



# Neural networks underlying parietal lobe seizures: A quantified study from intracerebral recordings

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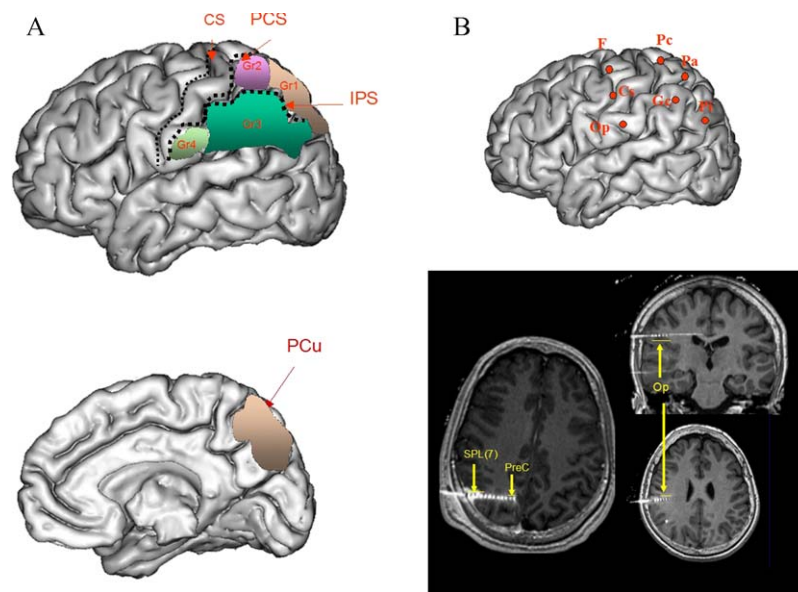
**Summary** In this study we have quantified the “epileptogenicity” of several brain regions in seizures originating in the posterior parietal cortex in 17 patients investigated by intracerebral recordings using stereotactic EEG (SEEG). Epileptogenicity of brain structures was quantified according to the “epileptogenicity index” (EI), a way to quantify rapid discharges at seizure onset. Seven patients had maximal epileptogenicity in the superior parietal lobule-BA area 7 (Gr1), 2 patients in the superior parietal lobule-area 5 (Gr2), 4 patients in inferior parietal lobule (Gr3) and 4 in the opercular region (Gr4). A large majority of patients (15/17 (88%)) reported to have at least one aura during the course of their disease. Somato-sensory manifestations were reported in the four groups. Vestibular disturbance was observed mainly in seizures from the superior parietal lobule (Gr1 and 2). Ipsilateral version was the most frequent objective manifestation (64%). Hyperkinetic behaviour (motor agitation) was found to be frequent, observed in 4/17 cases (23%) and observed in seizures from inferior parietal regions. In conclusion, the electrophysiological organization and the clinical manifestations of PLS are various and complex. The subjective manifestations are frequent and often suggestive, therefore must be actively sought.

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**Abbreviations:** EI, epileptogenicity index; EZ, epileptogenic zone; SEEG, stereoelectroencephalography.

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**Figure 1** (A) Schematic representation of the four subtypes of parietal seizures. CS, central sulcus; IPS, intraparietal sulcus; PCS, postcentral sulcus (see details in the text). (B) *Upper figure*. Example of depth electrode implantation for stereoelectroencephalographic (SEEG) exploration in parietal lobe epilepsy. A lateral view of all depth electrodes superimposed on a 3D reconstruction of the neocortical surface of the brain is shown. In this case, brain structures are explored with seven intracerebral multiple contact electrodes denoted by letters F, Pc, Pa, Pi, Op, Gc, Cs. The electrode F is located in the premotor cortex (Area 6 lateral and SMA in the internal contacts). Electrode Cs is a trans-rolandic electrode recording the pre and post-central sulci. Electrode Pc is located in area 5, electrode Pa in the superior parietal region, electrode Gc reaches the posterior cingulated region (internal contacts) and record the supramarginal gyrus. Electrode Pi record activity from the angular gyrus. *Lower figure*. Reconstruction of the trajectory of the electrodes Op and Pa superimposed on the coronal MRI view. In particular electrode Pa records the lateral part of area 7 (lateral contacts) and the precuneus (internal contacts). CT-scan/MRI data fusion was performed using MEDINRIA software (<http://gforge.inria.fr/projects/medinria>).

## Introduction

The parietal lobe seizures (PLS) are by far the least studied form of partial seizures. In the past only few studies have been dedicated to describe the anatomo-clinical correlations in PLS (Salanova et al., 1995) (Williamson et al., 1992; Ho et al., 1994; Fogarasi et al., 2003; Kim et al., 2004). Despite specific clinical and electrophysiological characteristics that PLS disclose, they are often regrouped with occipital seizures or occipito-temporal seizures into the categories of "posterior cortex" seizures (Blume et al., 1991). The semiology of PLS is often described as misleading as they can often mimic seizures originating from an extra-parietal cortex (Williamson et al., 1992).

Non invasive investigations, and particularly structural and/or metabolic neuroimaging largely contribute to the diagnosis of PLS (Kim et al., 2004). However, in many cases and particularly when MRI is non-contributive or show large lesional areas, studies using depth electrodes are often required. These investigations offer the unique opportunity to precisely study the electrical behaviour of various brain regions during seizure generation and propagation (McGonigal et al., 2007; Gavaret et al., 2009).

In this study we have investigated the role of the parietal cortex in seizure generation in patients having SEEG recordings undergoing pre-surgical evaluation.

The parietal lobe can be subdivided into four parts, the postcentral gyrus, the superior parietal lobule, the inferior parietal lobule and the parietal operculum (Nieuwenhuys et al., 2008).

We have limited the definition of PL seizures to seizures originating from the posterior parietal cortex (PPC), as previously proposed (Salanova et al., 1995). We have also included seizures from the parietal operculum. The PPC correspond to the superior parietal lobule and the inferior parietal lobule, separated by the intraparietal sulcus (Fig. 1a). The superior parietal lobule includes Brodmann area 5 (BA5) anteriorly which forms the somatosensory association cortex. The rest of this region corresponds to Brodmann area 7 (BA7). On the medial side, area 7 extends over the precuneus (PreCu). This area correspond to the superior polymodal parietal cortex, a region largely involved in visuo-motor coordination (Johnson et al., 1993, 1996). The inferior parietal lobule is composed of the angular and supramarginal gyri, corresponding roughly to Brodmann areas 39 and 40 (BA39, BA40). The parietal operculum has been shown to be constituted by four cytoarchitectonic areas (OP1-4) and involved in sensory processing (Eickhoff et al., 2007; Caspers et al., 2008; Naito et al., 2008).

The goal of this study was to determine whether sub-categories of PL seizures could be identified utilising a quantification study technique. We then wished to correlate these subtypes with clinical data.

## Methods

### Patient selection and SEEG recordings

Patients undergoing pre-surgical evaluation of drug-resistant PLE were selected from a series of patients in whom intracerebral recordings had been performed between 2001 and 2008.

All patients had a comprehensive evaluation including detailed history and neurological examination, neuropsychological testing, routine magnetic resonance imaging (MRI), surface electroencephalography (EEG) and stereo-electroencephalography (SEEG, depth electrodes).

SEEG exploration was carried out during long-term video-EEG monitoring. Recordings were performed using intracerebral multiple contact electrodes (10–15 contacts, length: 2 mm, diameter: 0.8 mm, 1.5 mm apart) placed according to Talairach's stereotactic method (Bancaud et al., 1970; Talairach et al., 1992), as illustrated in Fig. 1b.

The anatomical targeting of electrodes was established in each patient according to available non-invasive information and hypotheses about the localization of the epileptogenic zone (for details see previous reports (Bartolomei et al., 2008; Vaugier et al., 2009). CT-scan/MRI data fusion was performed to accurately check the anatomical location of each contact along the electrode trajectory using MEDINRIA software (<http://gforge.inria.fr/projects/medinria>). In selected patients, several distinct functional regions of the parietal lobe were explored. The schematic position of electrodes and the terminology used in our group is indicated in the Fig. 1. However the electrode map may be different from one patient to the other. The explored structures in each patient are indicated in supplemental table\*.

Signals were recorded on a 128 channel Deltamed™ system. They were sampled at 256 Hz or 512 Hz and recorded on a hard disk (16 bits/sample) using no digital filter. A high-pass filter (cut-off frequency equal to 0.16 Hz at –3 dB) was used to remove very slow variations that sometimes contaminate the baseline. Table 1 provides clinical information about the patients selected for the purpose of this study.

### SEEG signal analysis: computation of the epileptogenicity index

The epileptogenicity index (EI) is intended to quantify two important features of SEEG signals when recorded during the transition from pre-ictal to ictal activity: (i) the redistribution of signal energy from lower frequency band (theta, alpha) toward higher frequency band (beta, gamma) and (ii) the delay of appearance of these high-frequency components in a given structure with respect to the first structure, itself involved on a “rapid discharge mode” (Bartolomei et al., 2008; Aubert et al., 2009; Vaugier et al., 2009).

In this respect, the EI is built on the same information as the one that is searched for during visual review of EEG seizure recordings. In practice, we use a semi-automatic approach: using a handy graphical user interface, the user can easily inspect and validate automatically detected change points indicating the accurate onset of

rapid discharges. From this validation performed on a “structure-by-structure” basis, the EI is then computed.

In this section, we provide a short summary about the main features of this index along with the main methodological aspects. The “EI” is a normalized quantity (ranging from 0 to 1) that is computed from SEEG signals. This quantity may be estimated using a two-stage procedure.

- (a) First, over a sliding window, the signal energy ratio ( $ER$ ) is computed, between high ( $\beta$  (12.4–24 Hz) and  $\gamma$  (24–90 Hz)) and low ( $\theta$  (3.4–7.4 Hz) and  $\alpha$  (7.4–12.4 Hz)) frequency bands of the EEG from the signal spectral density  $\Gamma(w)$  (squared modulus of its Fourier transform).
- (b) Second, we detect change-points in the  $ER[n]$  quantity which is sensitive to frequency changes in the signal. In particular, we use an optimal algorithm (“cumulative sum algorithm” or “CUSUM”) to automatically determine the time instant when  $ER[n]$  increases, i.e. when  $\theta - \alpha$  activity (that is predominant in background SEEG signals) changes into  $\beta - \gamma$  activity (that is predominant in SEEG signals during rapid discharges) (see examples in Figs. 3 and 4).

These two steps allow for the computation of the epileptogenicity index  $EI_i$  from the SEEG signal  $s_i$  recorded from brain structure  $S_i$ :

$$EI_i = \frac{1}{N_{d_i} - N_0 + \tau} \sum_{n=N_{d_i}}^{N_{d_i}+H} ER[n], \quad \tau > 0$$

where  $N_0$  is the time instant corresponding to seizure onset (defined hereafter),  $N_{d_i}$  is the detection time in signal  $s_i$  recorded from structure  $S_i$  and  $H$  is the duration over which  $ER[n]$  is integrated. Parameter  $\tau$  accounts for the particular where  $S_i$  is the first structure that generates the fast activity ( $N_{d_i} = N_0$ , seizure onset) and avoids division by zero. It was arbitrarily set to 1. Parameter  $H$  was set to be equal to 5 s as previously defined to detect the onset of rapid discharges (Bartolomei et al., 2008).

Finally, in order to obtain a normalized value ranging from 0 (no epileptogenicity) to 1 (maximal epileptogenicity) for considered structures  $S_i$ ,  $EI_i$  values were divided by the maximal value obtained in each patient. In the sequel, normalized  $EI_i$  values are simply denoted by “EI values”.

In practice, we use a semi-automatic approach: using a handy graphical user interface, the user can easily inspect and validate automatically detected change points indicating the accurate onset of rapid discharges. From this validation performed on a “structure-by-structure” basis, the EI is then computed.

EI were calculated from regions of the parietal cortex shown on the sketch of Fig. 1b: area 5 (electrode placed immediately behind the post-central sulcus, electrode Pc), area 7 lateral (lateral part of electrode Pa), area 7 medial (precuneus, medial leads of electrode PA), inferior parietal region (electrode Gc medially reaching the posterior cingulate region and the supramarginal gyrus, electrode PI exploring the angular gyrus region) and the parietal operculum (electrode Op). Some patients had only a part of these regions explored but the majority of patients ben-

**Table 1** Main clinical features of the 17 studied patients (P1-P17).

	Sex	Age	Age at onset	Aetiology	Side	Aura	LOC	Main objective features	EZ network	Propagation network	Surgery	Engel's Class	FU (years)
P1	M	15	6	PO ischemic sequel	L	Vertigo, visual hallucination (numbers, letters)	Early	Arrest of activity, slow left version of head, clonic jerks right hemibody	Precuneus (left and right), parahippocampal gyrus	Supracalcarinian region, SMA	CI	—	—
P2	F	26	13	Cryptogenic	L	Fall sensation, vertigo, epigastric sensation, sometimes tunnel vision	No	Tonic contraction right arm, balance disturbance	SPL(area 5)	Postcentral rolandic, premotor	Yes	IA	2
P3	F	36	10	FCD precuneus	R	Fear, vertigo, complex visual hallucination (reptile monsters)	Early	arrest of activity, rapid left version of the head, automatisms, vocalization, left hemibody clonic jerks	Precuneus, pCG	Amygdala, SMA	Yes	IA	2
P4	F	30	12	FCD SPL	R	Somato sensory (tingling left arm)	Occasional	Tonic contraction left arm followed by clonic jerks	SPL(area 7 lateral)	Premotor	Yes	III	5
P5	F	34	12	FCD SPL(5)	R	Left arm asomatognosia or deformation	no	Tonic contraction left arm, screaming, painful expression	SPL(area5)	Postcentral rolandic, SMA	Yes	IB	3
P6	M	30	4	Cryptogenic	R	Pleasant vague sensation, respiratory blockage	Early	Tonic elevation of both arms, version of the head on the right	SPL(area 7 lateral)	SPL (area 7), contralateral, SMA	CI	—	—
P7	F	50	14	FDC (IPL)	R	Somatosensory (itching in left arm) feeling of shrinking left arm, autoscopia	Early	Hyperkinetic agitation, slight version of the head on the right, rapid movement of the right arm	IPL (SMG)	SMA, paracentral lobule, MTL	Yes	IA	3

Table 1 (Continued)

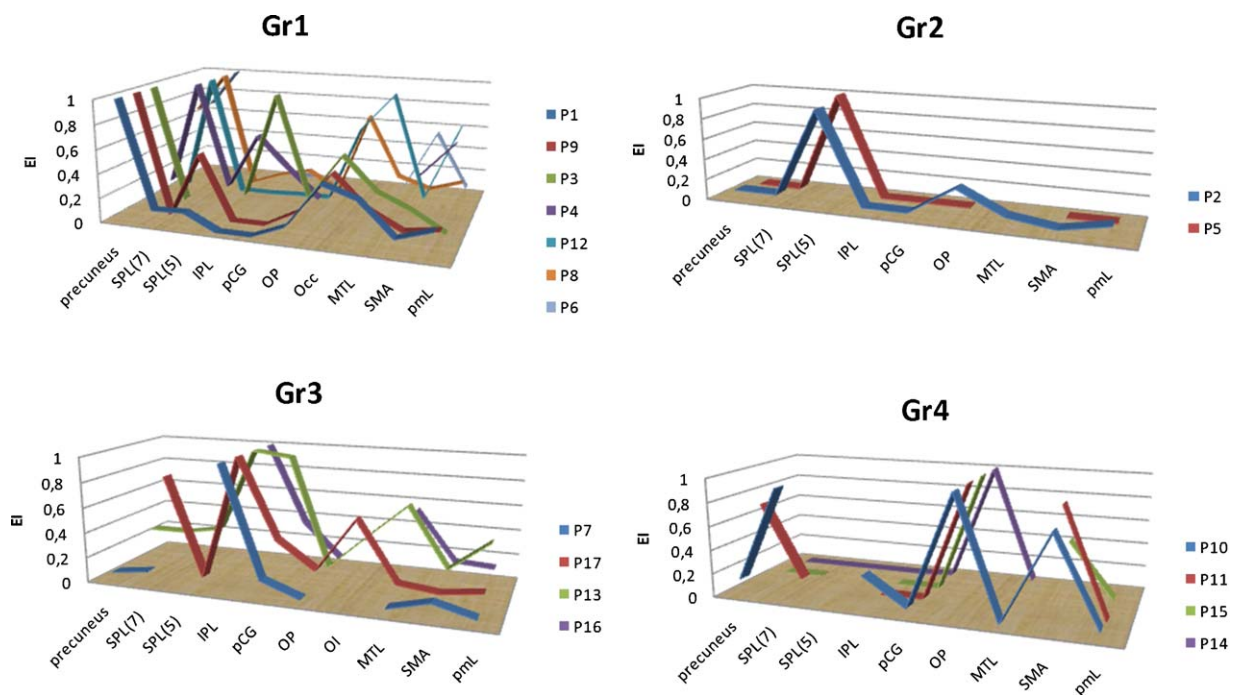
	Sex	Age	Age at onset	Aetiology	Side	Aura	LOC	Main objective features	EZ network	Propagation network	Surgery	Engel's Class	FU (years)
P8	M	38	7	FCD(IPL)	L	Fear, head pressure-like sensation	Early	Bilateral proximal tonic contraction of the arms (max right) bilateral facial contraction, version of the head on the left	IPL(AG)	SPL, PM lateral, Occipital lateral	Yes	IA	1
P9	M	13	6	P ischemic sequel	L	Vertigo, fall sensation, sensation of right ocular movement	Early	Tonic contraction of the right arm, version on the right, screaming	Precuneus	Parahippocampal, SMA	Yes	III	1
P10	F	35	13	FCD (OP)	L	Visual illusion (teleopsia), somatosensory (paresthesia right hemiface and shoulder)	Early	Tonic contraction of right arm, hyperkinetic agitation, version of the head and body on the left	Parietal operculum	SPL (area 7)	Awaiting	—	
P11	F	24	5	Cryptogenic	R	Somatosensory (diffuse paresthesia left arm)	Early	Hyperkinetic violent agitation	Parietal operculum(internal, insula/SII)	SPL(area 7), SMA	Refused	—	
P12	M	30	6	PO ischemic sequel	R	No	Early	Arrest of activity, right slow version on the right, eyelid flutter	IPL(AG, bilateral)	PM6, precuneus	CI	—	
P13	M	25	8	P ischemic sequel	L	Head pressure-like sensation	Early	Slight version of the head on the right, falls down, bilateral tonic clonic, jerks	SPL(area 7 lateral), IPL(SMG)	Lateral temporal, PM	CI	—	

Table 1 (Continued)

	Sex	Age	Age at onset	Aetiology	Side	Aura	LOC	Main objective features	EZ network	Propagation network	Surgery	Engel's Class	FU (years)
P14	M	16	3	DNET (OP)	L	No	Early	Version on the right, hyperkinetic agitation, contraction of the right arm, rapid movements of the left arm	Parietal operculum	Frontal operculum, SMA	Yes	II	1
P15	M	9	2	Cryptogenic	R	Paresthesia left hand	Early	hypotonia, salivation, clonic jerk left hemiface	Parietal operculum, insula	SMA	Yes	III	1
P16	M	26	2	FCD (IPL)	R	Fear, auditory illusion (sound distortion)	Early	Arrest of activity, automatisms of the right upper limb, nystagmus	IPL (AG)	PM6, Insula	Yes	I	0.5
P17	M	11	2	FCD (parieto-Temporal)	R	Feeling of general discomfort	Early	Version of the head and body on the right, hyperkinetic agitation, contraction of the left arm, rapid movements of the right arm	IPL (SMG) Parietal operculum	MTL	Awaiting	—	—

LOC, loss of consciousness; DNET, dysembryoplastic neuroepithelial tumour; FCD, focal cortical dysplasia; PO, parieto-occipital; SPL, superior parietal lobule; IPL, inferior parietal lobule; SMA, supplementary motor area; pCG, posterior cingulate gyrus; SMG, supramarginalis gyrus; PM, premotor; OP, parietal operculum; MTL, mesial temporal lobe; Occ, occipital region. Surgical outcome refers to the Engel's classification (NO, not operated; CI, contraindicated; FU, follow up duration >2 years for all patients).





**Figure 2** Different profiles of epileptogenicity according to the four groups of parietal seizures (see comments in the text). The EI values (mean of two seizures) in explored brain regions are indicated for each patient. For example in Gr1, the maximal values are in the precuneus for patient P1, P3 and P9 and in the lateral superior parietal lobule (SPL 7) in the other patients. Abbreviations: SPL(7), superior parietal lobule (BA area 7); SPL(5), superior parietal lobule (BA area 5); IPL, inferior parietal lobule; pCG, posterior cingulate gyrus; OP, parietal operculum; MTL, mesial temporal region; Occ, occipital cortex; SMA: supplementary motor area; pml, lateral premotor cortex (BA area 6).

efited from complete exploration of parietal subregions. Extra-parietal cortices were investigated in the majority of patients, including premotor cortex/SMA region, the occipital region or the temporal lobe. The two first spontaneous seizures recorded during video-SEEG monitoring were studied. [Supplemental table\\*](#) provides a list of the different explored structures along with corresponding EI values.

### Statistical analysis

A link between epilepsy duration and the number of brain areas disclosing high values of EI ( $\geq 0.4$ ) was investigated using non parametric Spearman correlation. A  $p$  value  $\leq 0.5$  was considered significant.

### Results

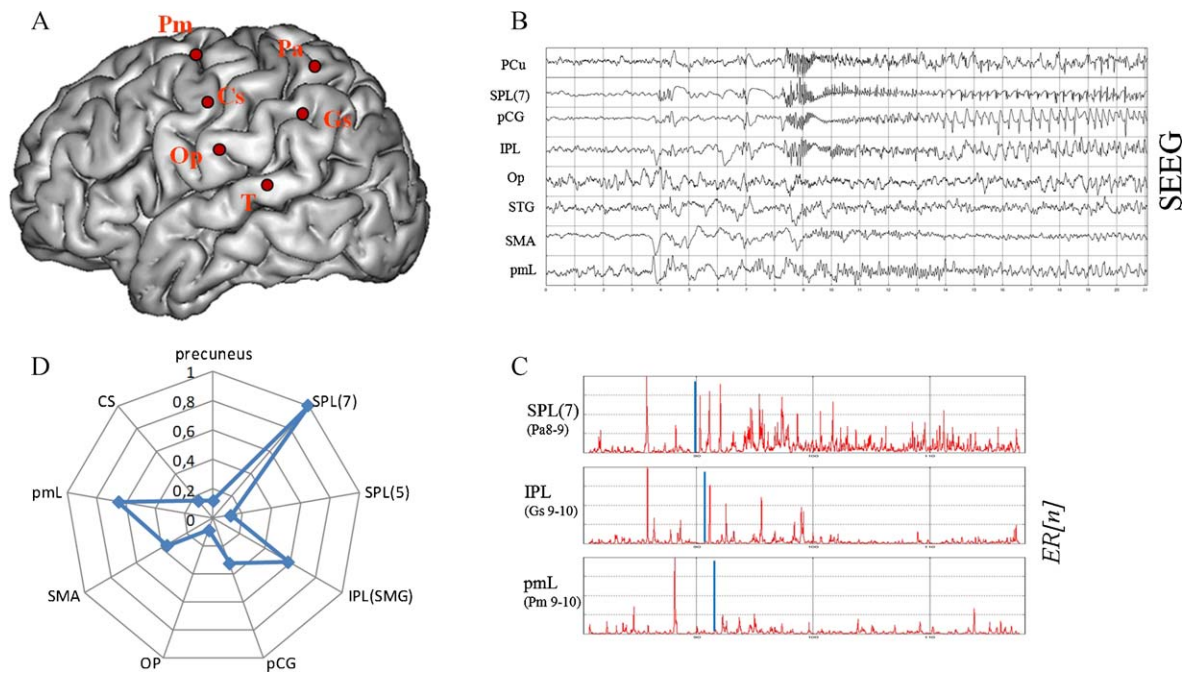
Among 170 consecutive SEEG procedures performed in our department, 17 patients were chosen on the basis of prominent involvement of parietal cortex at seizure onset. Visual analysis was further complemented by quantification of EEG signals changes at seizure onset (see below). [Table 1](#) summarizes the clinical characteristics of the 17 included patients. They were 7 females and 10 men. Age at SEEG ranged from 9 to 50 (mean 26). MRI disclosed features suggestive of focal cortical dysplasia in 8 cases, prenatal stroke in 4, neurodevelopmental tumours in 1 and was normal in 4. The EZ was localized in the left hemisphere in 7 and the right in ten. Ten patients had undergone surgery at the time of the manuscript's writing. Satisfactory results (Engel class I and II) were observed in 6 patients (60%). Surgery was contraindicated

in 4 patients, due to the extent of the EZ to the contralateral side (3 pts) or to a language related area (1 pt). One patient refused surgery and two currently wait for surgery.

### Subtypes of PLE networks

EI values from different explored brain structures were computed (and averaged from 2 seizures) in each patient (indicated in [supplemental table\\*](#)). The mean number of structures in which EI was determined in each patient was 8.3 (range 5–12). According to the inclusion criteria, most of the patients had maximal values in the parietal lobe. It is noteworthy however that high EI could be observed at distant sites, in particular in the occipital region, the premotor cortex or the temporal lobe.

According to the maximal value of EI, we have separated the patients into four subgroups. The first group included 7 patients with maximal values (EI=1) in area BA7 within the superior parietal lobule (Gr1). In this group, epileptogenicity was maximal either in the precuneus (3 cases) or in the lateral part of the superior parietal lobule (4 cases). Interestingly in this group relative low values were observed in the inferior parietal lobule, showing that epileptogenic networks are involved differentially within these two parietal subregions ([Fig. 2](#)). Most of the patients in this group disclosed relative high epileptogenicity in distant cortices, showing the more complex organization of epileptogenic networks among the four proposed groups. The mean number of structures disclosing EI  $> 0.4$  was  $3 (\pm 0.5)$ .



**Figure 3** Figure illustrates one patient from group 1 (SPL7). (A) SEEG implantation scheme. Electrodes explore the premotor cortex (Pm, exploring SMA on the internal contact and premotor lateral cortex on the lateral contacts), the central sulcus (Cs), the opercular parietal cortex (Op), the inferior parietal lobule (Gs, internal contact in posterior cingulated gyrus), the superior temporal gyrus (T) and the superior parietal lobule (Pa exploring the precuneus on its internal contacts). (B) SEEG traces showing rapid discharges prominent in the superior parietal lobule (SPL 7), and also visible over the contact exploring the precuneus, the posterior cingulated gyrus (pCG) and the inferior parietal lobule (IPL). (C) Increase in energy ratio  $ER[n]$  is shown in three SEEG signals from inferior parietal lobule (IPL, contacts Gs 9–10), superior parietal lobule (SPL 7, contacts of electrode Pa 8–9), and premotor cortex (pmL, contacts 9–10, electrode Pm). The Page-Hinkley algorithm provides a detection time Ndi (blue marks) for each brain structure if involved in the generation of a rapid discharge. (D) EI values quoted on web chart demonstrating maximal epileptogenicity in the lateral part of the superior parietal lobule. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

**Fig. 3** illustrates one patient (Pt4) from group 1 in whom analysis demonstrated maximal epileptogenicity in the lateral part of the superior parietal lobule.

A second group included 2 patients with maximal values in area 5 within the superior parietal lobule (Gr2). In these two patients epileptogenicity was confined to this region and tended to involve the region of the central sulcus (electrode Cs **Fig. 1b**, see epileptogenicity profile in **Fig. 2B**). Low values of epileptogenicity were observed in the other explored regions. **Fig. 4** illustrates a patient with epileptogenicity maximal in the BA 5 area. The two other groups involve seizures in which the epileptogenicity is maximal in the inferior parietal regions. The third group included 4 patients with highest values in the IPL (Gr3, **Fig. 3**). Example of such type of epileptogenicity is provided in **Fig. 5A**. The last group includes 4 patients with maximal values in the parietal operculum region (Gp4, **Fig. 3**). An example is shown in **Fig. 5B**.

### Relationship between PLS subtypes and clinical manifestations

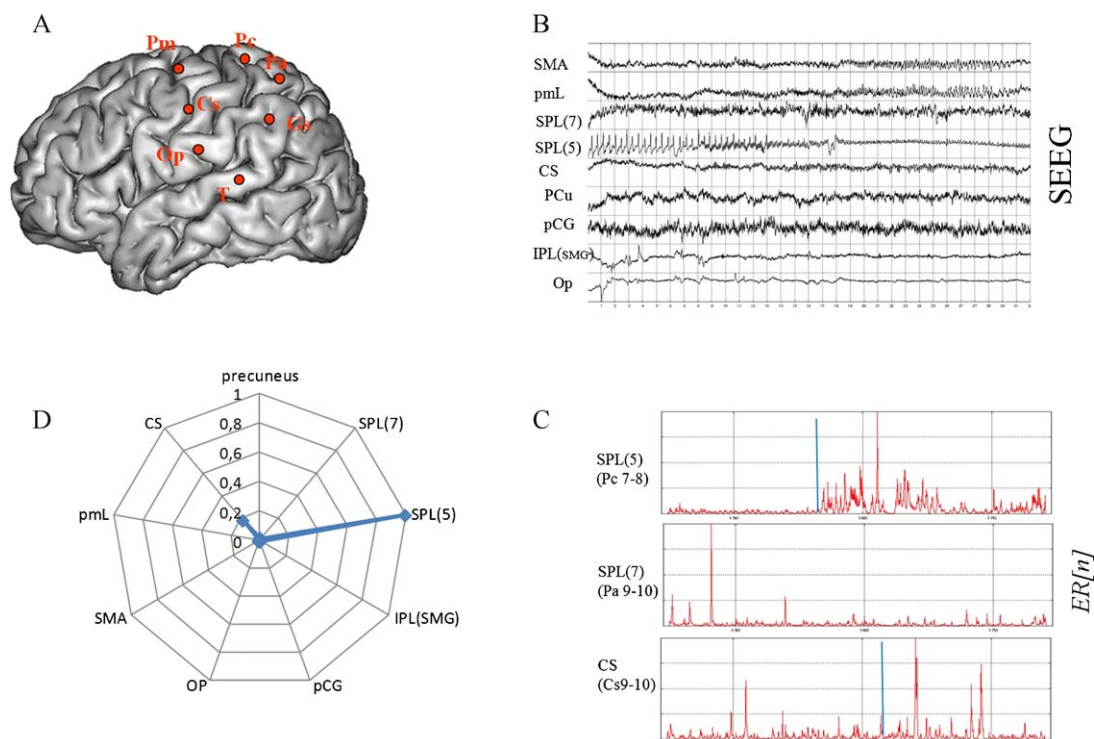
The main subjective manifestations observed in patients are indicated in **Table 2** and main objective symptoms in **Table 3**. A large majority of patients (15/17 (88%)) reported to have

at least one aura during the course of their disease. The most frequent symptoms were somato-sensory aura contralateral to the EZ (35%); vestibular symptoms (loss of balance, vertigo) (23.5%), fear (17%) and complex visual hallucinations (17%) including one case of autoscopy, one case with hallucination of numbers and letters and one case with hallucination of complex scenes. Two patients had visual illusion (tunnel vision, teleopsia) and two had body image alteration (ictal hemiasomatognosia, arm distorsion).

Versive phenomena were the most frequent objective manifestation occurring in 11 cases, (64%). In 7/11 the version of the head and/or eyes was ipsilateral (63%). Tonic postural changes, often asymmetric were observed in 7 cases (63%) of cases. Hyperkinetic manifestations (motor agitation) was found to be frequent, observed in 4/17 cases (23%). A particular pattern associating ipsilateral automatism and contralateral dystonia (Geier et al., 1977) was observed in 3 patients. In these three patients, the clinical manifestations included hyperkinetic behaviour with particular movement of the ipsilateral upper limb mimicking hemiballism (flinging involuntary movements). Early loss of consciousness was obvious in 15/17 cases.

**Fig. 6** shows the different subjective (A) and objective (B) clinical manifestations according to the PLS subtypes. The low number of patients in each group does not allow us to perform statistical comparison. However, it appears





**Figure 4** Figure illustrates one patient (Pt5) from group 2 (SPL 5). (A) SEEG implantation scheme. (B) SEEG traces showing rapid discharges prominent in the superior parietal lobule (SPL 5). (C) Energy ratio  $ER[n]$  is shown in three SEEG signals from superior parietal lobule BA 5 lateral (SPL 5, contacts Pc 7–8), superior parietal lobule BA 7 (SPL 7, contacts of electrode Pa 8–9), and precentral rolandic cortex (CS, contacts Cs 9–10,). Maximal increase and earliest detection is observed in SPL 5. (D) EI values quoted on web chart demonstrating maximal epileptogenicity in the superior parietal lobule 5.

that somato-sensory manifestations were reported in all four groups, particularly frequent in group 4 (operculum group). Fear was unexpectedly found to be a frequent symptom and was observed in 2 cases of seizures from superior parietal cortex (area7, Gr1) and one case from group 3 seizures (IPL). Vestibular disturbance (loss of balance, vertigo) was observed mainly in seizures from superior parietal lobule (Gr1 and 2).

As far as objective manifestations are concerned, the most frequent manifestation was version, and was a prominent feature of superior parietal lobe seizures (area 7, Gr1). Interestingly, hyperkinetic seizures were observed in two cases of group 4 and two cases of group 3 suggesting that this kind of manifestation is related to an epileptogenic zone located in the infero-parietal region.

### Relationship between PLS subtype and other clinical data

Quantification of the regions generating seizures may allow a study of the relationship between the extent of the EZ and the duration of epilepsy, in order to search for a progression of the epileptogenicity in the brain (Bartolomei et al., 2008; Aubert et al., 2009).

We then determined, for each patient, the number of explored brain structures exhibiting  $EI > 0.4$ , a value previously defined as a reliable cut-off value for determining potential epileptogenicity of the structure in extratemporal seizures (Aubert et al., 2009). This number will be

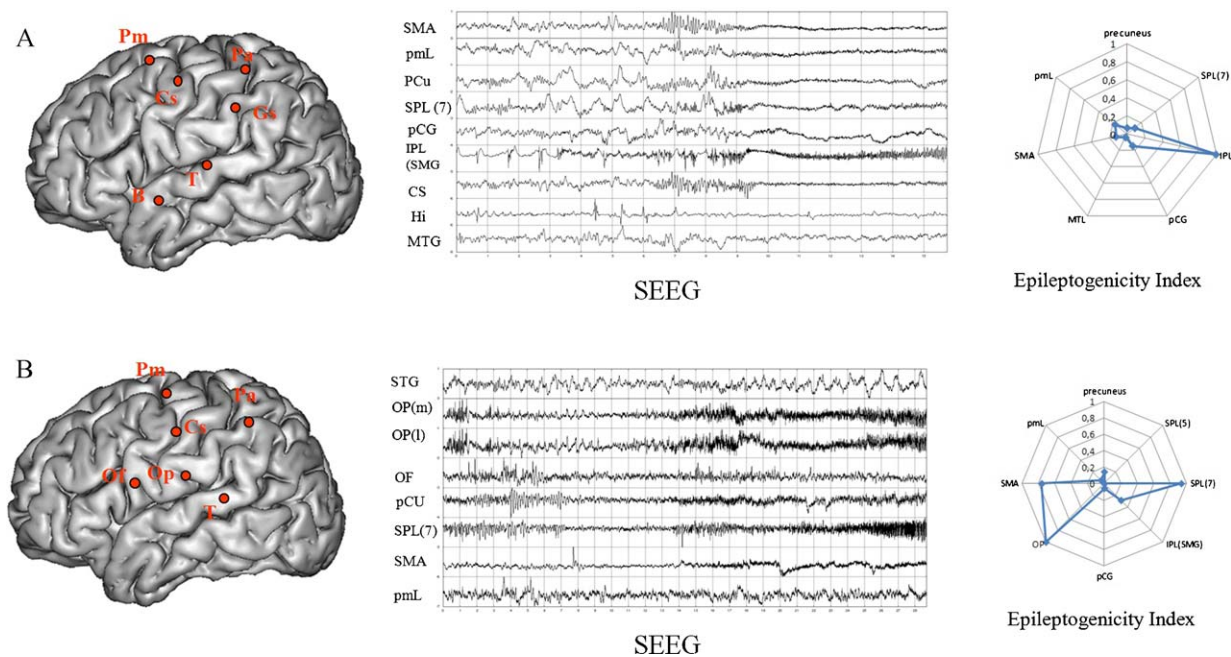
denoted by  $N_{EI \geq 0.4}$ . Given that the total number of structures studied was different from one patient to the other, for each patient we have divided the  $N_{EI \geq 0.4}$  by the number of studied regions. This quantity will be called  $R_{EI \geq 0.4}$ . The mean  $R_{EI \geq 0.4}$  was 0.32, ranging from 0.11 to 0.71.

A non-parametric Spearman correlation found no correlation between age at epilepsy onset and  $R_{EI \geq 0.4}$  ( $p = 0.41$ ) and between duration of epilepsy and  $R_{EI \geq 0.4}$  ( $p = 0.41$ ). In addition, we did not find clear difference between mean  $R_{EI \geq 0.4}$  when considering etiological factors (FCD: 0.26; post-ischemic: 0.36; cryptogenic: 0.34,  $p > 0.05$ ).

## Discussion

### Subtypes of epileptogenic networks in PLS

We found that neural networks involved in seizure generation in parietal lobe epilepsies follow several distinct organizations. In this paper we have restricted our analysis to patients with well-defined PL seizures according to accurately recorded SEEG signals. The main objective of this study was thus to quantify the brain structures involved in the generation of PL seizures, complementing visual interpretation. We have used a method that allows objective assessment of the EZ and characterization of the involved networks based on the "epileptogenicity index, EI". The index combines two factors in a single quantity: the appearance of beta-gamma oscillations concomitantly with the



**Figure 5** (A) Example of seizure from group 3 (inferior parietal region, IPL, P7). The SEEG implantation scheme, the diagram of epileptogenicity and the SEEG traces are provided. Epileptogenicity is found to be maximal in the IPL region. Abbreviations: for electrodes names and region explored see Figs. 4 and 5. In addition, (B) explores the hippocampus and the temporal neocortex. SMG, supramarginalis gyrus; pCG, posterior cingulate gyrus; HI, hippocampus; MTG, middle temporal gyrus. (B) Example of seizure from group 4 (opercular parietal region, P10). The SEEG implantation scheme, the diagram of epileptogenicity and the SEEG traces are provided. Epileptogenicity is found to be maximal in the opercular region. Abbreviations: for electrodes names and region explored see Figs. 4 and 5. In addition, (B) explores the hippocampus and the temporal neocortex. SMG, supramarginalis gyrus; PCg, posterior cingulated gyrus; HI, hippocampus; MTG, middle temporal gyrus.

attenuation of slower alpha-theta oscillations and the time at which rapid discharges occur.

EI is a new proposed way to quantify the epileptogenicity of explored brain structures: the absence of a rapid discharge and late involvement in the seizure process contributes to a low EI value whereas the presence of a rapid discharge with early involvement produces a high EI value (Bartolomei et al., 2008; Aubert et al., 2009).

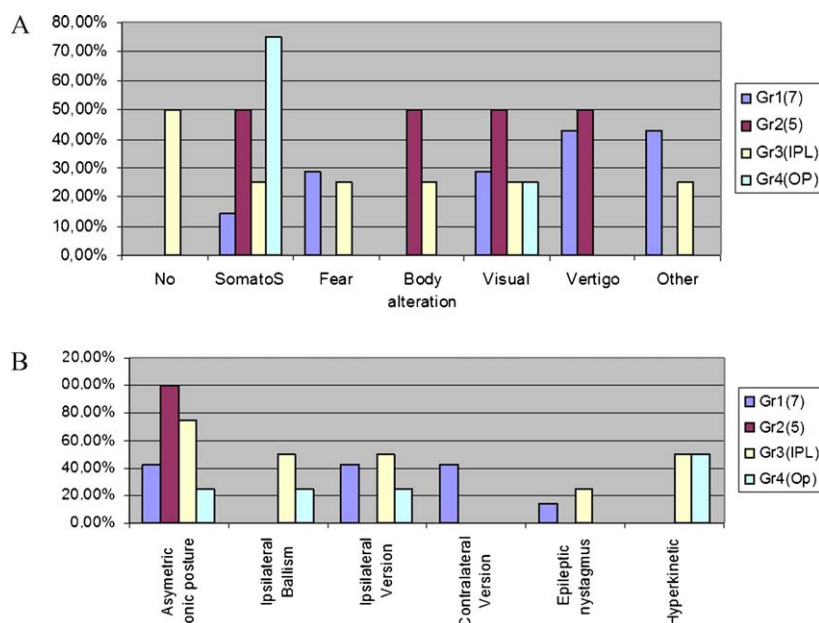
We propose to classify PL seizures into four main subgroups. Two groups were characterized by maximal epileptogenicity in the superior parietal cortex, affecting either a region close to the post-central sulcus (corre-

sponding to area 5, Gr2) or for the majority of patients a region corresponding to the area 7 (medial or lateral, Gr1). Two other groups included patients with the EZ affecting mainly the inferior parietal cortex, either the inferior parietal lobule (Gr3) or the parietal operculum cortex (Gr4).

These subtypes follow different patterns of epileptogenicity. Seizures from group 1 showed more complex networks, often disclosing relative high EI values in occipital, temporal and frontal regions. The complexity of the involved networks may be paralleled with the high level of connectivity of these regions. Monkey studies have revealed large connections between superior parietal cortices and both occipital and premotor cortices (Wise et al., 1997). Using new neuroimaging approaches (tractography) it has been shown that in humans the posterior parietal cortex

Table 2 Main reported subjective manifestations (n= 17 patients).		
	Number of patients	%
Somato-sensory	6	35
Vertigo	4	23.5
Fear	3	17.6
Complex visual hallucination	3	17.6
Body image alteration	2	11.7
Visual illusion	2	11.7
Cephalic tension	2	11.7
Pleasant feeling	1	5.8
Ocular movement	1	5.8
Epigastric sensation	1	5.8

Table 3 Main observed objective manifestations (n= 17 patients). LOC, loss of consciousness.		
	Number of patients	%
LOC	15	88
Tonic phenomenon	9	52
Ipsilateral automatism/ballism	3	17
Version	11	65
Nystagmus	1	5
Hyperkinetic manifestations	4	23



**Figure 6** (A) Subjective symptoms in patients from groups 1–4 PL seizures. No, no reported subjective symptom; SomatoS, somato-sensory. (B) Main objective signs in patients from groups 1–4 PL seizures.

and particularly the precuneus is one of the most connected regions of the brain (Teipel et al., 2009). In monkeys studies, the superior parietal cortex was shown to be reciprocally connected with distant regions including the visual cortex, area 5, and the dorsal part of area 8 containing the frontal eye field (Nieuwenhuys et al., 2008). The superior parietal lobule largely projects to the premotor cortex (area 6 and SMA) (Wise et al., 1997; Leichnetz, 2001). In addition, monkey and human studies have revealed that the intraparietal sulcus is a highly functional region particularly involved in visuomotor function and in oculomotor control (Andersen and Buneo, 2002; Connolly et al., 2003; Grefkes and Fink, 2005; Andersen and Cui, 2009). In contrast, the two patients with seizures starting from area 5 disclosed more restricted epileptogenicity with a profile of epileptogenicity maximal in area 5 and associated with relative high values in the rolandic cortex. This is in line with the large interconnection between primary motor and sensory cortex with area 5 in monkey (Padberg et al., 2005).

Groups 3 and 4 include patients with epileptogenicity mainly affecting the inferior parietal cortices. Group 3 is characterized by epileptogenicity maximal in the inferior parietal lobule while patients in group 4 disclosed maximal values in the parietal-opercular region. In this last group particular high values were observed in the SMA region. The relationship between these two regions is striking and may reflect the privileged connections between these two regions seen in primates (Luppino et al., 1993) and between these regions and the premotor cortex in humans (Rushworth et al., 2006). They also may be an anatomical basis for the prominent motor manifestation (and particularly hyperkinetic features) observed in this group (see below).

In contrast to what we have observed in patients with TLE (Bartolomei et al., 2008; Aubert et al., 2009), we did not observe any relationship between the duration of epilepsy and the extent of the epileptogenicity.

### Clinical subjective manifestations

The reported subjective manifestations agree with previous reports. They were reported by 88% of our patients. In the literature, the incidence of subjective manifestations ranged from 57% to 94% (Williamson et al., 1992; Ho et al., 1994; Salanova et al., 1995; Kim et al., 2004).

Sensory manifestations were found to be the most frequent symptom, observed in the four subgroups of parietal seizures. In the literature the incidence of sensory symptoms ranged from 30% (Williamson et al., 1992; Kim et al., 2004) to 63% (Salanova et al., 1995). They are unilateral, rarely bilateral and contralateral to the EZ. They may reflect the involvement of the secondary sensory areas from area 5 or SII or the extension of the discharge to the primary sensory cortices (Salanova et al., 1995). Vestibular manifestations were reported in 23.5% of the present series and in a significant proportion of patients in previous reports (11% in Salanova et al., 1995). They consisted of various sensations including loss of posture, vertigo, or imminent fall. They probably reflect the involvement of the vestibular cortex (Kahane et al., 2003). However, in contrast to the hypothesis of its localization in the human parietal operculum (Dieterich, 2007) we found this symptom mainly in seizures from the superior parietal region (groups 1 and 2). This is also in agreement with results of direct cortical stimulation applied near the intraparietal sulcus and eliciting vestibular responses in a patient undergoing invasive monitoring (Blanke et al., 2000).

To our knowledge, only one short report has mentioned fear/anxiety as a possible manifestation of parietal seizures (Alemayehu et al., 1995). The role of parietal cortex in fear and emotional regulation is not well known. However, patients with lesions affecting the parietal cortex may have difficulties in fearful face recognition, proving a link between this region and fear physiology (Adolphs, 2002).



## Objective manifestations in PLE

Objective manifestations in PLS reflect the local involvement of systems participating in oculomotor controls and the involvement of more distant cortices, in particular the premotor regions and the temporal lobe. In their seminal paper, Salanova et al. (1995) suggested that seizures from the superior parietal lobule involve preferentially the premotor cortex while the temporal lobe was the site of preferential spreading of seizures from the inferior parietal region. Our experience differs from this assumption. In particular, seizures starting from the opercular region seem particularly prone to involve the SMA region. In contrast, patients with seizures from the superior parietal region disclosed frequently early involvement of the medial temporal region (see profiles in Fig. 3).

Among objective signs, versive phenomena were the most frequent (65%). They were in the majority of cases ipsilateral to the epileptic side. Version in posterior seizures is probably not restricted to one mechanism. They could be related to the involvement of parietal regions involved in oculo-motor control, in particular the intraparietal sulcus where the equivalent of the monkey "parietal eye field" has been found (Grefkes and Fink, 2005). This may explain why version is a frequent phenomenon in seizures affecting regions close to or within the intraparietal sulcus (Gr1 seizures).

A frequent motor manifestation found in these series (23% of patients) is hyperkinetic behaviour. Hyperkinetic seizures (HS) were observed in seizures from the inferior parietal lobule or the parietal operculo-insular region. HS are classical manifestation of frontal lobe seizures (Chauvel et al., 1995) but are also reported in patients with temporo-frontal seizures (Vaugier et al., 2009) and anterior operculo-insular cortex (Ryvlin et al., 2006). It has previously been reported in PLS. Ho et al. (1994) found that 6/14 patients with PLS exhibited hyperkinetic seizures generally preceded by somatosensory aura. As proposed in other hyperkinetic seizures, this behaviour is probably related to the release of innate motor schema from subcortical structures. A particular pattern found in this context is the association of motor agitation with ipsilateral hemiballism and contralateral dystonia.

This pattern is probably close to that described by Geier et al. (1977) in which the ipsilateral manifestations were described as discreet automatism or athetotic movements.

Most of the patients suffered loss of consciousness during seizures, with the exception of the two patients with seizures located in the area 5. This result is not surprising since the associative parietal cortex is involved in the processing of normal consciousness (Dehaene and Naccache, 2001) and abnormal synchrony in brain networks involving the parietal cortex has been proposed to underlie loss of consciousness in temporal lobe seizures (Blumenfeld et al., 2004; Arthuis et al., 2009).

In conclusion, the electrophysiological organization and the clinical manifestations of PLS are various and complex. The subjective manifestations are frequent and often suggestive, therefore must be actively sought during a patient's investigation. Objective signs that often include motor manifestations can be misleading. Hyperkinetic seizure is a

frequent and often underestimated manifestation of these seizures.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.eplepsyres.2010.12.005.

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