Brain (2000), **123,** 1733–1751

Stereoelectroencephalography in focal cortical dysplasia

A 3D approach to delineating the dysplastic cortex

Francine Chassoux,[1] Bertrand Devaux,[1] Elisabeth Landré,[1] Baris Turak,[1] François Nataf,[1] Pascale Varlet,[2] Jean-Paul Chodkiewicz[1] and Catherine Daumas-Duport[2]

[1]*Department of Neurosurgery, Centre Hospitalier Sainte-Anne and* [2]*Department of Neuropathology, Centre Hospitalier Sainte-Anne, Paris, France*

Correspondence to: Francine Chassoux, MD, Service de Neurochirurgie, Centre Hospitalier Sainte-Anne, 1, rue Cabanis, 75014 Paris, France
E-mail: chassoux@chsa.broca.inserm.fr

Summary

Focal cortical dysplasia (FCD) is an increasingly recognized cause of intractable epilepsy. Surgical data suggest that the dysplastic cortex should be removed to obtain freedom from seizures, but the prognosis remains poor as FCD is difficult to delineate by imaging. We retrospectively analysed a series of 28 patients (aged 5–41 years, median 16.5 years) with FCD who had been investigated by stereoelectroencephalography (SEEG) between 1964 and 1995. Neurophysiological data were correlated with histological findings and surgical outcome. MRI was available for only seven patients. Severe partial epilepsy of early onset, pre-existing neurological deficit (68%) and cognitive impairment were the main clinical features. FCD was distributed equally between all lobes except for the temporal lobe, and was found predominantly on the mesial aspect of the cerebral hemispheres. SEEG findings provided evidence of dysplastic tissue epileptogenicity, as demonstrated by intralesional rhythmic spike discharges, the onset of ictal discharges and a low epileptogenic threshold. The epileptogenic zone corresponded to histologically defined FCD in 82% of the cases. Despite the lack of adequate neuroimaging in most cases, 64% of the patients became seizure-free after surgery. The main predictors of a favourable outcome were complete removal of the epileptogenic zone ($P < 0.01$) and complete removal of the dysplastic cortex ($P < 0.01$). These results emphasize the usefulness of neurophysiological data in accurately assessing the extent of the FCD.

Keywords: cortical dysgenesis; epilepsy surgery; EEG; intracranial recordings; neuropathology

Abbreviations: EZ = epileptogenic zone; FCD = focal cortical dysplasia; IZ = irritative zone; LZ = lesional zone; RSD = rhythmic spike discharge; SEEG = stereoelectroencephalography

Introduction

Focal cortical dysplasia (FCD) is increasingly recognized as a cause of intractable epilepsy of early onset (Palmini *et al.*, 1991*a*; Hirabayashi *et al.*, 1993; Polkey, 1996; Wyllie *et al.*, 1998). Although the classification of cortical dysplasia remains under debate, FCD usually refers to the lesion described by Taylor and colleagues, which consists of congregations of large, bizarre neurons that are littered throughout the cortex and are associated in most instances with voluminous glial cells (balloon cells) in the affected cortex and the underlying white matter (Taylor *et al.*, 1971). FCD accounts for 3–7.5% of all histological diagnoses in general epilepsy surgery series (Taylor *et al.*, 1971; Robitaille *et al.*, 1992; Hirabayashi *et al.*, 1993; Brännström *et al.*, 1996; Daumas-Duport, 1996) and for 18–26% in paediatric epilepsy surgery series (Polkey, 1996; Wyllie *et al.*, 1998). FCD is detectable by contemporary imaging, particularly with high-resolution MRI (Palmini *et al.*, 1991*c*; Kuzniecky *et al.*, 1995, 1997; Barkovich and Kuzniecky, 1996; Chan *et al.*, 1998). Epilepsy usually begins in early childhood, soon proves to be intractable (Chugani *et al.*, 1990; Chugani and Conti, 1996; Wyllie *et al.*, 1996) and may be associated with developmental delay and focal neurological deficits (Guerrini *et al.*, 1996).

Focal surgical resection may relieve the patients of their seizures, but the prognosis remains poor when compared with that of patients undergoing resective surgery for other types of lesion (Palmini *et al.*, 1991*b*; Hirabayashi *et al.*, 1993; Raymond *et al.*, 1995*a*; Wyllie *et al.*, 1998). One early report suggested that the extent of dysplastic cortex removal was the determining factor for a favourable outcome

(Palmini *et al.*, 1991*b*). Further studies demonstrated that all of the dysplastic tissue needed to be resected because of intrinsic epileptogenicity (Kuzniecky *et al.*, 1993; Palmini *et al.*, 1995). However, small dysplastic lesions may be hard to detect, even with high-resolution MRI (Duncan, 1997), and lesional boundaries are often difficult to delineate by neuroimaging or on the basis of the macroscopic appearance of the cortex during the surgical procedure (Olivier *et al.*, 1996; Polkey, 1996).

Neurophysiological investigations are usually considered unhelpful in determining the extent of lesions because the epileptogenic area appears larger than the dysplastic cortex (Palmini *et al.*, 1991*a*; Hirabayashi *et al.*, 1993; Kuzniecky *et al.*, 1995). More recently, specific interictal and ictal patterns on electrocorticography have been reported as a means of identifying the dysplastic cortex (Palmini *et al.*, 1995). However, the exact relationship between the extent of the lesion and the epileptogenic zone (EZ) remains unclear.

Stereoelectroencephalography (SEEG) provides a unique opportunity for obtaining direct intralesional recordings and correlating interictal and ictal activity in three-dimensionally orientated areas of the brain. Furthermore, the distribution of the neurophysiological abnormalities can be compared with that of histologically defined FCD in surgical brain samples. However, no reports focusing on cortical dysplasia investigated by SEEG have yet appeared. We analysed the neurophysiological and histological data in a series of 28 patients with FCD. The aim of the study was to assess the epileptogenicity of the dysplastic tissue and of the surrounding cortex, to analyse the interictal and ictal patterns, and to identify the factors influencing the postoperative seizure outcome. Only cases of FCD that conformed to the histological definition of Taylor and colleagues (Taylor *et al.*, 1971) were considered in this study.

Patients and methods

Twenty-eight of the 500 patients with intractable epilepsy undergoing corticectomy at Sainte-Anne Hospital, Paris, between 1964 and 1995 were identified as having FCD. The patient population consisted of 17 females and 11 males. Age at the time of operation ranged from 5 to 41 years (median 16.5 years); 14 patients were children <16 years old. Age at the onset of epilepsy ranged from the first days of life to 11.5 years (median 2.75 years). In eight cases, seizures occurred during the first year of life. The preoperative duration of epilepsy ranged from 3.5 to 38 years (median 12 years).

Presurgical evaluation consisted of an anatomical and electroclinical correlation study, based on the history of epilepsy, interictal and ictal EEG recordings, stereotaxic imaging and SEEG, as previously described by Bancaud (Bancaud, 1980) and Talairach and colleagues (Talairach *et al.*, 1992). The stereotaxic mapping procedure included angiography and, until 1990, ventriculography, which was subsequently replaced by stereotaxic MRI. Most patients were investigated before the era of modern brain imaging. Therefore, only 10 patients had a CT scan and seven had MRI. SEEG was performed in all cases, twice in four patients; in two of these four patients the second SEEG was performed after failure of surgery; in the other two surgery was initially withheld because of functional risks, and a second evaluation was done 6 and 11 years later, respectively, because of catastrophic deterioration. Intracerebral activity was recorded for several hours after the depth electrodes had been positioned, either during a single session (28 cases) or over several days (four cases). Based on SEEG data, the lesional zone (LZ) was defined by the presence of slow waves or depression of activity, the irritative zone (IZ) by interictal spiking and the EZ as the site of subclinical ictal discharges or of the onset of spontaneous, chemically or electrically induced seizures.

Cortical resections were individually tailored according to anatomical and neurophysiological data, including the EZ and ictal spread areas. The operation was guided by a diagram using the AC–PC stereotaxic landmarks defined by Talairach and Tournoux (Talairach and Tournoux, 1988, 1993). Cortical samples were fixed in formalin and paraffin sections were made. The whole corticectomy specimen was examined histologically in 22 cases; microscopic examination was limited to macroscopic cortical abnormalities in six cases.

The localization and assessment of the extent of FCD were based on histological findings in the cortical samples and compared with imaging data when available, as well as on the intra-operative findings. FCD was defined as limited if its volume was less than one-third of a lobe, as lobar when greater than one-third of but confined to one lobe, and as multilobar if it extended over more than one lobe. The extent of cortical resection was classified using the same criteria. The central area, defined as the paracentral lobule, the pre- and postcentral gyri and the corresponding part of the operculum, was considered as a separate lobe. The cortical specimens were labelled according to the anatomical location of intracranial electrodes; this allowed the establishment of a precise correlation between neurophysiological data (LZ, IZ, EZ) and the histological abnormalities in each cortical sample examined. Abnormal intracerebral activity was considered as co-localized with FCD when it was confined to lesional areas, as more extended when recorded both in lesional and perilesional or distant areas, as more restricted when recorded in an area smaller than the lesional areas, and as distinct when recorded outside the lesional areas. The EZ was considered as completely removed if the area of ictal discharge onset was totally included in the resection, and as incompletely removed in all other cases. FCD removal was considered complete when no dysplastic cortex was identified on resection borders, incomplete when the surgical limits clearly ran through the pathological zone or if all cortical samples were pathological, and possibly incomplete if the resection margins corresponded to the transitional area between the dysplastic and the non-dysplastic cortex.

Postoperative seizure outcome was evaluated according to

Table 1 *Location and spread of FCD in 28 cases*

Location	Mesial/lateral	Spread	Precise location
Frontal (n = 9)	Mesial (8) Mesial + lateral (1)	Limited (8) Lobar (1)	Frontopolar (1) Orbitocingular (1) Anterior cingular gyrus (3) Prefrontal–premotor (3) SMA (1)
Frontocentral (n = 1)	Mesial + lateral (1)	Multilobar (1)	All frontal and central areas
Central (n = 6)	Mesial 5 Lateral 1	Limited (6)	Paracentral lobule (1) Paracentral lobule + SMA (4) Precentral (1)
Parietal (n = 6)	Mesial (1) Lateral (3) Mesial + lateral (2)	Limited (5) Lobar (1)	Postcentral (3) Area 7 (3)
Occipital (n = 1)	Mesial (1)	Lobar (1)	
Occipito-parietal (n = 2)	Mesial (1)	Multilobar (2)	
Occipito-parieto-temporal (n = 2)	Mesial + lateral (2)	Multilobar (2)	All areas examined
Temporal (n = 1)	Mesial (1)	Limited (1)	Ammon's horn, parahippocampal gyrus, basal temporal cortex

SMA = supplementary motor area.

the classification proposed by Engel and colleagues (Engel *et al.*, 1996). Statistical analysis consisted of the calculation of non-parametric Spearman rank correlation coefficients, which were used to assess the degree of association between pairs of markers, and a logistical regression study to identify the main factors influencing seizure outcome. The threshold of significance was fixed at a probability of 0.05 for all tests.

Results

Location of the cortical dysplasia and histological findings

Table 1 shows that there was an equal distribution of FCD between the various locations except for the temporal lobe, which was affected in only one case. The posterior frontal lobe and the central and postcentral areas were involved in 11 cases (39%). In 18 cases (64.3%), the dysplastic cortex was located on the mesial aspect of the brain. The lateral cortex was involved in four cases (14.3%), and both the mesial and the lateral cortex in six cases (21.4%). FCD was limited in 20 cases, lobar in three and multilobar in five. The extent of FCD was accurately assessed histologically in the 22 cases in which the totality of the corticectomy tissue was examined. Most small FCD (nine out of 20 limited FCDs) were located in the mesial frontal, central and parietal areas, but multilobar FCD was found preferentially in posterior areas (four out of five cases). All cases met FCD criteria of cytomegaly. Both abnormal neurons and balloon cells were found in 24 cases. Balloon cells were lacking in four lobar or multilobar FCDs, three of which were located in the posterior areas and one in the frontocentral area. Two cases exhibited focal calcifications in association with an exuberant astrocytic component, showing a pseudotumoral appearance. In the other parts of the corticectomy specimens, more or less severe secondary parenchymal changes, i.e. gliosis and neuronal loss, were found. In some FCDs of central location, neuronal loss associated with axonal degeneration was particularly marked.

Clinical data

The early childhood onset of epilepsy stood out in our patient population. The earliest onset correlated with posterior localization ($P < 0.01$) and multilobar FCD ($P < 0.01$). The average age at onset was 0.9 years for posterior FCD (neonatal in three of five patients) and 3.27, 3.5, 4 and 7.5 years for frontal, temporal, parietal and central FCD, respectively.

Seizure frequency was one to several per day in 26 cases and several per week in two cases. In 18 cases, clusters were frequent, with 10–80 seizures per day. Epilepsia partialis continua was observed in three cases and status epilepticus in 10 cases. Despite the severity of epilepsy, a transitory seizure-free period lasting >2 years was reported in nine cases. All patients had partial seizures, which were simple in 11 cases, complex in three cases and undetermined in three cases. Secondary generalized seizures were observed in only four patients (rare in three and frequent in one). Fourteen patients had more than one seizure type. Seizure semiology was stereotyped for each patient and was clearly related to the location of FCD (Table 2). Auras were reported in 21 cases. The seven patients who did not report initial subjective manifestations (auras) were all children with severe cognitive disturbances. Sudden and traumatizing falls were observed in 11 patients, all of whom had central, precentral or postcentral FCD.

Neurological deficits were noted in 19 cases (68%). Mild to moderate limb motor or sensory–motor deficits (10 cases), facial paresis (three cases) and bilateral incoordination of the

Table 2 *Seizure semiology according to location of FCD*

	Aura	First signs	Loss of consciousness	Postictal deficit	Duration of seizures
Frontal ($n = 9$)	Fear (3) Autonomous (1) Indefinable (3) Not reported (2)	Frightened face (4) Screaming (4) Sudden agitation (2) Tonic posturing (2) Deviation of head and eyes (2)	8/9 Incomplete/ inconstant (5)	None (6) Brief confusion (2) Motor deficit (1)	20–40 s; 30–90 s if involving anterior cingular gyrus
Central ($n = 6$)	Somatomotor (3) Sensory (5)	Somatomotor: tonic (5) clonic (1)	0/6	Motor deficit (6)	15–60 s
Fronto-central ($n = 1$)	Headache (1) Not reported (1)	Vocalization (1)	1/1		
Parietal ($n = 6$)	Somatomotor (2) Sensory (1) Pain (2) Asomatognosia (2) Vertigo (1) Indefinable (1) Not reported (1)	Fixed gaze (4) Somatomotor (4) Autonomous (2) Version (2) Vocalization (2) Deviation of head and eyes (1)	3/6 Incomplete/ inconstant (2)	Motor deficit (2) Spatial agnosia (1)	30–60 s
Occipital Parieto-occipital Parieto-occipito-temporal ($n = 5$)	Visual Hallucination (1) Ocular Movements (1) Not reported (3)	Deviation of eyes jerking (1) tonic (1) ocular jerks (4) Head deviation (4) Somatomotor (3) Groaning 1 Hiding eyes (1)	4/5 Incomplete/ inconstant (4)	Not observed	$\geqslant$30–60 s (90–150 s/ $>$ 4 mn in 1 case)
Temporal $n = 1$	Anxiety Autonomous	Somatomotor Head deviation	1/1	Temporospatial disorientation	60 s

hands (two cases) were noted in patients with central or parietal FCD. Hemianopsia (two cases) and nystagmus (two cases) were observed in patients with posterior FCD. The motor deficit became permanent after status epilepticus in two patients, was apparently progressive in two cases with continuous myoclonus, and worsened with increased seizure frequency in one case.

Mental impairment was observed in 11 of the 14 children studied (78.5%) and in five out of 14 adults (35%). The IQ (intelligence quotient; Wechsler Intelligence Scale) was within the average range (90–109) in only three children. Borderline scores (70–79) were obtained in two children, three were classified as mentally deficient (IQ < 69) and six children could not be formally assessed because of severe mental retardation. Nine of the 14 adults had a normal IQ, whereas five others had IQs ranging from borderline to mentally deficient. Ten patients had major psychiatric disturbances (35%). Severe cognitive disorders were correlated with early onset of epilepsy ($P < 0.01$). Normal functioning or mild impairment was correlated with limited FCD ($P = 0.01$). Psychiatric disturbances were correlated with early onset of epilepsy ($P = 0.03$) and with a posterior location of the FCD ($P = 0.02$).

No patient had dermatological or neuroimaging features typical of tuberous sclerosis. However, one patient presented both mild cutaneous lesions and two cerebral calcifications.

Electroencephalographic data (Table 3)

The EEG background was abnormal in 19 cases, slow and/or asymmetrical in 15, and not identifiable in four patients, in whom the activity consisted of slow waves or continuous rhythmic spikes. It was normal in limited or lobar FCD affecting the anterior areas, but was severely abnormal in multilobar and posterior FCD.

Interictal spikes were focal (nine cases), regional (13 cases) or bilateral (six cases). In addition, spikes at a distance from the main focus were recorded in three cases: frontal spikes in two cases with occipitoparietal FCD and posterior spikes contralateral to a mesial premotor FCD in the third case. The site of maximum spike activity was concordant with the location of FCD in 17 cases (60%). Well-localized spikes were seen only in limited FCD. Regional spikes were seen in lobar and multilobar FCD, but were also recorded in limited FCD (five cases). Bilateral spikes were found only in limited mesial frontal FCD (six cases), with bilateral paroxysmal activity triggered by photic stimulation in one patient who had a family history of photosensitive epilepsy. The most characteristic interictal pattern consisted of rhythmic or pseudorhythmic spikes (16 patients), which was continuous in 14 patients, and was seen only during the postictal phase or after chemical activation in two patients. This pattern was observed mainly in limited FCD lying near the convexity of the brain, or in multilobar FCD.

Table 3 *Interictal and ictal EEG scalp recordings according to FCD spread*

FCD spread	Limited (20)	Lobar (3)	Multilobar (5)
EEG background			
Normal	8	1	0
Slow/asymmetrical	12	1	2
Not identified	0	1	3
Slow waves			
Absent	8	0	1
Focal	7	1	2
Regional	3	2	2
Bilateral	2	0	0
Spiking activity			
Focal spikes	9	0	0
Regional spikes	5	3	5
Bilateral spikes	6	0	0
Rhythmic or pseudorhythmic spikes	13	0	3
Ictal discharges (n = 27)			
Focal/lobar	6	0	0
Regional/multilobar	4	3	5
Bilateral/not identified	9	0	0

A scalp ictal recording was obtained in 27 cases, with 155 spontaneous seizures (1–65 per patient) and 16 chemically induced seizures. The onset of the ictal discharge was characterized by low-voltage fast activity (22 cases) or rhythmic spikes (five cases); the latter cases corresponded to posterior FCD. Ictal activity onset coincided with FCD location in 14 cases (six limited, eight lobar or multilobar FCD). In contrast, among 13 cases with limited FCD, the onset of ictal discharge appeared to be multilobar in four and no localization was possible in nine. In these latter cases, the location of the FCD was mesial frontal (five cases), mesial central (four cases), lateral central (one case), parietal (two cases) or temporal (one case). Thus, the ictal discharge recorded on the surface EEG had a localizing value in half the cases, and failure to localize usually implied a mesial FCD location.

SEEG data

The position of each intracranial electrode was decided on the basis of scalp electroclinical data, taking into account the lesional areas when they could be detected on MRI (six patients). A total of 257 intracranial electrodes were implanted (6–11 per patient, average 8). Their placement was unilateral in 13 cases and bilateral in 15. SEEG was carried out with electrodes located in multiple lobes (2–5) in 26 cases. Correlation with histological findings retrospectively demonstrated that 1–6 electrodes were clearly placed within the FCD in 25 patients. The electrodes were located at the periphery of the FCD in only three patients.

In 20 patients, the intralesional interictal activity was characterized by a peculiar electrical pattern consisting of continuous, rhythmic or pseudorhythmic spike or polyspike activity, the frequency of which varied from 0.5 to 10 Hz, usually between 1 and 3 Hz. In five other patients the activity consisted of pseudoperiodic spikes or bursts of spikes interrupted by depression or suppression of activity for 2–5 s (Fig. 1). These rhythmic spike discharges (RSDs) were either restricted to one or few closed electrodes or involved large areas. The RSDs were recorded simultaneously on the surface EEG in 14 cases (50%) (Figs 2 and 3). In three cases, RSDs appeared only after clinical or subclinical seizures, or became continuous after hyperventilation or chemical activation. Intravenous injection of diazepam (15 cases) did not suppress RSDs but decreased both the amplitude and frequency of the spikes for 20–30 s after injection (Fig. 4). Thus, RSDs were observed in all patients who had intralesional electrodes, including those whose surface EEG before or during SEEG did not show rhythmic spiking activity. The site of maximal RSD, in terms of rapidity and frequency, correlated with the location of FCD in

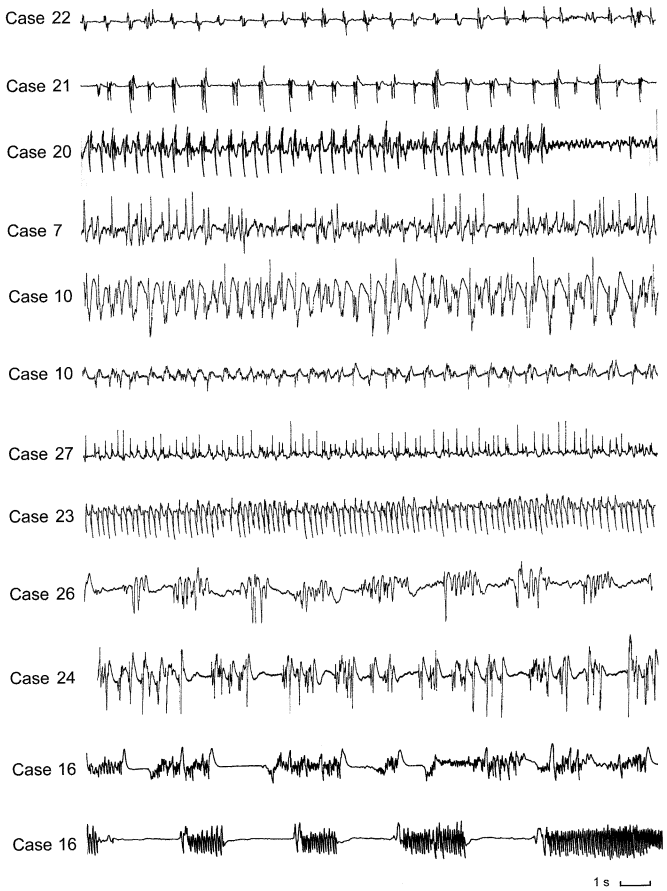


Fig. 1 SEEG recordings. Intralesional interictal activity in FCD is characterized by continuous or subcontinuous RSDs with frequency varying from 1 to 10 Hz. Various patterns were observed in areas that were close together in a given patient (Case 10). Case 16, with frontocentral FCD, illustrates one of the most severe patterns of this series, with pseudoperiodic bursts of spikes interrupted by suppression of activity. For this later case, the upper line shows central area activity and the lower line shows frontal lobe activity (recorded after failure of central resection).

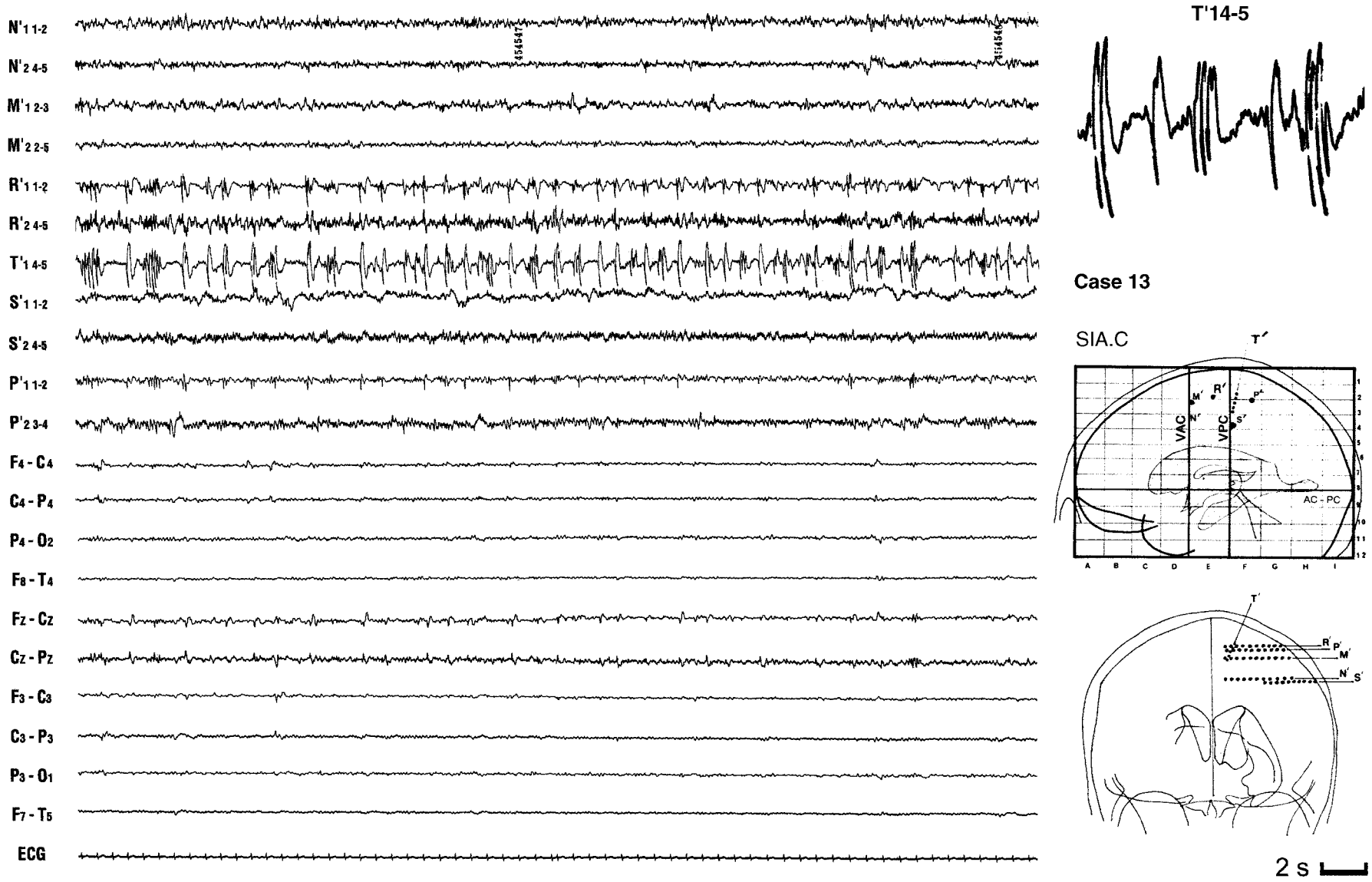


Fig. 2 Interictal activity in a small mesial central FCD. The mesial part of each electrode corresponds to code 1 (i.e. N′1, M′1, . . .) and the lateral part to code 2, the contacts being denoted 1–2, 2–3, etc. The RSDs are recorded in a limited area (R′1–T′1), that corresponded to the FCD. The rhythmic spiking activity was recorded simultaneously on surface EEG (Cz).

all cases. A gradual change from intralesional to perilesional activity was observed, with the appearance in the perilesional areas of background activity combined with spikes (Fig. 5A and B).

The interictal activity was recorded only in perilesional areas in three patients. For two of these patients, interictal activity remained rhythmic but consisted of slow spikes or sharp waves, similar to that observed in the perilesional areas in the other cases. The third patient was a 5-year-old child with continuous subclinical seizures due to limited mesial frontopolar FCD, in whom RSD were observed in the whole frontal lobe.

The LZ, defined by slow waves or depression of activity, was located in the same lobe or lobes containing FCD in 16 cases, also affecting a larger area than FCD in one-third of the cases. LZ was found to be multilobar in four limited FCDs and one lobar FCD, and hemispheric in one lobar FCD. It could not be identified in six cases, corresponding

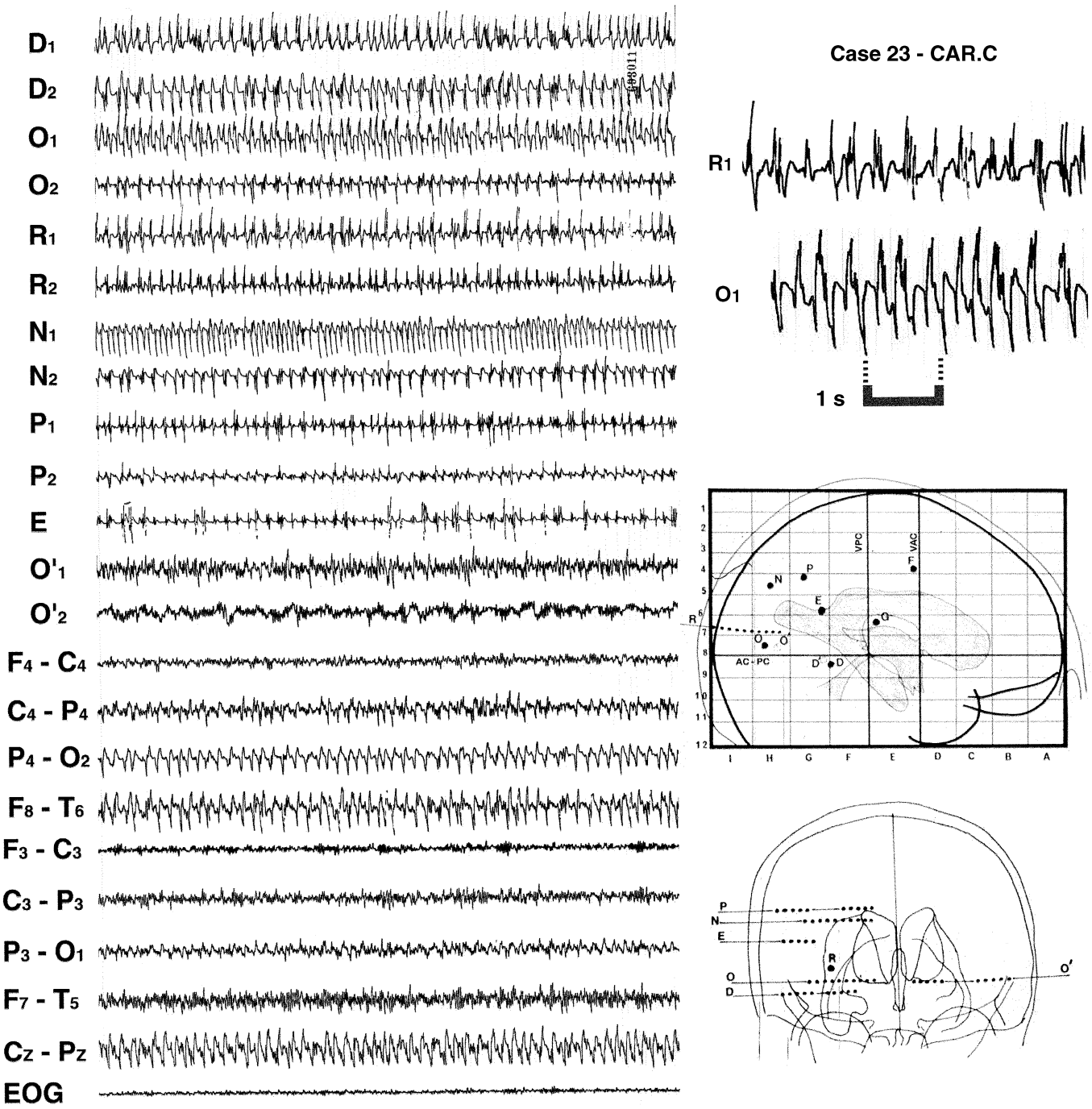


Fig. 3 Interictal activity in a multilobar occipitoparietotemporal FCD. All right posterior areas are involved, although RSD frequency varies in different parts of the FCD. Histologically, all areas displaying RSDs corresponded to the dysplastic cortex. The surface EEG shows the rhythmic activity in the right posterior areas. EOG = electrooculography.

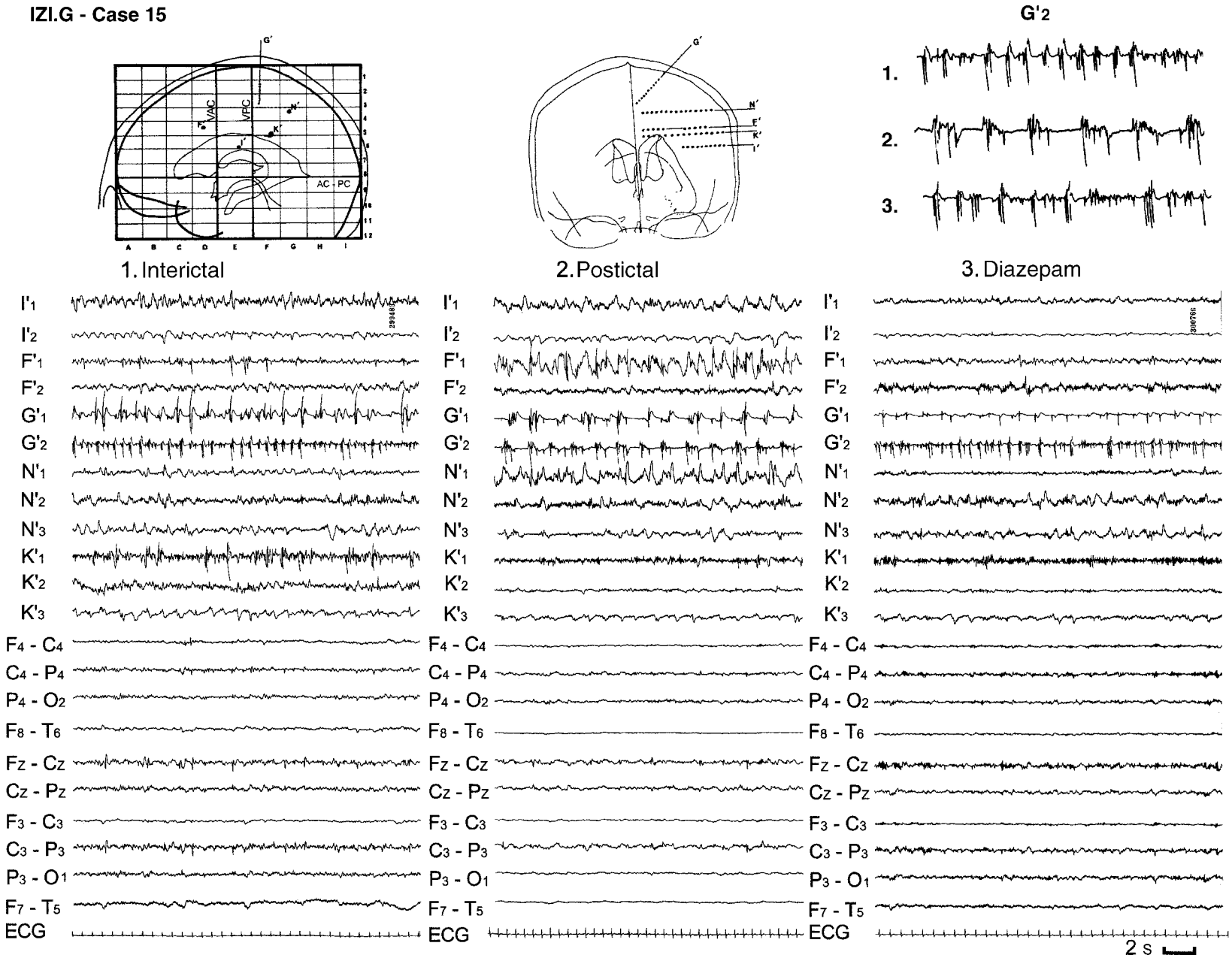


Fig. 4 Effect of intravenous diazepam on RSD activity (limited left central FCD). Interictal recording demonstrates focal RSDs (G′1–G′2), apparent on the surface EEG on the left central area (Fz–Cz, C3–P3). A large frontocentroparietal spiking activity occurs in the postictal state, whereas after intravenous injection of diazepam the RSDs persist only in a restricted area (G′1–G′2), corresponding to the FCD.

to a limited FCD in five out of six cases. Therefore, LZ did not appear to be an indicator of FCD.

The IZ was confined to the RSD areas in 15 cases, independently of the size of FCD. In the other cases, IZ included RSD and asynchronous spikes spreading to surrounding areas (11 cases including eight limited, one lobar and two multilobar FCD) or bursts of diffuse spikes (two cases with limited mesial frontal FCD). One of these last two patients had a personal and family history of photosensitivity. The extent of the IZ increased after seizures and diminished after injection of diazepam.

The EZ was defined in all patients except one who had neither seizures nor subclinical ictal discharges during SEEG. Spontaneous seizures were recorded in 20 patients (72 seizures, 1–11 per patient) and subclinical paroxysmal discharges (electrographic seizures) in five patients (65 paroxysmal discharges, 1–30 per patient). Eleven seizures were obtained after chemical activation in nine patients, and 100 seizures were obtained after electrical stimulation in 20 patients (1–13 per patient). Subclinical paroxysmal discharges were recorded within the area of maximal RSD activity, alternating with RSD areas in most cases but sometimes seen on only one electrode, while RSD activity persisted unchanged nearby. The ictal discharges mostly arose from the same areas as RSD (22 cases). However, ictal discharges arose from an area that was larger than the RSD in four cases and smaller than the RSD in one case. In most cases, low-voltage fast discharges were preceded by a brief acceleration of the RSDs (Fig. 6). Moreover, sustained subclinical discharges were noted before clinical seizures of posterior origin. In half of the cases, an early reappearance of RSD after a brief depression or disorganization of activity characterized the postictal pattern (Fig. 7).

High-frequency electrical stimulation (monophasic rectangular pulses of 1–2.5 mA and 1 ms duration at 50 Hz for 5 s), performed in 27 cases, induced seizures similar to spontaneous electroclinical seizures in 20 patients. In each case, stimulation-induced seizures were obtained when the current was applied to the same electrodes as those recording RSD, within the dysplastic cortex.

The functional organization of the central area was studied by low-frequency stimulation (1 Hz, 1.5–3 mA) in nine patients who had FCDs in central, precentral or postcentral areas. Normal motor and/or sensory responses were obtained in all cases, suggesting no displacement of the motor strip. An unexpected finding was the triggering of 10 seizures in five patients using low-frequency stimulation. In these cases, the stimulation was performed within the FCD located in central or parietal areas.

Comparison between SEEG findings and the extent of the FCD was possible in the 22 patients for whom all surgical samples were available for histological examination (Table 4). LZ and IZ had limited value in estimating the extent of the FCD because they coincided with the dysplastic cortex in only 18 and 41% of the cases, respectively. Conversely, RSD and EZ co-localized with the FCD in 86 and 82% of the cases and, therefore, had a high value for the delineation of the dysplastic cortex. A close correlation could not be established in the three patients in whom no intralesional electrode was implanted and in one other patient with central FCD in whom the EZ appeared more widespread than the FCD.

No complications as result of the presurgical investigation occurred in this series, except for minor subdural haemorrhage with uneventful outcome in one patient.

Neuroimaging findings

The CT scan was normal in four out 10 patients. In four cases, abnormalities consisted of hypodense areas apparently located in the white matter, and in two cases they consisted of cortical calcifications. The MRI was abnormal in six of seven cases and demonstrated a localized broad gyrus (one case), gyral abnormalities (four cases), a global increase in the volume of the occipital lobe (one case), increased signal on T_2-weighted images with blurring of the demarcation between the grey and white matter (three cases), and an area of prolonged T_2 relaxation in the underlying white matter (one case). MRI was normal in one of the seven cases. In all cases, FCD was histologically more widespread than the abnormal areas on CT scan, whereas on MRI this was true in three of six cases. In only three of the six patients who had abnormal MRI did the EZ correspond to the lesion as identified on MRI.

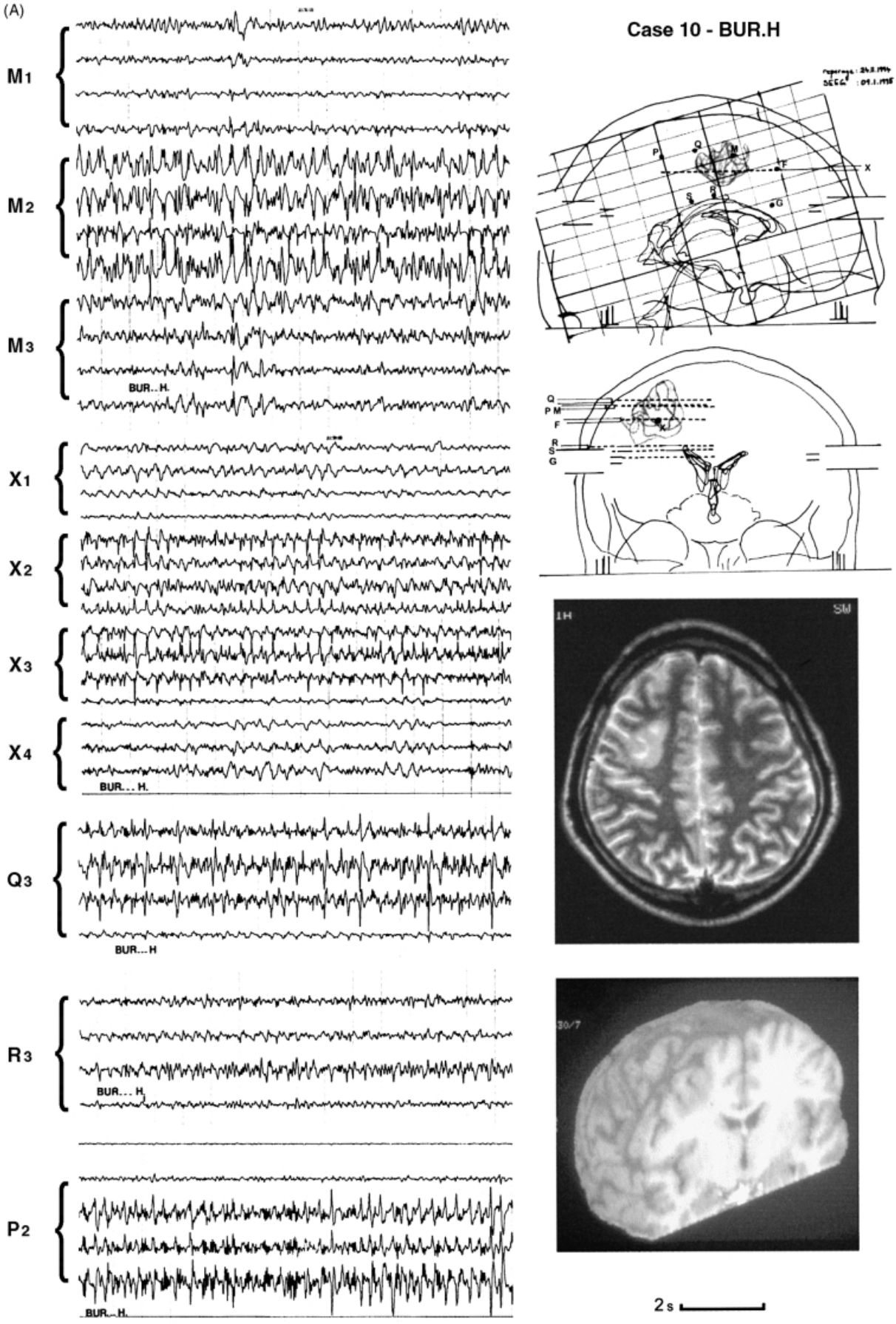
Surgical data

The extent of corticectomy was limited to part of a lobe in 14 patients, lobar in nine and multilobar in five. When compared with the extent of FCD, the corticectomy was often larger than the extent of the dysplastic cortex, because both the EZ and the ictal discharge spread areas were included in the resection. The EZ was considered to be included in the resected tissue in 22 cases. In five cases, the resection was smaller than the EZ, essentially because of functional risks. One patient was operated on without definition of the EZ, but had a localized area of RSD in the parietal lobe.

Histological examination of the whole corticectomy specimen (22 cases) showed that all resection margins were beyond the limits of the dysplastic cortex FCD in nine cases, whereas three cases had margins in the transitional zone and six cases had one margin in the pathological zone. In four cases, all samples were pathological, but in one case the boundary consisted of calcifications without abnormal neurons. Based on histological findings, FCD removal was complete in nine cases, possibly incomplete in three and incomplete in 10.

Seizure outcome

For each patient, seizure outcome was evaluated with a minimal follow-up of 2 years (up to 14 years, average 6


(A)
M1
M2
M3
BUR...H.
X1
X2
X3
X4
BUR... H.
Q3
BUR... H
R3
BUR... H.
P2
BUR... H.
Case 10 - BUR.H
2 s

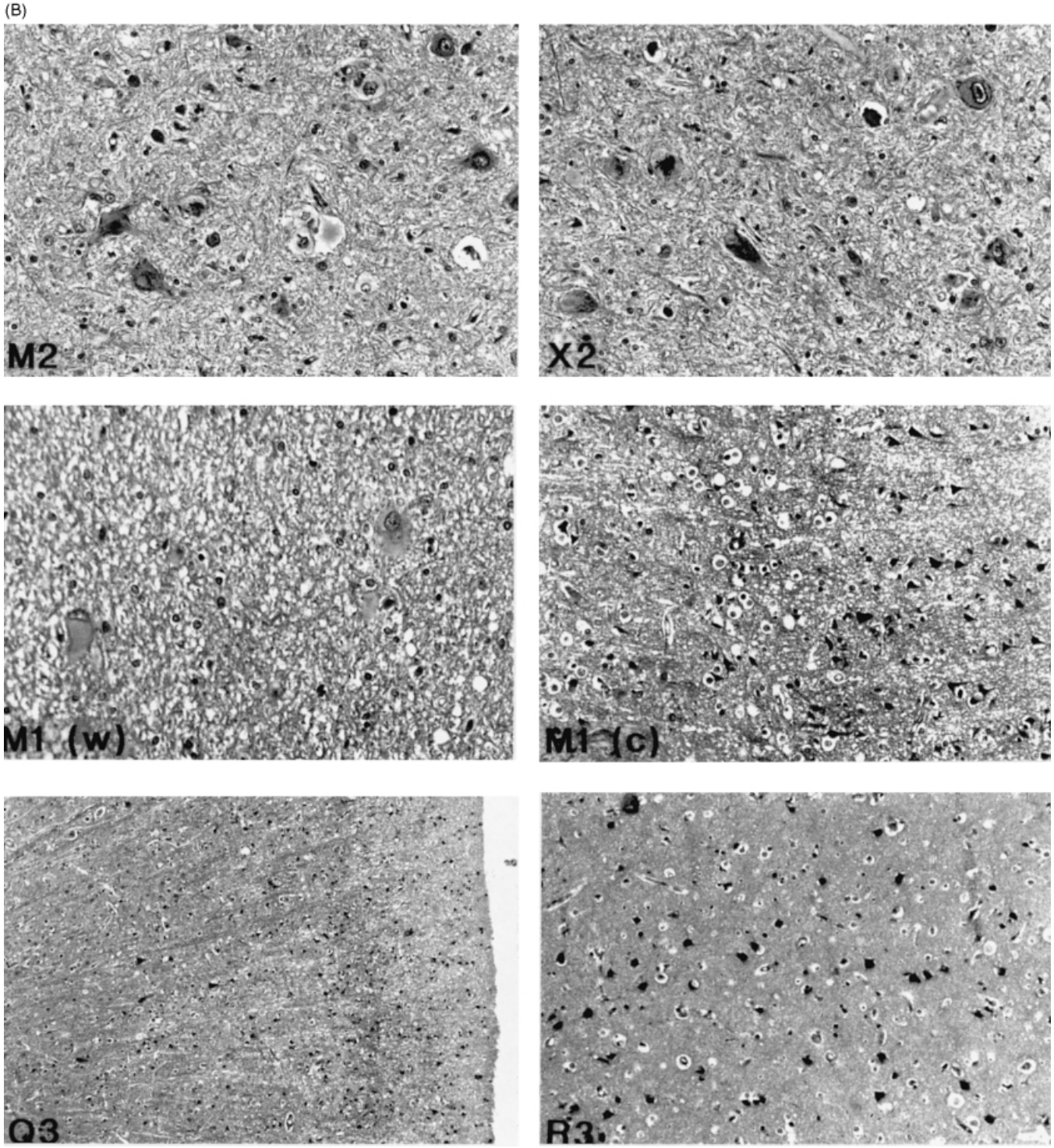


Fig. 5 SEEG and histological correlations in a limited right precentral FCD. (**A**) The site of maximal RSDs corresponds to the FCD (M2–X2–X3), which presented as a localized broad gyrus on MRI (T_2-weighted image and 3D reconstruction). A less continuous spiking activity was recorded in perilesional areas (especially Q3) and areas distant from them (P2). The patient became seizure-free after precentral resection that did not affect the parietal area (electrode P). Note the normality of the activity in the mesial white matter and cortex (M1). (**B**) Histological findings (haemalum–phloxin–safranin staining). The cortical specimens corresponding to M2 and X2 activity demonstrated characteristic features of FCD, with abnormal large neurons and balloon cells. Balloon cells were also seen in the adjacent white matter [M1 (w)]. However, there were no cortical abnormalities (except neuronal damage) in the mesial cortex [(M1 (c)] or in the posterior and inferior boundaries of the resection (Q3–R3). Magnification: M2, X2 and M1 (w), ×300; M1 (c) and R3, ×150; Q3 ×70.

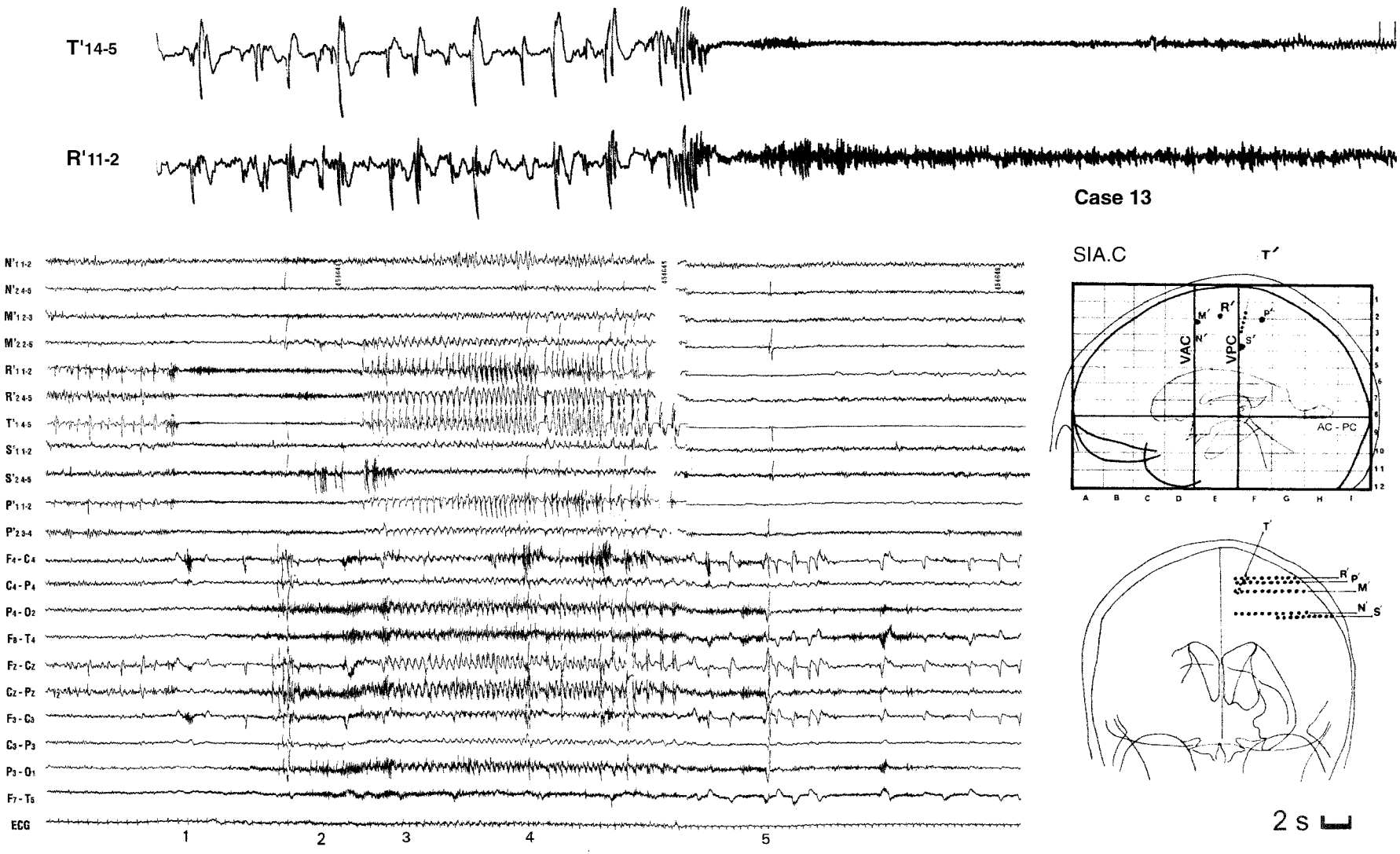


Fig. 6 Left central seizure in a case of left mesial central FCD (same patient as in Fig. 2). 1, Tonic stretching of the right leg; 2 tonic stretching of the 4 limbs; 3, right arm flexion; 4, clonic jerks of both lower limbs; 5, right lower limb paresis. The rapid discharge arose from the areas displaying RSDs, within FCD, after a brief speeding of the spiking frequency (T′1–R′1). It propagated immediately to the lateral cortex (R′2) and the mesial parietal area (P′1, S′1). The discharge appears bilateral on the surface EEG. The patient was seizure-free after restricted resection of the left mesial central area.

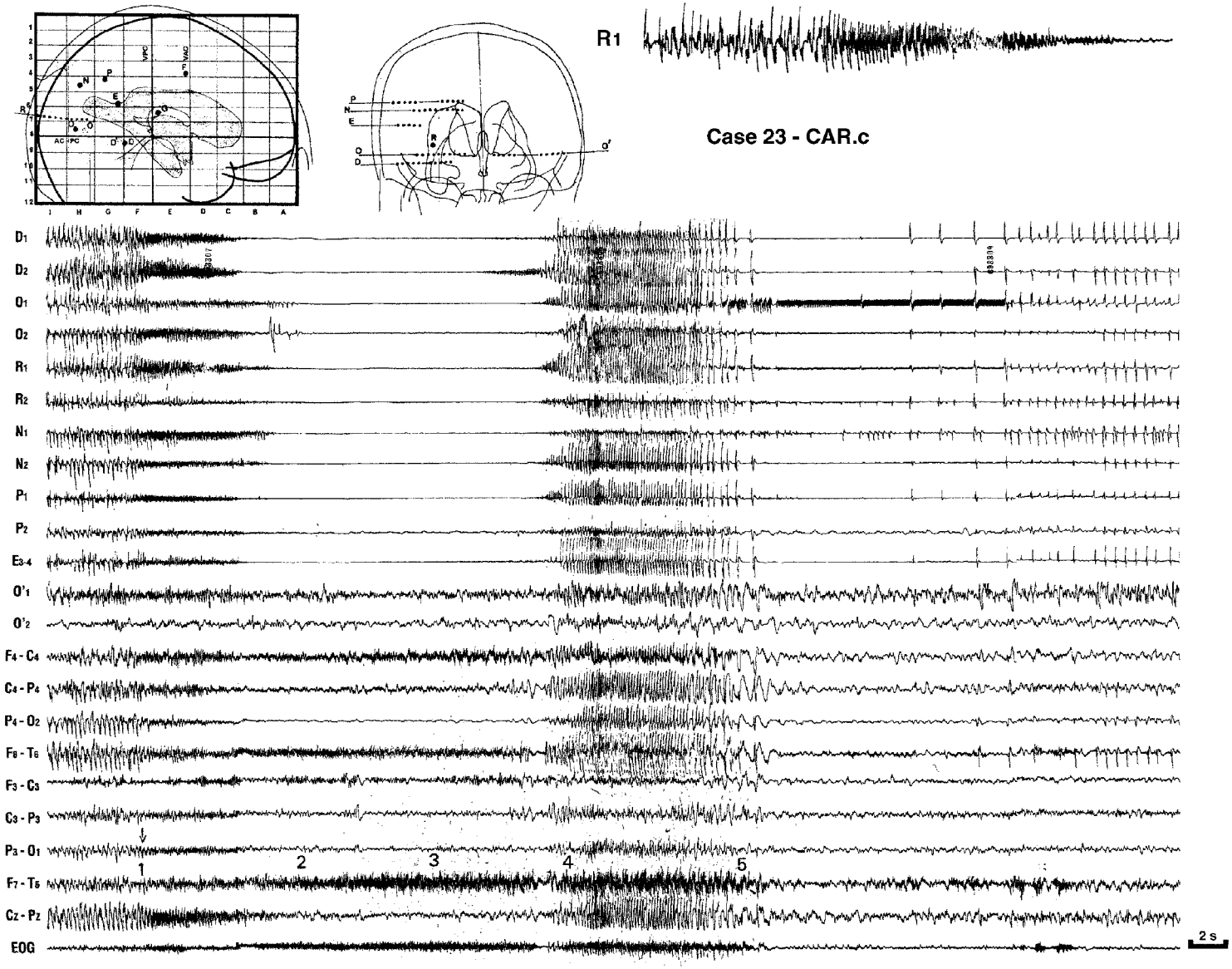


Fig. 7 Right posterior seizure in an occipitoparietotemporal FCD (same patient as in Fig. 3). 1, Right ocular deviation, blinking; 2, stretching of both lower limbs; 3, raising of the right arm; 4, clonic jerks of the left leg; 5, left ocular deviation. The discharge started after RSD acceleration, continued as a fast activity of very low amplitude and then as clonic activity, which was synchronous on all right electrodes, and stopped in the temporal and parietal areas before the occipital area. Note the fast activity (O1–O2–R1) at the end of the seizure. RSDs reappeared immediately after the end of the discharge. The seizure was visible on the right occipitoparietotemporal areas of the surface EEG. Despite a large multilobar (occipitoparietotemporal) resection, seizures persisted, although they were briefer and less frequent than before the operation (class III). All corticectomy specimens corresponded to FCD. EOG = electrooculography.

Table 4 *Relationship between histologically defined FCD extent and SEEG data*

SEEG data (neuropathology) $n = 22$	LZ/FCD	IZ/FCD	RSD/FCD	EZ/FCD
Limited FCD $n = 14$	= 2 Not identified (5) >4 Distinct (2)	= 5 >9	= 11 >1 Uncertain (2)	= 10 >4
Lobar FCD $n = 3$	= 1 >1 <1	= 2 >1	= 3	= 3
Multilobar FCD $n = 5$	= 1 Not identified (1) >3	= 2 >3	= 5	= 5
Total $n = 22$	LZ = FCD 4 18%	IZ = FCD 9 41%	RSD = FCD 19 86%	EZ = FCD 18 82%

>, more extended; <, more restricted; =, co-localized.

Table 5 *Seizure outcome according to histologically defined FCD removal and epileptogenic zone (EZ) removal*

	Class I	Class II	Class III	Class IV
FCD removal/seizure outcome ($n = 22$)				
Complete FCD removal $n = 9$	9 (8 IA, 1 ID)	0	0	0
Margins in transitional area $n = 3$	1 (ID)	2 (1 IIA, 1 IIC)	0	0
Incomplete FCD removal (single pathological boundary) $n = 6$	3 (2 IB, 1 IC)	0	1 (IIIA)	2 (IVB)
Incomplete FCD removal (all pathological boundaries) $n = 4$	1 (IA)	0	1 (IIIA)	2 (IV B)
EZ removal/seizure outcome ($n = 27$)				
Complete EZ removal $n = 22$	17 (11 IA, 2 IB, 1 IC 3 ID)	2 (1 IIA, 1 IIC)	1 (IIIA)	2 (IVB)
Incomplete EZ removal $n = 5$	0	0	3 (IIIA)	2 (IV B)

years). According to Engel's classification (Engel *et al*., 1996), 18 patients (64%) were found to be in class I (12 IA, two IB, one IC, three ID), two patients in class II (one IIA, one IIC), four patients in class IIIA and four patients in class IVB. Freedom from seizures was correlated both with the histologically confirmed complete removal of the dysplastic lesion ($P < 0.01$) and the complete removal of the EZ ($P < 0.01$) (Table 5).

When considering the status of FCD removal (22 patients), all patients in whom cortical resection included the totality of the FCD (nine cases) were seizure-free. Of the three patients whose resection boundaries were within the transitional zone, one was in class ID and two were in class II. Of the six patients with partial removal of FCD with one abnormal margin, three were in class I but none was in class IA; the other three had a less favourable outcome or no improvement (classes III and IV). Of the four patients in whom all tissue samples were pathological, three were in classes III or IV and only one was in class IA; in this patient, the edge of the resected tissue consisted of calcifications without abnormal neurons. In other words, the residual dysplastic cortex was found to be associated with postoperative seizures, even though some patients were greatly improved. However, a seizure-free outcome might still be observed, despite incomplete lesion removal, if the resection boundaries do not contain abnormal neurons.

When considering the status of EZ removal (27 patients), of the 22 patients for whom EZ resection was considered to be complete, 19 had an excellent or good outcome (17 in class I and two in class II). However, three patients had a less favourable or poor outcome (one in class III, two in class IV). For these latter patients, it was retrospectively

concluded that SEEG had underestimated the EZ. The patient who was operated on without definition of the EZ but with evidence of a limited RSD area was in class IA. Among the five patients with incomplete EZ resection, three were in class IIIA and two were in class IVB. Thus, complete EZ removal was clearly related to favourable outcome, although SEEG failed to demonstrate the real extent of EZ in three cases. Conversely, resections that did not include the EZ were associated with an unfavourable outcome in all patients. FCD removal status could not be determined with precision in four patients with a favourable outcome (class I) with complete EZ removal, as well as in two other patients with less favourable outcome (class III) and incomplete EZ removal.

Insufficient information was available for six patients, but analysis of the remaining 22 patients demonstrated that outcome results according to EZ removal or histologically defined dysplastic cortex removal were similar, suggesting that they tend to co-localize.

Discussion

This series of 28 cases constitutes a histologically homogeneous group of FCDs, as described by Taylor and colleagues (Taylor *et al.*, 1971), for which SEEG findings have not been reported previously. Moreover, precise orientation of the cortical specimen according to the location of the intracerebral electrodes demonstrated that the dysplastic tissue generated RSDs, and was the site of onset of spontaneous ictal discharges, and that intralesional electrical stimulation elicited seizures similar to spontaneous seizures. We found that the EZ corresponded to the histologically defined FCD in 82% of the cases. The co-localization of the EZ and FCD is supported by analysis of the surgical results. Seizure-free outcome was correlated with complete removal of the EZ ($P < 0.01$) and with complete removal of the histologically defined FCD ($P < 0.01$). The high rate of freedom from seizures after surgery guided by SEEG (64%) confirms the value of neurophysiological investigations, and particularly of SEEG in determining the extent of corticectomy, even in the absence of adequate neuroimaging. Failure of surgery can be explained by constraints on resection due to eloquent areas of the brain that have dysplastic involvement.

Except for the temporal lobe, which was affected in a single case, FCD was represented equally in all lobes. Crucial areas, such as the posterior frontal lobe and the central and postcentral areas, were affected in 39% of the cases. The smallest FCDs were seen in the central and parietal areas and in the anterior cingular gyrus. The largest FCDs were located primarily in the posterior areas. In most series, FCDs are found predominantly in frontal and central locations (Perot *et al.*, 1996; Palmini *et al.*, 1991*a*; Hirabayashi *et al.*, 1993; Kuzniecky *et al.*, 1996; Polkey, 1996). However, paediatric series show a mainly posterior or hemispheric location (Chugani and Conti, 1996; Wyllie *et al.*, 1996). Such differences can be explained by an earlier onset of epilepsy in larger and more posteriorly situated FCDs, as noted in our population. Temporal involvement is rare in our series, but not uncommon in other studies (Taylor *et al.*, 1971; Palmini *et al.*, 1991*b*; Raymond *et al.*, 1995*a*; Brännström *et al.*, 1996). This discrepancy may be the result of a bias in selection for surgery, or of the inclusion of different types of cortical dysplasia. On the other hand, in most reported cases involving the temporal lobe, including our single temporal case, seizures persisted after temporal lobectomy, suggesting the involvement of extratemporal areas associated with temporal FCD. We found FCD located predominantly on the mesial aspect of the brain (64%). This high frequency of mesially situated FCD is not reported by other authors, except by Kuzniecky (Kuzniecky, 1996) for the frontal lobe. This mesial location can explain some of the peculiarities of EEG patterns and the difficulties encountered during intracranial recording.

The major clinical features in this series are the early onset of epilepsy, a high seizure frequency with occurrence of clusters and status epilepticus, the severity of the cognitive impairment, especially in children, and the high frequency of neurological deficits (68%), which were concordant with the location of the FCD. The motor deficit was clearly acquired secondarily with central FCD in five patients (26% of neurological deficits), after bouts of high seizure frequency, including epilepsia partialis continua and status epilepticus. Partial seizure semiology, as previously described (Bancaud *et al.*, 1991; Bancaud and Talairach, 1992; Chauvel *et al.*, 1992), clearly corresponded to the site of the FCD except for the only temporal case in which there were perisylvian signs (Munari *et al.*, 1980). Secondarily generalized seizures were rare (14%). This series presents most of the characteristics already mentioned in earlier series of histologically demonstrated FCD. Early onset and severity of epilepsy (Palmini *et al.*, 1991a; Hirabayashi *et al.*, 1993; Polkey, 1996; Wyllie *et al.*, 1996) with the occurrence of status epilepticus (Perot *et al.*, 1966; Palmini *et al.*, 1991*a*; Kuzniecky *et al.*, 1995; Wyllie *et al.*, 1996) and of epilepsia partialis continua (Palmini *et al.*, 1991*a*; Kuzniecky and Powers, 1993; Aicardi, 1994) appear to be characteristic of FCD. A relationship between the location of FCD and the neurological deficit has been noted in central (Barkovich and Kjos, 1992; Raymond *et al.*, 1995*a*) and posterior FCD (Taylor *et al.*, 1971; Kuzniecky *et al.*, 1997). Progressive motor deficits related to epilepsy have been described (Perot *et al.*, 1966; Kuzniecky and Powers, 1993; Guerrini *et al.*, 1996; Polkey, 1996; Wyllie *et al.*, 1996). Autistic features combined with severe mental retardation in children with posterior or anterior involvement have also been reported (Jambaque *et al.*, 1993; Rossi *et al.*, 1996). Few data concerning ictal semiology are available, but reported partial seizure manifestations consist of focal motor features or drop attacks in frontocentral FCD (Palmini *et al.*, 1991*b*; Barkovich and Kjos, 1992; Kuzniecky *et al.*, 1995) and of visual symptoms in occipital FCD (Kuzniecky *et al.*, 1997). A distinct feature of our series is the low incidence of secondary

generalization (14%) instead of the 35–73% reported in other studies (Palmini *et al.*, 1991*b*; Hirabayashi *et al.*, 1993; Kuzniecky *et al.*, 1995). Such differences in secondarily generalized seizure frequency may be explained by heterogeneity in the histological diagnosis of focal dysplasias. It may also be difficult to distinguish generalized seizures from seizures with somatomotor manifestations due to rapid bilateral involvement of the mesial premotor areas (Chauvel *et al.*, 1992).

Continuous or subcontinuous spikes or rhythmic sharp waves were observed on the surface EEG in 57% of our cases. This striking pattern of rhythmic epileptiform discharges is considered characteristic of surface EEG recordings in FCD and is found in about half the cases in some studies (Palmini *et al.*, 1995; Raymond *et al.*, 1995*b*; Gambardella *et al.*, 1996). Rhythmic epileptiform discharges are spatially more restricted than intermittent sharp waves and spikes, correspond to maximally epileptogenic areas, as demonstrated by electrocorticography, and are concordant with FCD location in 80% of the cases (Gambardella *et al.*, 1996). Comparison with SEEG recordings allowed us to show that rhythmic epileptiform discharges observed on the surface EEG clearly correspond to RSDs recorded within the dysplastic cortex, although the pattern appears to be attenuated and distorted on surface recordings: intracerebral rapid spikes may correspond to slow and low-amplitude spikes or sharp waves on the surface EEG. However, intracerebral and surface recordings may be similar in some cases. Rhythmic epileptiform discharges are recorded on EEG in larger FCDs, but also when small dysplastic lesions are located near the convexity or the cerebral poles. Conversely, RSDs generated by FCD located on the mesial aspect of the hemispheres may not be recorded on the surface EEG, which will show only propagated or bilateral interictal spikes. Scalp ictal EEG recordings are often considered unhelpful in locating FCD (Palmini *et al.*, 1991*a*; Hirabayashi *et al.*, 1993; Kuzniecky *et al.*, 1995). In this series, ictal EEG proved to be useful for localization in half of the cases. Comparison with intracerebral recordings demonstrates that clearly lateralized discharges on SEEG can appear bilateral on the surface EEG, especially in central mesial FCD. Thus, interictal and ictal EEG patterns appear to be determined by the location, orientation and extent of FCD.

Surface EEG evaluation was of considerable help when planning an adequate SEEG procedure. Since most patients were investigated without contemporary imaging, it is noteworthy that the intracranial implantation plan, based on electroclinical correlation, led to the placement of at least one electrode in the dysplastic cortex in all cases but three. Direct intralesional recordings demonstrated unequivocally the epileptogenicity of the dysplastic cortex, which was the site of interictal RSD, spontaneous ictal discharge onset, and induced seizures after electrical stimulation. In most of our cases, a clear correlation between the extent of FCD and the EZ could be demonstrated. The few discrepancies observed may have been due to methodological reasons (i.e. the lack of an intralesional electrode, an inadequate number of electrodes or the absence of a recorded seizure). Overall, FCD was delineated by SEEG in 82% of the cases. The main difficulties in accurately assessing the extent of FCD occurred in the central area, where the EZ may be larger than the dysplastic lesion, probably because of a low epileptogenic threshold. In this area, the RSD interictal pattern appeared to be of particular interest for delineating the dysplastic cortex. In the only previously reported case of FCD investigated using SEEG (Munari *et al.*, 1996), the authors found that EZs were more widespread than the lesion on MRI, and postulated that ictal discharges may start in the surrounding cortex. However, the histologically defined extent of the dysplastic cortex found at surgery was not given, and therefore their hypothesis does not necessarily contradict our data.

Epileptogenic areas defined by electrocorticography are often more widespread than the structural lesion on MRI (Palmini *et al.*, 1991*a*; Hirabayashi *et al.*, 1993; Kuzniecky *et al.*, 1995). They can also be larger than the hypometabolic area identified by PET (Olson *et al.*, 1990). The usefulness of peculiar patterns of ictal or continuous epileptogenic discharges recorded on electrocorticography from electrodes overlying the dysplastic cortex, even in cases with normal imaging or visual inspection, has been stressed recently by Palmini and colleagues (Palmini *et al.*, 1995). These authors concluded that the described electrocorticographic pattern allowed the identification of the dysplastic cortex. They emphasized the intrinsic epileptogenicity of FCD, which they found to be more epileptogenic than other structural lesions. However, other authors found that this electrocorticography pattern was correlated with high seizure frequency and a subtype of balloon cell cortical dysplasia, but could be also observed in other types of lesions (Rosenow *et al.*, 1998). We reach conclusions similar to Palmini and colleagues, as we demonstrated that a striking pattern (RSD) was highly valuable in identifying and delineating the FCD. However, as mentioned (Rosenow *et al.*, 1998), this pattern cannot be considered to be specific for dysplastic tissue. We indeed observed it in other conditions, mainly in Rasmussen encephalitis and in some cases of dysembryoplastic neuroepithelial tumours (personal observation). Therefore, this pattern appears to be a marker of high lesional epileptogenicity rather than a histological marker.

Both electrocorticography and SEEG allowed detection of dysplastic cortex. However, some differences related to methodology should be noted. First, we observed RSDs on intracerebral recordings in all but two patients (93%), whereas a similar pattern was found in 67% of the cases by electrocorticography (Palmini *et al.*, 1995). Secondly, we demonstrated that both subclinical ictal discharges and electroclinical seizure onset clearly arose from the dysplastic cortex that also generated RSD. Thus, keeping in mind that the definition of the EZ is based on ictal discharges in our method, we showed that only part of the interictal spiking (RSDs) could be considered to have a similar value to ictal discharges for the identification of the EZ. Thirdly, SEEG

permits a satisfactory evaluation of mesial FCD. Furthermore, it provides a three-dimensional approach to the delineation of the FCD, despite the fact that depth electrode recording implies limited sampling of lesional and perilesional areas.

The epileptogenicity of dysplastic cortex may be accounted for by several mechanisms. Seizures elicited by low-frequency stimulation of the dysplastic cortex in this study and one other study (Munari *et al.*, 1996) suggest a low epileptogenic threshold, since such stimulation does not usually elicit seizures outside the hippocampal structures (Kahane *et al.*, 1993). Persisting RSDs in the dysplastic cortex after intravenous injection of diazepam when surrounding spikes have disappeared and [^{11}C]flumazenil-PET findings (Chassoux *et al.*, 1995; Richardson *et al.*, 1996) both suggest that abnormal benzodiazepine receptors are involved in FCD. Moreover, abnormal synaptic interconnectivity (Mattia *et al.*, 1995), changes in the pattern of catecholaminergic innervation (Trottier *et al.*, 1994) and serotonergic hyperinnervation (Trottier *et al.*, 1996) and abnormalities in GABAergic neurons (Ferrer *et al.*, 1992) have been found in dysplastic cortical specimens.

Because EZ and FCD areas tend to co-localize, it can be postulated that lesion removal is both necessary and sufficient for the achievement of freedom from seizures. However, in this series corticectomies were often larger than the dysplastic cortex as they included areas of ictal spread, and it is therefore not possible to arrive at a conclusion concerning the necessity of removing perilesional areas. When removal of the EZ was considered to be complete, the outcome was favourable in the majority of cases. Surgical failure in three patients was interpreted as being due to an insufficient definition of the EZ. Incomplete EZ removal was performed because of functional risks in the eloquent cortex and was associated with poor outcome in all patients. Complete removal of the FCD led to results in class IA. The residual dysplastic cortex was clearly associated with an unfavourable outcome, except in patients who presented no abnormal neurons at the margins of the resection. Although Taylor and colleagues reported half the cases to be seizure-free (Taylor *et al.*, 1971), in later series freedom from seizures was $<$20% (Palmini *et al.*, 1991*b*; Hirabayashi *et al.*, 1993; Raymond *et al.*, 1995*a*; Brännström *et al.*, 1996). Poor surgical outcome was explained by difficulty in identifying the margins of the dysplastic cortex on imaging and at surgery (Kuzniecky *et al.*, 1995; Palmini *et al.*, 1995; Olivier *et al.*, 1996; Polkey, 1996). A more favourable outcome has been reported in children, the proportion of seizure-free patients ranging from 52% (Wyllie *et al.*, 1996) to 65% (Chugani *et al.*, 1993), but wider resections, including hemispherectomy, may account for this discrepancy. With 64% seizure-free patients, our results figure among the best reported, despite the lack of adequate brain imaging and limited cortical resections in extratemporal areas in the vast majority of cases; these results therefore validate SEEG methodology. It must be recalled that, until the advent of modern imaging techniques, neurophysiological investigation was the only method available for planning surgical resection in epileptic patients. The value of the information provided by SEEG data is more than just historical as it has led to a better understanding of the epileptogenicity of FCD and the organization of the EZ. It also aids in the delineation of the dysplastic cortex for surgical resection. We conclude that, despite the risks and costs entailed, the combination of neurophysiological criteria with high-resolution MRI will retain its usefulness in planning adequate resection for focal cortical dysplasia until invasive procedures can be replaced by newer, more advanced imaging techniques.

Acknowledgements

We wish to thank Suzanne Trottier, Catherine Chiron and Olivier Dulac for reviewing the manuscript and P. Chauvel, C. Munari, D. Broglin, L. Merienne, D. Toussaint, J. P. Gagnepain, S. Baudouin-Chial, P. Buser, M. Lamarche, S. Liminana and F. Semah for their constructive advice and assistance. This manuscript is dedicated to Jean Bancaud and Alain Bonis, in memoriam, and to Jean Talairach, in respectful homage.

References

Aicardi J. The place of neuronal migration abnormalities in child neurology. [Review]. Can J Neurol Sci 1994; 21: 185–93.

Bancaud J. Surgery of epilepsy based on stereotactic investigations—the plan of the SEEG investigation. Acta Neurochir Suppl (Wien) 1980; 30: 25–34.

Bancaud J, Talairach J. Clinical semiology of frontal lobe seizures. [Review]. Adv Neurol 1992; 57: 3–58.

Bancaud J, Talairach J, Munari C, Giallonardo T, Brunet P. Introduction à l'étude clinique des crises épileptiques rétrorolandiques. Can J Neurol Sci 1991; 18 (4 Suppl): 566–9.

Barkovich AJ, Kjos BO. Nonlissencephalic cortical dysplasias: correlation of imaging findings with clinical deficits. AJNR Am J Neuroradiol 1992; 13: 95–103.

Barkovich AJ, Kuzniecky RI. Neuroimaging of focal malformations of cortical development. [Review]. J Clin Neurophysiol 1996; 13: 481–94.

Brännström T, Silfvenius H, Olivecrona M. The range of disorders of cortical organization in surgically treated epilepsy patients. In: Guerrini R, Andermann, F, Canapicchi R, Roger J, Zifkin BG, Pfanner P, editors. Dysplasias of cerebral cortex and epilepsy. Philadelphia: Lippincott-Raven; 1996. p. 57–64.

Chan S, Chin SS, Nordli DR, Goodman RR, DeLaPaz RL, Pedley TA. Prospective magnetic resonance imaging identification of focal cortical dysplasia, including the non-balloon cell subtype. Ann Neurol 1998; 44: 749–57.

Chassoux F, Landré E, Semah F, Ghossoub M, Turak B, Devaux B et al. Epilepsie pariétale et dysplasie corticale: corrélations anatomo-cliniques et imagerie fonctionnelle. Epilepsies (Montrouge) 1995; 7: 397–404.

Chauvel P, Trottier S, Vignal JP, Bancaud J. Somatomotor seizures of frontal lobe origin. [Review]. Adv Neurol 1992; 57: 185–232.

Chugani HT, Conti JR. Etiologic classification of infantile spasms in 140 cases: role of positron emission tomography. J Child Neurol 1996; 11: 44–8.

Chugani HT, Shields WD, Shewmon DA, Olson DM, Phelps ME, Peacock WJ. Infantile spasms: I. PET identifies focal cortical dysgenesis in cryptogenic cases for surgical treatment. Ann Neurol 1990; 27: 406–13.

Chugani HT, Shewmon DA, Shields WD, Sankar R, Comair Y, Vinters HV, et al. Surgery for intractable infantile spasms: neuroimaging perspectives. Epilepsia 1993; 34: 764–71.

Daumas-Duport C. Dysembryoplastic neuroepithelial tumors in epilepsy surgery. In: Guerrini R, Andermann F, Canapicchi R, Roger J, Zifkin BG, Pfanner P, editors. Dysplasias of cerebral cortex and epilepsy. Philadelphia: Lippincott-Raven; 1996. p. 71–80.

Duncan JS. Imaging and epilepsy. [Review]. Brain 1997; 120: 339–77.

Engel J Jr, Van Ness PC, Rasmussen TB, Ojemann LM. Outcome with respect to epileptic seizures. In: Engel J Jr, editor. Surgical treatment of the epilepsies. 2nd ed. Philadelphia: Lippincott-Raven; 1996. p. 609–21.

Ferrer I, Pineda M, Tallada M, Oliver B, Russi A, Oller L, et al. Abnormal local-circuit neurons in epilepsia partialis continua associated with focal cortical dysplasia. Acta Neuropathol (Berl) 1992; 83: 647–52.

Gambardella A, Palmini A, Andermann F, Dubeau F, Da Costa JC, Quesney LF, 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.

Guerrini R, Dravet C, Bureau M, Mancini J, Canapicchi R, Livet MO, et al. Diffuse and localized dysplasias of cerebral cortex: clinical presentation, outcome, and proposal for a morphologic MRI classification based on a study of 90 patients. In: Guerrini R, Andermann F, Canapicchi R, Roger J, Zifkin BG, Pfanner P, editors. Dysplasias of cerebral cortex and epilepsy. Philadelphia: Lippincott-Raven; 1996. p. 255–69.

Hirabayashi S, Binnie CD, Janota I, Polkey CE. Surgical treatment of epilepsy due to cortical dysplasia: clinical and EEG findings. J Neurol Neurosurg Psychiatry 1993; 56: 765–770.

Jambaque I, Chiron C, Dulac O, Raynaud C, Syrota P. Visual inattention in West syndrome: a neuropsychological and neurofunctional imaging study. Epilepsia 1993; 34: 692–700.

Kahane P, Tassi L, Francione S, Hoffmann D, Lo Russo G, Munari C. Manifestations électrocliniques induites par la stimulation électrique intracérébrale par 'chocs' dans les épilepsies temporales. Neurophysiol Clin 1993; 23: 305–26.

Kuzniecky RI. MRI in focal cortical dysplasia. In: Guerrini R, Andermann F, Canapicchi R, Roger J, Zifkin BG, Pfanner P, editors. Dysplasias of cerebral cortex and epilepsy. Philadelphia: Lippincott-Raven; 1996. p. 145–150.

Kuzniecky R, Powers R. Epilepsia partialis continua due to cortical dysplasia. J Child Neurol 1993; 8: 386–8.

Kuzniecky R, Mountz JM, Wheatley G, Morawetz R. Ictal single-photon emission computed tomography demonstrates localized epileptogenesis in cortical dysplasia. Ann Neurol 1993; 34: 627–31.

Kuzniecky R, Morawetz R, Faught E, Black L. Frontal and central lobe focal dysplasia: clinical, EEG and imaging features. Dev Med Child Neurol 1995; 37: 159–66.

Kuzniecky R, Gilliam F, Morawetz R, Faught E, Palmer C, Black L. Occipital lobe developmental malformations and epilepsy: clinical spectrum, treatment, and outcome. Epilepsia 1997; 38: 175–81.

Mattia D, Olivier A, Avoli M. Seizure-like discharges recorded in human dysplastic neocortex maintained in vitro. Neurology 1995; 45: 1391–5.

Munari C, Talairach J, Bonis A, Szikla G, Bancaud J. Differential diagnosis between temporal and 'perisylvian' epilepsy in a surgical perspective. Acta Neurochir (Wein) 1980; Suppl 30: 97–101.

Munari C, Francione S, Kahane P, Tassi L, Hoffmann D, Garrel S, et al. Usefulness of stereo EEG investigations in partial epilepsy associated with cortical dysplastic lesions and gray matter heterotopia. In: Guerrini R, Andermann F, Canapicchi R, Roger J, Zifkin BG, Pfanner P, editors. Dysplasias of cerebral cortex and epilepsy. Philadelphia: Lippincott-Raven; 1996. p. 383–94.

Olivier A, Andermann F, Palmini A, Robitaille Y. Surgical treatment of the cortical dysplasias. In: Guerrini R, Andermann F, Canapicchi R, Roger J, Zifkin BG, Pfanner P, editors. Dysplasias of cerebral cortex and epilepsy. Philadelphia: Lippincott-Raven; 1996. p. 351–66.

Olson DM, Chugani HT, Shewmon DA, Phelps ME, Peacock WJ. Electrocorticographic confirmation of focal positron emission tomographic abnormalities in children with intractable epilepsy. Epilepsia 1990; 31: 731–9.

Palmini A, Andermann F, Olivier A, Tampieri D, Robitaille Y, Andermann E, et al. Focal neuronal migration disorders and intractable partial epilepsy: a study of 30 patients. [Review]. Ann Neurol 1991a; 30: 741–9.

Palmini A, Andermann F, Olivier A, Tampieri D, Robitaille Y. Focal neuronal migration disorders and intractable partial epilepsy: results of surgical treatment. Ann Neurol 1991b; 30: 750–7.

Palmini A, Andermann F, Olivier A, Tampieri D, Robitaille Y, Melanson D, et al. Neuronal migration disorders: a contribution of modern neuroimaging to the etiologic diagnosis of epilepsy. Can J Neurol Sci 1991c; 18 (4 Suppl): 580–7.

Palmini A, Gambardella A, Andermann F, Dubeau F, da Costa JC, Olivier A, et al. Intrinsic epileptogenicity of human dysplastic cortex as suggested by corticography and surgical results. Ann Neurol 1995; 37: 476–87.

Perot P, Weir B, Rasmussen T. Tuberous sclerosis. Surgical therapy for seizures. Arch Neurol 1966; 15: 498–506.

Polkey CE. Cortical dysplasia: resective surgery in children. In: Guerrini R, Andermann F, Canapicchi R, Roger J, Zifkin BG, Pfanner P, editors. Dysplasias of cerebral cortex and epilepsy. Philadelphia: Lippincott-Raven; 1996. p. 435–9.

Raymond AA, Fish DR, Sisodiya SM, Alsanjari N, Stevens JM, Shorvon SD. Abnormalities of gyration, heterotopias, tuberous sclerosis, focal cortical dysplasia, microdysgenesis, dysembryo-

plastic neuroepithelial tumour and dysgenesis of the archicortex in epilepsy: clinical, EEG and neuroimaging features in 100 adult patients. [Review]. Brain 1995a; 118: 629–60.

Raymond AA, Fish DR, Boyd SG, Smith SJ, Pitt MC, Kendall B. Cortical dysgenesis: serial EEG findings in children and adults. Electroencephalogr Clin Neurophysiol 1995b; 94: 389–97.

Richardson MP, Koepp MJ, Brooks DJ, Fish DR, Duncan JS. Benzodiazepine receptors in focal epilepsy with cortical dysgenesis: an ^{11}C-flumazenil PET study. Ann Neurol 1996; 40: 188–98.

Robitaille Y, Rasmussen T, Dubeau F, Tampieri D, Kemball K. Histopathology of nonneoplastic lesions in frontal lobe epilepsy. Review of 180 cases with recent MRI and PET correlations. Adv Neurol 1992; 57: 499–513.

Rosenow F, Luders HO, Dinner DS, Prayson RA, Mascha E, Wolgamuth BR, et al. Histopathological correlates of epileptogenicity as expressed by electrocorticographic spiking and seizure frequency. Epilepsia 1998; 39: 850–6.

Rossi PG, Parmeggiani A, Santucci M, Baioni E, Amadi A, Berloffa S. Neuropsychological and psychiatric findings in cerebral cortex dysplasias. In: Guerrini R, Andermann F, Canapicchi R, Roger J, Zifkin BG, Pfanner P, editors. Dysplasias of cerebral cortex and epilepsy. Philadelphia: Lippincott-Raven; 1996. p. 345–50.

Talairach J, Tournoux P. Co-planar stereotaxic atlas of the human brain. Stuttgart: Thieme; 1988.

Talairach J, Tournoux P. Referentially oriented cerebral MRI anatomy. An atlas of stereotaxic anatomical correlations for gray and white matter. Stuttgart: Georg Thieme Verlag; 1993.

Talairach J, Tournoux P, Musolino A, Missir O. Stereotaxic exploration in frontal epilepsy. [Review]. Adv Neurol 1992; 57: 651–88.

Taylor DC, Falconer MA, Bruton CJ, Corsellis JA. Focal dysplasia of the cerebral cortex in epilepsy. J Neurol Neurosurg Psychiatry 1971; 34: 369–87.

Trottier S, Evrard B, Biraben A, Chauvel P. Altered patterns of catecholaminergic fibers in focal cortical dysplasia in two patients with partial seizures. Epilepsy Res 1994; 19: 161–79.

Trottier S, Evrard B, Vignal JP, Scarabin JM, Chauvel P. The serotonergic innervation of the cerebral cortex in man and its changes in focal cortical dysplasia. Epilepsy Res 1996; 25: 79–106.

Wyllie E, Comair YG, Kotagal P, Bulacio J, Bingaman W, Ruggieri P. Seizure outcome after epilepsy surgery in children and adolescents. Ann Neurol 1998; 44: 740–8.

Received November 1, 1999. Revised February 10, 2000
Accepted March 20, 2000