Magnetic resonance imaging abnormalities in the resection region correlate with histopathological type, gliosis extent, and postoperative outcome in pediatric cortical dysplasia

Clinical article

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Object. The authors conducted a study to correlate histopathological features, MRI findings, and postsurgical outcomes in children with cortical dysplasia (CD) by performing a novel resection site–specific evaluation.

Methods. The study cohort comprised 43 children with intractable epilepsy and CD. The MR image review was blinded to pathology but with knowledge of the resection location. An MRI score (range 0–7) was calculated for each resection region based on the number of imaging features of CD and was classified as “lesional” or “nonlesional” according to all imaging features. Outcome was determined using the International League Against Epilepsy (ILAE) scale. The determination of pathological CD type was based on the ILAE 2011 consensus classification system, and the cortical gliosis pattern was assessed on GFAP staining.

Results. There were 89 resection regions (50 ILAE Type I, 29 Type IIa, and 10 Type IIb). Eleven (25.6%) of 43 children had more than one type of CD. The authors observed MRI abnormalities in 63% of patients, characteristic enough to direct resection (lesional) in 42%. Most MRI features, MRI score ≥3, and lesional abnormalities were more common in patients with Type II CD. Increased cortical signal was more common in those with Type IIb (70%) rather than Type IIa (17.2%) CD (p = 0.004). A good outcome was demonstrated in 39% of children with Type I CD and 72% of those with Type II CD (61% in Type IIa and 100% in Type IIb) (p = 0.03). A lesional MRI abnormality and an MRI score greater than 3 correlated with good outcome in 78% and 90% of patients, respectively (p < 0.03). Diffuse cortical gliosis was more prevalent in Type II CD and in resection regions exhibiting MRI abnormalities. Complete surgical exclusion of the MRI abnormality was associated with a better postoperative outcome.

Conclusions. This study provides a detailed correlation of MRI findings, neuropathological features, and outcomes in children with intractable epilepsy by using a novel resection site–specific evaluation. Because 25% of the patients had multiple CD subtypes, a regional analysis approach was mandated. Those children with lesional MRI abnormalities, Type II CD, and surgical exclusion of the MRI abnormality had better outcomes. Type II CD is more detectable by MRI than other types, partly because of the greater extent of associated gliosis in Type II. Although MRI findings were correlated with the pathological CD type and outcome in this study, the majority of patients (58%) did not have MRI findings that could direct surgical therapy, underscoring the need for improved MRI techniques for detection and for the continued use of multimodal evaluation methods in patient selection.

Keywords: • cortical dysplasia • MRI • histopathology • children • surgical outcomes • epilepsy

Epilepsy surgery is an increasingly recognized therapeutic option in children with intractable epilepsy for both MRI lesional and MRI normal cases.12,29

Multimodal imaging, including different MRI modalities, positron emission tomography (PET), ictal and interictal single-photon emission computed tomography (SPECT), subtraction ictal SPECT coregistered to MRI (SISCOM), in addition to magnetoencephalography (MEG), conventional electroencephalography (EEG), and neuropsychological assessments, can aid in the identification of appropriate surgical candidates.
MRI abnormalities in pediatric cortical dysplasia

logical testing, is used in an attempt to accurately select patients, maximize achievable seizure reduction, and minimize postoperative neurological and neuropsychological deficits.  

Cortical dysplasia (CD) is the most common pathology encountered in children undergoing surgery for intractable epilepsy and, by definition, represents abnormal organization of the cerebral cortex (that is, “dyslamination”). Our understanding of CD has undergone significant evolution in the last 10 years with publication of the Palmini classification in 2004 and the revised International League Against Epilepsy (ILAE) consensus classification in 2011. The consensus classification describes CD as follows: Type I is radial or tangential dyslamination; Type IIa, dyslamination with dysmorphic neurons; Type IIb, dyslamination, dysmorphic neurons, and balloon cells; and Type III, dyslamination associated with another principal lesion. Type III is subclassified into 4 forms: IIIa is temporal cortex dyslamination associated with hippocampal sclerosis; IIIb, dyslamination in association with tumors; IIIc, dyslamination associated with vascular malformations; and IIId, dyslamination associated with early acquired destructive brain lesions. Using these classification systems, differences in clinical behavior, imaging appearance, and outcomes have been identified among CD subtypes. These findings have significant implications for improving/deloping diagnostic techniques to assist in patient selection for surgical therapy. Multiple dysplasia types in one patient have been rarely described, but may not be evident, unless spatially distant resections are performed, and pathologically analyzed.

Lesion detection by MRI has consistently been shown to be one of the key prognostic factors for postoperative seizure freedom; however, the imaging spectrum and the relationship of imaging to outcomes have been primarily evaluated in mixed-age or adult populations. Although MRI findings and outcome assessments have been described in some children with CD, the underlying pathological basis for imaging findings in a consistent cohort of children has been incompletely assessed. We could find no prior study in which a resection region-specific evaluation was used to directly relate histopathological and imaging findings in pediatric subjects. The goals of the present study were to determine direct correlations between histopathological findings in children with CD and imaging findings based on a detailed resection site-specific evaluation and to correlate imaging and pathological findings with outcomes after epilepsy surgery.

Methods

Patient Selection

We identified a single-institution cohort of pediatric patients (≤ 20 years of age) with medically intractable epilepsy and CD identified on histopathological analysis after resection of the presumed epileptogenic regions. Subject identification was performed by searching the institutional epilepsy surgery database as well as pathology and radiology reports from January 1, 2006, until July 1, 2012. The term “cortical dysplasia” was used as a key term for report review. This study was reviewed and approved by the institutional review board at our institution, with a waiver of informed consent.

Extensive presurgical evaluation was performed as part of the selection process, described in detail previously. In brief, our standard presurgical evaluation included a detailed history and clinical examination, scalp video-EEG monitoring, MRI, PET, ictal/interictal SPECT with SISCOM, and MEG. All patients underwent scalp video-EEG monitoring and MRI, but not all patients necessarily received all the noninvasive functional tests. Invasive EEG (subdural grid placement) was used when indicated for further localization of the ictal onset zone and to map eloquent cortices. Clinical decisions regarding surgical candidacy and resection plan were made on the basis of all available data.

For the purposes of this study, patients were excluded if they had undergone prior surgery (adjacent to the study resection site or without preoperative imaging), had poor-quality MRI studies, CD and associated destructive lesions (encephalomalacia from encephalitis or infarct) or tumor. Type IIIa CD (hippocampal sclerosis and adjacent Type I CD), only mild malformation of cortical development, a diagnosis of tuberous sclerosis, less than 1 year of postoperative clinical follow-up, or were age ≥ 21 years. After exclusion, a group of 43 pediatric patients with intractable neocortical epilepsy, high-quality MRI studies, and definite CD based on neuropathological analysis formed the study cohort.

Surgical Procedure

Localized or multilobar surgery was performed by a single neurosurgeon (F.T.M.) based on all clinical data, as detailed above, using standard operative techniques. Intracranial electrographic data were used to identify the seizure-onset zone as detailed previously. Surgical extent was determined based on preoperative testing, intracranial EEG, MRI results, and proximity to eloquent brain regions as described previously. In general, standard craniotomy techniques were used to expose the desired cortical surface. The resection margin selected was determined by ictal onset zone using intracranial EEG (primary ictal onset zone plus secondary spread zone). Resections spared the eloquent cortex (language and motor). This resulted in spatially distant cortical and/or lobar resections in some patients (see Results). Method of resection varied depending on the region selected for resection, its proximity to eloquent cortex, and the objective of the resection. In general, lobectomies were performed using standard surgical techniques. In regions such as the posterior temporal lobe or parietal lobe, inter sulcal cortical resections were performed to avoid injury to passing draining veins. In selected patients in whom seizures were poorly localized but were clearly lateralized, a functional hemispherotomy was recommended after weighing all surgical risks and functional outcomes. The functional hemispherotomy was performed using a modified perinsular technique. Tissue resected with this approach included the frontal and temporal opercula, insula, amygdala, and hippocampus. For the purposes of this study, this technique typically provided specimens.
for histological evaluation of the frontal and temporal lobes. Only resection regions with adequate cortical tissue for accurate pathological analysis were evaluated in this research study. Resection specimens (for neuropathological review) were labeled with relationships to anatomical landmarks, ictal onset zone, and grid positions (when applicable). Intraoperative photographs of subdural grid positions and resection sites were acquired and available in each individual.

**MRI Technique and Evaluation**

In each patient, a dedicated seizure-protocol MRI study was acquired as part of the presurgical workup. In 37 patients 3-T MRI was performed and in 6 patients 1.5-T MRI was performed. The 1.5-T protocol included sagittal T1-weighted (5-mm slice thickness, at 6-mm intervals), axial fast spin echo (FSE) T2-weighted (5-mm slice thickness at 6.5-mm intervals), axial T2-weighted FLAIR (5-mm slice thickness at 6.5-mm intervals), corona 3D surface rendering of the brain surface from preoperative CT and MR images; 2) images of the operative field (including subdural grid placement, brain surface without the grid in place, and brain surface after resection); 3) CT scans with grids in place (including 3D segmentation of grid location superimposed on 3D surface rendering of the brain surface from preoperative MR images); and 4) detailed operative notes from the neurosurgeon (which included specimen nomenclature for subsequent pathological analysis). Resection regions involving the amygdala and hippocampus were excluded, as the purpose of this study was to assess neocortical regions. Insular resection regions were not further evaluated, as neuropathological evaluation for CD in this region is difficult and imprecise. A total of 89 discrete resection locations, identifiable by imaging, each resulting in a neuropathological evaluation was made, blinded to pathological diagnosis but with knowledge of resection specimen location. Resection locations were determined in each case (Fig. 1) by simultaneously reviewing the following: 1) all available postoperative CT and MR images; 2) images of the operative field (including subdural grid placement, brain surface without the grid in place, and brain surface after resection); 3) CT scans with grids in place (including 3D segmentation of grid location superimposed on 3D surface rendering of the brain surface from preoperative MR images); and 4) detailed operative notes from the neurosurgeon (which included specimen nomenclature for subsequent pathological analysis). Resection regions involving the amygdala and hippocampus were excluded, as the purpose of this study was to assess neocortical regions. Insular resection regions were not further evaluated, as neuropathological evaluation for CD in this region is difficult and imprecise. A total of 89 discrete resection locations, identifiable by imaging, each resulting in a separate specimen for pathologic analysis, were assessed.

Each resection region was specifically evaluated for known imaging findings of CD. These included abnormal sulcal/gyral pattern, abnormal white matter signal, abnormal gray matter signal, cortical thickening, blurred gray matter–white matter junction, “transmantle” (that is, extending to the ventricular margin) subcortical signal changes, and localized volume loss. An MRI score was calculated for each resection region (range 0–7) giving 1 point for each MRI feature identified. Additionally, to reflect clinical practice, the resection region was also classified as “lesional” or “nonlesional” based on the combination of imaging features as previously detailed. Lesional classification was made if the combination of imaging features was strongly suggestive of CD and could potentially direct the resection (typically at least two MRI features of CD). Nonlesional classification was made if the MRI features were normal or if there were only nonspecific, nonlocalizing findings (for example, only small foci of abnormal white matter signal, only volume loss) that could not direct a potential resection.

Dedicated imaging review (research review) was performed by a board-certified radiologist with a certificate of added qualification in neuroradiology and 15 years of experience interpreting neuroimaging in patients undergoing surgery for intractable epilepsy. The clinical MRI report on each case was subsequently reviewed, and any discrepancies between the research interpretation and clinical interpretation (including any unmentioned MRI findings of CD or uncertainty regarding localization) in each resection region were reviewed by an additional board-certified radiologist (secondary review) with fellowship training in both pediatric radiology and pediatric neuroradiology (M.K.). Twelve resection regions in 11 subjects required secondary review. The secondary review agreed with the research review in all cases. Thus, the imaging findings in each case were reviewed and agreed upon by at least two radiologists.

Evaluation of the completeness of resection of MRI-documented lesional abnormalities was performed using the same resection site evaluation technique as above, by evaluating all available intraoperative and postoperative imaging data. A classification of complete resection was given if the entirety of the MRI-documented cortical abnormality was removed. For the purposes of this study, those patients who had functional hemispherotomies and lesional MRI studies with complete resection were considered to have had a complete resection. As this study was not focused on electrophysiology, the relationship of EEG abnormalities and resection was not specifically assessed.

**Neuropathological Assessment**

The neuropathological assessment was made, blinded to patient’s clinical and radiographic data, using a previously described method. In brief, brain tissue specimens were sectioned perpendicular to the surface to be examined grossly to identify any lesions and to evaluate the gyral pattern and the gray and white matter junction. Smaller specimens (< 3 cm in maximum diameter) were totally submitted, and for larger specimens every other section was submitted. Staining with H & E was performed on all sections. Based on the H & E findings or if the resection specimen included the epileptogenic focus, glial fibrillary acidic protein (GFAP), neuronal nuclei (NeuN), and neurofilament staining was performed on selective sections. Cortical dysplasia was defined according to the 2011 ILAE classification by using H & E,–, neurofilament-, and NeuN-stained slides. Types Ia, Ib, and Ic were denoted as Type I CD for the purposes of this study. A pediatric pa-
MRI abnormalities in pediatric cortical dysplasia

Fig. 1. Resection locations were determined in each case by simultaneously reviewing the following: Images of the operative field with subdural grids in place (A); CT scan with subdural grids in place (B); 3D segmentation of grid location superimposed on 3D surface rendering of the brain surface from preoperative MR image (C); intraoperative photograph after resection (D); all available postoperative CT and MR scans (E), as well as detailed operative notes from the neurosurgeon (which included specimen nomenclature for subsequent pathologic analysis). Each resection location was estimated (F) and imaging findings within the resection region were evaluated (arrows).

Pathologist subspecializing in neuropathology (L.M.), who was blinded to clinical and radiographic data, reviewed all cases including all H & E and immunohistochemistry slides and patients’ clinical pathology reports. In the few cases with minor discrepancies between the primary and study pathologists, the slides were re-reviewed by both pathologists to reach a consensus on final classification. Based on GFAP stains, cortical gliosis was classified as follows: superficial (involving only subpial and first layer of cortex) or diffuse (extensively involving all 6 layers of cortex). GFAP-stained sections were available for review in all patients but only 82 specimens.

Clinical Follow-Up/Outcome Assessment

Surgical outcome was based on the ILAE scale. The ILAE scale categorizes postsurgical outcomes based on scores ranging from 1 to 6 in which a score of 1 is defined as being seizure free; 2 as only having auras; 3 as having 1–3 seizure days/year; 4 as having 4 seizure days/year to 50% reduction of baseline seizure days; 5 as having less than a 50% reduction of baseline seizures to 100% increase of baseline seizure days; and 6 as having more than a 100% increase in baseline seizure days. For purposes of this study, an ILAE scale score of 1–3 was considered to reflect a good surgical outcome. All patients had at least a year of postsurgical follow-up, except one patient whose surgical outcome was poor and who required reoperation 350 days after the initial operation for continued seizures. In this patient, 350 days was used as the follow-up period. The mean follow-up period was 624 days (median 517 days; range 350–1322 days).

Statistical Analysis

The chi-square test or Fisher’s exact test for categorical variables and the t-test or Wilcoxon rank-sum test for continuous variables were used to assess the relationship among MRI findings, cortical gliosis extent, and pathological type. One-factor ANOVA was used when comparing continuous variables for more than 2 groups. Values for 2-sample t-test are expressed as mean ± SD unless stated otherwise. Logistic regression was used to assess the relationship among MRI findings, pathological type, and gli-
sis extent in relationship to the resection region and among MRI findings, pathological type, and surgical outcome. The final model was chosen based on model selection with stepwise criterion. A value of \( p < 0.05 \) was considered significant. All analyses were performed using SAS version 9.3 statistical software (SAS Institute Inc.).

Results

Patient Demographics, Seizure History, and Surgical Performance

The cohort contained 23 male and 20 female patients whose mean age was as follows: at surgery, 10.2 years (median 9.3 years, range 6 months to 19 years); at imaging, 9.2 years (median 8 years, range 4 months to 19 years); and at seizure onset, 4.1 years (median 3 years, range birth to 16 years). Mean duration patients had been experiencing seizures prior to surgery was 6 years (median 5.6 years, range 6 months to 14 years). There were 23 single lobar region resections (17 frontal, 3 parietal, and 3 temporal), 11 multilobar resections, and 9 functional hemispherotomies (resulting in multilobar specimens). In all subjects with MRI-documented abnormalities, the resection included at least part of the MRI-defined abnormality identified preoperatively.

Pathological Findings

There were 89 separate resection specimens analyzed in 43 patients: 14 patients had 1 resection region analyzed, 19 patients had 2 resection regions analyzed, 6 patients had 3 regions analyzed, 2 patients had 4 regions analyzed, and 1 patient each had 5 and 6 resection regions specifically assessed by imaging and histopathology. There were 50 resection regions with Type I dysplasia, 29 regions with Type IIa dysplasia, and 10 regions with Type IIb dysplasia. According to pathological criteria, 16 patients had only Type I CD, 12 patients had only Type IIa CD, and 4 patients had only Type IIb CD. Eight patients had both Type I and Type IIa dysplasia, 2 patients had both Type I and Type IIb dysplasia, and 1 patient had both Type IIa and IIb dysplasia. Different dysplasia subtypes were seen in the same lobe in 6 subjects (5 frontal and 1 parietal) and in different lobes in 5 patients (4 frontal and parietal; 1 frontal, temporal, and parietal), including 2 hemispherotomy patients. Thus overall, approximately one-quarter (11 [25.6%] of 43) of our patients had 2 types of CD detected on pathological analysis of different resection regions.

MRI Findings in the Resection Region and Neuropathological Findings

A greater number of MRI features suggesting CD in the resection region (a higher MRI score) related to a higher CD type and improved differentiation between more severe subtypes (Table 1). The presence of any abnormality was noted in 30% of Type I, 55% of Type IIa, and 80% of Type IIb regions (\( p < 0.005 \)). Overall, MRI abnormalities were seen in 24 (61.5%) of 39 Type II resection regions (\( p < 0.005 \), Type I vs Type II). Although MRI abnormalities were more common in Type IIb (80%) than Type IIa (55%) resection regions, this difference was not statistically significant. MRI findings consistent with CD in the resection region (a “lesional” designation) were significantly more prevalent in resection regions with Type II (51%) rather than Type I (12%) CD at histopathological examination (as well as Type IIa or IIb vs Type I CD) (see case examples in Figs. 2 and 3). Although the presence of MRI-identified CD (lesional) was more common in Type IIb than IIa CD (80% vs 41%, respectively), this did not reach statistical significance (\( p = 0.065 \)). An MRI score \( \geq 3 \) (3 or more MRI features of CD) was significantly more prevalent in resection regions with Type II versus Type I CD, Type IIb versus Type I CD, and Type IIb versus Type IIa CD at histopathological examination. Although the presence of 3 or more MRI features of CD was more common in Type IIa CD (28%) than Type I CD (10%), this did not reach statistical significance (\( p = 0.06 \), 2-tailed; 0.04, 1-tailed) (Table 1). Using the highest CD type per patient (more comparable to prior studies that did not use a resection region-specific evaluation), we found an MRI abnormality (but not one necessarily suggesting CD) in 56% of those with Type I CD and in 68% of those with Type II CD (61% of Type IIa, 86% of Type IIb) (Table 2), which was not statistically significant when comparing groups. Overall, MRI abnormalities were seen in 63% of patients, characteristic enough to direct resection (lesional) in 42%. Lesional abnormalities were significantly more common in patients with Type II CD (56%) than Type I CD (22%) and in Type IIb CD (86%) than Type I CD (\( p = 0.03 \) and 0.007, respectively). A maximum MRI score of 3 was significantly more prevalent in patients with Type IIb CD (86%) than in those with Type I (22%) CD (\( p = 0.007 \)) and in Type IIb CD than in those with Type IIa CD (33%) (\( p = 0.03 \), Table 2).

All MRI features except localized volume loss were more commonly identified in resection regions with Type II CD than Type I CD (Table 3). When modeled by logistic regression with stepwise model selection, a blurred cortical junction best predicted Type II CD versus Type I CD, although other features were also quite different in prevalence. Differences were less evident when comparing resection regions with Type IIa and Type IIb CD. Comparing these groups, only increased gray matter signal was significantly more common in Type IIb CD (70%) compared with Type IIa CD (17.2%) resection sites (\( p = 0.004 \), Fisher’s exact test, as well as by stepwise logistic regression). A blurred cortical junction, white matter signal, and abnormal gyral pattern were more common in Type IIa than in Type I CD.

The extent of gliosis differed significantly between dysplasia types: Full cortical thickness gliosis was demonstrated in 84% (32 of 38) of resection specimens with Type II CD compared with 18% (8 of 44) of resection specimens with Type I CD (\( p < 0.0001 \)). The extent of gliosis was less pronounced in Type I (18%) than it was in Type IIa (79%) and Type IIb (100%), but it was not significantly different between Types IIa and IIb (Table 4). A separate assessment of the relationship of MRI findings to the extent of cortical gliosis was performed (Table 5). Full cortical thickness (diffuse) gliosis was significantly more common in resection specimens that were lesional,
MRI abnormalities in pediatric cortical dysplasia

| Table 1: Summary of MRI findings correlated with dysplasia type in each resection region* |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| **MRI Finding** | **Dysplasia Type (%)** | **I (n = 50)** | **IIa (n = 29)** | **IIb (n = 10)** | **All** | **I vs II** | **I vs IIa** | **I vs IIb** | **IIa vs IIb** |
| any abnormality | yes | 15 (30) | 16 (55) | 8 (80) | 0.005 & 0.005 | 0.03 | 0.005 | 0.26 |
| | no | 35 (70) | 13 (45) | 2 (20) | <0.0001 | <0.0001 | 0.005 | <0.0001 | 0.65 |
| lesional | yes | 6 (12) | 12 (41) | 8 (80) | 0.0006 | 0.06 | <0.0001 | 0.007 |
| | no | 44 (88) | 17 (59) | 2 (20) | 0.0006 | 0.06 | <0.0001 | 0.007 |
| MRI score ≥3 | yes | 5 (10) | 8 (28) | 8 (80) | 0.0001 | 0.0006 | 0.06 | <0.0001 | 0.007 |
| | no | 45 (90) | 21 (72) | 2 (20) | 0.0006 | 0.06 | <0.0001 | 0.007 |

* Overall there were 89 resection regions: 50 Type I, 29 Type IIa, and 10 Type IIb.
† Determined using the chi-square test.
‡ Determined using the Fisher’s exact test.
§ 2-tailed test p = 0.06, 1-tailed test p = 0.04.

Those with ≥3 MRI features of CD, and those with all MRI features in isolation except localized volume loss (compared with resection regions with normal MRI features). Applying a stepwise logistic regression model, white matter signal change was most significantly associated with extent of cortical gliosis in the resection region. There were no significant differences in seizure onset, age at surgery, or seizure duration related to cortical gliosis extent or surgical outcome (data not shown).

MRI Features, Pathological Findings, and Outcomes

There was no significant difference in outcome (ILAE score of 1–3 vs > 3) based on age at seizure onset, seizure duration, and age at surgery.

Good postoperative surgical outcome (ILAE outcome scale score of 1–3) was significantly correlated with the severity of CD identified on histopathological examination after resection (p = 0.019; Table 6). Patients with only Type I CD had good surgical outcome in 39% of the cases whereas those with Type II CD had good surgical outcome in 72% of the cases (p = 0.03). There was good surgical outcome in 100% of patients with a Type IIb histology. There were no statistically significant differences in surgical outcome when comparing Type I with Type IIa CD (p = 0.31) or Type IIa with Type IIb CD (p = 0.13).

The presence of a lesional MRI abnormality or a maximum MRI score greater than 3 in any resection region correlated with a good surgical outcome (ILAE score of 1–3) in 77.8% and 90% of patients with these findings, respectively (Table 7). Although the median MRI score was greater in patients with a good surgical outcome than it was in patients with a poor surgical outcome, this difference was not statistically significant (p = 0.137). In patients with lesional MRI abnormalities (n = 18), when the abnormal MRI region was completely excluded or resected (including functional hemispherotomy subjects with lesional MRI findings), all patients (11 [100%] of 11) had good surgical outcome compared with 42.8% (3 of 7) of those with incomplete resection (p = 0.01).

No difference in seizure duration prior to surgery was noted when comparing all dysplasia types. In children with Type IIb CD, seizure onset occurred at an earlier age than in children with Type I or Type IIa CD (1.5 ± 1.4 years vs 4.2 ± 4.0 and 5.2 ± 4.9 years, respectively; p = 0.02 and p = 0.008). There was a significant difference in age at surgery when comparing dysplasia types (p = 0.028): Children with Type IIb CD presented earlier for surgery than others. We noted significant differences between Type I and IIb CD (11.0 ± 4.8 years vs 5.4 ± 3.3 years, respectively; p = 0.005) and between Type IIa and IIb CD (11.2 ± 5.3 years vs 5.4 ± 3.3 years, respectively; p = 0.005). Children with lesional MRI status were younger in age (mean 6.2 ± 4.79 years) at imaging than those without definite CD on preoperative imaging (mean 11.32 ± 4.14 years) (p < 0.001).

Applying a logistic regression analysis to examine sex, age at surgery, seizure duration, lesional MRI finding, maximum MRI score/patient, MRI score > 3, and highest CD type/patient in the model, the highest pathological type best described the statistical model predicting eventual patient outcome (p = 0.0128).

Discussion

Most prior imaging studies of CD have used mixed age populations of both children and adults. There have been a few studies specifically assessing MRI features of CD correlated with pathology and outcome in pediatric (or mostly pediatric) patients, with the investigators using more modern pathological classification systems.14,16,17,19,33 Most of these studies also included CD in the temporal lobe associated with hippocampal sclerosis (ILAE Type IIIa),3 which complicates evaluation of the imaging, pathology, and outcome correlations in this population. For our study, to provide the most homogeneous cohort for evaluation, we excluded these patients, as well as patients with other brain abnormalities and CD (Types IIb, IIIc, and dual pathology).4 As in most other studies of CD, we identified a higher prevalence of lesional MRI abnormalities in cases of...
Type II rather than Type I CD (51% vs 12%, respectively). Evaluating our cohort by the highest CD type per patient (more closely comparable to the existing literature), we found MRI findings suggesting CD in 22% of those with Type I CD and 56% of those with Type II CD. Previous studies specifically evaluating children are rare and have usually documented a higher MRI “positive rate” (38%–66% for Type I and 79%–88% for Type II).\textsuperscript{14,16,17,19} None of these studies used a resection region–specific analysis such as used in our evaluation, and some include patients with hippocampal sclerosis and, presumably, Type IIIa CD, which was specifically excluded in this study. In a recent study, Mellerio et al.\textsuperscript{22} utilizing a detailed evaluation approach in 71 adults and children (median age 20 years) with Type II CD, demonstrated an MRI abnormality in 59% of the patients, which was more similar to the 68% of patients identified in our study with Type II CD.

The lower overall rate of MRI abnormalities found in the present study compared with most previous studies may be explained by methodological and population-based differences. To make our results more clinically applicable, we were careful to define MRI abnormalities as either “lesional” (a combination of findings suggesting CD) or “nonlesional” (including completely normal or isolated nonspecific findings that could not be used to direct surgery). This distinction differs from many other studies that use any MRI-documented abnormality to identify the MRI-positive rate for CD. In addition to these methodological differences, our epilepsy surgery program has gained significant experience in treating and

![Fig. 2. Studies obtained in a 9-year-old right-handed boy with intractable complex partial seizures. A: Selected preoperative MR images (left to right: coronal T2-weighted FLAIR, coronal T2-weighted FLAIR, sagittal volumetric T1-weighted, and axial FSE T2-weighted images). Mild gyral thickening is noted in the inferior frontal lobe with poor definition of the gray matter–white matter interface (thick arrows), ill-defined white matter signal in the subcortical region (thin arrows), subtle signal in the gray matter at the sulcal depth (arrowhead), and ill-defined tapering signal extending toward the ventricle margin (thick arrows, far-right axial T2-weighted image). The MRI score was 5, and the imaging appearance was “lesional.” Interictal EEG demonstrated right frontal slowing and bifrontal rhythmic sharp waves (with a right-sided predominance). Phase II with right-sided grid placement revealed right inferior frontal onset with localization near the MRI abnormality. A right frontal lobectomy was performed, completely resecting the MRI-defined abnormality and ictal onset zone. B–E: Pathological analysis: H & E, original magnification × 200 (B); H & E, original magnification × 400 (C); NeuN, original magnification × 40 (D); and GFAP, original magnification × 40 (E). Multiple large irregularly shaped dysmorphic neurons were noted (arrows, B) as well as multiple balloon neurons (arrow, C). NeuN immunostaining (D) demonstrated distortion of cortical 6-layer laminar architecture and loss of cortical neurons. GFAP staining (E) showed diffuse cortical and white matter gliosis. The diagnosis was Type IIb CD. The patient is seizure free, with an ILAE outcome score of 1, at 1 year of follow-up.](image-url)
MRI abnormalities in pediatric cortical dysplasia

**Fig. 3.** Studies obtained in an 8-year-and-10-month-old, right-handed boy who had intractable complex partial seizures with frequent generalization. Interictal EEG demonstrated frequent spikes in the midline. Ictal EEG demonstrated a bilateral frontal onset. Bifrontal subdural grid placement was performed, and the ictal onset, based on analysis of intracranial EEG, was in the right frontal lobe. **A:** Selected images from preoperative MRI and postoperative CT scanning (left to right: axial volumetric T1-weighted, axial T2-weighted FLAIR image, coronal T2-weighted FLAIR image, and axial CT scan obtained 2 weeks postoperatively). No MRI abnormality was identified. The MRI score was 0, and the imaging appearance was “nonlesional.” A right frontal lobectomy was performed, encompassing the intracranial EEG–identified ictal onset zone. **B–E:** Pathological analysis: low-power photomicrograph stained with H & E, original magnification ×40 (B); high-power photomicrograph stained with H & E, original magnification ×400 (C); NeuN immunostaining, original magnification ×100 (D); and GFAP, original magnification ×100 (E). There was mild distortion of the cortical 6-layer lamellar architecture with pyramidal cells in the external granular layer, which was best seen on the NeuN-immunostained image (D). On the low-power H & E–stained image, a mix of giant neurons (arrow, C) and small immature neurons (arrowhead, C) was identified. GFAP immunostaining (E) revealed superficial subpial and molecular-layer gliosis. The diagnosis was Type Ib CD. The patient had a greater than 50% reduction of seizure frequency postoperatively and had an ILAE outcome score of 4, at 757 days of follow-up.

**TABLE 2:** Summary of MRI findings correlated with maximum dysplasia type in each patient (n = 43)

<table>
<thead>
<tr>
<th>MRI Finding</th>
<th>Dysplasia Type (%)</th>
<th>Group Comparison p Values*</th>
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<tbody>
<tr>
<td></td>
<td>I (n = 18)</td>
<td>IIa (n = 18)</td>
</tr>
<tr>
<td>any abnormality</td>
<td>yes</td>
<td>10 (56)</td>
</tr>
<tr>
<td></td>
<td>no</td>
<td>8 (44)</td>
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<tr>
<td>lesional</td>
<td>yes</td>
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<tr>
<td></td>
<td>no</td>
<td>14 (78)</td>
</tr>
<tr>
<td>MRI score ≥3</td>
<td>yes</td>
<td>4 (22)</td>
</tr>
<tr>
<td></td>
<td>no</td>
<td>14 (78)</td>
</tr>
</tbody>
</table>

* Determined using the Fisher’s exact test.
Evaluating the data reported by Krsek et al. also demonstrated the differentiation between the Type IIa and IIb CD subtypes. Only single imaging feature that allowed statistical differentiation was the increased gray matter signal on FLAIR sequences correlating most strongly with Type IIb CD, and this was the etiology of this finding is uncertain but may be related to gliosis, cell density, or potentially seizure-related edema.

Comparison of MRI Features and Pathological Findings

All specific MRI features except localized volume loss were significantly more prevalent in resection regions with Type II compared with Type I CD. Unlike other authors, we found no increased prevalence of volume loss in Type I versus Type II CD. This could relate to the exclusion of Type I CD associated with hippocampal sclerosis (now denoted as Type IIIa) in our study; however, evaluation of localized volume loss is also highly subjective. Transmantle signal changes are a useful predictor of Type II CD, and IIb CD specifically. We also found transmantle signal changes to be a specific finding in Type II CD but did not distinguish Type II subtypes in our analysis. Colombo et al. found transmantle signal changes in 83% of Type IIb CD compared with 26% of Type IIa CD (statistically significant [p < 0.05]). However, these studies were primarily of adult patients. In contrast, Krsek et al. studied an exclusively pediatric population and identified the transmantle sign in only 16% of those with Type II CD (9% in Type IIa and 21% in Type IIb), similar to the results of our study. It is possible that the findings of Type IIb CD become more apparent on imaging with age (including transmantle signal changes), potentially based upon myelination changes and progressive gliosis, but this relationship needs further study.

A potentially important finding in our study was that increased gray matter signal on FLAIR sequences correlated most strongly with Type IIb CD, and this was the only single imaging feature that allowed statistical differentiation between the Type IIa and IIb CD subtypes. Evaluating the data reported by Krsek et al. also demonstrates a higher prevalence of gray matter signal changes in Type IIb (71%) than in Type IIa CD (48%) in children, but this difference was not statistically significant. Colombo et al., assessing a mixed but predominately adult population, found increased gray matter signal in 20% of Type IIb, as compared with 6% of Type IIa CD (also not statistically significant). The cause for the increased prevalence in our study is uncertain; however, 3D 1-mm isotropic T2-weighted FLAIR sequences and predominately 3-T images were used and this differs from most prior studies. Interestingly, Wagner et al. in a selected group of 50 predominately adult patients with Type IIb CD (82% lesional), found increased cortical signal in 90% of their patients, 40% of whom underwent 3-T imaging, some with 3D T2-weighted FLAIR sequences. The etiology of this finding is uncertain but may be related to gliosis, cell density, or potentially seizure-related edema.

Multiple Dysplasia Subtypes

Another important finding of this study is the relatively common (in 25% of the patients) presence of multiple CD types in a single patient, typically both Type II and Type I (Fig. 4). This has been rarely reported, but based upon our analysis method, it may be more common than previously realized. It has important implications in the evaluation of imaging pathology correlations as well as understanding the pathophysiology of this condition. None of our patients with multiple CD types had imaging or clinical findings consistent with tuberous sclerosis; in fact, these patients were specifically excluded. On subgroup analysis, we observed no significant difference in surgical success between those with multiple CD types (64%) and those with one CD subtype (56%) histopathologically. Fauser et al. described 5 patients with multifocal CD detected by MRI and/or histological evaluation.

TABLE 3: Specific MRI features in 89 resection sites correlated with histopathological dysplasia type

<table>
<thead>
<tr>
<th>MRI Feature</th>
<th>Dysplasia Type (%)</th>
<th>Group Comparison p Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I (n = 50)</td>
<td>IIa (n = 28)</td>
</tr>
<tr>
<td>cortical thickening</td>
<td>3 (6.0)</td>
<td>6 (20.7)</td>
</tr>
<tr>
<td>blurred GM-WM junction</td>
<td>5 (10.0)</td>
<td>11 (37.9)</td>
</tr>
<tr>
<td>WM signal</td>
<td>8 (16.0)</td>
<td>13 (44.8)</td>
</tr>
<tr>
<td>GM signal</td>
<td>6 (12.0)</td>
<td>5 (17.2)</td>
</tr>
<tr>
<td>volume loss</td>
<td>6 (12.0)</td>
<td>6 (20.7)</td>
</tr>
<tr>
<td>abnormal gyral pattern</td>
<td>2 (4.0)</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td>transmante changes</td>
<td>0 (0.0)</td>
<td>2 (6.9)</td>
</tr>
</tbody>
</table>

* The Fisher’s exact test was used for statistical assessment (2-tailed). GM = gray matter; WM = white matter.
† < 0.05 (one-tailed). Logistic regression demonstrated that a blurred cortical junction best differentiated dysplasia Type I from Type II and that abnormal gyral pattern best differentiated Type Ia from Type Ib (based upon stepwise criteria).

TABLE 4: Extent of gliosis by histopathological evaluation and CD type

<table>
<thead>
<tr>
<th>Gliosis Extent</th>
<th>Dysplasia Type (%)</th>
<th>Group Comparison p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I (n = 44)</td>
<td>IIa (n = 28)</td>
</tr>
<tr>
<td>diffuse</td>
<td>8 (18.2)</td>
<td>22 (78.6)</td>
</tr>
<tr>
<td>superficial</td>
<td>36 (81.8)</td>
<td>6 (21.4)</td>
</tr>
</tbody>
</table>
In 1 pediatric patient 2 different types of CD were identified (Type Ib, from the anterior temporal lobe, which was MRI normal, and Type IIb, from the posterior temporal lobe, which was MRI visible), and the patient was free from seizures after surgery. The recent 2011 ILAE classification system indicates that abnormal cortical laminar bands can occur in the vicinity of Type II CD variants, and whether this represents a separate Type III subtype or simply a gradation of cortical disorganization within Type II CD is uncertain at this time. Our cases in which different CD subtypes (Types I and II) were found in a single lobe could fall into this category, but how to classify those with different types of CD in different, non-contiguous lobes is uncertain at this time. The etiology of CD is unknown, but it is thought to arise from abnormal maturation, migration, and apoptosis during ontogenesis. According to evolving classification systems of malformations of cortical development, Type II CD seems to evolve from a disturbance of cellular proliferation, likely developing during the first trimester of pregnancy. Type I CD may result from later disturbances in cortical organization during the third trimester of pregnancy (or even postnatally). It is possible that some cases of Type I CD could represent an acquired condition, potentially more widespread in distribution, occurring as a sequela of early acquired seizures in patients with Type II CD, although this remains speculative. The existence of Type I CD in association with destructive brain lesions has also been documented (Type IIId), supporting the idea that CD can be acquired in relation to sustained plasticity and neurogenesis in the postnatal brain. Whatever the etiology, it is clear that different CD subtypes may occur in disparate brain regions in surgically treated children with intractable epilepsy. Further assessment of this interesting subgroup is needed.

**Patient Outcomes**

In patients with CD, most studies have demonstrated that the most important features relating to a good surgical outcome are identification of a focal lesion on MRI, complete resection of the lesion and/or seizure-onset zone, and more severe CD subtypes identified histopathologically. Some studies, however, have shown better outcomes for patients with Type I CD, and other studies have shown no difference in outcome between patients with milder and those with more severe CD subtypes. The few studies specifically evaluating children are less conclusive. Krsek et al. documented postoperative seizure freedom in 48% of the children with Type I CD and in 67% of those with Type II CD (60% of Type IIa CD and 74% of Type IIb), although this was not statistically significant. Kim et al. excluded patients with hippocampal sclerosis, which makes the two comparable. It is likely that Type I CD associated with hippocampal sclerosis (ILAE Type IIIa) is associated with better outcomes than isolated neocortical Type I CD subtypes, similar to the principal lesion itself.

---

**TABLE 5: Summary of MRI features correlated with cortical gliosis extent**

<table>
<thead>
<tr>
<th>MRI Feature</th>
<th>Diffuse Gliosis</th>
<th>Total Regions</th>
<th>% of Regions</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>13</td>
<td>45</td>
<td>28.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>lesional</td>
<td>21</td>
<td>26</td>
<td>80.8</td>
<td>0.0008</td>
</tr>
<tr>
<td>MRI score ≥3</td>
<td>17</td>
<td>21</td>
<td>80.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>any abnormality</td>
<td>27</td>
<td>38</td>
<td>71</td>
<td>0.0002</td>
</tr>
<tr>
<td>cortical thickening</td>
<td>11</td>
<td>13</td>
<td>84.6</td>
<td>0.0004</td>
</tr>
<tr>
<td>blurred GM-WM junction</td>
<td>19</td>
<td>23</td>
<td>82.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WM signal</td>
<td>22</td>
<td>28</td>
<td>78.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>GM signal</td>
<td>14</td>
<td>18</td>
<td>77.8</td>
<td>0.0006</td>
</tr>
<tr>
<td>volume loss</td>
<td>6</td>
<td>10</td>
<td>60</td>
<td>0.07</td>
</tr>
<tr>
<td>abnormal gyral pattern</td>
<td>12</td>
<td>13</td>
<td>92.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>transmantle changes</td>
<td>4</td>
<td>4</td>
<td>100</td>
<td>0.01</td>
</tr>
</tbody>
</table>

* Diffuse gliosis = number of resection regions with diffuse full-thickness gliosis; total regions = total number of resection regions with this MRI feature; % of regions = percentage of regions with specific MRI feature or imaging finding with diffuse cortical gliosis on histopathological evaluation.
† Compared with MRI-documented normal resection regions, using the Fisher’s exact test. White matter signal changes correlated best with gliosis extent on stepwise logistic regression analysis.

**TABLE 6: Most severe cortical dysplasia histopathologic type in each patient (n = 43) and surgical outcome**

<table>
<thead>
<tr>
<th>ILAE Outcome Score</th>
<th>Dysplasia Type (%)</th>
<th>Group Comparison p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I (n = 18)</td>
<td>Ila (n = 18)</td>
</tr>
<tr>
<td>1–3</td>
<td>7 (38.9)</td>
<td>11 (61.1)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>11 (61.1)</td>
<td>7 (38.9)</td>
</tr>
</tbody>
</table>
The detection of MRI abnormalities preoperatively, in particular imaging findings consistent with CD ("lesional" by our definition), correlated with improved outcome in our study as well as several previous studies (although performed primarily in adult or mixed-age populations).5,28,31 In children, the older studies of Park et al.26 and Hader et al.13 did not demonstrate a significant difference in outcome related to MRI abnormalities, but the authors had relatively few MRI-negative cases (18%–25%), limiting statistical evaluation. In a study of 48 children with CD or mild malformations of cortical development, Kim et al.15 showed no differences in seizure-free outcome between those with localizing MRI abnormalities and those without. Their study also included mild malformations of cortical development, thus limiting comparisons among CD subtypes. The completeness of resection of MRI-identified abnormalities (when present) has been described as an important factor relating to operative success.5,13,17,19,28,32 Our study also supports this finding. Although better outcome was noted in our study in patients with MRI abnormalities, previous studies have demonstrated good results in MRI-negative cases with careful selection.6,29 Increased reliance on multimodality functional imaging and more extensive EEG evaluation is often necessary in these patients.

**TABLE 7: Summary of MRI features and surgical outcome**

<table>
<thead>
<tr>
<th>ILAE Outcome</th>
<th>MRI Findings (%)</th>
<th>Maximum MRI Score (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>Lesional</td>
<td>Nonlesional</td>
</tr>
<tr>
<td>1–3</td>
<td>14 (77.8)</td>
<td>11 (44.0)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>4 (22.2)</td>
<td>14 (56.0)</td>
</tr>
</tbody>
</table>

* At the patient level, presence of an MRI lesion correlated with ILAE score of ≤ 3 (good surgical outcome). The median maximum MRI score within resection regions in each patient was slightly greater in those with good surgical outcomes; however, this was not statistically significant. A maximum MRI score within the resection regions of > 3 was associated with ILAE outcome score of ≤ 3.
† Determined using the chi-square test.
‡ Determined using the Wilcoxon rank-sum test.
§ Determined using the Fisher’s exact test.

The detection of MRI abnormalities preoperatively, in particular imaging findings consistent with CD ("lesional" by our definition), correlated with improved outcome in our study as well as several previous studies (although performed primarily in adult or mixed-age populations).5,28,31 In children, the older studies of Park et al.26 and Hader et al.13 did not demonstrate a significant difference in outcome related to MRI abnormalities, but the authors had relatively few MRI-negative cases (18%–25%), limiting statistical evaluation. In a study of 48 children with CD or mild malformations of cortical development, Kim et al.15 showed no differences in seizure-free outcome between those with localizing MRI abnormalities and those without. Their study also included mild malformations of cortical development, thus limiting comparisons among CD subtypes. The completeness of resection of MRI-identified abnormalities (when present) has been described as an important factor relating to operative success.5,13,17,19,28,32 Our study also supports this finding. Although better outcome was noted in our study in patients with MRI abnormalities, previous studies have demonstrated good results in MRI-negative cases with careful selection.6,29 Increased reliance on multimodality functional imaging and more extensive EEG evaluation is often necessary in these patients.

**Extent of Cortical Gliosis and MRI Visibility**

Correlating specific pathological findings with specific MRI abnormalities in CD has been challenging.

**Fig. 4.** Studies obtained in an 8-year-old left-handed boy with history of infantile spasms starting at 4 months. Intractable focal complex partial epilepsy (staring, eye twitching, and postictal left leg paralysis) with common secondary generalized tonic-clonic seizures. A–D: Selected images from preoperative MRI and postoperative CT scanning: coronal T2-weighted FLAIR image (A), coronal volumetric T1-weighted MR image (B), axial T2-weighted FLAIR image (C), and postoperative CT scan (D). Interictal EEG demonstrated right central, parietal, and posterior temporal spikes. Ictal EEG revealed low-amplitude fast activities over the right hemisphere most prominent at F4/Fz. Resection specimens and regions from the right posterior temporal and parietal lobe (blue outline), and right frontal operculum (white outline) were evaluated. Abnormal cortical thickening (thick arrows), focal and hazy ill-defined increased white matter signal (thin arrows), and a small region of subependymal heterotopic gray matter along the occipital horn (arrowheads) were identified in the right parietal, posterior temporal, and occipital lobes. The right frontal operculum was normal on MRI. The right temporal parietal resection region was given an MRI score of 4, and the imaging appearance was “lesional.” The right frontal operculum resection region was given an MRI score of 0, and the imaging appearance was “nonlesional.” Pathological evaluation of the right parietal and posterior temporal lobes revealed significant distortion of the cortical 6-layer laminar architecture and clusters of dysmorphic neurons containing irregularly shaped processes as well as Nissl substances. There was diffuse, full-thickness gliosis of the cortex. No balloon cells were identified. The diagnosis was Type IIa CD. Evaluation of the right frontal opercular resection region revealed mild distortion of the cortical 6-layer laminar architecture with many pyramidal neurons in the external granular cell layer. No dysmorphic neurons were seen. GFAP revealed superficial subpial- and molecular-layer gliosis. The diagnosis was Type I CD. Additional resection region in the posterior frontal lobe, above the level of the operculum, had similar pathology to the temporal parietal resection region (Type IIa CD), with the exception of superficial gliosis, and less cortical laminar architectural distortion. Magnetic resonance imaging in this region was normal.
MRI abnormalities in pediatric cortical dysplasia

and precise correlation of specific pathological features with MRI features has not been well investigated. In a recently published neuropathological study by Miles et al., analyzing much of the same cohort as the present imaging-focused study, cortical gliosis was found to be more extensive in cases of Type II CD than in those of Type I CD, potentially as a consequence of long-term brain injury. Given the correlation between increased T2 signal on MRI and gliosis,1,18,27 we hypothesized that more pronounced gliosis (involving the full thickness of the cortex) would correlate with MRI visibility, particularly those features that relate to increased T2 or FLAIR signal intensity in either the cortex or white matter. In our analysis, all MRI features, with the exception of volume loss, were significantly more prevalent in those resection regions with diffuse gliosis. On multivariate analysis, white matter signal intensity correlated most strongly with MRI visibility, particu larly those features that relate to increased T2 or FLAIR signal intensity in either the cortex or white matter. In our analysis, all MRI features, with the exception of volume loss, were significantly more prevalent in those resection regions with diffuse gliosis. On multivariate analysis, white matter signal intensity correlated most strongly with a diffuse gliosis pattern. Other possibilities for the abnormal white matter and cortical signal commonly seen in Type II CD would include neuronal heterotopia; abnor mal white matter and cortical signal commonly seen in Type II CD would include neuronal heterotopia; hypo-, de-, or dys-myelination; and presence of balloon cells or cellular edema.24 Differentiation between these possibilities was not possible with the methods used in our study and represents an area for further research.

Limitations

This study is retrospective, and both the pathologic and imaging analyses were subjective, although this reflects clinical practice. Although the imaging analysis is subjective and the findings of CD on MRI are sometimes subtle, these findings have been well described, applied successfully in other studies, and are clinically applicable. Each MRI study and pathological specimen was reviewed by 2 reviewers with consensus evaluation in discrepant cases, improving consistency. Compared with other papers, the relatively small number of Type II CD is notable, but this reflects our practice and in fact provides a wider spectrum for evaluation. The identification of the resection region was subjective but carefully performed and has been used successfully by our group in other studies.23 Although all of our patients had at least 1 year of postsurgical follow-up, longer-term outcomes are not known for some patients.

Conclusions

This study provides a detailed correlation of MRI, neuropathology, and outcomes in children with intractable epilepsy when using a novel resection site–specific evaluation. Those children with lesional MRI abnormalities, Type II CD, and surgical exclusion of the MRI abnormality had better outcomes. Type II CD is more detectable by MRI, partly because of the greater extent of associated gliosis. Multiple CD subtypes were present in 25% of our patients, mandating a regional analysis approach and suggesting that in some cases CD may not necessarily be “focal.” Because many children with pathologically proven CD have no detectable MRI abnormalities, continued development and improvement of MRI techniques for identifying CD are necessary.

Acknowledgment

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Disclosure

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

Author contributions to the study and manuscript preparation include the following. Conception and design: Leach, Miles, Zhang, Mangan. Acquisition of data: Leach, Miles, Henkel, Greiner, Holland, Rose, Mangan. Analysis and interpretation of data: Leach, Miles, Henkel, Greiner, Gukrema, Mangan. Drafting the article: Leach, Henkel. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Leach. Statistical analysis: Leach, Zhang. Study supervision: Leach.

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