical intervention, intracarotid amobarbital testing is used to determine the dominant cerebral hemisphere in the cooperative patient.

### Surgical Considerations

The goal of clinical, EEG, and neuroimaging preoperative assessment is to identify the cortical area producing seizures and generating discharges and its anatomical and functional relationships. Concordance amongst the different modalities used to identify the lesion producing seizures is critical for surgical planning. A 3D preoperative understanding of the epileptogenic zone, surrounding, or encompassing functional cortex, and the characteristic vascularization of the area in individual patients provides a map for planning the surgical approach, the limits of excision, and determining the potential risk to function.

The purpose of surgical intervention in the management of intractable epilepsy with underlying histological evidence of cortical dysplasia is to improve seizure control and maximize the potential for normal neuropsychological development. The surgical approach to FCD is dependent on the presence of a lesion visible on MR imaging, its location to eloquent cortex, and the concordance of presurgical EEG and functional neuroimaging with identifiable lesions. If a well-defined lesion is visible on MR imaging that correlates with EEG localization of the epileptogenic focus, resection may be performed in a single-stage procedure with intraoperative electrocorticography as a guide. If no lesion is visible on MR imaging or if it is localized within eloquent cortex based on the results of noninvasive preoperative studies, a 2-stage procedure with invasive EEG monitoring should be considered for the purpose of localizing the primary and secondary ictal epileptogenic zones, irritative zones, and cortical mapping of eloquent cortex to guide the focal cortical resection. Once the epileptogenic zone is identified, 3 different surgical strategies can be used: lesionectomy, focal cortical resections, or regional or regional.
Focal cortical dysplasia and epilepsy surgery

hemispheric surgical disconnection (Fig. 3). En-bloc resection between cortical vessels, sparing as many vessels as possible to avoid local arterial or venous infarction is essential.24 An important reason for incomplete resection is the intentional avoidance of the eloquent cortex.34 Morrell et al.35 have demonstrated that this risk may be circumvented by the use of multiple subpial transections in eloquent cortex where there is extension of the lesion as seen on imaging or EEG studies. Widespread regional cortical dysplasias such as hemi-hemimegalencephaly or multilobar cortical dysplasia, more commonly identified in the posterior quadrant, may be approached with multilobar resection. However, disconnection of the entire posterior quadrant has been advocated in an attempt to limit complications associated with extensive cortical removal, and has met with excellent success.39 A hemispheric disconnection procedure such as a functional hemispherectomy may be used when multiple independent spike foci are present throughout the hemisphere or when neuroimaging or surface EEG cannot identify unique loci of seizure onset.38 Anterior corpus callosotomy may be considered in patients with bitemporal MCD or FCD who suffer from drop attacks or intense head drop seizures35,62 and who would not be candidates for focal cortical or lesion resections due to multifocal disease. The rate of repeated operation for FCDs is 3–14%.27 When patients present with recurrent frequent seizures or status epilepticus after the first surgical procedure, careful consideration of their anticonvulsant therapy and reassessment of the epileptogenic cortical lesion on neuroimaging and EEG studies should be undertaken. Repeated operation after a failed first surgery generally consists of extension of the previous resection margin in the zone of epileptogenesis.27 Intraoperative corticography or invasive EEG monitoring prior to extension of resection may be considered if the lesion is not well defined on preoperative neuroimaging or noninvasive EEG studies. The extent of further surgery after a first procedure is often limited by the proximity of the remnant epileptogenic zone to the functional cortex. Subsequently, there is a greater risk of neurological impairments such as paresis or visual field deficits after repeated surgery, depending on the location of the surgical target.

Invasive Monitoring

Invasive video-EEG monitoring with subdural grids or depth electrodes may be indicated to aid in localization of the epileptogenic zone particularly in patients with cryptogenic lesions on MR imaging, lesions located in or near eloquent cortex, or evidence of bilateral or multifocal seizure onset as determined by scalp video-EEG. Some groups advocate the use of 3D MR imaging after depth electrode placement to generate a stereo-EEG model of the lesional zone characterized by attenuation of background activity or the presence of slow waves, the irritative zone (characterized by the presence of spikes and waves), and the epileptogenic zone, identified as the cortical areas with primary origin of ictal discharges.10,11,53 Subdural electrodes allow extraoperative mapping of the eloquent cortex including critical somatosensory, motor, and language areas. These techniques can be used on any patient, but may be more important in children in whom intraoperative cortical mapping is possible. This technique provides important information about the function and spatial relationship of the epileptogenic zone to functional cortex. The complication rate after subdural electrode placement is < 10%, with the most common complication being epidural hemorrhage.25

Seizure Outcome After Surgery

In a large series of pediatric patients, the average time from seizure onset to surgery was 5.7 years.52 The authors of a study that included adult patients demonstrated a mean epilepsy duration of 21 years, with mean age at surgery of 28 years.51 In their surgical series, Wang et al.53 showed an overall postoperative seizure freedom or reduction in frequency rate of ≥ 70% in 58% (range 33–89%) of their patients with FCD. In 2 long-term prospective studies, the rate of seizure freedom was < 50%, which suggests an overall decline in the rate of long-term seizure control.31,40 Cumulative rates may be somewhat misleading as to the potential for a successful surgery in an individual patient because there are several preoperative and surgical factors that may influence seizure outcome. Temporal location of FCD lesions is associated with an 87% rate of freedom from seizures.1 Negative prognostic factors include long duration of epilepsy before surgery, older age at surgery, multiple seizure types, the occurrence of secondary generalized seizures before surgery, the need for invasive EEG recording, and incomplete resection of the epileptogenic area.21,65 In a series of patients who underwent frontal lobectomy for frontal lobe epilepsy, independent predictors of seizure recurrence were no MCD/FCD found on MR imaging, extrafrontal MR imaging abnormalities, generalized ictal EEG patterns, acute postoperative seizures, and incomplete resection.36 When no lesion was visible on preoperative MR images, only 37% of 24 adults and children were seizure-free 1 year postoperatively.4 Positive prognostic factors for good seizure control include the presence of focal epileptogenic discharges, a well-defined lesion on preoperative MR images, and coincidence of ictal SPECT findings with the resection site.31,44,57 Predictors of a seizure-free outcome after repeated operation include an age at seizure onset of > 15 years, a duration of epilepsy ≤ 5 years, and preoperative focal interictal discharge.54 There is debate over whether greater cytoarchitectural disorganization of the cortex is predictive of good seizure outcome.5,12,33,55 In a large recent study in patients who underwent resection for FCD, the authors found that patients with more severe histopathological abnormalities (FCD Type IIb, including balloon cells) had the best surgical outcome.54

The completeness of resection appears to have the most predictive power for long-term seizure-free outcome.31 Surgical failure, defined as the presence of persistent or recurrent seizure activity, is highly dependent on the completeness of resection of the epileptogenic cortex.16,20 Intraoperative challenges to complete resection include poorly defined epileptogenic zone margins on neuroimaging or EEG, the presence of important vascular structures in the epileptogenic zone, proximity of the epileptogenic zone to eloquent cortex, or an epileptogenic zone that has important cortical function. It is important to understand that...
epileptic foci and underlying cortical dysplasia may occur outside of the clearly delineated areas of abnormality demonstrated on MR imaging. Although the use of intraoperative MR imaging, neuronavigation, and intraoperative transcranial ultrasonography may improve the extent of resection of the lesion as visualized on MR imaging, the surgical target includes the area of electrical abnormality. Therefore, concurrent use of preoperative EEG and stereo-EEG data or intraoperative electrocorticography for 1-stage procedures is essential. Cortical areas displaying ictal or continuous epileptogenic discharges should be included within the resection margin to the extent that it is safe to do so.

Complications of Surgical Treatment

The rate of transient postoperative complications after cortical resection, lobectomy, or hemispherectomy for cortical dysplasia has been reported as 10.9%. The risks of multiple subpial transections include intraparenchymal hemorrhage, cerebral edema, and fine motor abnormalities. Significant permanent neurological deficits are rare, but initial neurological deterioration (for example hemiparesis, dysphasia, dysnomia, and/or memory disturbance) is very common in a high proportion of cases.

Developmental Outcome

Early surgical intervention in patients who develop intractable epilepsy in infancy or childhood may improve quality of life and possibly cognitive outcomes in the developing child. In a study in infants treated surgically for catastrophic epilepsy, Wyllie observed marked “catch-up” development in patients with at least 50% reduction in seizures. In a series of 25 children who underwent extra-temporal resection for epilepsy, stable overall IQ or improvements in attention and nonverbal reasoning were observed, and there was also a trend towards improvement in behavioral functioning. Furthermore, early surgical intervention after onset of medically refractory epilepsy is supported by studies demonstrating better seizure outcome and improved developmental development in patients with shorter epilepsy duration.

Conclusions

Focal cortical dysplasia is a common and important cause of medically intractable epilepsy in adults and children. Complete resection of the entire epileptogenic zone including focal cortical dysplastic lesions visible on MR images is essential for achieving the best seizure outcome. The majority of patients experience a good seizure outcome after complete resection of FCDs. The recurrence of seizures in patients with incompletely resected FCDs is high, however, and long-term follow-up is essential to determine the surgical outcome.

Acknowledgment

The authors thank Dr. Harvey Sarnat, Alberta Children’s Hospital, Calgary, for his preparation of pathological specimens and contribution of photomicrographs to this paper.

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Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Focal cortical dysplasia and epilepsy surgery


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Accepted June 25, 2008.
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