Case Report

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Microsurgical lesionectomy for drug-resistant insular cortex epilepsy in focal cortical dysplasia type IIB: a pediatric case report

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Introduction and importance: Focal cortical dysplasia (FCD) is a significant cause of drug-resistant epilepsy, often necessitating surgical intervention. Type IIb FCD poses challenges due to its strong association with drug-resistant seizures. Effective management involves advanced imaging, intraoperative neurophysiological monitoring, and precise surgical techniques. This case study illustrates these strategies in an 11-year-old female with drug-resistant epilepsy attributed to Type IIb FCD.

Case presentation: The patient, an 11-year-old female, had drug-resistant seizures despite various anticonvulsant treatments. Preoperative 3 Tesla (3T) MRI revealed an ill-defined lesion in the right frontal operculum. The surgical team used neuro-navigation for intraoperative guidance and electrocorticography for lesionectomy. Pathology confirmed Type IIb FCD with rare concentric calcifications.

Clinical discussion: Drug-resistant seizures in FCD often require surgery when medications fail. This case highlights the importance of comprehensive preoperative evaluations and advanced imaging, such as 3T MRI, to accurately identify lesions. Intraoperative neurophysiological monitoring, including electrocorticography, ensures precise resection of the epileptogenic zone. The unusual finding of concentric calcifications in Type IIb FCD is noteworthy, suggesting the need for further research to understand their impact on the disease.

Conclusion: Microsurgical lesionectomy is crucial for managing drug-resistant seizures in Type IIb FCD. Combining advanced imaging with intraoperative monitoring improves surgical precision and outcomes. The rare pathological finding of calcifications highlights the diversity of FCD manifestations, warranting further study. These techniques can significantly enhance seizure control and quality of life in patients with drug-resistant epilepsy.

Keywords: calcification, focal cortical dysplasia, intractable seizures, microsurgical lesionectomy

Introduction

Focal cortical dysplasia (FCD) is a type of cortical development anomaly and stands as the primary cause of medically resistant epilepsy in children and one of the top three causes of unmanageable seizures in adults[1]. Seizures associated with FCD are typically triggered by abnormal circuitry resulting from the presence of cytomegalic dysmorphic neurons (CDN) and balloon cells (BC)[2]. Initially, medications are utilized to manage seizures stemming from cortical dysplasia. However, if anticonvulsants prove ineffective in controlling seizure activity, lesionectomy becomes a viable option for treating FCD[3].

FCD is one of the most common causes of drug-resistant epilepsy, particularly in children, accounting for about 10–50% of epilepsy cases undergoing surgical treatment. In pediatric patients, FCD is the leading cause of refractory epilepsy, responsible for 30–50% of epilepsy surgeries. While specific mortality rates directly attributable to FCD are not well-documented, refractory epilepsy is associated with an increased risk of sudden unexpected death in epilepsy, with an incidence of about 1–2 per 1000 patient-years. Surgical intervention can

HIGHLIGHTS

- Focal cortical dysplasia and drug-resistant epilepsy: Surgery essential for control.
- Pediatric case: Precision lesionectomy for 11-year-old's seizures.
- Surgical precision: Tech aids accuracy in lesion removal.
- Unusual finding: Concentric calcifications in focal cortical dysplasia type IIb.
- Multidisciplinary approach: Enhances surgical success.
- Future research: Explore calcifications' clinical role.

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significantly improve prognosis, with 60–70% of patients achieving favorable outcomes, thereby reducing the risks associated with uncontrolled seizures.

Case description

An 11-year-old female child presented with a history of seizures starting at 18 months of age. Each episode lasted 5–10 sec, characterized by behavioral arrest, a vacant stare, and left upper limb posturing, indicative of complex partial seizures likely originating from the right hemisphere. Until the age of 7, the episodes occurred once a week and were managed using Sodium Valproate & Clobazam. Medications were discontinued, and the child remained seizure-free for 2 years. However, seizures recurred, and the child was subsequently treated with Oxcarbazepine and Lamotrigine. Despite medication, the seizures became refractory, progressing from two episodes per week to almost daily occurrences. The patient's management was provided in a specialized neurosurgical center equipped with advanced diagnostic and therapeutic facilities for the comprehensive evaluation and treatment of epilepsy and related neurological disorders. This center likely included a multidisciplinary team comprising neurologists, neurosurgeons, epileptologists, neuroradiologists, neuropsychologists, and other allied healthcare professionals. An initial brain MRI (1.5 Tesla) in 2011 showed no evident abnormalities, and an EEG was also normal. A further brain MRI (3 Tesla) with a seizure protocol revealed an ill-defined lesion in the right frontal operculum (1.61.21.6 cm) consistent with type IIb FCD. A fused positron emission tomography with screening MRI confirmed the lesion's location in the right insula, exhibiting a transmantle sign extending to the right frontal horn of the lateral ventricle[4]. positron emission tomography-computed tomography brain scan demonstrated significant hypo-metabolism in the right insular cortex (asymmetrical index (AI) of – 54.57%) (Fig. 1). Functional MRI (fMRI) indicated language function in the left hemisphere. Additionally, Diffusion tensor imaging revealed part of the cortico spinal tract near the FCD mantle. Video EEG recorded epileptiform activity over the right fronto-parieto-temporal regions during wakefulness and multifocal epileptiform discharges during sleep over the midline frontal, bi-frontal, and right fronto-temporal regions. Four complex partial seizures of probable right hemispheric origin were observed. Neuro-psychological assessment exhibited impaired visuo-conceptual and visuo-perceptive memory, suggesting right hemisphere abnormality. The Epilepsy committee at the center decided, after comprehensive discussions, to proceed with an image-guided resection of the right frontal opercular FCD under ECOG monitoring.

Surgical procedure

A right pterional craniotomy was performed with navigation assistance (Medronic Stealth Station S8) under general anesthesia. Neuro monitoring involved scalp electrode placement and testing various modalities such as EcoG, subcortical motor fiber mapping, motor evoked potentials, and somatosensory evoked potentials. Upon opening the sylvian fissure, the frontal operculum revealed ill-defined abnormal gyri confirmed by navigation as the site of FCD. The lesion was resected with EcoG guidance. Subsequently, the mantle was localized with neuro-navigation and excised carefully, monitoring the subcortical motor fibers. Intraoperative MRI (3T) showed residual FCD in the inferior lip of the right frontal operculum, which was excised. EcoG remained silent post-lesionectomy, while motor evoked potentials and somatosensory evoked potentials remained intact throughout the procedure. Following the surgical procedure, the patient was transferred to the neurological rehabilitation ward for thorough postoperative monitoring. During the initial 24 h, continuous monitoring was conducted to assess neurological stability and any immediate complications. In the early hours post-surgery, the patient was closely observed to monitor intracranial pressure and prevent the risk of hemorrhage or cerebral edema. Throughout the immediate postoperative period, the patient showed signs of gradual recovery from sedation. Transient weakness in the movements of the left upper and lower limbs was observed in the early postoperative period. This weakness was assessed as 4-/5 on the Medical Research Council muscle strength scale. However, over the following days, the patient demonstrated gradual improvement in muscle strength and mobility of the affected limbs.

During the hospital stay, the patient underwent continuous EEG monitoring to detect any abnormal epileptic activity. Additionally, regular neurological examinations were conducted to assess brain function and cognitive abilities. The patient reported no further epileptic seizure episodes since the immediate postoperative period. This absence of seizures was corroborated by continuous EEG monitoring, which did not detect any abnormal epileptic activity.

Histopathological examination revealed several dysmorphic neurons, some displaying coarse Nissl substance, balloon cells with glassy eosinophilic cytoplasm and vesicular nucleus with prominent nucleoli (formerly known as Taylor cells). Mitotic activity was virtually negative, and increased astroglial cell density along with concentric calcifications (an unusual finding in focal cortical dysplasia) were observed (Fig. 2). These pathological features confirmed a diagnosis of FCD, ILAE/PALMINI TYPE IIB variant[5].

Postoperative axial T1 and T2 MRI brain views illustrated complete resection of the right insular lesion. Coronal MRI brain views further demonstrated complete resection of the mantle (Fig. 3). We have followed the Surgical CAse REport 2023 criteria for the preparation of this case[6].

At the 3-month follow-up, the patient exhibited significant progress in their recovery. Neurological assessments showed continued improvement in motor function, with the transient weakness in the left upper and lower limbs completely resolved. There were no signs of muscle weakness or motor deficits during the follow-up evaluations.

Discussion

FCD represents a congenital anomaly of brain development, characterized by improper neuronal migration in specific brain regions during fetal development. It stands as a primary cause of intractable epilepsy in both pediatric and adult populations. FCD manifests in three types with various subtypes, namely type 1a, 1b, 2a, 2b, 3a, 3b, and 3c, each displaying distinct histopathological features[7] (Table 1). Mutations associated with FCD subtypes 2a and 2b involve genes such as mechanistic target of rapamycin, PI3KCA, AKT3, and DEPDC5. These mutations lead to heightened mechanistic target of rapamycin pathway signaling during critical stages of brain development. Recent evidence

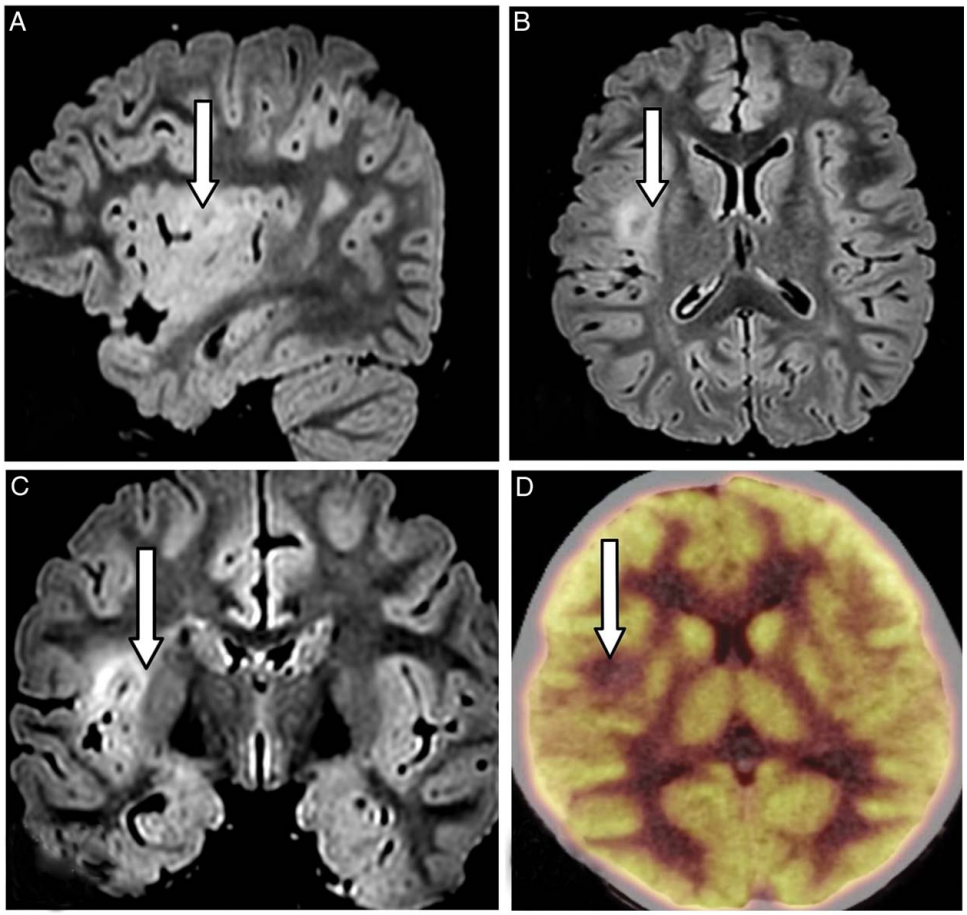

Figure 1. Radiological findings of focal cortical dysplasia type IIb. (A) Sagittal view of MRI brain displaying an ill-defined lesion in the right frontal operculum. (B) Coronal view of MRI brain indicating the transmantle sign with the lesion extending into the right frontal horn of the lateral ventricle. (C) Axial view of MRI brain highlighting the right frontal opercular lesion. (D) PET-CT brain scan revealing marked asymmetrical hypo-metabolism in the right insular cortex. PET-CT, Positron emission tomography-computed tomography.

suggests a potential association between in-utero viral infections, such as cytomegalovirus and human papillomavirus, and the development of FCD[8].

Seizures in FCD are believed to arise from aberrant circuitry prompted by the presence of CDNs and BCs. Initial treatment involves medication to manage seizures resulting from cortical dysplasia. In cases where anticonvulsants fail to control seizure activity, lesionectomy emerges as a viable option for FCD management. During surgical intervention, careful consideration is required to remove the mantle adequately to prevent postoperative

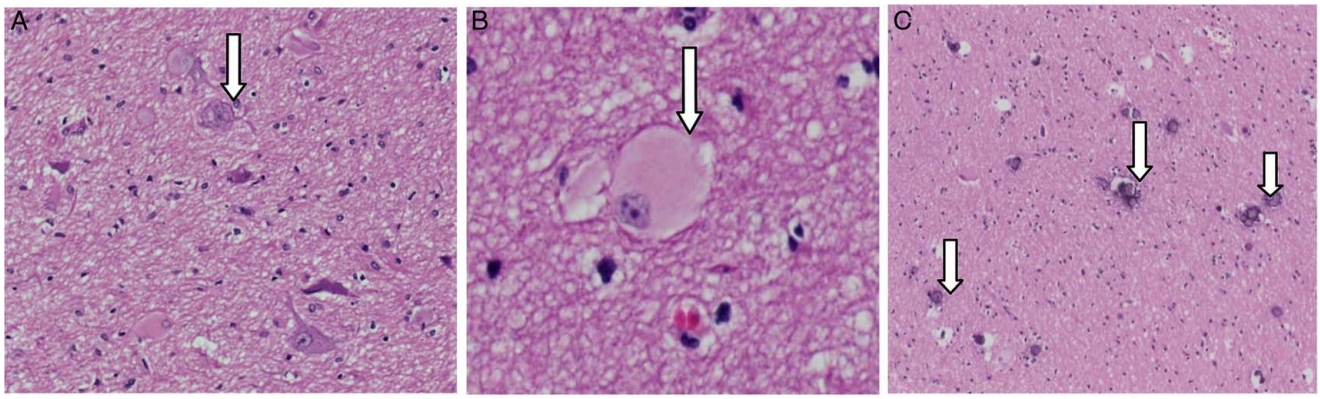

Figure 2. Histopathological examination of focal cortical dysplasia type IIb. (A) Cortex exhibiting several dysmorphic neurons, some displaying coarse Nissl substance. (B) Neurons depicting glassy eosinophilic cytoplasm and vesicular nuclei with prominent nucleoli, characteristic of Taylor-type balloon cells. (C) Unusual concentric calcifications observed in focal cortical dysplasia, along with a dysmorphic neuron and reactive glial cells in the background. BC, balloon cells.

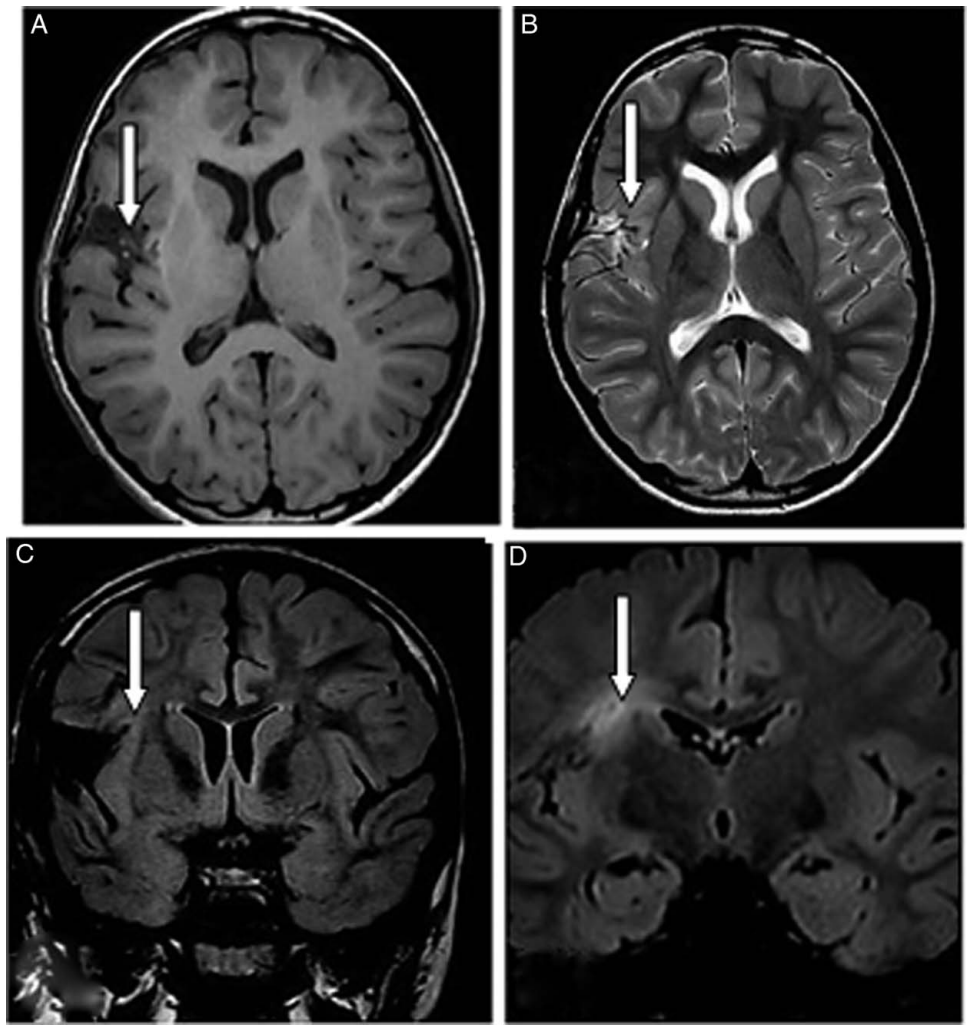

Figure 3. Postoperative radiological assessment. (A, B) Axial T1 and T2 MRI brain views illustrating complete resection of the right insular lesion. (C, D) Coronal MRI brain views demonstrating complete resection of the mantle.

status epilepticus. Accurate imaging, preferably utilizing 3T MRI, becomes essential as routine 1.5 Tesla MRI may not effectively identify these ill-defined lesions. Successful surgical resection following proper localization aids in achieving seizure freedom.

Table 1

ILAE three-tiered classification system for focal FCD

	Three-tiered ILAE classification system of FCD
Type I	Isolated FCD
Ia	Abnormal radial cortical lamination
Ib	Abnormal tangential cortical lamination
Ic	Abnormal radial and tangential cortical lamination
Type II	Isolated FCD
IIa	Dysmorphic neurons
IIb	Dysmorphic neurons with balloon cells
Type III	Cortical lamination abnormalities
IIIa	In the temporal lobe associated with hippocampal sclerosis
IIIb	Adjacent to glial or glioneuronal tumor
IIIc	Adjacent to vascular malformation
IIId	Adjacent to any other lesion acquired during early life (encephalitis etc.)

BC, balloon cells; FCD, focal cortical dysplasia.

Type 2b FCD is characterized by complete loss of laminar structure, the presence of CDN, and balloon cells displaying specific morphological features. Typically, calcifications are not observed in FCD[9], a characteristic not previously reported in the literature. However, in our case, concentric calcifications were present, rendering it an unusual variant. Calcification refers to the deposition of calcium salts in tissue, which can be detected radiologically and confirmed histopathologically. When present in FCD, calcification may appear as small, dense areas within the dysplastic cortex on imaging studies such as computed tomography scans. Histologically, it manifests as basophilic deposits within the affected cortical areas, sometimes associated with glial scarring or neuronal damage.

The presence of calcification in a patient with FCD may prompt consideration of other pathological entities that can present with cortical calcification. These include tuberous sclerosis complex, Sturge–Weber syndrome, and various infectious or metabolic conditions. Calcifications can affect the interpretation of imaging studies. Radiologists and clinicians must be aware of this possibility to avoid misdiagnosis or oversight of the underlying FCD. Additionally, the presence of calcifications could indicate a different pathophysiological mechanism at play within the dysplastic

tissue, which may involve chronic inflammation, neuronal injury, or aberrant mineral metabolism.

This case underscores the importance of comprehensive pathological evaluation in epilepsy surgery. The detection of calcifications should lead to a broader differential diagnosis and a thorough investigation of potential underlying causes. Furthermore, understanding the mechanisms behind calcification in FCD could offer insights into the disease's progression and potentially reveal new therapeutic targets.

The implications of finding calcifications in FCD are significant for both diagnosis and treatment. From a diagnostic perspective, identifying calcifications necessitates considering a wider range of differential diagnoses and may require additional diagnostic tests to rule out other conditions. From a treatment perspective, the presence of calcifications may influence surgical planning and outcomes. Surgeons need to account for these calcified areas to ensure complete resection of the epileptogenic tissue, which is crucial for achieving seizure freedom. Unidentified risk factors: Despite detailed case analysis, there may be unidentified risk factors that could influence the effectiveness of the surgical intervention and the postoperative course of the patient. These may include genetic factors, medical comorbidities, or other patient-specific risk factors that could affect long-term outcomes.

Limitations

- Each case of epilepsy associated with focal cortical dysplasia is unique and may respond differently to surgical intervention and postoperative therapy. The results of this case may not be generalizable to all patients with similar conditions and may vary based on individual factors.
- Although neurocognitive examinations were conducted, there may be limitations in assessing the patient's cognitive functions. Further assessment may be necessary to fully understand the impact of the neurological condition and surgical intervention on the patient's cognitive abilities.

Conclusion

Microsurgical lesionectomy should be considered for patients with drug-resistant refractory seizures associated with FCD. A comprehensive preoperative assessment, coupled with the optimal utilization of new adjuncts such as intraoperative neurophysiological monitoring and image guidance, significantly enhances surgical outcomes and contributes to achieving substantial seizure freedom. Notably, the presence of pathological calcifications represents an unusual finding in Type IIb FCD, warranting further exploration and clarification.

Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient's next of kin.

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Author contribution

S.V., V.R.R.K.: conceptualization, data curation, methodology; A.R., M.J.: investigation, methodology, resources; G.S., G.E.U.: supervision, validation, visualization, writing—review and editing; B.C.: supervision, validation.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

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References

[1] Kabat J, Król P. Focal cortical dysplasia—review. Pol J Radiol 2012;77:35–43.
[2] Fauser S, Huppertz HJ, Bast T. Clinical characteristics in focal cortical dysplasia: a retrospective evaluation in a series of 120 patients. Brain 2006;29:1907–16.
[3] Blümcke I, Thom M, Aronica E, *et al*. The clinicopathologic spectrum of focal cortical dysplasias: aconsensus classification proposed by an ad hoc task force of the ILAEdiagnostic methods commission. Epilepsia 2011;52:158–74.
[4] Kimura Y, Shioya A, Saito Y, *et al*. Radiologic and pathologic features of the transmantle sign in focal cortical dysplasia: the t1 signal is useful for differentiating subtypes. . AJNR Am J Neuroradiol 2019;40:1060–6.
[5] Kim YH, Hoon-Chul K, Dong-Seok K, *et al*. Neuroimaging in identifying focal cortical dysplasia and prognostic factors in pediatric and adolescent epilepsy surgery. Epilepsia 2011;52:722–7.
[6] Sohrabi C, Mathew G, Maria N, *et al*. The SCARE 2023 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg Lond Engl 2023;109:1136.
[7] Marsan E, Baulac S. Mechanistic target of rapamycin (mTOR) pathway, focal cortical dysplasia and epilepsy. Neuropathol Appl Neurobiol 2018;44:6–17.
[8] Taylor DC, Falconer MA, Bruton CJ, *et al*. Focal dysplasia of the cerebral cortex in epilepsy. J NeurolNeurosurg Psychiatry 1971;34:369–87.
[9] Blümcke I, Thom M, Aronica E, *et al*. The clinicopathologic spectrum of focal cortical dysplasias: a consensus classification proposed by an ad hoc task force of the ILAE diagnostic methods commission. Epilepsia 2011;52:158–74.