# Clinical commentary with video sequences

# Gelastic seizures: not always hypothalamic hamartoma

Christina S. Cheung, Andrew G. Parrent, Jorge G. Burneo

Epilepsy Programme, Department of Clinical Neurological Sciences,
University of Western Ontario, London, Canada

**ABSTRACT** – Gelastic seizures are often associated with hypothalamic hamartomas. However, focal cortical dysplasias can also cause "laughing seizures", and such cases can be difficult to localize with EEG. This case report presents a 29-year-old woman who was successfully rendered free of gelastic seizures after resection of a frontal cortical dysplasia, localized through MRI and SPECT imaging. *[Published with video sequences]*

**Key words:** gelastic seizures, cortical dysplasia, hypothalamic hamartoma frontal lobe seizures

**Correspondence:**
Jorge G. Burneo, MD, MSPH
Epilepsy Programme
University of Western Ontario
London Health Sciences Centre
339 Windermere Rd
London, ON, Canada, N6A5A5
<jburneo2@uwo.ca>

Gelastic (laughing) epilepsy has been thought to represent less than 0.5% of all other types of epilepsy (Chen and Forster 1973). Its most common cause is hypothalamic hamartoma, and gelastic seizures are thought to be one of the hallmark features of this condition (Arzimanoglou *et al.* 2003, Anderman *et al.* 2003, Kerrigan *et al.* 2005). However, it has been postulated that they may originate from neural activity in the cingulate gyrus and temporal region as well as the frontal lobe (Loiseau *et al.* 1971, Arroyo *et al.* 1993, McConachie and King 1997). Often, MR imaging may not detect a lesion and such cases are deemed cryptogenic (Arroyo *et al.* 1993, Iannetti *et al.* 1997, Garcia *et al.* 2000). There has been study of subtle findings on MRI, associated with cortical dysgenesis and abnormalities of cortical organization that should trigger closer evaluation (Bronen *et al.* 2000). Ictal EEG can demonstrate various patterns in gelastic seizures of frontal lobe origin, and SPECT has demonstrated hypoperfusion post-ictally, particularly in cases of focal cortical dysplasia (Iannetti *et al.* 1997, Sasaki *et al.* 2000).

Frontal lobe epilepsy manifests clinically more typically as motor symptoms, which is a useful distinguishing characteristic of frontal *versus* temporal lobe epilepsy (Geier *et al.* 1977). Much discussion has surrounded the affective component of gelastic seizures, with feelings of mirth associated with seizures from the temporal lobe. Mirth or pleasant sensations are not usually present in cases of frontal origin (Arroyo *et al.* 1993). It is worth noting however, that temporal lobe gelastic seizures can also be associated with motor activity, such as running or kicking (Chen and Forster 1973, McConachie and King 1997). We present the case of a patient with frontal lobe epilepsy who presented with laughing seizures. EEG, MRI, and single photon emission computed tomography (SPECT) evaluation allowed localization of seizure onset to the frontal lobe.

## Case report

The patient was a 29-year-old female, first seen by the epilepsy service for evaluation of seizures, which had be-

**Figure 1.** Scalp EEG before and during a typical seizure. No EEG changes were seen. The red line indicates onset of the clinical event.

gun a year earlier, when she was 28 years old and 38 weeks pregnant, and after a long, seizure-free period.

Her first seizure occurred following pertussis vaccination at age five. She continued to have generalized and complex partial seizures after that and was treated with carbamazepine and clobazam, which controlled her seizures. By age 15, she had complete seizure control. She gradually came off both medications when she became pregnant, but in her 3rd trimester, began to have frequent seizures (1-5 times during the day, 10-15 times a night), with a sensation comparable to the seizures she had had as a teenager. She was thus started back on her previous medications.

The seizures were described as an initial aura of abdominal discomfort that ascended upward, and then a sensation of being on a roller coaster. She was able to speak and understand during these episodes, and complained of feeling restless. She would then occasionally lose awareness, her body would rock or she would aimlessly wander.

Events usually lasted 10-30 seconds. She had no manual automatisms or dystonic posturing.

Two years after her pregnancy and safe delivery of her child, she had no further generalized episodes, but frequent partial events continued, and it was noted that they were catamenial in nature. Some of the seizures consisted of a brief period of laughing followed by some confusion, while others were staring spells and not very obvious.

Upon admission to the epilepsy monitoring unit, continuous video-EEG monitoring confirmed the semiology of the events, but without clear EEG changes *(see video sequence and figure 1)*. An MRI showed a right frontal transmantle cortical dysplasia extending from the right superior frontal gyrus down to the upper outer border of the right lateral ventricle *(figure 2)*. An ictal SPECT showed hyperperfusion over the right frontal regions corresponding with the area of cortical dysplasia *(figure 3)*. At this time it was felt that epileptogenesis was from the right frontal area and surgery was considered.
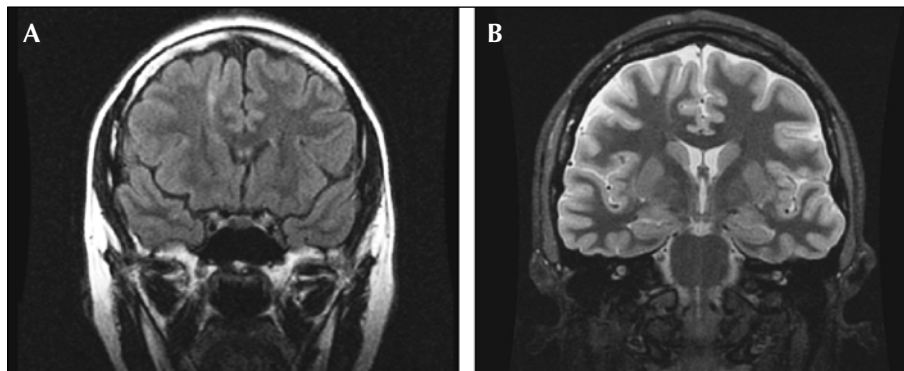
**Figure 2. A**) MRI of the patient, FLAIR sequence, coronal, demonstrating an area of high signal in the right frontal lobe that extends from the surface of the cortex into the subcortical area close to the lateral ventricle. **B**) The same MRI, T1 sequence, high resolution, coronal, demonstrating the same abnormality.
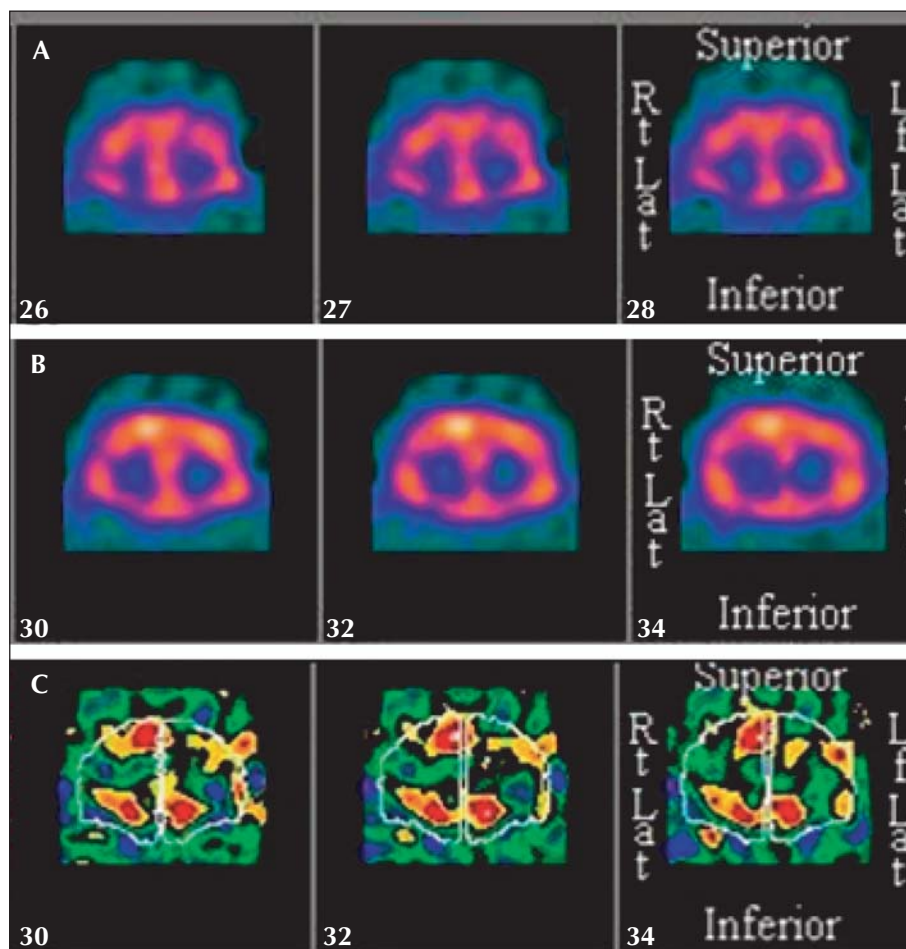


**Figure 3. A**) Interictal SPECT not revealing any area of hypo- or hyper-perfusion. **B**) Ictal SPECT, coronal section, revealing a small area of hyperperfusion in the right frontal area, concordant with the MRI findings. **C**) Subtraction analysis, showing the area of hyperperfusion (white surrounded by red coloration) in the right parasagittal frontal region.

Intracranial electrodes were implanted and these showed a broad field *(figure 4)* corresponding to the obvious cortical, dysplastic lesion.

Resection of the right superior frontal tissue and white matter was performed and pathological analysis showed focal, cortical dysplasia with subcortical ballooned astrocytes.

She had been seizure-free for 12 months post-operatively and was driving again when she began to experience rare auras reminiscent of her previous seizures. These consisted of a brief, rising, abdominal sensation that was not associated with any change in level of consciousness, ability to speak or understand, and there were no associated involuntary movements. She continues to be on antiepileptic medications to control these auras.

## Discussion

Malformations of cortical development are divided into three categories based upon the three major processes in cortical development: cell proliferation and apoptosis, neuronal migration, and cortical organization. Cortical dysplasia in particular is due to a defect in neuronal migration, with disruption of normal cortical lamination. Taylor type cortical dysplasias are focal epileptogenic abnormalities of the cerebral cortex containing dysplastic neurons within. These and various other types of dysplasias are characterized histologically by the presence of balloon cells (Taylor *et al.* 1971, Barkovich *et al.* 2001).

In dysplasias where there are abnormalities of cell type from the time they are generated, radiological appearance reflects the inability of this cell type to migrate normally or organize correctly after arrival in the cortex. Thus, imaging should show abnormalities that extend from cortex to germinal zone near the ventricular margin (Barkovich *et al.* 2001) as would seem to be the case in our patient.

EEG investigation of patients with epilepsy due to Taylor-type cortical dysplasia has revealed distinctive ictal and interictal patterns characterized by disruption of background activity, high frequency fast spikes and polyspikes, interspersed with flattening and fast lower amplitude activity (Tassi *et al.* 2002). Focal, fast, rhythmic epileptiform discharges have also been found in patients with focal cortical dysplasia (Kuruvilla and Flink 2002. Gambardella *et al.* 1996). While present only in approximately half the patients studied, when present, such discharges would appear to be useful for identification of epileptogenic foci amenable to surgical removal. A review by Kutsy (1999) identifies several types of interictal patterns seen in patients with extratemporal epilepsy, including various focal, regional and generalized epileptiform discharges that may or may not localize to the site of seizure origin. Also noted is the distinct possibility that no epileptiform discharges may be seen at all, which was the case in our patient, likely due to her discrete area of activation. Scalp

EEG findings are often poorly localizing (Raymond *et al.* 1995), necessitating further imaging to determine seizure focus.

SPECT brain imaging has proven helpful in localizing epileptogenic foci in patients with medically refractory epilepsy. The sensitivity of SPECT in localizing epileptic foci is highest for ictal, then post-ictal, then interictal recording, as noted in one meta-analysis (Devous *et al.* 1998). A similar pattern of sensitivity is noted for the relationship of SPECT to surgical outcome in the localization of seizure focus. In the case of our patient, the EEG was not helpful, and ictal SPECT was capable of revealing hyperperfusion over the right frontal regions corresponding to the area of cortical dysplasia seen on MRI.

Extensive imaging is often necessary to localize the lesion for epilepsy surgery as the completeness of resection correlates with degree of seizure-freedom (Alexandre *et al.* 2006). Even with extensive imaging however, focal cortical dysplasias are often missed on initial scan, and because they often occur concurrently with other pathology (Bautista, Foldvary-Schaefer *et al.* 2003), a consistent outcome is difficult to achieve. Malformations of cortical development can worsen the probability of complete resection as compared to hippocampal sclerosis or tumour, possibly because such malformations can extend microscopically beyond the resected region (Hirabayashi *et al.* 1993). Our patient was rendered completely seizure-free (Engel Class 1) after partial frontal lobe resection, which is consistent with Class I seizure relief obtained by 72% of patients with resection according to Kral *et al.* (2003), but somewhat unusual as the percentage of those seizure-free post-operatively tend to decrease progressively from childhood, through adolescence and adulthood (Edwards *et al.* 2000, Kral *et al.* 2003).

While gelastic seizures are commonly deemed a hallmark of hypothalamic hamartomas (Kerrigan *et al.* 2005), many studies have linked gelastic seizures to lesions of the temporal lobes, frontal lobes, pituitary tumours, astrocytomas of mamillary bodies, third ventricular papillomas, and various other locations (Loiseau *et al.* 1971, Ianetti *et al.* 1992, Arroyo *et al.* 1993, McConachie and King 1997). Our patient's gelastic seizures were due to focal cortical dysplasia in the frontal lobe, not detected by EEG and identified only after MRI and SPECT localization. As frontal seizures, our patient's episodes were also somewhat atypical in that they lacked prominent motor manifestations and presented instead with laughter and various sensations of restlessness or abdominal discomfort.

Finally, a possible explanation for the remaining auras in our patient is that perhaps not all the epileptogenic area was resected, as the changes during intracranial recordings were more regional than focal (Iannetti, 1992).

In conclusion, it is worth noting that gelastic seizures are not pathognomonic of hypothalamic hamartoma exclusively. Consideration should also be given other brain areas. □
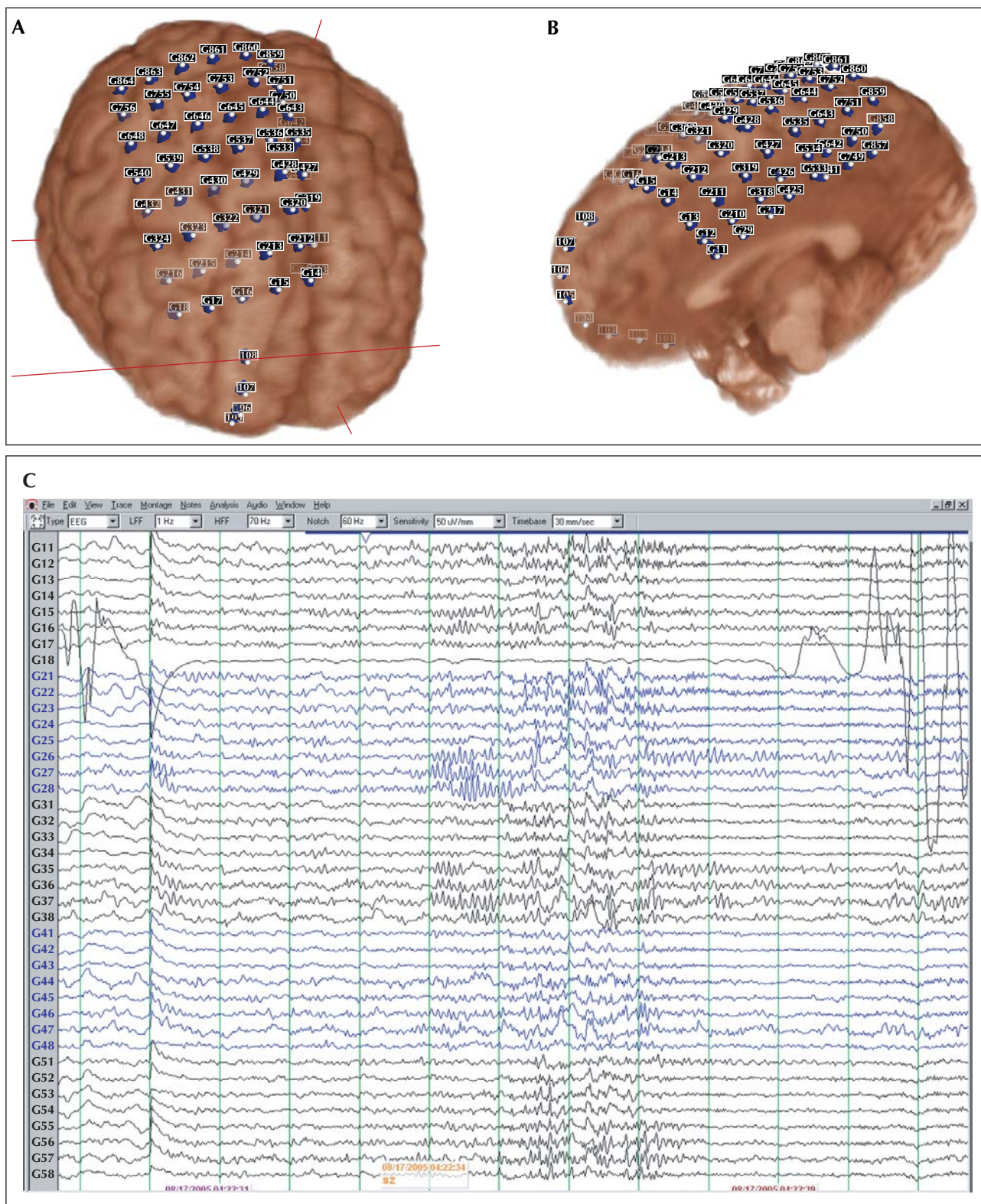
**Figure 4.** CT performed with the patient having a subdural grid and one line of electrodes, superimposed onto a pre-surgical MRI using Atamai software (London, ON, Canada). The grid is covering the right frontal convexity (**A**) and the mesial portions (**B**), while the line is covering the right orbitofrontal region. The recordings using these electrodes revealed an onset concordant with the MRI lesion and the SPECT findings (**C**).

## Legend for video sequence

The patient felt an avra that made her triggered the alarm. Immediatly after that, she began to laugh and have some movements of her lower extremities. Despite the short duration of the event, she appeared to be unresponsive. There was no EEG correlation.

## References

Alexandre Jr. V, Walz R, Bianchin MM, *et al.* Seizure outcome after surgery for epilepsy due to focal cortical dysplastic lesions. *Seizure* 2006; 15: 420-7.

Andermann F, Arzimanoglou A, Berkovic SF. Hypothalamic hamartoma and epilepsy: the pathway of discovery. *Epileptic Disord* 2003; 5: 173-5.

Arroyo S, Lesser RP, Gordon B, *et al.* Mirth, laughter and gelastic seizures. *Brain* 1993; 116: 757-80.

Arzimanoglou A, Hirsh E, Aicardi J. Hypothalamic hamartoma and epilepsy in children: illustrative cases of possible evolutios. *Epileptic Disord* 2003; 5: 187-99.

Barkovich AJ, Kuzniecky RI, Jackson GD, *et al.* Classification system for malformations of cortical development: update 2001. *Neurology* 2001; 57: 2168-78.

Bautista JF, Foldvary-Schaefer N, Bingaman WE, *et al.* Focal cortical dysplasia and intractable epilepsy in adults: clinical, EEG, imaging, and surgical features. *Epilepsy Res* 2003; 55: 131-6.

Bronen RA, Spencer DD, Fulbright RK. Cerebrospinal fluid cleft with cortical dimple: MR imaging marker for focal cortical dysgenesis. *Radiology* 2000; 214: 657-63.

Chen RC, Forster FM. Cursive epilepsy and gelastic epilepsy. *Neurology* 1973; 23: 1019-29.

Devous Sr. MD, Thisted RA, Morgan GF, *et al.* SPECT brain imaging in epilepsy: a meta-analysis. *J Nucl Med* 1998; 39: 285-93.

Edwards JC, Wyllie E, Ruggeri PM, *et al.* Seizure outcome after surgery for epilepsy due to malformation of cortical development. *Neurology* 2000; 55: 1110-4.

Gambardella A, Palmini A, Andermann F, *et al.* Usefulness of focal rhythmic discharges on scalp EEG of patients with focal cortical dysplasia and intractable epilepsy. *Electroencephalogr Clin Neurophysiol* 1996; 98: 243-9.

Garcia A, Gutierrez MA, Barrasa J, *et al.* Cryptogenic gelastic epilepsy of frontal lobe origin: a paediatric case report. *Seizure* 2000; 9: 297-300.

Geier S, Bancaud J, Talairach J, *et al.* The seizures of frontal lobe epilepsy. A study of clinical manifestations. *Neurology* 1977; 27: 951-8.

Hirabayashi S, Binnie CD, Janota I, *et al.* Surgical treatment of epilepsy due to cortical dysplasia: clinical and EEG findings. *J Neurol Neurosurg Psychiatry* 1993; 56: 765-70.

Iannetti P, Chessa L, *et al.* Gelastic epilepsy. A clinical contribution. *Clin Pediatr* 1992; 31: 467-70.

Iannetti P, Spalice A, Raucci U, *et al.* Gelastic epilepsy: video-EEG, MRI and SPECT characteristics. *Brain Dev* 1997; 19: 418-21.

Kerrigan JF, Ng YT, Chung S, *et al.* The hypothalamic hamartoma: a model of subcortical epileptogenesis and encephalopathy. *Semin Pediatr Neurol* 2005; 12: 119-31.

Kral T, Clusmann H, Blumcke I, *et al.* Outcome of epilepsy surgery in focal cortical dysplasia. *J Neurol Neurosurg Psychiatry* 2003; 74: 183-8.

Kuruvilla A, Flink R. Focal fast rhythmic epileptiform discharges on scalp EEG in a patient with cortical dysplasia. *Seizure* 2002; 11: 330-4.

Kutsy RL. Focal extratemporal epilepsy: clinical features, EEG patterns, and surgical approach. *J Neurol Sci* 1999; 166: 1-15.

Loiseau P, Cohadon F, Cohadon S. Gelastic epilepsy. A review and report of five cases. *Epilepsia* 1971; 12: 313-23.

McConachie NS, King MD. Gelastic seizures in a child with focal cortical dysplasia of the cingulate gyrus. *Neuroradiology* 1997; 39: 44-5.

Raymond AA, Fish DR, Sisodiya SM, *et al.* Abnormalities of gyration, heterotopias, tuberous sclerosis, focal cortical dysplasia, microdysgenesis, dysembryoplastic neuroepithelieal tumour and dysgenesis of the archicortex in epilepsy: Clinical, EEG, and neuroimaging features in 100 adult patients. *Brain* 1995; 118: 629-60.

Sasaki K, Ohsawa Y, Sasaki M, *et al.* Cerebral cortical dysplasia: assessment by MRI and SPECT. *Pediatr Neurol* 2000; 23: 410-5.

Tassi L, Colombo N, *et al.* Focal cortical dysplasia: neuropathological subtypes, EEG, neuroimaging and surgical outcome. *Brain* 2002; 123: 1719-32.

Taylor DC, Falconer MA, Bruton CJ, *et al.* Focal dysplasia of the cerebral cortex in epilepsy. *J Neurol Neurosurg Psychiatry* 1971; 34: 369-87.