■ Clinical commentary

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Inferior parietal lobule gyrations in refractory epilepsy

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ABSTRACT – Posterior parietal epilepsy can be difficult to identify due to complex clinical presentation and non-localisable electrophysiological findings. The inferior parietal lobule (IPL) exhibits normal gyral variation, and hidden among this are cases of refractory surgically remediable epilepsies. We present a case series of four patients with refractory parietal epilepsy in which IPL gyral variation was associated with dysplasia, confirmed histopathologically in three of the cases. All patients underwent extensive presurgical evaluation including 3T MRI-volumetric T1, FLAIR and T2 SPACE sequences. Awareness is essential as these cases can be easily missed. Interpretation of volumetric brain MRI on sagittal plane is important to identify these cases. With better awareness and understanding of foetal development of the sylvian fissure and operculisation, inferior parietal gyral refractory epilepsies may be more common than currently recognized.

Key words: inferior parietal lobe; gyral variations; refractory epilepsy.

The inferior parietal lobule (IPL) consists of the supramarginal gyrus (SMG) and angular gyrus (AG). Variable gyral morphology of the IPL has been described based on healthy volunteers and brain specimens [1,2]. The IPL can be classified into four different patterns: typical, in which the supramarginal gyrus and angular gyrus are seen behind the post-central sulcus with no additional gyrations; PreSMG with an additional gyrus between the post-central sulcus and the supramarginal gyrus; PreAG with an additional gyrus between the supramarginal gyrus and angular gyrus; and others (PreSMG + Pre, AG, and non-identifiable patterns) [1]. This variability, ranging from normal occurrence to abnormalities that lead to epilepsy, can be overlooked. Here, we report four cases of refractory parietal lobe epilepsy (PLE) associated with these gyral patterns.

Case series

Patient 1 (PreSMG pattern) (*figures 1, 2*)

An 18-year-old, right-handed engineering student was evaluated for refractory epilepsy with onset at 13 years of age. Semiology sequentially consisted of paresthesias of the tongue, a twitching sensation of the lips, palpitations, fear, tinnitus in the right ear, followed by right facial tonic contraction with right upper limb tonic posturing lasting for about 30 seconds. Additionally,

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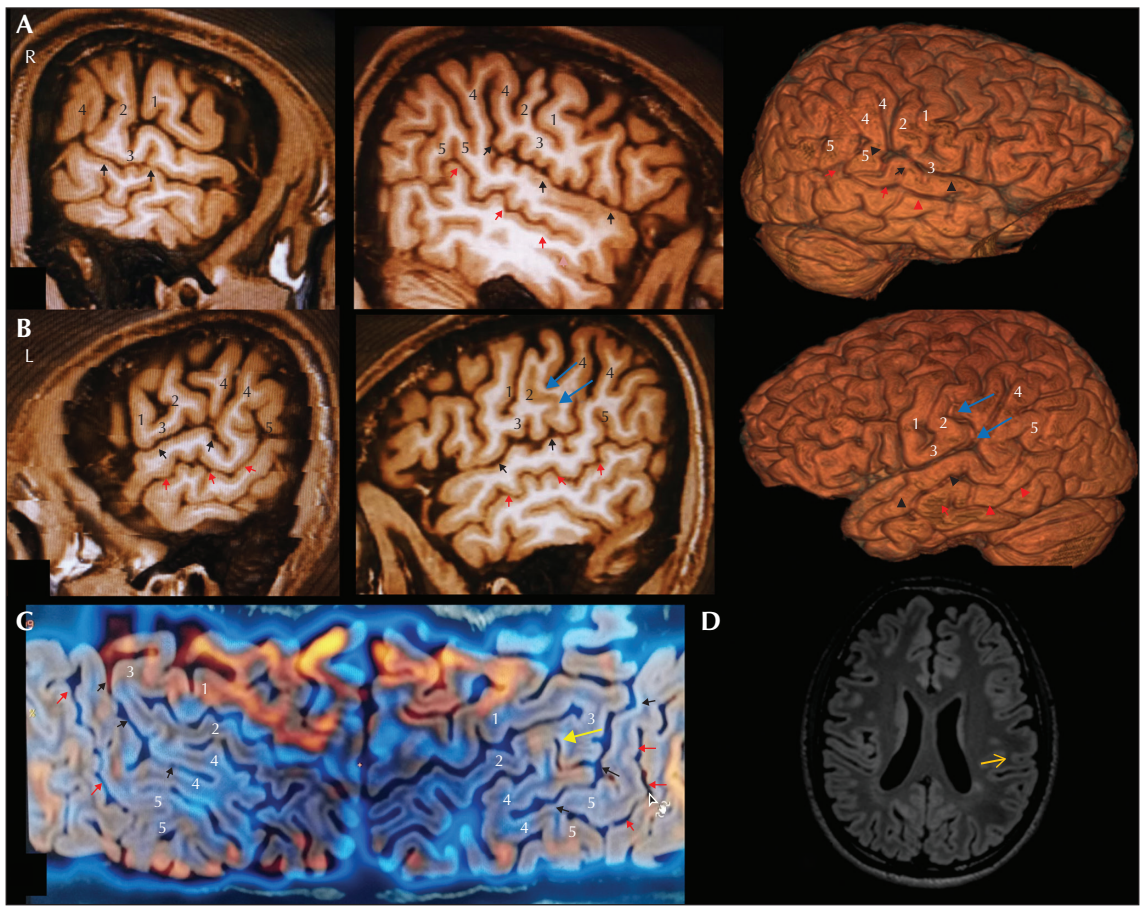
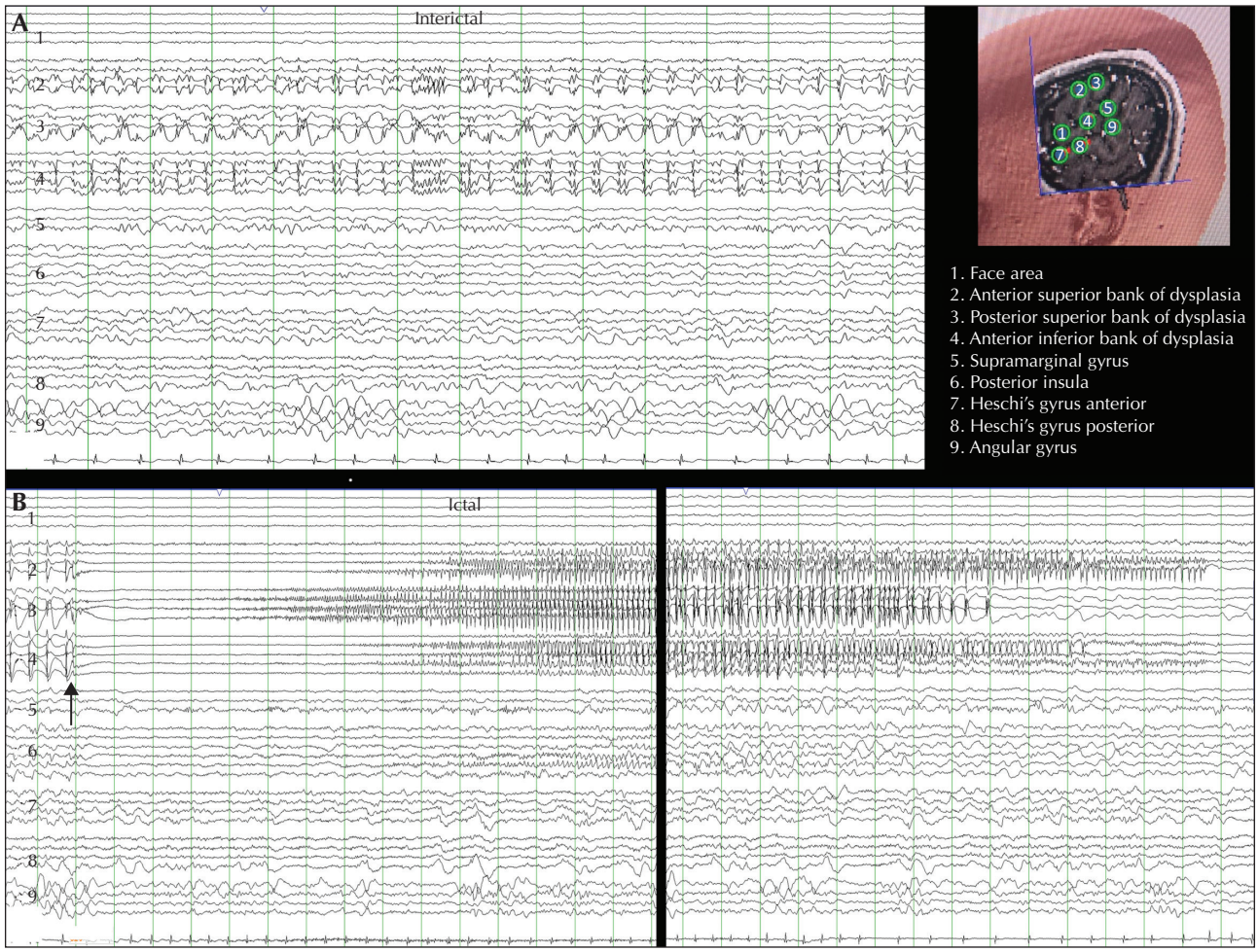
during recorded seizures, clonic jerking of the tongue to the right, eye movements to the right with blinking and head turned downwards and to the right was noted. Postictally, he had no speech disturbance or Todd's paresis. He had multiple daily seizures. The family also reported rare secondary generalized tonic-clonic seizures during non-compliance to medications. EEG showed frequent interictal epileptiform discharges (IEDs) over the left temporal regions (T3). Ictal EEG was lateralizing to the left hemisphere at onset. Neuropsychology showed mild left temporal dysfunction. Brain MRI was reported to be normal. On review, a preSMG gyrus was noted to be hypometabolic on FDG-PET. This was unclear on the axial section, but was best visualized on sagittal sequences. fMRI showed bilateral language representation. The patient underwent SEEG which confirmed the preSMG gyrus as the epileptogenic zone. Habitual seizures could be reproduced with 50-Hz (2-mA) stimulation of the preSMG gyrus. Angular gyrus stimulation produced word finding difficulty and paraphasia, suggesting language localisation (1 Hz-4 mA and 50 Hz-2 mA). The patient underwent awake craniotomy and



■ **Figure 1.** Brain MRI and FDG-PET of Patient 1. (A) Brain MRI of the right hemisphere. (B) Brain MRI of the left hemisphere showing abnormal preSMG (blue arrows) on the left side. (C) MRI and FDG-PET co-registration in a curved surface projection (pancake view) showing hypometabolism in the left sensory motor area and the deep preSMG gyrus (yellow arrow). This gyrus was indistinguishable on axial MRI FLAIR sequences (D, yellow arrow). Annotations: 1=precentral gyrus; 2=postcentral gyrus; 3=subcentral lobule; 4=supramarginal gyrus; 5=angular gyrus; black arrow=sylvian fissure; red arrow=superior temporal sulcus; long yellow arrow=abnormal preSMG sulcus. R: right; L: left.

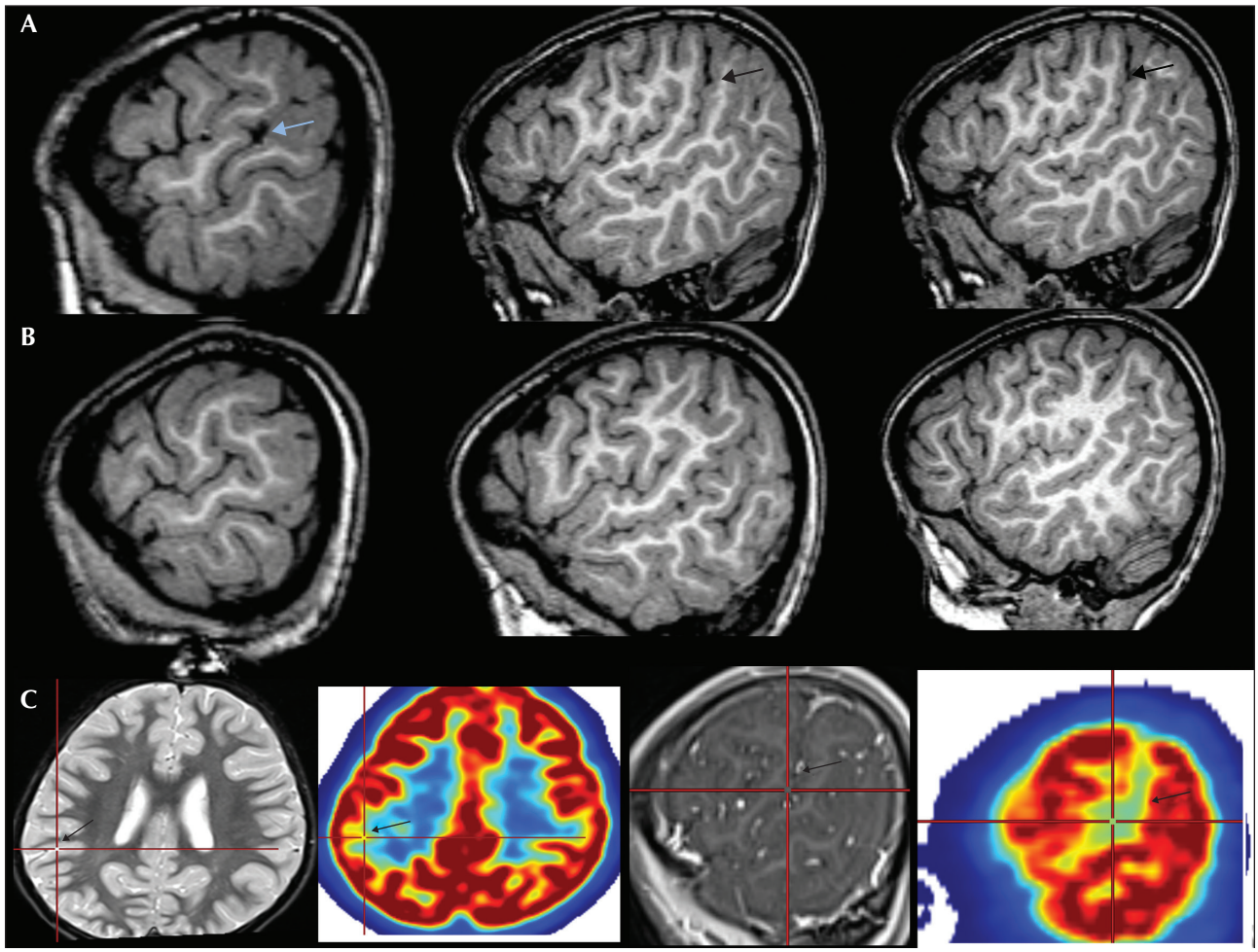


■ **Figure 2.** Stereo-EEG of Patient 1 showing continuous rhythmic discharges from the left preAG gyrus during the interictal tracings (A). Ictal pattern in the same area was noted as low-voltage fast activity (B, arrow). The SEEG plan is shown in the insert.

excision of the abnormal preSMG gyrus. Histopathology was reported as FCD IIa. The patient is seizure-free at 24 months of follow-up (Engel Class 1a) without neurological deficits.

Patient 2 (PreAG pattern) (*figures 3 ,4*)

A four-and-a-half-year-old, right-handed male child was evaluated for refractory daily seizures since three years of age. Semiologically, he occasionally reported aura, would say that he is falling down, and would then have left upper and lower limb tonic posturing with right-sided automatisms, lower limb cycling automatisms, eyes and head deviation downwards and to the right along with eye blinking followed by whole-body turning to either side. He was also noted to have cyanosis, salivation and mydriasis during the events recorded in the epilepsy monitoring unit. Events lasted for about a minute. IEDs were located in right parietal (P4), centro-parietal (C4-P4) and posterior temporal (T6) regions. Ictal EEG showed low-voltage fast activity from the right parietal and posterior temporal regions, many seconds prior to the clinical onset, later evolving into a right hemispheric seizure. Neuropsychology showed adequate social and occupational functioning. Brain MRI was reported to be normal. On review, a preAG gyrus on the right was noted. Interictal FDG-PET showed hypometabolism of the preAG gyrus, posterior insula and superior temporal gyrus. SEEG confirmed the preAG gyrus as the epileptogenic zone. Stimulation studies reproduced

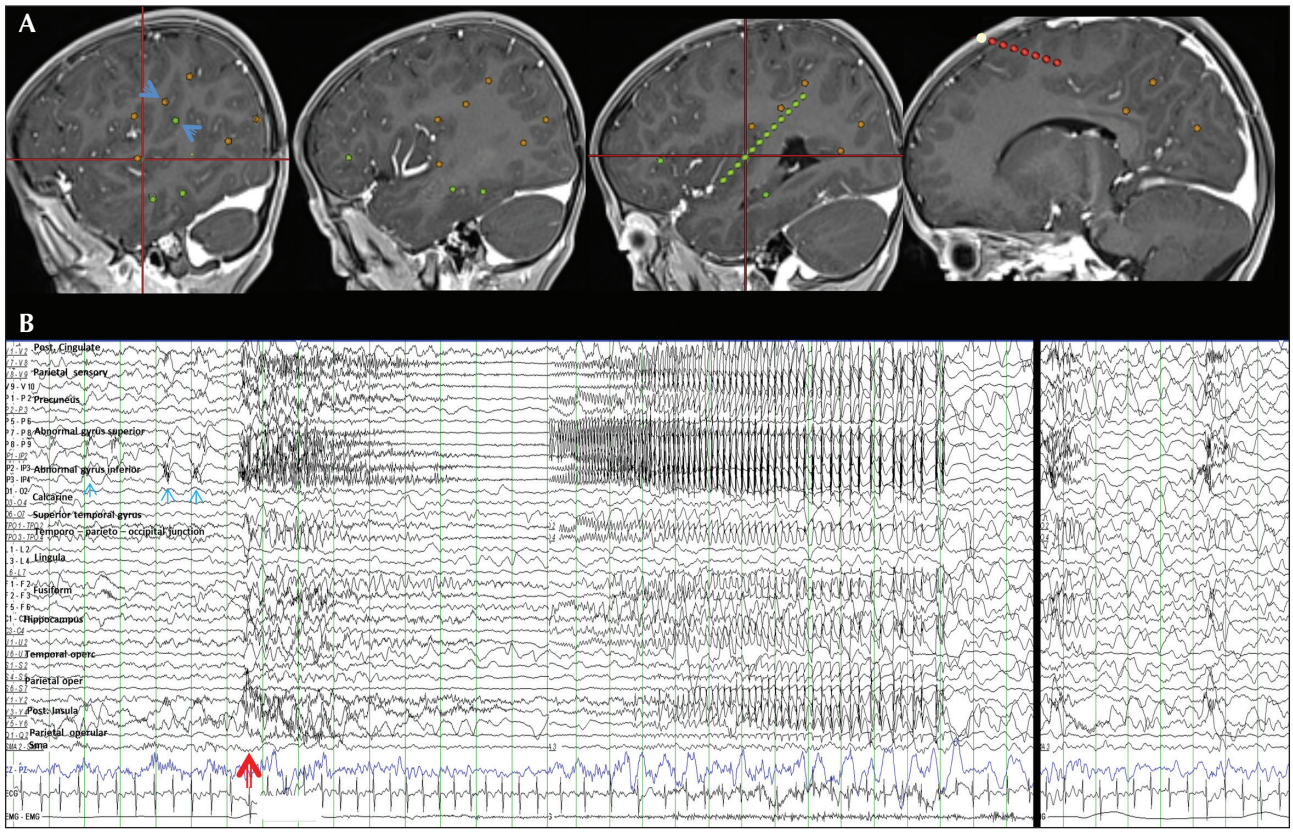


■ **Figure 3.** Imaging of Patient 2 with right hemispheric refractory epilepsy showing abnormal preAG on the right side (A, black arrow) along with a surface cortical dimple (blue arrow) and normal gyration on the left side (B). This preAG on the right showed intense interictal FDG-PET hypometabolism (C).

habitual seizures at 1 Hz with 1 mA. He underwent excision of the PreAG gyrus. Histopathology was reported as FCD IIa. The patient is seizure-free at three years off medications (Engel Class 1a).

Patient 3 (PreAG) (*figure 5*)

A 40-year-old, right-handed male patient was evaluated for refractory epilepsy since nine years of age. Semiologically, he would have intermittent waves of paraesthesias ascending from the right hand upwards to the shoulder, along with weakness of the right hand, and would drop objects held in his right hand. Events last for about 10 to 40 seconds with immediate recovery. If seizures were prolonged, posturing of the right upper limb occurred. During recorded seizures, he also had slow head deviation downwards and to the right with eye blinking, with mild increase in right lower limb tone. These events were often triggered by cold sensation (for example, dipping the right hand in water). No speech disturbance was reported postictally. The patient is currently on four antiepileptic drugs. Video-EEG showed frequent left central-parietal-temporal spikes (C3, P3, and T3-T5, spreading to CZ), with periodic build-up preictally. Ictal EEG showed initial desynchronization over the left hemisphere for a few seconds, followed by evolving fast rhythm over the left parietal-central-temporal regions. Brain MRI was reported to be normal. On review, a preAG on the left side was noted. PET showed hypometabolism

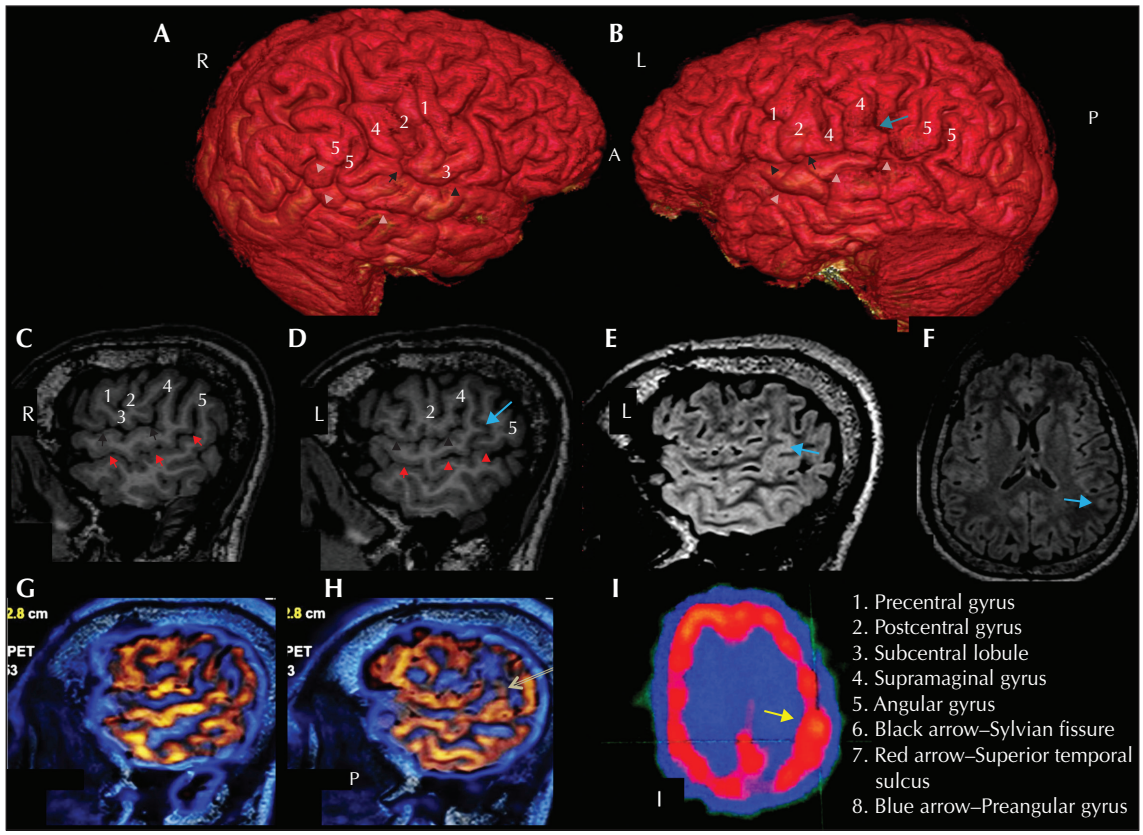


■ **Figure 4.** (A) SEEG of Patient 2 with refractory right hemispheric seizures. (B) Interictal spikes from the right preAG (blue arrows); ictal onset from the right parietal preAG (blue arrow head on SEEG plan) is shown as bursts of high-amplitude fast activity that evolves to low-voltage fast activity (red arrow). (C) Postictally, bursts of polyspikes continued in the right parietal preAG.

of the left preAG gyrus. Early ictal-SPECT (with 10-second injection time) showed hyperperfusion in the left parietal region. Left preAG gyrus epilepsy was concluded. Functional MRI lateralised language to the left. The patient is presently not keen on surgical management and is under follow-up.

Patient 4 (Other patterns) (*figures 6, 7*)

An eight-year-old male child with normal birth and development was evaluated for refractory daily seizures with onset at three years of age. His semiology consisted of vague tingling over the left side of the forehead and left hand, followed by behavioural arrest, asymmetric upper limb tonic posturing, slow head turning downwards and to the right, with frequent eye blinking, lasting for about 10-15 seconds. He would recover immediately. EEG showed continuous right parietal and right parietal-temporal spikes with right parietal-temporal slowing. Multiple right hemispheric seizures lasting about 10 seconds were recorded. Ictal EEG showed initial desynchronization, followed by right parietal-posterior temporal rhythmic activity. Neuropsychology showed above-average IQ and right parietal dysfunction. Brain MRI showed high extension of the posterior ascending ramus of the right sylvian fissure into the supramarginal gyrus with corresponding hypometabolism on FDG-PET. A subtle transmantle sign was noted. He underwent resection of the abnormal gyrus. Intraoperative corticography using grid and depth electrodes recorded seizures arising from the abnormal gyrus starting as low-voltage fast activity. Intraoperative ultrasound identified the gyrus as hyperechoic when compared to neighbouring gyri. The tail was not resected. Histopathology showed type IIb FCD. The patient has had no further seizures.



■ **Figure 5.** Patient 3 with refractory left parietal epilepsy. Brain MRI brain and 3D reconstruction demonstrating normal anatomy on the right side (A, C) and additional preAG on the left side (B, E, blue arrow). This was not clearly definable on axial FLAIR MRI sequence (blue arrow). This preAG gyrus showed hypometabolism on FDG-PET (yellow arrow) (G right, H left). Early SPECT study showed hyperperfusion involving the same area. Annotations: 1=precentral gyrus; 2=postcentral gyrus; 3=subcentral lobule; 4=supramarginal gyrus; 5=angular gyrus; black arrow=sylvian fissure; red/pink arrow=superior temporal sulcus; blue arrow=abnormal preAG gyrus. R: right; L: left.

A summary of the clinical details of the patients is presented in *table 1*.

Discussion

PLE accounts for less than 5% of surgical epilepsy cases. Presurgical assessment of PLE remains challenging. The extensive connections of the parietal lobe add to the clinical and electrophysiological difficulties. Bilateral interictal epileptiform discharges, non-localisable ictal changes, and unclear complex or absent aura are common [3,4,5,6,7,8]. Seizure propagation to the supplementary motor area or temporo-limbic network leads to varied clinical manifestation [9]. MRI is evolving as an important tool to identify PLE [10]. Additional radiological features may aid in the identification of PLE.

The parietal lobe is divided into the postcentral gyrus and posterior parietal lobule. The latter is divided into the superior parietal and inferior parietal lobules. While the superior parietal lobule (SPL) is anatomically more consistent, the IPL has variable anatomy among individuals and between hemispheres [1,2]. IPL is bound anteriorly by the postcentral sulcus, posteriorly by the occipital ramus of the intra-parietal sulcus and superiorly by the intra-parietal sulcus. The supramarginal gyrus is an inverted horse shoe-shaped gyrus, formed over the posterior ascending ramus of the sylvian fissure, and the angular gyrus is an inverted horse shoe-shaped gyrus formed over the posterior portion of the superior temporal sulcus. These two are separated by the sulcus intermedius primus. Four patterns of IPL gyration have been described, as detailed in the introduction. A typical pattern is reported less frequently on the left hemisphere. The PreSMG

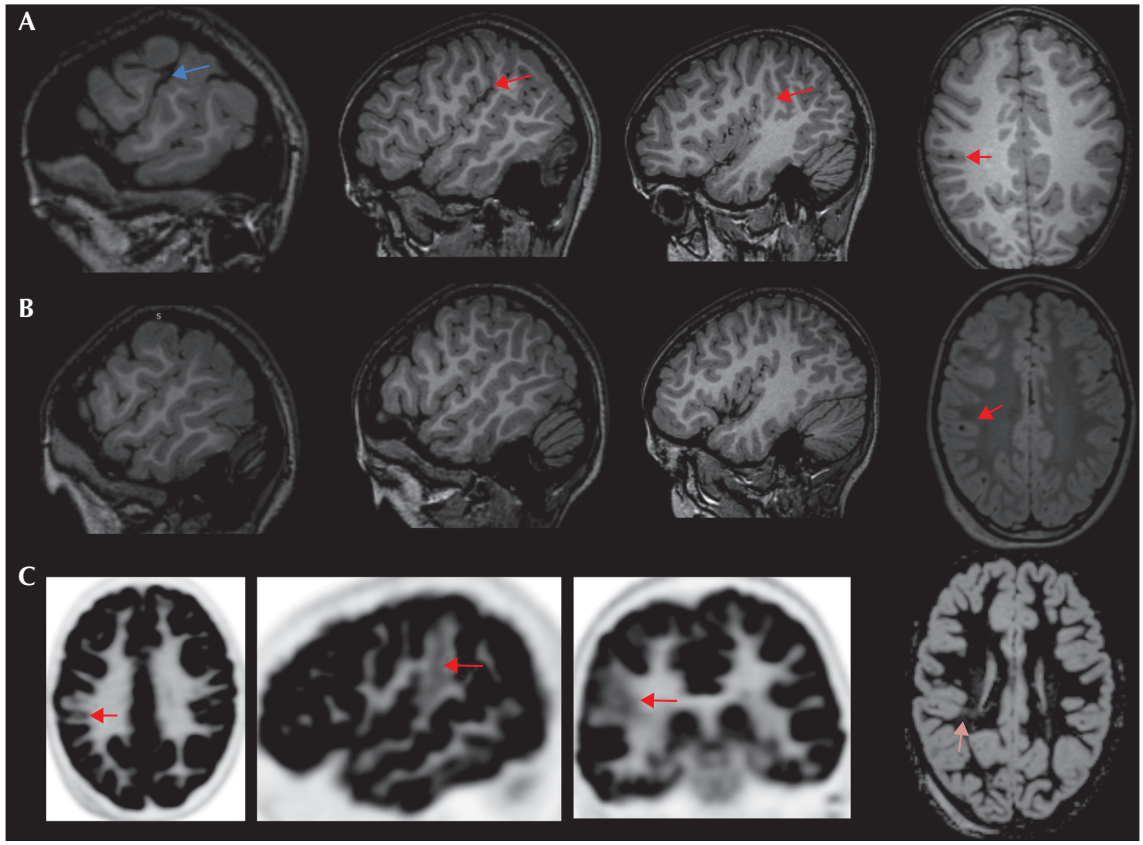
▼ **Table 1.** Details of patients with inferior parietal lobule epilepsy associated with abnormal gyration.

Patient	Age (years)/sex/ handedness	Onset age (years)/ frequency	Semiology	Interictal spikes	VEEG-ictal	MRI	Hypometabolism on PET /other tests	SEEG	Histopathology/ outcome
1 (***figures 1,2***)	18/male/R	13 years/ daily seizures-rare secondary GTCS	Tongue/ lip paresthesia, palpitations, fear, tinnitus in R ear, R facial tonic contraction and R upper limb tonic posturing. Duration ~ 30 seconds.	T3 spikes (low-amplitude, frequent)	Early L hemisphere changes, no clear localisation subsequently	L PreSMG gyrus	L sensori-motor strip and preSMG gyrus	Frequent spikes and polyspikes from preSMG. Ictal-LVFA from preSMG. Corroborative stimulation studies (50 Hz)	FCD 2a Engel Class 1A at 2 years
2 (***figures 3,4***)	4 ½/male/R	3 years/daily seizures	Occasional aura as falling from bed, L upper limb and lower limb tonic posturing, R hand automatisms, lower limb cycling automatism, eyes and head deviation to R, whole body turning to R. Cyanosis, salivation and mydriasis in EMU-recorded events. Duration ~ minute.	P4, P4-C4, T6	Low-voltage fast activity form R parietal and posterior temporal regions, many seconds prior to the clinical onset and later evolving as R hemispheric seizure.	R PreAG gyrus	PreAG gyrus/ posterior Insula	Frequent spikes and polyspikes from R PreAG. Ictal bursts of polyspikes and LVFA from R PreAG. Corroborative Stimulation studies (1 Hz/50 Hz)	FCD 2a Class 1A at 4 years

▼ **Table 1.** Details of patients with inferior parietal lobule epilepsy associated with abnormal gyration *(continued)*.

Patient	Age (years)/sex/ handedness	Onset age (years)/ frequency	Semiology	Interictal spikes	VEEG-ictal	MRI	Hypometabolism on PET /other tests	SEEG	Histopathology/ outcome
3 (***figures 5***)	40/male/R	9 years/daily seizures	Intermittent waves of paraesthesia ascending from the R hand upwards to shoulder, along with weakness of the R hand and R hand posturing. Duration ~10 to 40 seconds. Cold temperature-triggered seizures were common.	C3, P3, T3-T5, spreading to Cz (very frequent)	Initial desynchronization over the L hemisphere for a few seconds followed by evolving fast rhythm over the L parietal-central-temporal regions.	L PreAG gyrus	PreAG gyrus	Not done	Under follow-up
4 (***figures 6,7***)	8/male/R	3 years/daily seizures	Tingling over the L side of the forehead and L hand, behavioural arrest, asymmetric upper limb tonic posturing, slow head turn downwards and to the R, frequent eye blinking (L more than R) and drooling. Duration ~ 10-15 seconds.	P4-T6 (very frequent rhythmic spikes)	Initial desynchronization, then R parietal rhythmic theta.	Abnormal posterior ascending ramus of the R sylvian fissure into the SMG. Transmantle sign.	Posterior ascending ramus of the sylian fissure in IPL.	Intraoperative corticography. Spikes and seizures as LVFA from abnormal gyrus.	Operated on recently FCD2b Seizure-free

L: left; R: right.

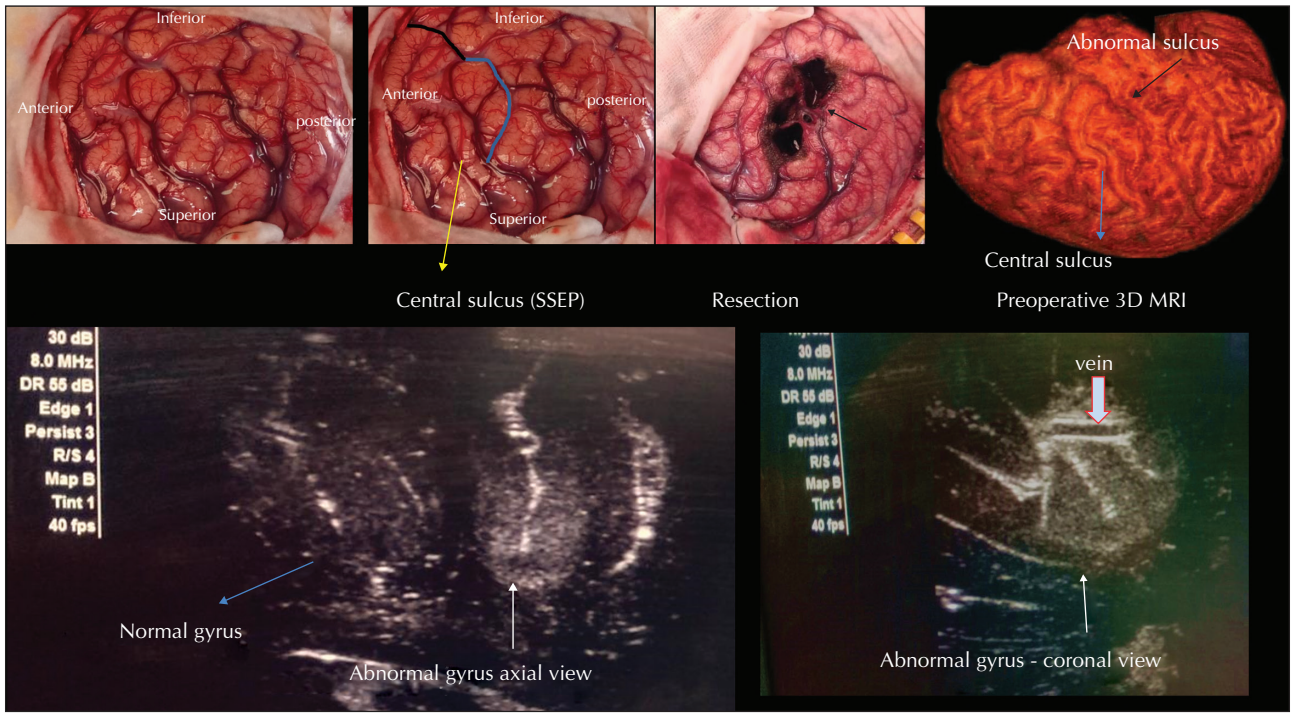


■ **Figure 6.** Brain MRI of Patient 4 showing posterior extension of the right sylvian fissure to form a high supramarginal gyrus on the right side that shows intense hypometabolism on FDG-PET. Blue arrow: cortical dimple at the surface; red arrow: abnormal sulcus; pink arrow: subtle transmantle sign at the bottom of the sulcus. (A) Right sagittal T1 and axial T1 sequence. (B) Left sagittal T1 and axial FLAIR MRI. (C) Brain FDG-PET and T2 SPACE axial sequence.

pattern is more common on the left hemisphere compared to the right, and the preAG is more common on the right side. This variability, ranging from normal occurrence to abnormalities with hidden cortical dysplasia within these gyral patterns leading to epilepsy, can be overlooked.

The complexity of the IPL is related to embryogenesis. During embryogenesis, the sylvian fissure is one of the earliest structures to develop by 14 to 16 weeks and is completed by 33 weeks [11]. Lateral temporal lobe embryogenesis occurs slightly later and the superior temporal sulcus starts appearing by 27-32 weeks and is completed by 33 weeks. Multiple genes are involved in the development of these sulci and operculisation. Abnormal sulcation can be an early indicator of migrational disorder on foetal ultrasound [13, 14, 15]. Anomalies of this process may lead to varied effects, from bilateral perisylvinan syndromes to very focal gyral dysplasia or dysgenesis [16].

In our analysed PLE patients, we identified four patients with abnormal gyration patterns. Patient 1 had a left preSMG pattern, Patient 2 had a right preAG pattern, and Patient 3 had a left preAG pattern. Patient 4 had abnormal extension of the sylvian fissure posteriorly consistent with the dysgenesis pattern reported previously [16]. Clinically, three patients had contralateral sensory aura (one with reflex temperature trigger). One patient had an occasional sensation of fall as aura. Failure to report initial sensory aura complicated the localisation in one patient. All patients had ipsilateral eye and head movement and eye blinking suggesting spread to the SPL or intraparietal sulcus. Prominent tinnitus and amnesia suggested temporolimbic spread in Patient 1. Hypermotor behaviour in Patient 2 suggested frontal spread. All patients had electro-clinical-radiological concordance with regards to localisation. All patients had 3T-MRI including volumetric T1, FLAIR and T2-SPACE and



■ **Figure 7.** Upper panels: intraoperative image of Patient 4 showing abnormal extension of the right sylvian fissure (black line) into the parietal gyrus (blue line) and the resection (arrow). This abnormal gyrus is depicted on preoperative 3D MRI (arrow). Lower panels: intraoperative ultrasound showing this gyrus to be hyperechoic in comparison to the neighbouring gyri.

were initially considered MRI-negative. There was no obvious gyral thickening or distinct abnormal cortical signal changes on MRI that could indicate dysplasia in these cases. During pre-surgical workup of these cases, the clinical, EEG and FDG-PET information suggested a parietal origin of seizures. Review of the imaging subsequently helped us identify these abnormalities. We observed that these gyri of the IPL were oriented in sagittal plane but missed on axial sequences. SEEG and intraoperative electrocorticography confirmed these gyral patterns as epileptogenic in three of our patients. Patient 3 chose medical therapy.

Chassoux et al. demonstrated a high degree of sensitivity and specificity for FDG PET MRI in identifying subtle FCD IIb with improved surgical outcomes [17]. The presence of balloon cells has been attributed to the reduction of FDG uptake despite very high seizure frequency in these patients. We found similar FDG PET findings. All patients had PET hypometabolism that helped us further localize the abnormality. In two of the four patients, the hypometabolism was regional rather than gyral (Patient 1 and 2), and both these patients underwent SEEG that clearly demonstrated electrophysiological abnormalities consistent with FCD. Histopathology showed FCD IIa. Patient 3 and 4 had clear focal gyral hypometabolism. Patient 4 on further 3T SPACE MRI demonstrated the transmantle sign consistent with FCD IIb, that was confirmed on histopathology.

Conclusion

Based on the data presented, we suggest that high-resolution 3D-MRI should be performed and that these patterns should be investigated carefully in the IPL, especially on sagittal plane, in MRI-negative PLE cases. FDG-PET coregistered with brain MRI may further aid in detecting FCD within these gyral patterns. Larger studies on parietal epilepsies should be performed in order to further elucidate their association with these patterns. ■

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None of the authors have any conflict of interest to declare.

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TEST YOURSELF

(1) Parietal lobe epilepsy exhibits the following features:

A. heterogeneous symptoms that are often obvious on propagation to other areas of the brain
B. more than one spike population may be present
C. MRI is the most useful tool for diagnosis
D. all the above

(2) Which of the following is incorrect regarding the inferior parietal lobule:

A. the inferior parietal lobule is anatomically more consistent than the superior parietal lobule
B. the inferior parietal lobule is bound anteriorly by the post-central sulcus, posteriorly by the occipital ramus of the intra-parietal sulcus and superiorly by the intra-parietal sulcus
C. the supramarginal gyrus is formed over the posterior ascending ramus of the sylvian fissure
D. the angular gyrus is formed over the posterior portion of the superior temporal sulcus

(3) Which of the following is correct regarding the inferior parietal lobule:

A. variable anatomy of the inferior parietal lobule is common in healthy subjects
B. inferior parietal lobule epilepsy is often accompanied by somatosensory aura
C. during embryogenesis, the sylvian fissure is one of the earliest features to develop
D. anomalies of development of the sylvian fissure and operculisation may lead to abnormalities that result in epilepsy
E. all the above

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".