Original article

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Subjective signs in premotor epilepsy: confirmation by stereo-electroencephalography

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ABSTRACT – Subjective manifestations inaugurating frontal seizures are less well known than those observed in temporal seizures. We report eleven consecutive patients who underwent surgery for premotor epilepsy. Six of them had focal cortical dysplasia. Ictal symptomatology was analysed to establish electroclinical correlations. The localisation of the epileptogenic zone was assessed by stereoelectroencephalographic studies. Subjective manifestations were described in all cases, more frequently in a sensory rather than an emotional or psychological fashion. Focal seizures limited to subjective features were recorded in two patients. In one, psychological illusions and visual hallucinations were related to the superior frontal sulcus. Another presented isolated paraesthesia in the left arm with the implication of the supplementary motor area. Electrical stimulation of an electrode located in the premotor area evoked isolated subjective manifestations in three other patients. One patient reported sensory manifestations and another, ideational manifestations. Cephalic sensations and emotional manifestations were associated in one case. Subjective manifestations were observed in all patients, and were proved to be related to a discharge restricted to the premotor area in five. These were non-specific signs, but were always the same in a given patient. Spontaneous, isolated sensations and stimulation data tended to be contradictory. This illustrates the complexity of analyzing subjective signs, as well as the complexity of the neuronal networks participating in the propagation of discharges arising in the premotor frontal area.

Key words: frontal epilepsy, premotor area, partial seizures, subjective manifestations, epilepsy surgery, stereo-EEG

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Subjective signs inaugurating frontal lobe seizures are less well known than those observed in temporal seizures. In the literature, the frequency varies from 56% to 90% (Broglin *et al*. 1992, Williamson *et al*. 1992, Laskowitz *et al*. 1995). Studying retrospectively and prospectively two groups of patients, Palmini and Gloor found respectively 61% and 49% of those with frontal lobe epilepsies were experiencing auras (Palmini and Gloor 1992). The diversity of reported subjective manifestations is extreme. Clinically, it is generally considered that some of those subjective manifestations do not point to any particular localization, when others have a more or less precise localizing value (Broglin *et al*. 1992). For instance, psychointellec-

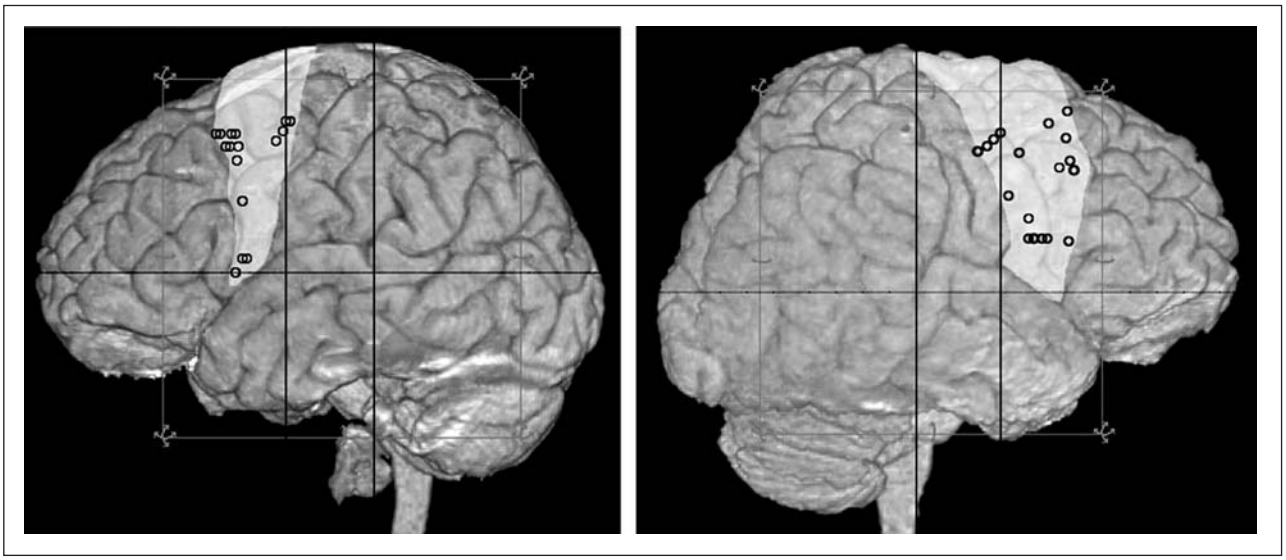

Figure 1. Position of the implanted electrodes in the premotor areas in the 11 patients. **A**) Left side. **B**) Right side. In white: premotor areas. Vertical lines figure AC (anterior commissure) and PC (posterior commissure).

tual auras and in particular forced thinking are considered to indicate an onset in the anterior frontal associative cortex. The urge to urinate is supposed to indicate an onset in the mediobasal cortex. Additionally, because of the large volume involved and the multiple connections and networks established in cortical and subcortical structures, seizures arising in the frontal lobe vary greatly, complicating classification. The premotor area appears to be one of the most homogeneous. Between 1990 and 2003, we explored by means of intracerebral electrodes, eleven consecutive patients who underwent surgery for premotor epilepsy. We present ictal symptoms, focusing on subjective signs and their possible correlation with electroencephalographic findings.

Patients and methods

Eleven patients presented premotor epilepsy. The premotor region involves areas 6, 8 and 44 as well as the supplementary motor area (SMA) considered to include the anatomic SMA and the pre-SMA. We studied the subjective manifestations observed in these patients, looking for categories which could be classified together. Data collected included past medical history, the history of the epilepsy, a precise description of the seizures (provided by patients and family), results of the interictal clinical observations and the neuropsychological examination, video-electroencephalography, and imaging findings. Stereo-electroencephalography (SEEG) was used to identify the epileptogenic focus, map the lesional and irritative zones, and perform electrical stimulations (Talairach *et al.* 1974, Chauvel *et al* 1992). An epileptologist or a specialized nurse observed the seizure in all patients and performed a complete examination during the post-ictal period. History taking was thus particularly reliable and detailed because it was conducted shortly after the seizure. Patient questioning also provided crucial information for SEEG during focal discharges. Each patient underwent an individualized surgical procedure to resect the epileptogenic zone found in the SMA or pre-SMA, the superior frontal sulcus, or the premotor cortex, and occasionally in the opercular region. The Engel classification was used for outcome (Engel 1987).

Results

Mean age at onset of epilepsy was 6.6 years, and age at the time of the SEEG recording was about 27 years. The neurological examination was normal in all patients. Demographic data are summarized in *table 1*.

Seizures, SEEG localization and imaging findings are described in *table 2*. *Figure 1* shows the position of the electrodes implanted in the premotor areas of the eleven patients. All patients reported subjective signs, from onset of the seizure (for 5 patients) or *a posteriori* (6 patients). They were more generally sensorial (in 6 patients) than intellectual (1 patient), 4 patients having both types. The postoperative outcomes are presented in *table 1*. Pathological studies reported focal cortical dysplasia in six patients.

Results of the search for correlations between the subjective manifestations and SEEG findings are presented in *table 3* for the five patients in whom they were possible. For the six other patients, the subjective features were too short-lasting or reported *a posteriori*, which did not allow

entirely reliable correlations. Isolated subjective signs were recorded in two patients. The first patient (PA) (*figure 2*) experienced psychic illusions, and visual and auditory hallucinations related to a superior frontal sulcus focus. The second patient (BH) (*figure 3*) had paresthesia of the left arm related to a focus in the SMA. In three other patients, electrical stimulations of the premotor area triggered the same isolated subjective manifestations as observed during spontaneous ictus. Sensorial illusions, including an epigastric sensation and an "electrical discharge" in the head and sometimes in the entire body, was observed in one case (CS). A patient (TL) experienced headache-like and emotional sensations, while another reported ideational manifestations (LC).

Discussion

All 11 patients had premotor epilepsy. Ten achieved cure (Engel class I, including three patients with a short follow-up). Cure was not achieved in patient PA, probably due to insufficient resection of the posterior part of the focus on the lateral aspect of the cortectomy. After surgery the subjective part of the seizures disappeared completely, with persistence of the objective features. This patient declined further examinations to prepare for a second operation, but there was no reason to question the localization after the surgical failure. Patient TL experienced recurrence after more than 2.5 years of seizure-free remission. Reviewing her chart, we noted that the cortectomy planned had not been done and that the removal of the dysplasia was not complete. The subjective manifestations of the new seizures, recorded with video-EEG, were similar to those seen preoperatively, but they were of longer duration (more than 20 seconds). She underwent a second cortectomy in July 2004, to remove residual dysplasia and has remained seizure-free since. After a 5-year, seizure-free period, patient LC experienced a few seizures, but only when her treatment dose was tapered. These disappeared completely after increasing the medication; she is now more than five years seizure-free.

Apart from the surgical results, another way of assessing the origin of seizures is to observe objective semiology as described in *table 2*. Objective ictal features are quite well-known and indicate the propagation of the seizure (Broglin *et al.* 1992). Anatomo-electroclinical correlations performed using electrodes implanted in the ictal onset zone and the propagation areas can give reliable data when SEEG is used as described by Talaraich et al. (1974). Moreover, when electrical stimulation of several close contacts evokes the subjective manifestation with a limited afterdischarge or no electrical change, it has a good localizing value.

Ten patients reported sensorial signs, five subjective intellectual manifestations, related to seizures arising in the superior frontal sulcus or the SMA. These manifestations varied. Patient PA reported changes in the environment due to psychic illusions, while patient TL had a scary impression of falling into a void. Another patient, CS, whose primary epileptogenic focus was also in the superior frontal sulcus, did not experience any subjective intellectual manifestations. She did however report somatosensorial manifestations perceived as an electrical discharge with no particular systematization. This manifestation was somewhat like the painful cephalic sensation reported by TL, and the vertiginous sensation reported by CaS. The most frequent auras reported by Palmini and Gloor were cephalic impressions and vertigo. From their paper, it is difficult to implicate the same origin (Palmini and Gloor 1992). For Broglin *et al.* (1992), a cephalic aura has no clear localizing value. Only one patient (LC), whose attacks involved the SMA and the middle frontal gyrus, experienced isolated, intellectual manifestations with no associated sensorial sensations. Three patients (LC, BP, CaS) had ideational manifestations; the epileptogenic focus was in the SMA in all three.

Using SEEG, we were able to identify precise electroclinical correlations in two patients who had spontaneously isolated subjective manifestations. In BH, who had somatosensorial sensations, they were related to an epileptic discharge limited to SMA. PA had visual illusions correlated with trains of polyspikes or polyspike-waves or rapid local discharges at the site of the electrode in the dysplastic zone of the superior frontal sulcus. In three patients electrical stimulations triggered isolated subjective manifestations identical to those occurring during their spontaneous attack. In LC, the ideational manifestations were related to discharges limited to SMA. Electrical stimulation of the superior frontal sulcus triggered epigastric sensations and electrical discharges in CS, was associated with a local spikes afterdischarge while stimulation of the same region produced painful cephalic and emotional manifestations in TL.

Eight of our patients (CS, PA, TL, PD, LC, BP, CaS, BH) had attacks with only subjective manifestations, no objective sign being detectable. For 6 of these patients, dysplasia was proved, for another (PD) dysplasia was probable. This raises the question of whether the nature of the lesion could affect the causal mechanism of local discharges leading to isolated subjective manifestations. Specific continuous rhythmic discharges have been described in dysplastic lesions explored by intra-cerebral electrodes (Palmini *et al.* 1995, Tassi *et al.* 2002), but without any concomitant clinical manifestation. The clinical manifestations may appear at a specific discharge frequency or more probably when the discharges propagate outside the lesion. As such discharges may exist since the early development level, they may have stabilized specific pathways in the surrounding healthy brain during maturation. When some specific frequency of the discharge is adapted, they may trigger conscious sensations from elsewhere in the brain.

Table 1. Demographic data, pathological findings and follow-up.

Patients	Age at onset (years)	Age at SEEG recording (years)	Full scale intellectual quotient	Epilepsy side	Hemispheric dominance[a]	Surgery type	Pathologic findings	Engel classification	Follow-up duration
CS	2.5	28	99	Left	Left	Internal frontal and superior frontal sulcus resection	Focal cortical dysplasia	Id	3 years 5 months
PA	3	41	86	Right	Left	Internal frontal and superior frontal sulcus resection	Focal cortical dysplasia	IV	3 years 11 months
TS	2	23	69	Right	Left	Internal frontal and superior frontal sulcus resection	Focal cortical dysplasia	Ia	3 years 4 months
TL	4	14	102	Left	Left	Internal frontal, superior frontal sulcus and lateral premotor resection	Focal cortical dysplasia	Ia	5 months
LA	2	19	71	Right	Left	PreSMA and lateral premotor resection including operculum	Normal	Ia	3 years
PD	9	38	85	Left	Right[b]	PreSMA and lateral premotor resection including operculum	Normal	Ia	2 years 8 months
LC	8	20	ND	Right	Left	SMA resection	Normal	Ic	10 years 6 months
BP	8	32	ND	Right	Left	SMA resection	Normal	Ia	10 years
CaS	3	40	62	Left	Left	Internal frontal and superior frontal sulcus resection	Focal cortical dysplasia	Ia	9 months
TG	28	33	ND	Right	Left	Lateral premotor and pre SMA resection	Normal	Ia	14 years
BH	3	14	68	Right	Left	SMA resection	Focal cortical dysplasia	Ia	4 months

ND : no data.
[a] Indicated by clinical and electrical stimulation data.
[b] Confirmed by amobarbital testing.

The subjective signs recorded in these patients were variable and localization of the focus was never identical, the clinical and electrical data showing differences. The convergence of all the sensorial regions towards the frontal cortex *via* numerous connections could explain these differences. Fuster (1997) showed in animals that the premotor cortex is directly connected to the neighboring motor cortex and prefrontal area, as well as to the somatosensorial cortex. Auditory and visual projections reach the frontal cortex, and the ventro- and dorsolateral regions of the main sulcus receive projections from the inferior parietal lobule (connections with the polymodal areas); the main sulcus receives projections from the limbic cortex. The posterior parietal cortex projects onto areas 6 and 8 and both the SMA and the pre-SMA.

These inaugural subjective manifestations are short-lived, exceptionally described in detail, and sometimes considered to be too fleeting for analysis, the patient often quickly forgetting them as the attack continues. This situation differs from temporal epilepsy where the initial aura may last longer (Bancaud *et al.* 1991). They are nevertheless suggestive of a frontal origin, even though other

Table 2. Seizure description, SEEG and MRI findings.

Patient	Subjective manifestations	Objective manifestations	Ictal onset zone	Area of fast propagation	MRI findings
CS	Epigastric sensation, electrical sensation in the head, sometimes in the whole body	Tachycardia, impairment of consciousness, inferior limbs movements, right turning of the eyes and head, tonic facial expression, agitation	Posterior area of superior frontal sulcus		Hyperintense left superior frontal sulcus on FLAIR
PA	Sensation of unreality, disorientation, blurred vision, auditory hallucinations	Impairment of consciousness, inferior limbs and head movements, upper limbs flexion	SMA Superior frontal sulcus	Precentral gyrus	Hyperintense right superior frontal sulcus
TS	Left wrist shivering and paresthesia, sometimes in the back	Right turning of the eyes and head, left upper limb tonic postural sign, lower limb extension, impairment of consciousness	External premotor cortex SMA		Hyperintense right superior frontal gyrus spreading to the right precentral region
TL	Cephalic sensations like a weight on the head, dizziness	Systematically puts hands on the head, hypertonia of the right upper limb, lower limbs agitation, impairment of consciousness	Superior frontal sulcus		Hyperintense left superior frontal sulcus on FLAIR
LA	Blurred vision, sometimes discharge in the hands	Right turning of the eyes and head, ocular jerks, left upper limb tonic postural sign, extension of the lower limbs, impairment of consciousness difficult to assess	Superior frontal sulcus PreSMA Opercular region		Normal
PD	Sensation of constriction and paresthesia of the throat and tongue	Oroalimentary automatisms, anarthria, no impairment of consciousness	Opercular region Superior frontal sulcus PreSMA		Hyperintense left preSMA
LC	Feeling of motor and intellectual inhibition	Right turning of the eyes and head, bilateral tonic facial expression, impairment of consciousness	Middle frontal gyrus SMA	Inferior area of postcentral gyrus	Normal (no FLAIR)
BP	Blurred vision, fixed gaze, indefinable sensation in the head	Left turning of the eyes and head, left upper limb tonic postural sign, vocalization, sometimes left trunk rotation, no impairment of consciousness	SMA	Medial frontal cortex Left SMA Opercular region	Normal (no FLAIR)
CaS	Dizziness in the head, visual zoom, difficulties with not fixing something with the eyes	Bilateral tonic facial expression, impairment of consciousness, agitation	Superior frontal sulcus	SMA Anterior cingular gyrus External promotro cortex	Hyperintense left superior frontal sulcus and hyperintense lesion spreading to the ventricule
TG	Blurred vision	Complex ocular movements, impairment of consciousness, vocalization, gestural automatisms	SMA Middle frontal gyrus	Anterior cingular gyrus Supraorbital region	Normal (no FLAIR)
BH	Sensation in the left upper limb	Forward and left propulsion of the head, right turning of the eyes, extension of the left upper limb, impairment of consciousness	SMA	Anterior cingular gyrus External premotor cortex Opercular region	Hyperintense SMA on FLAIR

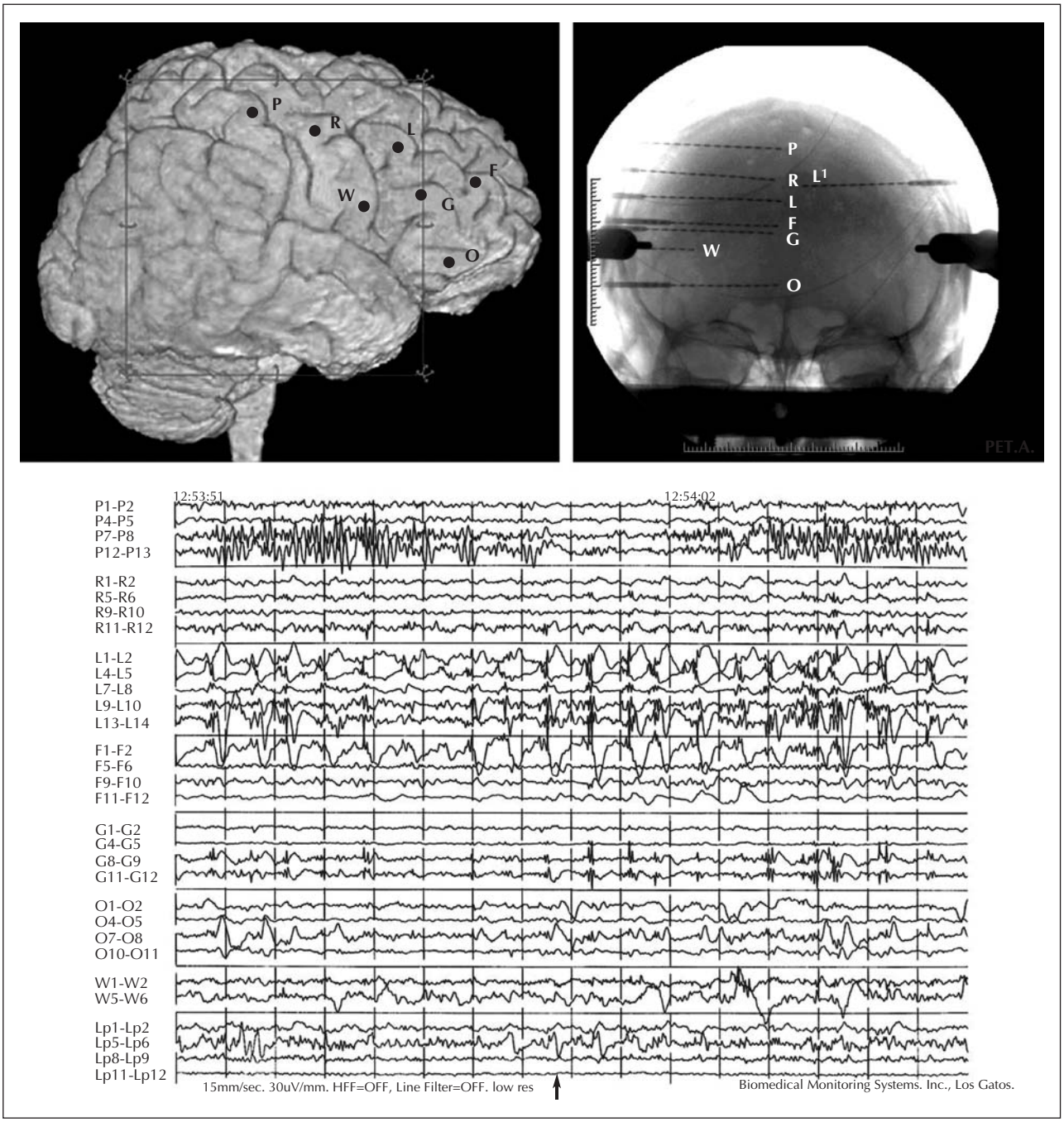

Figure 2. Patient PA. **A**) Position of the implanted electrodes. Top: on right side of surfacic MRI. Bottom: on X-ray front view of the skull. **B**) SEEG recording: psychic illusions, visual and auditory hallucinations with polyspikes and waves discharge on L electrode, maximal on L4-L5 contacts exploring superior frontal sulcus. Arrow points when patient indicates.

localizations can be evoked in certain cases. The epigastric sensation CS described as a "knot" corresponds to an aura frequently reported in temporal epilepsy (French et al. 1993), but without the classical sensation of retrosternal ascension. She did not report any other subjective signs, suggesting involvement of internal temporal structures. Moreover, as the seizure progressed (spreading of the lower limbs and cephalogyric ocular movements followed by uncoordinated agitation) the objective signs were not particularly suggestive of temporal involvement in which automatic or dystonic motor phenomena predominate (Bancaud *et al.* 1991). Likewise, patient PA

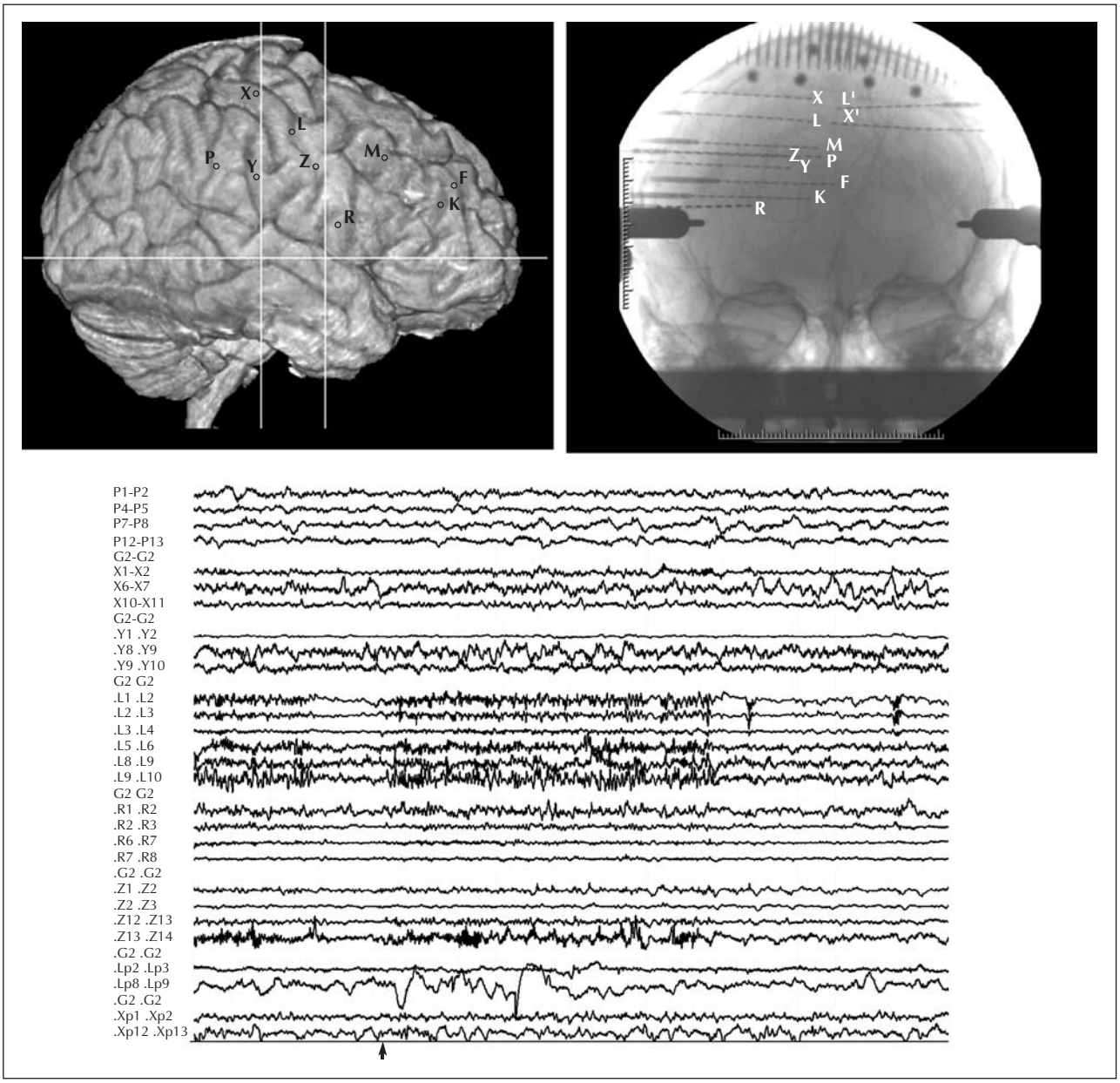

Figure 3. Patient BH. **A**) Position of the implanted electrodes. Top: on right side of surfacic MRI. Bottom: on X-ray front view of the skull. **B**) SEEG recording: paresthesia of the left arm with a discharge on the L electrode, maximal on the L1-L2 contacts exploring the SMA. Arrow points when patient indicates, the discharge began 11 seconds before, as seen on the recording.

reported that the environment seemed to change, with strange objects around her. She did not however have any *déjà-vu* or *déjà-entendu* sensations and there were no associated hallucinations or illusions as can sometimes be observed in the dreamy state arising from the temporal lobe (Bancaud *et al.* 1991). The double-vision sensations reported by LA (area 8 involvement), or the visual haze reported by BP and TG, were difficult to describe and quite different from occipital hallucinations or illusions (Williamson *et al.* 1991, Salanova *et al.* 1992). Sensory changes were widely described in SMA seizures (Morris *et al.* 1988). The sensations were described as pulling, pulsing, heaviness or numbness and tingling. They could have been contralateral or ipsilateral to the epileptogenic zone, and jacksonian march was unusual. As in our patient, the clinical description was clearly different from those given in post-central seizures.

The subjective signs observed in our 11 patients explored by SEEG for premotor epilepsy corresponded to clearly identified, localized cortical foci in five of them. It is

Table 3. Electro-clinical correlations at SEEG.

Patients	Spontaneous, isolated subjective manifestations	Isolated subjective signs evoked by electrical stimulations of electrodes located in EZ
CS		Superior frontal sulcus
PA	Superior frontal sulcus	
TL		Superior frontal sulcus
LC		SMA
BH	SMA	

EZ: epileptogenic zone.

important to identify these manifestations during or immediately after the seizure since they are short-lived, quite difficult to describe and isolate from other critical signs. They are an expression of the participation of polymodal areas. Subjective signs, which can be the only detectable manifestations, sometimes last a few seconds, are shorter than those observed in temporal auras. These non-specific signs are always the same in a given patient. It is tempting to associate the somesthesic sensations with the SMA, and the psychic impressions with the superior frontal sulcus. Nevertheless, this type of dichotomy was apparent in only 2 patients with spontaneous isolated sensations. Furthermore the stimulation data did not confirm this hypothesis. This illustrates the difficulty in analyzing subjective signs and the need for further study in a larger group of patients, as well as the complexity of the neuronal networks participating in the propagation of discharges arising in the premotor frontal area. □

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