■ Original article

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Epileptic Disorders

Children with seizures and radiological diagnosis of focal cortical dysplasia: can drug-resistant epilepsy be predicted earlier?

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ABSTRACT

Objective. Focal cortical dysplasia (FCD) is a malformation of cortical development and is associated with drug-resistant epilepsy. Standard indication for epilepsy surgery is drug resistance (as defined by the ILAE). Given the high incidence of drug resistance in these children, this delay may not be warranted. The aim of the study was to determine the proportion of patients with a presumed FCD who develop drug resistance, and evaluate post-operative outcomes.

Methods. This study incorporated a survey within a regional paediatric epilepsy network and a retrospective database review of a paediatric epilepsy centre serving the network to identify children with epilepsy and a presumed FCD on MRI.

Results. The survey revealed that 86% of the patients with epilepsy and presumed FCD on MRI within the network were referred to our centre. Of 139 paediatric patients included in the study, 131 (94.2%) had drug-resistant epilepsy. One hundred and ten (83.9%) patients were referred to epilepsy surgery, of whom 97 underwent surgery. Of 92 with one-year postoperative follow-up, 59.8% had an Engel Class 1 (seizure-free) outcome. Concordance of location between MRI and ictal EEG was strongly associated with Engel Class 1 outcome ($p<0.001$), as was older age at seizure onset ($p=0.03$). Time from diagnosis to surgery, number of medications, type of surgery and histology were not associated with improved outcome.

Significance. Our data suggest that most children presenting with seizures and a radiological diagnosis of FCD will develop drug-resistant epilepsy and are candidates for epilepsy surgery. The main outcome predictors are the correlation between MRI and ictal EEG localization and age at onset. This suggests that patients with FCD and epilepsy may be considered for surgery before traditional criteria of drug resistance are met. This change in practice has the potential to improve quality of life and cognitive function, and reduce burden on epilepsy services.

Key words: drug-resistant epilepsy, epilepsy surgery, focal cortical dysplasia

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Focal cortical dysplasia (FCD) is a localized malformation of cerebral cortical development believed to form between Weeks 10 and 20 of human embryonic development [1-12]. FCDs are classified according to the ILAE task force consensus, based on histopathology and associated additional pathology [1]. Numerous publications have noted an association between FCDs and drug-resistant focal epilepsy, and it is the most common pathology responsible for focal-onset epilepsy in children who are scheduled for surgical resection [13-17].

The standard indication for epilepsy surgery in patients with focal-onset seizures as a result of FCD is drug resistance. This is defined by the International League Against Epilepsy (ILAE) as failure of two adequately tolerated and appropriately dosed antiepileptic agents to achieve seizure control [18]. These data, however, are based on epilepsy as a result of all aetiologies and is not specific to either focal cortical dysplasia or epilepsy caused by parenchymal brain lesions. In the context of surgically treated FCDs, less than 10% of the patients will respond to a third antiepileptic medication as opposed to 50-75% of patients who will become seizure-free after surgery [12, 19-22]. However, it may be possible to predict drug resistance at an earlier stage, thus allowing earlier epilepsy surgery and potentially improving long-term outcomes. There have been several studies, including from our own institution, examining disease course and outcomes following epilepsy surgery in the context of low-grade brain tumours [23–25]. These have shown that the majority of cases do not respond to medical treatment alone and will eventually go on to require epilepsy surgery.

Seizure freedom is not the only aim of epilepsy surgery in many patients. There is evidence to suggest treating seizures in a timely manner improves not only seizure outcome but also long-term cognitive functioning [20, 23, 26-29], possibly related to the deleterious effect of long-term anti-epileptic medication [30]. Another possibility is the negative correlation demonstrated between both the number of seizures prior to an operation and the length of time from first seizure to surgery with regards to seizure outcome and cognitive ability [20, 23, 26-29]. This raises the possibility that early identification of surgical candidacy may result in better long-term outcomes. Thus, if the risk of drug resistance and hence indication for surgical management, in a particular cohort, is high, then postponing surgical intervention to complete the two-drug-resistance paradigm may not be optimal, and the delay may produce a poorer outcome. In order to determine whether early epilepsy surgical treatment for FCD might be warranted, we set out to ascertain the natural history of children presenting with seizures and presumed FCD.

Our study aimed to determine the proportion of patients with seizures and presumed FCDs on MRI who go on to develop drug resistance and become surgical candidates. We also investigated factors associated with drug resistance and predictors for seizure-free outcome after epilepsy surgery. In order to be able to generalize the applicability of our findings, we also assessed our referral patterns from secondary providers. Our hypothesis was that the vast majority of patients with epilepsy and a radiological diagnosis of FCD would develop drug resistance and become surgical candidates, raising the possibility of considering surgical resection at an earlier stage relative to current treatment paradigms.

Methods

Study design

This two-part study involved a survey of clinicians in the north London paediatric epilepsy referral network and a single-centre retrospective cohort study. These two parts were undertaken simultaneously.

Cohort study

A single-centre retrospective case study of a series of children with presumed FCD on MRI, who had been reviewed in the epilepsy service at Great Ormond Street Hospital (GOSH) for Children between 2012 and 2019, was performed.

Inclusion and exclusion criteria

The electroencephalogram (EEG) and the magnetic resonance imaging (MRI) report databases at GOSH were interrogated for the term 'dysplasia' between 2012 and 2019 in order to identify all children with FCD who attended the hospital. All MRIs were formally reviewed by an experienced tertiary-centre paediatric neuroradiology consultant with a special interest in paediatric epilepsy. Patients were eligible for inclusion if they were under 18 years of age at the time of diagnosis, with MRI findings suggestive of focal cortical dysplasia (blurring of grey/white matter junction, smooth cortical thickening, subcortical abnormal signal and/or transmantle sign) and epilepsy. Patients were excluded if the pre-surgical brain MRI findings were unclear, or if the imaging revealed non-isolated FCD, *e.g.* in the context of tuberous sclerosis or hemimegalencephaly. Seizure freedom was defined as a minimum of 12 months from the last seizure to the date of the last documented review of the patient.

Data collection

Demographics, clinical assessment, imaging, neurophysiology, and surgical procedure data were collected retrospectively. Scalp video-EEG reports, performed as part of pre-surgical evaluation, were reviewed. Interictal and ictal epileptiform discharges were recorded and classified as concordant if the interictal discharges and ictal onset arose from the same lobe (or brain region in cases of multilobar involvement). Interictal and ictal epileptiform discharges were categorised according to their location in relation to the anatomical region of the FCD on MR imaging. EEG data and MRI were considered concordant if the EEG report stated that interictal discharges, or ictal onset, was derived from the same lobe or quadrant (in cases in which the EEG findings arose from more than one lobe *e.g.* occipito-parietal) as the MRI lesion, or the report specifically stated they were in keeping with the known lesion. The surgical decision making was at the discretion of the epilepsy surgery multidisciplinary team (MDT). In the context of a presumed epileptogenic lesion on MRI, a lack of complete concordance between MRI and EEG was discussed on a case-by-case basis. Patients with significantly discordant findings were considered for intracranial EEG evaluation.
Seizure outcome postoperatively was calculated using the Engel scale [31] after 12 months of follow-up. Information regarding any adverse events was obtained from a prospectively maintained neurosurgical operative database.
Post-operative EEGs were reviewed for presence of epileptiform discharges, and post-operative MRI scans were reviewed for residual lesion by a neuroradiologist. Drug reduction typically commences six months postoperatively, with two to three months of tapering for each drug. This is evaluated for every patient individually and remains under the decision of the clinician.

Survey

Great Ormond Street Hospital for Children provides specialist paediatric epilepsy services together with three other neurology centres in North London. Out of four paediatric epilepsy surgery centres in England, GOSH neurosurgery is the largest, receiving some of the most challenging patients. To address bias that might arise from the group of patients presented to GOSH, as those with drug-resistant epilepsy (DRE), and not representing the general population of patients with FCD, we conducted an online survey, addressing paediatricians and paediatric neurologists of the North Thames Paediatric epilepsy network (NTPN); a network in our geographical referral area consisting of hospital and community clinic-based paediatric services, as well as three other paediatric neurology centres. The survey was sent to the whole referral network, comprising a total of 52 consultant paediatricians or paediatric neurologists primarily involved in the care of patients with epilepsy.
Clinicians were asked, using an online questionnaire, whether they referred all patients with epilepsy, and presumed FCD on MRI, to our specialist epilepsy service/epilepsy surgery programme for evaluation, or confined their referrals to only those with DRE (the online questionnaire is available under the accompanying *supplementary material*). The survey was undertaken anonymously in order to protect confidentiality.

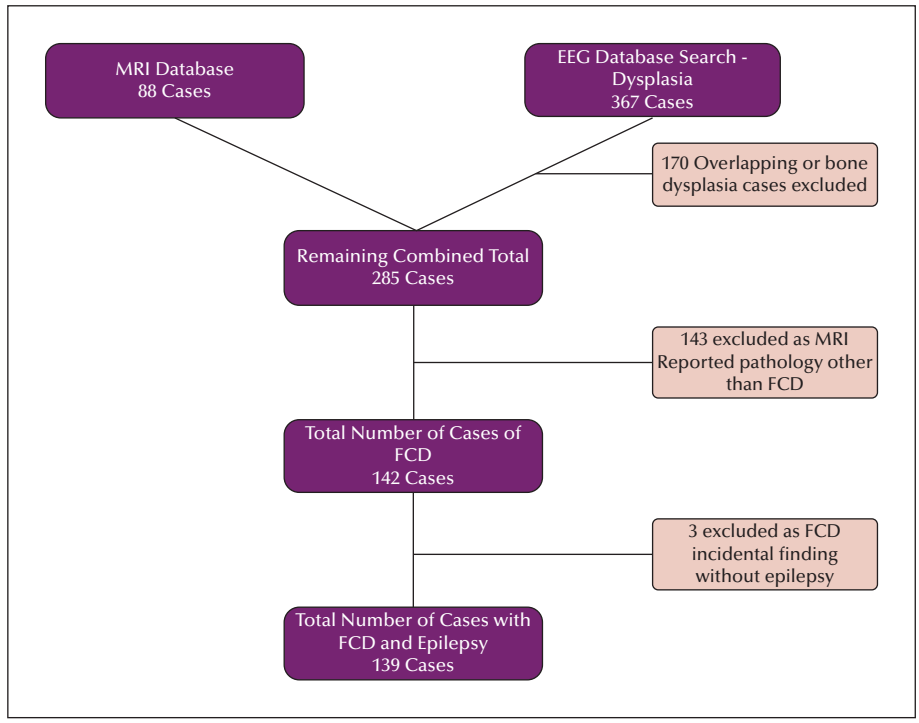
Statistical analysis

Differences between groups were assessed using one-way analysis of variance (ANOVA) (or Kruskal Wallis), t-test, or Fischer's exact test, as appropriate. Odds ratio (OR) with a 95% confidence interval (CI) was used to predict factors relating to seizure outcome. Multiple logistic regression was used to determine factors which predict Engel Class 1 at one year of follow-up. The model included age at seizure onset, the number of medications used prior to surgery, the duration of epilepsy at the time of surgery (these were included as both continuous and categorical variables), concordance of interictal or ictal EEG with the MRI, whether or not PET or invasive EEG was performed, FCD confirmation on histology, epileptiform discharges on post-operative EEG, and residual pathological tissue on postoperative MRI.
Institutional approval for this study was waved by the ethics committee as it was a retrospective anonymous internal audit.

Results

Cohort study

Patient records from 2012 to 2019 were scrutinised. Eighty-eight cases were identified from the MRI database. A further 367 cases were identified from a search of the EEG database. Once duplicates and cases with a bony dysplasia were excluded, a total of 285 cases were collated. On further chart review, 143 cases were excluded as their MRI scans were not reported as suggestive of focal cortical dysplasia (FCD) and the diagnosis had been erroneously entered in their EEG request or report, or they had an additional diagnosis such as polymicrogyria, tuberous sclerosis, or lissencephaly. Three patients with FCD had never had seizures and their FCD was found incidentally on MRI performed for other reasons; these were excluded.



■ **Figure 1.** Flowchart describing patient identification, eligibility assessment and the included cohort.

The final sample analysed in this study consisted of 139 cases (*figure 1*). These were divided into two groups: Group 1 consisted of 131 children (94.2%) with DRE. Over time, seven of these children (5.3%) went on to become seizure-free, following additional medical treatment (three to seven medications in total) and so a recommendation for conservative treatment was made. The majority of Group 1 (116) had been referred for surgical assessment and subsequently discussed at the epilepsy surgery MDT meeting. Group 2 consisted of eight children (5.8%), who were seizure-free on pharmacological treatment. There were slightly more males than females (56.5% vs 43.5% in the drug-resistant group, and 37.5% vs 62.5% in the drug-responsive group). The complete group characteristics are described in *tables 1, 2*.

Drug-resistant versus drug-responsive epilepsy

The average age at seizure onset in the drug-resistant group (Group 1) was 2.8 years (range <one month-14 years), with an average age at referral to GOSH of 5.94 years (one month – 16 years). The average age at epilepsy surgery was eight years of age (six months - 18 years). The average time from seizure onset to referral was 3.2 years (<one month – 14 years), whereas the average time from initial referral to surgery was 2.2 years (<one month – 13 years). The average time from seizure onset to surgery was 5.5 years (two months – 18 years).

The average age at seizure onset in the drug-responsive group (Group 2) was 4.1 years (<one month – 14). The average number of medications tried was 1.13 (vs 4.6 in the drug-resistant group; $p<0.001$). In total, 62.5% ($n=5$) became seizure-free after commencing their first anti-seizure medication (ASM). A further 25% ($n=2$) became seizure-free after addition or replacement with a second medication. One child had seizures which resolved without the need for medication. In Group 2, the average time from seizure onset to referral was less than that in Group 1 (2 years vs 3.2 years). This reached statistical significance with $p=0.023$. Children with drug-responsive epilepsy were referred at an earlier timepoint, which may have introduced a bias. However, we found no association between time from seizure onset to surgery when analysing surgical outcomes (*see table 3*). Mean time of follow-up for Group 2 was 4.87 years.

Ictal EEG abnormalities, concordant with the MRI findings, were significantly associated with drug resistance (*see table 1*) (ictal EEG: OR = 7.62, 95% CI: 1.79-37.86; $p=0.011$). However, for 50% ($n=4$) of those with pharmacoresponsive epilepsy (Group 2), an ictal EEG was not performed, thus restricting our ability to infer conclusions from the ictal data. In addition, 3/131

▼ **Table 1.** Comparison of drug-resistant and drug-responsive groups.

	Drug resistant epilepsy (n=131) 94.2%	Drug responsive epilepsy (n=8) 5.8%	Odds ratio (95% CI)	p value
	n (%)	n (%)		
Males	74 (56.5%)	3 (37.5%)		
Females	57 (43.5%)	5 (62.5%)		
Average age at seizure onset (years [range])	2.8 (under 1 month-14)	4.1 (Under 1 month-14)		0.120
Average age at referral (years [range])	5.94 (1 month -16)	6.1 (1-15.3)		0.983
Average time from seizure onset to referral (years [range])	**3.2 (<1-12.34)**	**2 (0.4-9.75)**		**0.023**
Average time from seizure onset to epilepsy surgery (years [range])	5.5 (2 months-18 years)			
Average time from referral to epilepsy surgery (years [range])	2.2 (<1 month-13)			
Average age at epilepsy surgery (years [range])	8 (6 months-18 years)			
Average number of medications used (range)	**4.6 (1-10)**	**1.13 (0-2)**		**<0.0001**
Laterality of FCD	Right 71 (54.2%) Left 60 (45.8%)	Right 5 (62.5%) Left 3 (37.5%)	1.41 (0.35:5.48)	0.7285
Bilateral interictal EEG abnormalities	**16 (12.2%)**	**5 (33.33%)**	**0.08 (0.02:0.88)**	**0.0021**
Ictal EEG not captured	9 (6.9%)	4 (50%)		
Interictal EEG normal	**3 (2.3%)**	**2 (25%)**	**0.07 (0.01:0.47)**	**0.0263**
MRI and interictal EEG concordant	97 (74%)	4 (50%)	2.85 (0.79:10.15)	0.214
MRI and ictal EEG concordant	**94 (71.8%)**	**2 (25%)**	**7.62 (1.79:37.86)**	**0.011**
Ictal and interictal EEG concordant	**101 (77%)**	**1 (0.125%)**	**23.57 (3.86:267.4)**	**0.0004**
Ictal, interictal and MRI concordant	**88 (67.2%)**	**1 (0.125%)**	**14.33 (2.402:162.9)**	**0.0033**

EEG: electroencephalogram; MRI: magnetic resonance imaging; FCD: focal cortical dysplasia; CI: confidence interval.

(2.3%) patients of Group 1 had normal interictal EEG, as opposed to 2/8 (25%) of Group 2 (p=0.0263)

Epilepsy surgery outcome

Of the 131 patients with DRE, 116 were discussed at the epilepsy surgery MDT. Six children were not offered surgery. In five of these cases, it was concluded that surgery would result in a neurological deficit that would be too severe, and in one case, the child became seizure-free in the interim. Of those 110, 11 patients declined surgery and two patients were awaiting surgery at the time of data collection. In total, 97 (74%) went on to have epilepsy surgery, of whom 92 had one-year post-surgery follow-up (*table 2*). Of those scheduled for epilepsy surgery, 82/97 patients (84.5%) had resective surgery, while 15 (15.4%) had a disconnection surgery. Sixty-eight

▼ **Table 2.** Pharmacoresistant and epilepsy surgery patients.

Drug-resistant epilepsy	Number (percentage of total unless otherwise specified)
Total	131
Underwent epilepsy surgery	97 (74%)
Resective surgery	82 (62.6%)
Disconnection	15 (11.5%)
Surgery recommended but parents declined	11 (8.4%)
Evaluated but not felt to be a surgical candidate	6 (4.6%)
Awaiting discussion or surgery	4 (3.1%)
Not referred for surgical assessment	6 (4.6%)
PET scan performed	29 (22.1%)
Invasive monitoring performed	30 (22.9%)
>1 year post surgery follow-up	92 (70.2%)
Engel Class 1 at 1 year follow-up	55 (59.8% of those >1 year post surgery)
Engel Class 1-3 at 1 year follow-up	76 (82.6% of those >1 year post surgery)
Engel Class 4 at 1 year follow-up	16 (17.4% of those >1 year post surgery)
Required further epilepsy surgery	13 (14.1% of those >1 year post surgery). 1 underwent vagal nerve stimulator implantation
Histology confirmed FCD	68 (70% of surgical cohort); resection: 71.4%, disconnection: 60%, p=0.3762
Histology non-diagnostic	13 (13.4% of surgical cohort)
Engel Class 1 in those with confirmed FCD	41 (64% of FCD 1 year post surgery)
Engel Class 1 in those with non-FCD histology	14 (50% of those 1 year post surgery)
FCD subtypes (% total FCD)	FCD Type 2a: 12 (17.6%) FCD Type 2b: 47 (69.2%) FCD-subtype unknown: 9 (13.2%)
Other histology (n=29)	Non-diagnostic: 19 Gliosis: 3 Polymicrogyria: 2 Normal: 1 Glioneuronal tumour: 1 Low grade ganglioglioma (NOS): 1 Hippocampal sclerosis (no FCD): 1 Pleomorphic xanthoastrocytoma (PXA): 1

FCD: focal cortical dysplasia; PET: positron emission tomography; MDT: multidisciplinary Team.

patients had a confirmed histology of FCD and 29 had non-FCD histology. Subtypes and percentages are detailed in *table 2*.

Fifty-five (59.8%) were seizure-free (Engel Class I) at one-year post surgery with 76 (82.6%) achieving at least a worthwhile improvement (Engel Class III or better) (*table 2*). Unadjusted factors significantly associated with Engel Class 1 at one year included seizure onset after one year of age, no interictal epileptiform discharges on post-surgery EEG, location of FCD in the right hemisphere, and no residual FCD or unintended connection across the surgical track on post-surgery MRI (*table 3*). However, only an absence of interictal epileptiform discharges on post-surgery EEG, no residual FCD or connection on post-surgery MRI, and disease affecting the right hemisphere

▼ **Table 3.** Factors affecting surgical outcome based on 92 patients at >one year post surgery.

Unadjusted values	Odds ratio of Engel Class 1 at one year	95% Confidence interval	p value
Age >1 year at seizure onset	**2.56**	**1.15 to 6.04**	**0.0355**
Less than 2 years from presentation to surgery	1.62	0.59 to 4.11	0.457
Interictal and ictal EEG concordant	1.07	0.35 to 3.51	>0.9999
Interictal EEG and MRI correlate	2.176	0.8 to 6.49	0.182
Ictal EEG and MRI correlate	1.64	0.59 to 4.57	0.424
Ictal EEG, onterictal EEG and MRI all correlate	1.69	0.62 to 4.66	0.325
Right hemispheric FCD	2.66	1.15 to 5.92	0.033
PET scan performed	1.6	0.59 to 4.11	0.457
Invasive EEG performed	0.46	0.18 to 1.11	0.105
Resective surgery v disconnection	0.99	0.31 to 3.12	>0.9999
Histology confirmed FCD	1.78	0.76 to 4.2	0.251
No residual disease or connection on post-op MRI	**3.63**	**1.49 to 8.69**	**0.0048**
No epileptiform discharges on post-op EEG	**4.57**	**1.75 to 11.12**	**0.0017**

PET: positron emissions tomography; EEG: electroencephalogram; MRI: magnetic resonance imaging; FCD: focal cortical dysplasia; post-op: post-operative.

remained significant based on the multiple logistic regression model (*table 4*). In addition, lobar location of the FCD was assessed against Engel class, however, no lobe in particular was associated with Engel score at one year of follow-up, and this was also the case for multilobar disease.

We assessed the complete removal of the "tail" of FCD (radiological transmantle sign) separately. Of the lesionectomy/lobectomy patients, 33 presented with a radiological "tail". Of these, 27 patients had a complete resection of the tail, according to postoperative MRI; 16/27 (59.9%) had Engel Class 1,

▼ **Table 4.** Multiple logistic regression model of factors affecting likelihood of Engel Class 1 outcome at one year post surgery.

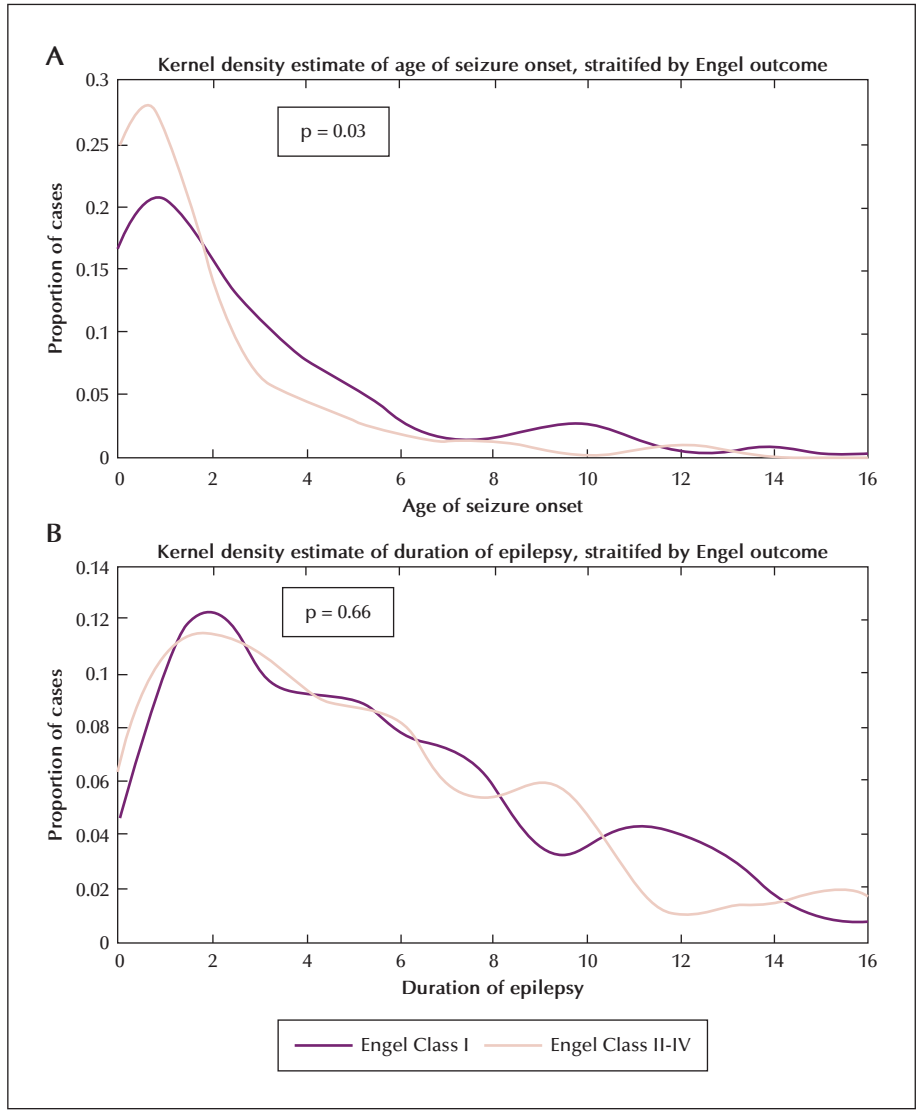
Adjusted values	Odds ratio of engel class 1 at 1 year	95% confidence interval	*P* value
Age at seizure onset	1.23	1.004 to 1.57	0.059
Number of AEDS	0.93	0.72 to 1.22	0.588
Number of years from seizure onset to surgery	0.96	0.82 to 1.11	0.558
Interictal EEG, ictal EEG and MRI concordant	2.71	0.70 to 11.78	0.158
Right hemispheric FCD	3.63	1.19 to 12.37	0.029
FCD confirmed on histology	2.23	0.66 to 8.11	0.204
Epileptiform discharges on post-surgery EEG	**0.27**	**0.1 to 0.84**	**0.023**
Residual disease on post-surgery MRI	**0.26**	**0.08 to 0.73**	**0.013**

compared to 4/6 (66.6%) who did not have a complete resection. The difference was not statistically significant. When assessing age at onset and duration of epilepsy for Engel Class 1 versus 2-4 as a continuous variable, we found a significant effect for age at onset (p=0.03), with children under the age of one year having a lower rate of seizure freedom postoperatively (*figure 2A*). The duration of epilepsy prior to an operation, however, did not seem to influence Engel score (*figure 2B*).

Fifty percent of the non-FCD histology group had an Engel score of 1. Even though this is a lower rate than that for the total, the difference between groups did not prove to be statistically significant.

Surgery safety outcome

Of the 97 cases who received surgery, there was no peri-operative mortality. The adverse event rate was 6%, and 4% had mild complications including transient mild paresis (one patient), anaesthesia-related drug reaction (one patient), urinary catheter complication (one patient) and superficial infection (one patient) treated with antibiotics only, without surgical management. Two cases (2%) had a moderate complication of new-onset motor deficit. However, at one year postoperative follow-up, both had regained normal neurological function. There were no cases of permanent neurological deficit.



■ **Figure 2.** Kernel density estimate of age at seizure onset (A) and duration of epilepsy (B) prior to surgery, stratified by Engel outcome.

Survey

Sixteen responses were obtained in total, representing 30.7% (16/52) of the north London paediatric epilepsy network consultants. Within the practices of this subset of physicians, a total of 130 patients with epilepsy and presumed FCD were being managed. In total, 112 of these had been referred to GOSH for management. That is, 86.2% of the patients with epilepsy and presumed FCD being treated within the network were referred to GOSH for further evaluation, regardless of whether seizures were controlled with medication.

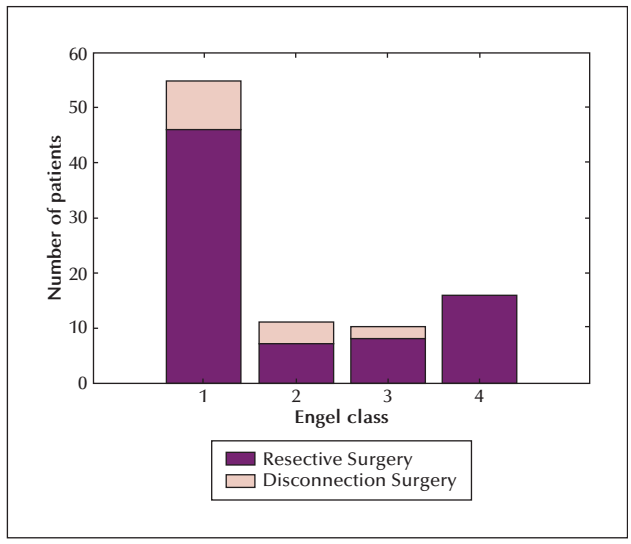
Discussion

More than 94% (131/139) of the patients in our cohort of children presenting with epilepsy and presumed FCD on MRI had DRE. In total, 110/139 patients (79%) were recommended for surgery. This demonstrates that most children presenting in this way will be surgical candidates and would likely benefit, as almost 60% of our surgical patients became seizure-free post-operatively, in comparison to only 10.8% (eight drug-responsive patients and seven patients with DRE who were seizure-free on more than two medications) of this patient group who were seizure-free on medical treatment alone. Focal cortical dysplasia is associated with DRE [13-17]. The high proportion of drug resistance found in the current cohort has also been reported in the literature for this group of patients (FCD), although most of these studies report the proportions in histologically defined cohorts, whereas this study reflects the clinical practice scenario considering a radiologically defined cohort, as this is what is available at the time of initial referral to the neurologist/epileptologist considering pre-surgical evaluation.

There was a higher proportion of patients with concordant ictal EEG abnormalities and MRI lesions in the drug-resistant cohort. Of note, one third of the children with drug-responsive epilepsy had bilateral interictal epileptiform discharges, raising the possibility that FCD may not be the only factor contributing to their epilepsy, or in fact, that the radiological diagnosis was incorrect, as these patients were not operated on and no histology was taken. In these cases, these findings could imply contribution of additional aetiological factors that are more responsive to medical treatment. In our patient group, only 1.4% of the patients who failed the first medication responded to a second. This is a much lower percentage than is found in the literature for epilepsy as a whole [18]. This highlights that the delay to consider patients with an MRI diagnosis of FCD as suitable for surgical treatment until traditional criteria for drug-resistance are met, might be unnecessary.

A negative correlation has previously been reported between the length of time from first seizure to an operation and both seizure outcome and cognitive ability [20, 23, 26-29]. In a study performed by our department on low-grade tumours, more than 20 seizures prior to surgical treatment were found to correlate with a worse cognitive prognosis [23]. There is also evidence that intelligence quotient (IQ) declines over time with continuing seizures [30], and IQ is more likely to increase post-surgery when medication is weaned, as observed in the "time to stop" study [33]. Our cohort did not demonstrate an advantage to earlier surgery in terms of seizure outcome. This study, however, was neither designed, nor powered to do this. We were unable to obtain complete and accurate data on cognitive outcomes in our cohort. Nevertheless, there is evidence in the literature suggesting that early surgical treatment, resulting in seizure control, improves cognitive outcome [20, 23, 26-29]. In a study by Pelliccia *et al*., two groups of patients with low-grade tumours, diagnosed at a young age, were compared; one was operated on in childhood and the other in adulthood. One of the key points in that study was that shorter duration of epilepsy significantly correlated with better seizure outcome [34]. With the increased likelihood of a worthwhile reduction in seizures and reduced anti-epileptic medication burden offered by surgical treatment, one would expect improvement in quality of life measures. With these factors in mind and the fact that in our cohort surgery was effective with regards to seizure control, very safe and associated with a low complication rate, with no long-term negative sequelae, the case can be made for surgical treatment at an earlier stage for lesions that are EEG-MRI concordant in non-eloquent areas, before the traditional definition of drug resistance is met. In cases in which the epileptogenic lesion overlaps with eloquent cortex, the risk:benefit balance for surgery will require more careful evaluation.

The rate of Engel Class 1 outcome, one year after surgery, was 59.8%. This is in line with literature reports of 50-75% in most studies [19-22]. We also accomplished an 82.6% rate of worthwhile seizure improvement (Engel Class III or better) (*figure 3*). Factors significantly associated with an Engel Class 1 outcome score were age above one year at diagnosis, no epileptiform activity on postoperative EEG, complete resection of the FCD on postoperative MRI, and right hemisphere operations. Even though we have demonstrated that the completeness of the resection is important for seizure outcome, the complete removal



■ **Figure 3.** Engel classification at one-year post surgery.

of the "tail", or radiological transmantle sign, did not prove to be significant. The difference between hemispheres with regards to seizure outcome could be due to the ability to perform a larger lesionectomy on the non-dominant side.

As stated before, the patients included were those with presumed FCD on preoperative MRI as well as epilepsy. On postoperative histology, however, only 69% of the samples showed a confirmed diagnosis of FCD (*table 2*) and 13% of the cases non-diagnostic histology. There was no significant association between histology findings and surgical outcomes. There are several possible explanations for this finding. In deep or peri-eloquent resections, the use of ultrasonic aspiration, whilst effective, may limit histological specimen quality, and much debate remains between histopathologists regarding the criteria for diagnosis or subtle malformations (*e.g.* FCD type 1 and mild malformations of cortical development) [1]. Nevertheless, resection of lesions without histopathological diagnosis of FCD still resulted in 50% becoming seizure-free.

There are several limitations to this study. One arises from the fact that GOSH is a specialist epilepsy centre with an epilepsy surgery programme, and selection bias towards referral of patients with DRE cannot be excluded. In order to assess possible referral bias, we performed a community-based survey. This indicated that the majority of children/young people with radiological FCD diagnosis, resident in the geographical catchment area (86.2%), were referred to us whether or not they had shown a response to medication. That being said, we only received response from 30% of the physicians who were requested to participate in the survey, thereby limiting our ability to draw meaningful conclusions. Furthermore, we cannot deduct that the referral pattern of our epilepsy network necessarily represents the pattern in other networks, both nationally and internationally. Another limitation lies in the retrospective nature of this study and the relatively short period of follow-up of the postoperative patients.

Conclusion

In our cohort of patients with epilepsy and a radiologically presumed FCD, we show high rates of drug resistance. Subsequent surgery results in favourable seizure outcomes with an excellent safety profile, and given the fact that earlier surgery has the potential to improve seizure and cognitive outcome, this study provides further support to consider surgery in this cohort at an earlier stage relative to current standard practice. Further evaluation is necessary and a prospective study to assess the outcomes of earlier surgery for children with FCD associated epilepsy is needed. ■

Disclosures.

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Key points

- The vast majority of FCD-related epilepsy patients have drug-resistant epilepsy
- Most of these patients are surgical candidates and will have a significantly higher rate of seizure freedom, compared to those on medical treatment.
- This patient group should be considered for surgical treatment earlier compared to current standard management.

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