Original article

Epileptic Disord 2012; 14 (3): 275-89

Extratemporal surface EEG features do not preclude successful surgical outcomes in drug-resistant epilepsy patients with unitemporal MRI lesions

Kyriakos Garganis [1], Vasileios Kokkinos [1], Basilios Zountsas [2]

[1] Epilepsy Monitoring Unit

[2] Neurosurgery Department, St Luke's Hospital, Panorama, Thessaloniki, Greece

Received September 11, 2011; Accepted May 29, 2012

ABSTRACT – Of 47 patients with onset of intractable partial seizures and temporal lobe MRI lesions, subjected to presurgical evaluation and temporal lobe surgery, we identified eight (mean age: 24 years; range: 7-52 years) demonstrating surface interictal and/or ictal EEG features suggestive of an extratemporal localisation. All eight patients underwent surgery aiming to predominantly resect the lesion, without extending to the extratemporal region. The patients were prospectively followed (mean follow-up duration: 38 months; range: 12-66 months) and all achieved excellent postoperative seizure control. Extratemporal surface interictal/ictal EEG features were more often encountered in tumoural and focal cortical dysplasia cases, compared with medial temporal sclerosis cases, and were most frequently localised over frontopolar and suprasylvian-pericentral locations. We postulate that propagation of interictal/ictal activity from the epileptogenic region of the temporal lobe to extratemporal neocortical areas, perhaps utilising the temporal pole and insula as intermediary nodes of a common epileptogenic network, accounts for the presence of our cohort's discordant lesion and EEG features.

Key words: surface EEG, temporal lobe lesion, epilepsy surgery

Correspondence:
Kyriakos Garganis
Epilepsy Monitoring Unit,
St Luke's Hospital,
55236, Panorama,
Thessaloniki, Greece
<gkkap@the.forthnet.gr>

doi:10.1684/epd.2012.0527

The concordance of surface interictal/ictal EEG and MRI data is traditionally considered as vital for non-invasive localisation of the epileptogenic region in patients with intractable, lesional, partial epilepsies. Medial temporal sclerosis (MTS), low-grade and developmental tumours, and focal cortical dysplasia (FCD) constitute the great bulk of epileptogenic substrates in temporal lobe epilepsy surgery. Many of the reports in the literature suggest that unitemporal MTS based on MRI and a concordant interictal sharp-wave (SW) focus are strongly predictive of a successful surgical outcome, even independent of the

localising information the ictal EEG may provide (Gilliam *et al*., 1997; Pataraia *et al*., 1998; Cendes *et al*., 2000). The prognostic significance of a concordant, unilateral-temporal SW focus is further strengthened by studies reporting less successful surgical outcome in MTS cases with bitemporal, independent (So *et al*., 1989; Radhakrishnan *et al*., 1998) or additional extratemporal interictal foci (Barry *et al*., 1992), which are believed to indicate bitemporal or more extensive neocortical epileptogenic pathology, respectively. While the prevalence of extratemporal interictal foci in MTS patients is very low, interictal SW foci with extratemporal localisation are reported more often in series of patients with temporal lobe tumours (Hammer *et al*., 1999). As a rule, the primary goal of resective strategy in lesional epilepsy is lesion removal, sometimes with modifications of resection margins guided by chronic or acute ECoG. There is not much information as to how much the presence of extratemporal EEG features affects surgical outcome in such cases, nor how it might influence preoperative work-up, thereby suggesting further investigations with intracranial electrodes. Similar questions also arise regarding ictal EEG interpretation; bitemporal independent ictal EEG onsets are often reported in the setting of temporal lobe epilepsy (Steinhoff *et al*., 1995), usually considered as indicative of bitemporal epileptogenicity rather than of an extratemporal "occult" localisation, and, depending on findings from the entire work-up, may support the decision for surgery or dictate further intracranial EEG studies or even no surgery at all (So *et al*., 1989; Hirsch *et al*., 1991; Sirven *et al*., 1997; Holmes *et al*., 2003). However, neither prevalence nor prognostic significance of ictal EEG patterns, suggesting an extratemporal localisation in patients with temporal lobe epileptogenic lesions, have been adequately appreciated, although it is often stated that ictal EEG should be utilised to rule out extratemporal seizure onsets (Castro *et al*., 2008).

The aim of our study was: a) to contribute information concerning the prevalence and topographical spectrum of extratemporal interictal and ictal EEG localising features in a cohort of surgical patients with partial seizures and unitemporal epileptogenic structural imaging lesions, and b) to determine whether the presence of such "discordant" features influences surgical outcome, as long as the main surgical target is lesion resection. The presence of extratemporal interictal and ictal EEG localisation may either indicate the presence of occult epileptogenic pathology in the areas associated with EEG abnormalities with variable degrees of contribution to seizure genesis, or simply reflect pathways of epileptic activity propagation to remote extratemporal neocortical areas, indicative of an epileptogenic neuronal network whose major "pacemaker" might be more or less firmly established in the region of imaging abnormality. Although these two interpretations may overlap to some degree, successful postsurgical outcomes following lesion resection would apparently favour the latter.

Materials and methods

This was a prospective study of 47 consecutive patients with temporal lobe drug-resistant partial epilepsy and unitemporal MRI structural lesions, undergoing presurgical evaluation at our centre from January 2003 to July 2010. A standard non-invasive protocol was employed which included: a) prolonged extracranial video-EEG monitoring with typical seizures recorded (in all cases additional bilateral inferior temporal chain electrodes were used [F9/T9/P9 and F10/T10/P10]), b) high-quality brain MRI (1.5T) studies with temporal lobe epilepsy protocol (perpendicular to the long hippocampal axis T1-IR, T2 and FLAIR sections for optimising identification of medial temporal pathology, especially MTS), and c) neuropsychological testing, including the Wada test in selected cases.

Extratemporal surface video-EEG localisation was defined and categorised as follows: a) *extratemporal interictal localisation,* if a dominant SW focus was detected that was localised over extratemporal scalp electrodes (*i.e.* electrodes other than the traditional temporal electrodes: F7/F9, T3/T9, T5/P9 and F8/F10, T4/T10, T6/P10); a dominant SW focus was defined as such when the focus accounted for at least 35% of the totally recorded interictal activity, and b) *extratemporal ictal EEG localisation*, if initial ictal EEG changes involved scalp electrodes other than the traditional temporal electrodes, as previously defined; excluded were the type 1b ictal EEG patterns, according to Ebersole's classification (Ebersole and Pacia, 1996), manifesting with an initial "theta/alpha" midline-parasaggital ictal rhythm, which were considered "temporal".

Sporadic and infrequent SWs in extratemporal locations were not considered in the analysis and the same was also applicable for generalised spike/sharp-wave complexes. Determination, localisation, and quantification of interictal SW foci was performed after reviewing all 24-hour recordings and included all SWs recorded throughout wakefulness and sleep. EEG data were evaluated by two of the authors (KG, VK) with many years of training and experience in the field of epileptology and EEG. Both have previously worked closely together for years and any apparent disagreements regarding EEG data interpretation were resolved after re-reviewing.

Thirty-two EEG channels were used for recording during the video-EEG session. They were AC recorded, amplified at a total gain of x1,000 (Pro Amp, LaMont

Medical Inc., Wisconsin, USA), band-pass filtered at 0.1-100 Hz, digitised through a 16-bit resolution A/D converter at a sampling frequency of 500 Hz by a Harmonie System (Stellate, Montreal, QC, Canada), and stored on hard disk along with synchronised video streams. Intraoperative ECoG was performed by strip and grid electrodes (Dixi Microtechniques, Besançon, France) connected to the above-described EEG system, strategically placed over the brain regions of interest.

Results

Of the 47 patients, based on qualitative MRI assessment, 26 had findings consistent with unilateral MTS, 17 with low-grade static tumours, and four with FCD. Eight cases (16%) (mean age: 24 years; range: 7-52 years) of this cohort showed extratemporal interictal/ictal surface EEG features, in particular, two of the 26 MTS, four of the 17 tumoural, and two of the four FCD cases (*table 1*). All eight patients underwent standard procedures (anteromedial temporal lobe resections or lesionectomies) with minor modifications based on intraoperative ECoG in selected cases. One patient (Patient 7) was lost during follow-up, after three years of being continuously seizure-free since operation and having suffered, at this point, a recurrence associated with lesion relapse. The other seven patients all had excellent postoperative outcomes (Engel class I) over a mean follow-up period of 38.3 months (range: 12 to 66 months).

Case studies

Patient 1

A 25-year-old, right-handed man presented with a history of seizures since age 10 years. He had no personal or family risk factors for epilepsy. Seizure semiology consisted of a rising epigastric sensation and a fearful feeling, clouding of consciousness, and oral and hand automatisms. The events usually presented in clusters of 3-4 within 48 hours, 2-3 times per month. The MRI revealed findings strongly consistent with right MTS (*figure 1A$_1$*). Interictal surface video-EEG

Table 1. Patient, lesion, EEG and surgical outcome data.

Patient	Age	Gender	MRI lesion	Interictal EEG	Ictal EEG	Surgical outcome
1	25	M	R MTS	RantT (F8/F10 & T4/T10) RF (Fp2/F4/Fz)	RF (Fp2/F4/Fz)	Seizure-free at 20 m PostOp
2	57	M	R MTS	RantT (F8/T4 & F10/T10)	BF (Fp2/F4 & Fp1/F3)	Seizure-free at 30 m PostOp
3	7	M	RT FCD type IIb	RmidT (T4/T6) RantT (F8/Fp2)	RF (Fp2/F4/Fz)	Seizure-free at 22 m PostOp (drug withdrawal-related seizure at 12 m PostOp)
4	8	M	LT FCD	LantT (F7/T3 & F9/T9)	LF (F3) LC (C3/P3)	Seizure-free at 66 m PostOp
5	25	M	LT astrocytoma	LC (C3)	LC (C3/P3 & T3/T5)	Seizure-free at 54 m PostOp
6	8	M	LT astrocytoma	LC (C3)	LCP (C3 & P3/Pz)	Seizure-free at 44 m PostOp
7	46	M	RT astrocytoma	RantT (F8/F10 & T4/T10)	RPT (T6/P4)	Seizure-free at 36 m PostOp (then lost during follow-up)
8	21	M	LT astrocytoma	LF (Fp1/F3)	LF (Fp1/F3/F7)	Seizure-free at 12 m PostOp

R: right; L: left; B: bilateral; F: frontal; T: temporal; C: central; P: parietal; PT: parietotemporal; ant: anterior; mid: middle; MTS: mesial-temporal sclerosis; FCD: focal cortical dysplasia; m: month.

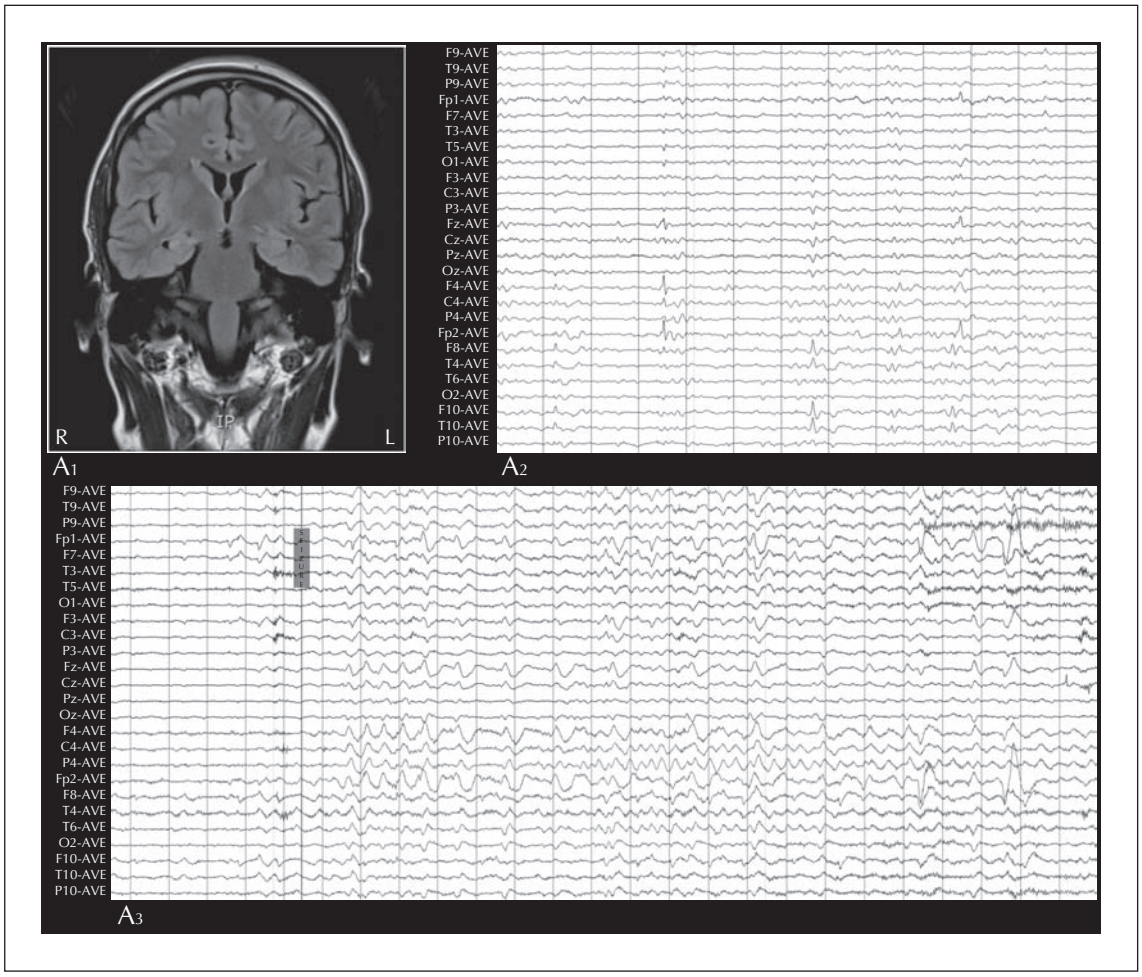

Figure 1. Patient 1. (A_1) MRI showing high signal intensity over the right hippocampus. (A_2) Interictal EEG of SW activity with a right temporal (F8/F10/T10) and right frontal (Fp2/F4/Fz) distribution. (A_3) Ictal EEG reveals repetitive SW activity over the right frontopolar and frontal area (Fp2/F4/Fz).

revealed an ipsilateral anterior temporal SW focus (F8/F10 and T4/T10), accounting for 65% of the total interictal activity and an additional right frontal SW focus (Fp2/F4/Fz), accounting for the remaining 35% (*figure 1A*$_2$). Four typical seizures were recorded, with a broadly distributed ictal rhythm consisting at onset of repetitive SW activity over the right frontopolar and frontal area (maximum over Fp2/F4/Fz), with rapid subsequent spread to the ipsilateral centroparietal and temporal region, and in a less well-organised manner, over the contralateral side as well (*figure 1A*$_3$). Acute intraoperative ECoG revealed active spiking from the right temporal pole and the right subtemporal region. Very rare spikes were recorded from the six-contact strip placed anteriorly, over the lateral-inferior frontal cortex. The patient underwent an ipsilateral temporal pole resection plus amygdalohippocampectomy and has been continuously seizure-free, currently at the twentieth postoperative month. Biopsy was consistent with severe hippocampal sclerosis (HS).

Patient 2

A 52-year-old, right-handed man, with a history of complicated febrile convulsions at age 18 months, had onset of typical seizures starting at age 14 years, with an aura of rising epigastric sensation, clouding of consciousness, oral automatisms, and posturing of the left upper extremity. Postictally, he was confused and hyperactive for a few minutes, sometimes suffering minor injuries. By the time of the evaluation, he was experiencing 3-4 seizures per week. MRI revealed features consistent with right MTS. Surface interictal EEG demonstrated a typical right anterior SW focus (maximum over F8/T4 and F10/T10), while ictal EEG, in three recorded seizures, showed a widespread pattern at onset consisting of bilateral frontopolar-frontal repetitive SW activity (maximum over Fp2/F4 and Fp1/F3) with subsequent emergence of a right temporal sustained and well-organised "theta/alpha" rhythm (*Appendix 1, supplementary figure 1*). Acute intraoperative ECoG

revealed active spiking from the polar and medial-basal temporal region, and less frequently from the lateral temporal neocortex. An ipsilateral anteromedial temporal resection plus amygdalohippocampectomy was performed and the patient has been continuously seizure-free, now at 2.5 years postoperatively. Biopsy revealed severe HS.

Patient 3

A 7-year-old, right-handed boy, with no apparent epilepsy risk factors from his personal and family history, started having seizures at age 4 years, consisting of an indescribable aura (he would shout "*... here it comes...*"), followed by motionless stare, clouding of consciousness, and mild hand automatisms. Brain MRI revealed an extensive right temporal lobe lesion, involving the pole, medial-basal and lateral temporal neocortex and extending as far back as the occipito-temporal junction. By the time of the evaluation and following multiple drug trials, he had 1-2 seizures weekly. Interictal EEG revealed right mid-posterior temporal SW activity (maximum over T4/T6), extending occasionally to the anterior temporal region (F8/Fp2), while ictal EEG onsets were poorly organised with a broadly distributed semi-rhythmic "delta" pattern, more prominent over the right frontal region and the anterior midline (Fp2/F4/Fz). A late, intraictal, posterior temporal-occipital activation, consisting of a focal (T6/O2) rhythmic theta pattern, was consistently seen in all four recorded seizures (*Appendix 1, supplementary figure 2*). Acute intraoperative ECoG demonstrated prominent spiking over the temporal pole and the medial-basal and lateral-inferior temporal

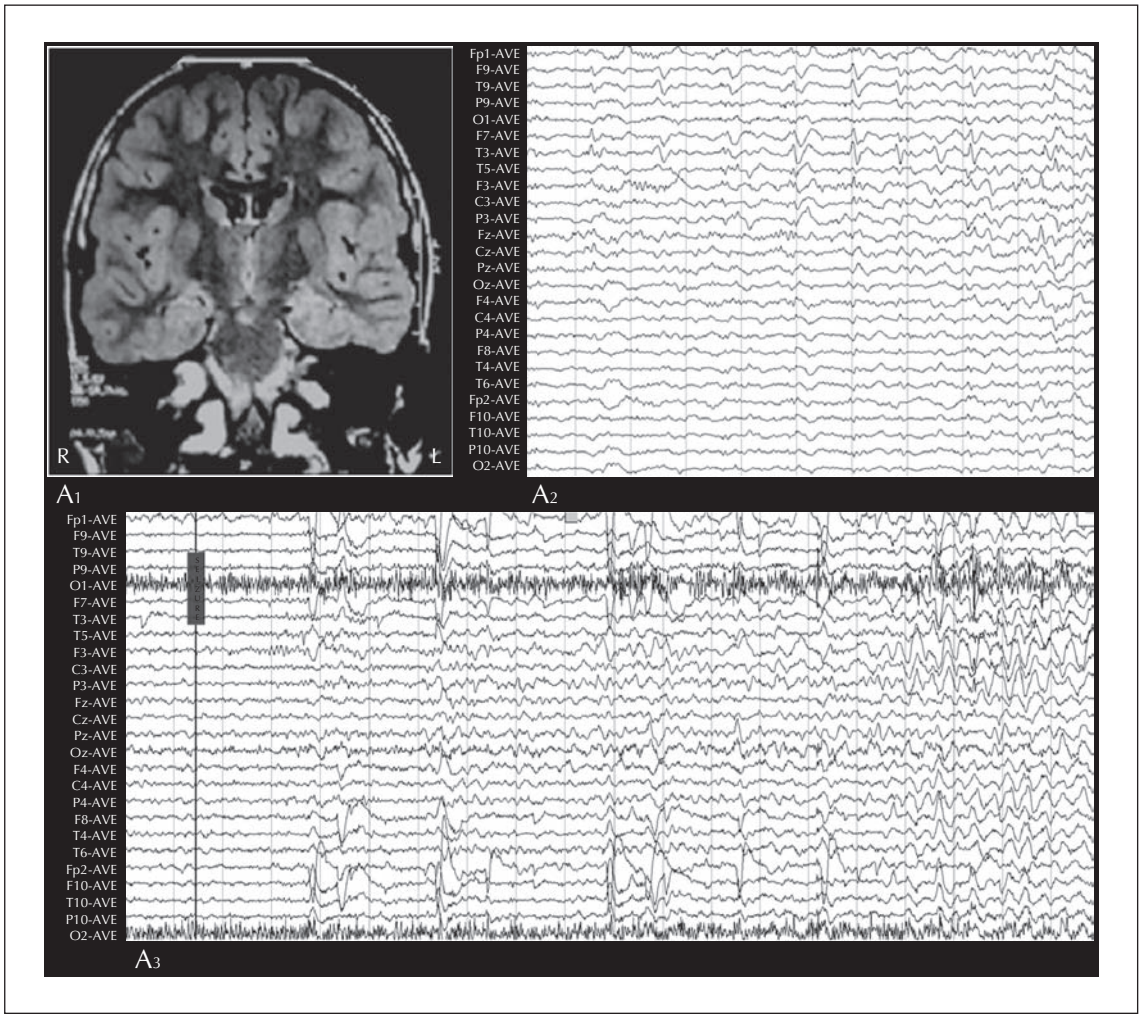

Figure 2. Patient 4. (A_1) MRI showing extensive left medial-basal and inferior lateral temporal FCD. (A_2) Interictal EEG shows anterior-midtemporal SWs (F7/T3/F9/T9). (A_3) Ictal EEG showing a low-amplitude fast rhythm over the left lateral frontal region (F3), subsequently spreading over the ipsilateral parasagittal region.

neocortex, up to the temporo-occipital junction. The largest part of the lateral temporal neocortex, although invaded by the lesion, was inactive and the same was true for the sampled areas from the lateral inferior and basal frontal cortex. A generous right temporal lobectomy, plus resection of the medial temporal structures, was performed. The patient has since been seizure-free, now at the twenty-second postoperative month, with the exception of a brief drug withdrawal-associated relapse at postoperative month 12. Biopsy revealed type IIb FCD.

Patient 4

An 8-year-old male presented with a long history of seizures since age 25 days and borderline intelligence. He reported feeling "*dizzy*" at the beginning of his seizures and was then unresponsive and motionless for 40-60 seconds. At the time of the evaluation, he was suffering multiple events daily. The MRI revealed an extensive left medial-basal and inferior lateral temporal lesion, consistent with FCD (*figure 2A$_1$*). Interictal EEG showed an anterior-midtemporal SW focus (maximum over F7/T3 and F9/T9) (*figure 2A$_2$*), however, the first ictal EEG changes, manifesting as a low-amplitude fast rhythm, were detected over the left lateral frontal region (maximum over F3), with subsequent spread over the ipsilateral parasaggital region (C3/P3) (*figure 2A$_3$*). The patient underwent an extensive left temporal lobectomy plus resection of the medial structures and to date, 5.5 years postoperation, has remained continuously seizure-free. Biopsy revealed immature and poorly organised neuronal elements, however, the lesion was not adequately categorised.

Patient 5

A 25-year-old, right-handed man presented with a history of seizures since age 13. They manifested with a sensation of dizziness, difficulty with speaking and comprehending language, clouding of consciousness, and some tonic posturing of both upper extremities. MRI revealed an extensive low-growth tumour involving the basal and inferior left temporal lobe, encroaching on the ipsilateral temporal horn and abutting the ipsilateral parahippocampal gyrus (*figure 3A$_1$*). Surface video-EEG revealed an interictal left central SW focus (maximum over C3) (*figure 3A$_2$*) and a co-localised focal ictal rhythm, consisting of repetitive SW activity maximum over C3/P3 and extending to the midtemporal region as well (T3/T5) (*figure 3A$_3$*). Acute intraoperative ECoG revealed infrequent spiking over the inferior and basal temporal region and much more frequently from the medial border of the lesion, corresponding to the parahippocampal gyrus. Total lesion resection was performed with additional resection of the ipsilateral parahippocampal gyrus and the patient, 4.5 years postoperation, remained continuously seizure-free. Biopsy revealed a pilocytic astrocytoma.

Patient 6

An 8-year-old, right-handed boy presented with a history of seizures since age 3 years, manifesting with behavioural arrest and unresponsiveness. MRI revealed a left temporal lobe tumour invading the basal temporal and inferior lateral temporal neocortex. At age 4, he underwent a partial tumour resection and remained seizure-free for one year postoperatively. Subsequently, seizures relapsed with identical semiological features, progressively increasing in frequency to multiple daily, by the time of the evaluation. A well-localised interictal SW EEG focus was shown over the left central region (C3), while ictal EEG onset was broader and less well-organised, with left-hemispheric rhythmic delta, more prominent over the parasaggital region (P3/Pz) (*Appendix 1, supplementary figure 3*). He was subjected to total resection of the lesion and acute intraoperative ECoG revealed spiking over the basal and lateral temporal neocortex, up to the superior temporal gyrus. This gyrus was not resected, in spite of persistent post-excisional spiking, due to concerns about damaging language cortex. Following a seizure cluster on postoperative days 19 and 25, the patient has remained seizure-free continuously for 44 months of postoperative follow-up. Biopsy revealed a pilocytic astrocytoma.

Patient 7

A 46-year-old man presented with a history of seizures since age 19 years, with a non-describable aura, motionless stare, and subsequent oral and hand automatisms. Although imaging revealed a right medial temporal lobe mass lesion and the seizures followed a drug-resistant course, he did not consider surgery until many years had passed. Presurgical video-EEG monitoring revealed a right anterior temporal interictal SW focus (F8/F10 and T4/T10), while ictal EEG consistently demonstrated focal onsets with 8-9 Hz sinusoidal activity from the posterior temporo-parietal region (T6 spreading to P4) (*Appendix 1, supplementary figure 4*). He underwent a gross lesion resection along with removal of medial temporal structures. Biopsy revealed an oligoastrocytoma. He was seizure-free for the first three postoperative years and subsequently had a seizure, associated with tumour recurrence. He was later lost during follow-up.

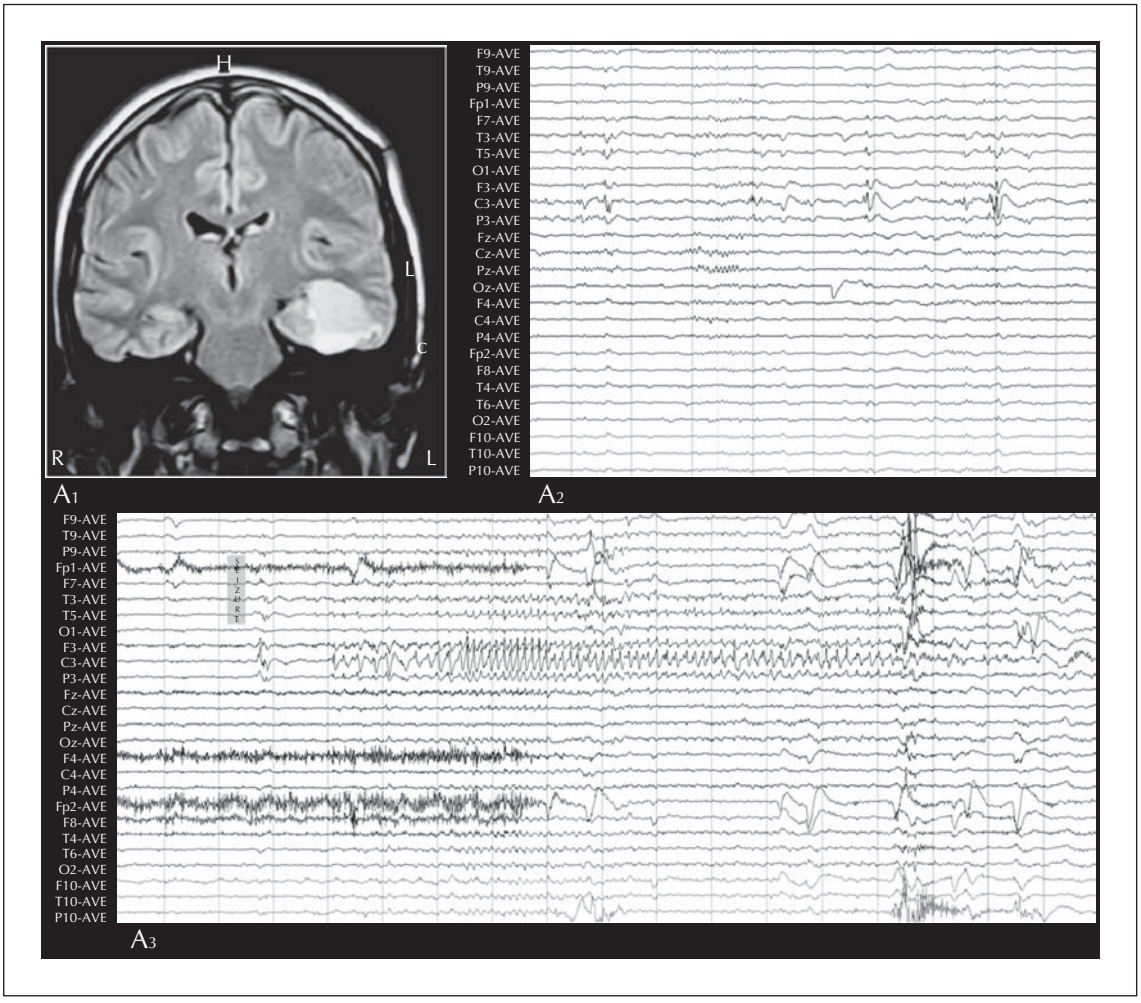

Figure 3. Patient 5. (A_1) MRI revealing an extensive low-growth tumour involving basal and inferior left temporal lobe, encroaching on the ipsilateral temporal horn and abutting the ipsilateral parahippocampal gyrus. (A_2) Interictal EEG with left central SW focus (C3). (A_3) Ictal EEG showing repetitive SW activity over C3/P3, extending to the midtemporal region (T3/T5).

Patient 8

A 21-year-old man presented with a history of seizures since age 17 years, with stereotyped episodes of auras described as *"...an altered sense of reality and nearby objects become larger..."*, accompanied occasionally by an abnormal numbness-like sensation of the entire left side of the body. He then lost awareness and became agitated and hyperkinetic. MRI revealed a left basal temporal, non-enhancing, cystic mass lesion (*figure 4A$_1$*). Prolonged video-EEG studies demonstrated a left frontotemporal interictal SW focus (maximum over Fp1/F3 with field spread to F7/F9) (*figure 4A$_2$*) and several typical events were recorded with an ictal, low-amplitude sinusoidal fast rhythm localised over Fp1, spreading quickly to F7/F3 and Fp2 (*figure 4A$_3$*). The patient underwent lesion resection with acute intraoperative ECoG, documenting spiking from the anterior and lateral lesion margin. On postoperative day 9, he experienced a cluster of partial seizures. He has otherwise been seizure-free, currently one year postoperation.

Discussion

Of 47 surgical patients with unitemporal structural imaging lesions, MTS, indolent tumours, and FCD, eight (16%) presented surface interictal and/or ictal EEG features suggesting an extratemporal localisation. These were not predictive of an adverse surgical outcome, as almost all of these cases showed excellent postoperative seizure control following temporal lobe resections aimed at removing the imaging abnormality, with only minor modifications of resection margins in some cases, guided by acute intraoperative

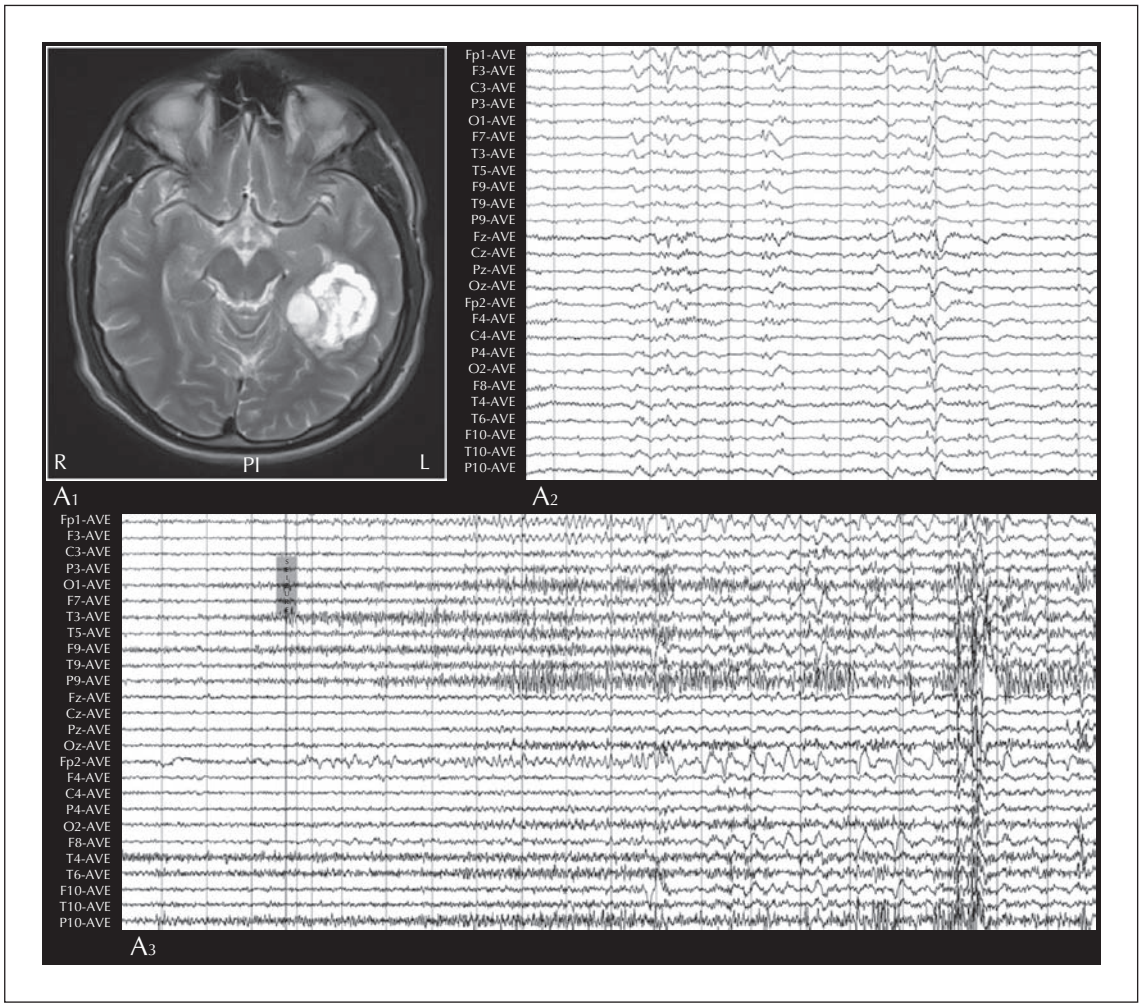

Figure 4. Patient 8. (A_1) MRI shows a left basal temporal cystic mass lesion. (A_2) Interictal EEG demonstrates a left frontotemporal interictal SW focus (Fp1/F3 spreading to F7/F9). (A_3) Ictal EEG reveals a low-amplitude fast rhythm localised over Fp1, spreading quickly to F3/F7 and Fp2.

ECoG, and not extending to extratemporal regions depicted by surface EEG. We recognise that there is no literature data for a quantitative definition of a dominant interictal extratemporal sharp wave focus in the setting of lesional temporal lobe epilepsy, against which to compare our own data. In this study, this was defined as at least 35% of total interictal activity localised over extratemporal electrodes; this was an arbitrary cut-off point we utilised to include patients with a significant proportion of extratemporal interictal activity (suggesting perhaps the presence of an active remote focus) and to exclude patients with rare and non-consistent extratemporal spiking. In a *post-hoc* analysis, we were able to identify two more cases (both with MTS) with less than 5% of total interictal spiking recorded over extratemporal areas (frontopolar and posterior temporal/parietal).

The prevalence of extratemporal EEG localising features was much lower in the MTS group (2/26 cases [7%] *versus* 6/21 for tumours and FCD [30%]), thus supporting a more concrete and predictable electrophysiological behaviour of MTS, compared to tumoural and FCD cases. Both of our two MTS cases demonstrated early ictal EEG features implicating frontopolar regions, while Patient 1 had a frontopolar-inferior frontal lobe interictal SW focus in addition to a predominant ipsilateral anterior-basal temporal focus. Apparently, frontopolar surface ictal EEG onsets have been described in cases with medial/basal temporal lobe lesions and concordant ictal onsets on intracranial EEG recordings with subdural (Mikuni *et al*., 1997) and foramen ovale electrodes (Alarcon *et al*., 2001). Seizures may readily propagate from the medial temporal region to the basal-orbitofrontal and thence to the anterior frontal cortex, utilising established

anatomo-functional connections in these areas, as has been shown by chronic recordings with depth electrodes implanted in the relevant regions (Lieb *et al*., 1991) and evoked potential studies documenting orbital frontal cortex responses to hippocampal stimulations (Catenoix *et al*., 2005). If this occurs before propagation to ipsilateral temporal neocortex takes place, erroneous frontal lobe localisation may be suggested. Frontopolar regions were the only extratemporal areas implicated in our MTS patients. Falsely localising lateral frontal and parietal surface ictal EEG onsets have been described in exceptional cases of medial temporal lobe epilepsy, verified by foramen ovale recordings (Alarcon *et al*., 2001).

Extratemporal suprasylvian, frontocentral, and centroparietal locations were observed in 3 of our 6 tumoural and FCD cases; frontopolar/frontal in 2 and posterior temporal-parietal in one. The lesion was located lateral to the collateral sulcus in three patients (Patients 5, 7, and 8), involved parts of the medial temporal lobe plus basal/lateral temporal neocortex in two (Patients 3 and 4), and was strictly mediotemporal in one (Patient 6). There was no obvious difference with regard to EEG localisation within particular extratemporal regions between the medial temporal lesion and the lateral temporal lesion subgroups, however, our sample was too small to be able to infer the presence of such differences. Studies focusing on the electroclinical features of lesional temporal neocortical epilepsies either do not report on the presence of extratemporal interictal/ictal EEG findings (O'Brien *et al*, 1996; Foldvary *et al*., 1997), or report such findings among 6-11% of their population (Pfander *et al*., 2002) without specifying particular localisation. Apparent discordant interictal and ictal EEG localisation was noted in 2 (Patients 4 and 7) of our 6 tumoural and FCD cases. In both of them, interictal EEG localisation was lesion-concordant and correctly localising, thus being more reliable compared to ictal EEG. This is in agreement with Pfander *et al*. (2002) reporting extratemporal interictal EEG localisation in 6% *versus* 11% with ictal EEG among their lesional neocortical temporal group. We postulate that ictal onset from the temporal neocortex may be hidden on surface EEG due to poor synchrony among discharging neurons and recruitment of neuronal substrate, not yet large enough to produce a detectable surface EEG signal (Tao *et al*., 2007). Subsequent propagation to extratemporal cortex by incorporating larger neuronal populations and achieving greater discharge synchrony may give rise to an obvious, nonetheless falsely localising, extratemporal ictal EEG pattern.

Of 9 patients with medial temporal lobe tumours (Hammer *et al*., 1999), 7 demonstrated extratemporal interictal SW activity, accounting for only a small proportion of the total recorded interictal activity. According to our criteria, the extratemporal interictal SW focus should account for at least 35% of the totally recorded interictal activity and thus our method is not comparable. Besides this, only one of our 6 tumoural/FCD patients (Patient 7) had a lesion strictly confined within the medial temporal region.

Propagation of interictal and ictal activity from temporal neocortex or from both medial and neocortical temporal areas and early involvement of extratemporal suprasylvian neocortical areas through corticortical connections, utilising most likely polar and insular cortex as intermediary nodes (Kahane *et al*., 2001; Chabardès *et al*., 2005; Bartolomei *et al*., 2010), appears to be the most likely explanation for suprasylvian-pericentral EEG localisation in the three (Patients 4, 5, and 7) of our tumoural and FCD patients. This could be consistent with the recently proposed concept of the "*temporosylvian epileptogenic network*" (Bartolomei *et al*., 2010), which especially applies to temporal lobe lesions other than HS. The temporopolar-orbital frontal pathway was most likely utilised for Patient 8, who showed very prominent hyperkinetic behaviours, consistent with recent reports linking this pathway to seizures of temporal lobe origin manifesting similar ictal behaviours (Rheims *et al*., 2008; Wang *et al*., 2008; Vaugier *et al*., 2009). The organisation of the epileptogenic zone for Patient 3 was probably more complex and extensive involving temporal, frontal, and occipital cortices. Patient 6 was the only patient demonstrating a posterotemporal/parietal ictal EEG onset, in obvious discordance with an ipsilateral medial temporal mass lesion and an anterior temporal interictal SW focus. According to the previous discussion, we postulate a seizure propagation phenomenon from the medial temporal region, perhaps utilising insula as an intermediary node. Temporo-occipital ictal EEG onsets have been reported in a recent series of lesional insular epilepsies (Lehe *et al*., 2009).

An alternative explanation for our findings is the presence of an additional epileptogenic pathology, non-detectable by MRI, underlying areas of extratemporal EEG abnormalities. Co-existence of MTS with FCD and other dysplastic features is reported in 10-50% of MTS patients in surgical series (Diehl *et al*., 2004; Kalnins *et al*., 2004; Fauser and Bongahe, 2006). Both pathologies, however, are usually co-localised in the same temporal lobe, often in the anterior and basal portion (Srikijvilaikul *et al*., 2003; Kalnins *et al*., 2004), and it is very questionable whether they could generate discordant EEG foci. The same holds true for some types of developmental tumours (DNET, GG) that may also be associated with occult cortical malformations in their vicinity (Prayson *et al*., 1993; Ferrier *et al*., 2006). In any case, it is difficult to consider that a hypothetically non-visible intratemporal pathology, nonetheless in close proximity to the main lesion, may account for

such prominent extratemporal EEG activity. In addition, the excellent surgical outcome following temporal lobe resections only argues against an extratemporal epileptogenic pathology. We certainly recognise that a longer follow-up time is needed to confirm successful outcome in the long-term, as three of our eight patients were followed postoperatively for periods of between one and two years and another (Patient 3) had an isolated seizure, most likely related to drug withdrawal, 12 months postoperatively and is currently seizure-free following reinstitution of drug treatment for 10 months. However, the remaining patients have been continuously seizure-free since surgery for follow-up periods ranging between 2 and 5.5 years.

French groups have introduced the concept of "*temporal lobe plus*" epilepsies (Chabardès *et al*., 2005; Barba *et al*., 2007) and utilised sophisticated signal analysis ("*epileptogenicity index*") (Bartolomei *et al*., 2008; Aubert *et al*., 2009; Bartolomei *et al*., 2010) to describe seizures of multilobar origin based on intracranial EEG depth recordings involving the temporal lobe and neighbouring areas. They have suggested that the presence of extratemporal surface EEG features is predictive of such cases (Barba *et al*., 2007). Their patients differed from ours, with a much higher prevalence of MTS and a considerable proportion of normal MRI cases. Nevertheless, the topographical spectrum of extratemporal EEG localisations, when described (Barba *et al*., 2007), was comparable to that of our mixed MTS and tumoural/FCD group, involving frontocentral, frontotemporal, and posterotemporal/parietal regions. Most cases of the French series were subjected to invasive monitoring and tailored resections, however, failures still occurred, reflecting intricacies and complexities of the epileptogenic zone organisation in this group.

In conclusion, we obtained excellent results with resections aiming to primarily remove lesions. Sample sizes for each pathology (HS, tumoural, and FCD) subgroup were too small to draw any conclusions regarding valid statistical differences. Another source of difficulty with statistical analysis was that our definition of "*surface extratemporal EEG features*" included either or both interictal (provided it was >35% of totally recorded) and ictal extratemporal activity. Although we suspect that tumoural and FCD cases may more often show extratemporal surface EEG features and specific constellations of findings, such as interictal and ictal activity exclusively localised to extratemporal areas, we elected to simply report actual numbers and percentages, recognising the need for stronger samples in order to prove statistically significant differences. We recognise difficulties with reproducing our findings in larger comparable cohorts, given the adoption of different presurgical approaches among epilepsy surgery centres. We proceeded to surgery without previous intracranial EEG studies and in spite of the presence of such EEG findings. Our decision was based on the constellation of: 1) seizure semiology consistent with temporal lobe involvement; 2) unitemporal structural abnormalities of high epileptogenic potential, ipsilateral to EEG findings; 3) absence of any other imaging evidence suggesting pathology over areas depicted by remote EEG signals; and 4) recognition that the discordant EEG signals may well utilise a common epileptogenic network. We certainly do not advocate that utilisation of invasive monitoring should be dogmatically rejected in every case comparable to ours. Instead, we propose that the presence of this kind of EEG discordance should not discourage the surgical option, does not necessitate non-invasive evaluations in an as yet undetermined, but perhaps significant, proportion of such patients, and may well be compatible with excellent surgical outcomes provided a generous lesion resection is accomplished. □

Disclosures.
The authors have no conflict of interest to disclose.

References

Alarcon G, Kissani N, Dad M, *et al*. Lateralizing and localizing values of ictal onset recorded on the scalp: evidence from simultaneous recordings with foramen ovale electrodes. *Epilepsia* 2001; 42: 1426-37.

Aubert S, Wendling F, Regis J, *et al*. Local and remote epileptogenicity in focal cortical dysplasias and neurodevelopmental tumors. *Brain* 2009; 132: 3072-86.

Barba C, Barbati G, Minnoti L, Hoffmann D, Kahane P. Ictal clinical and scalp-EEG findings differentiating temporal lobe epilepsies from temporal "plus" epilepsies. *Brain* 2007; 130: 1957-67.

Barry E, Sussman N, O'Connor M, Harner R. Presurgical electroencephalographic patterns and outcome from anterior temporal lobectomy. *Arch Neurol* 1992; 49: 21-7.

Bartolomei F, Chauvel P, Wendling F. Epileptogenicity of brain structures in human temporal lobe epilepsy: a quantified study from intracerebral EEG. *Brain* 2008; 131: 1818-30.

Bartolomei F, Cosandier-Rimele D, McConigal A, *et al*. From mesial temporal lobe to temporosylvian seizures: a quantified study of temporal lobe seizure networks. *Epilepsia* 2010; 51: 2147-58.

Castro L, Serpa M, Valerio R, *et al*. Good surgical outcome in discordant ictal EEG-MRI unilateral mesial temporal sclerosis patients. *Epilepsia* 2008; 49: 1324-32.

Catenoix H, Magnin M, Guenot M, Isnard J, Maugiere F, Ryvlin P. Hippocampal-orbitofrontal connectivity in human: an electrical stimulation study. *Clin Neurophysiol* 2005; 116: 1779-84.

Cendes F, Watson C, Andermann F, Dubeau F, Arnold D. Is ictal recording mandatory in temporal lobe epilepsy? *Arch Neurol* 2000; 57: 497-500.

Chabardès S, Kahane P, Minnoti L, *et al*. The temporopolar cortex plays a pivotal role in temporal lobe seizures. *Brain* 2005; 128: 1818-31.

Diehl B, Najm I, La Presto E, *et al*. Temporal lobe volumes in patients with hippocampal sclerosis with or without cortical dysplasia. *Neurology* 2004; 62: 1729-35.

Ebersole J, Pacia S. Localization of temporal lobe foci by scalp ictal EEG patterns. *Epilepsia* 1996; 37: 386-99.

Fauser S, Bongahe A-S. Epileptogenicity of cortical dysplasia in temporal lobe dual pathology: an electrophysiologic study with invasive recordings. *Brain* 2006; 129: 82-95.

Ferrier C, Aronica E, Leijten F, *et al*. Electrocorticographic discharge patterns in glioneuronal tumors and focal cortical dysplasia. *Epilepsia* 2006; 47: 1477-86.

Foldvary N, Lee N, Thwaites G, *et al*. Clinical and electrographic manifestations of lesional neocortical temporal lobe epilepsy. *Neurology* 1997; 49: 757-63.

Gilliam F, Bowling S, Bilir E, *et al*. Association of combined MRI, interictal EEG, ictal EEG results with outcome and pathology after temporal lobectomy. *Epilepsia* 1997; 38: 1315-20.

Hammer M, Najm M, Mohamed A, Wyllie E. Interictal epileptiform discharges in temporal lobe epilepsy due to hippocampal sclerosis *versus* medial temporal lobe tumors. *Epilepsia* 1999; 40: 1261-8.

Hirsch L, Spencer S, Spencer D, Williamson P, Mattson R. Temporal lobectomy in patients with bitemporal epilepsy defined by depth electroencephalography. *Ann Neurol* 1991; 30: 340-6.

Holmes M, Miles A, Dodrill C, Ojemann G, Wilensky A. Identifying potential surgical candidates in patients with evidence of bitemporal epilepsy. *Epilepsia* 2003; 44: 1075-9.

Kahane P, Huot J-C, Hoffmann D, Lo Russo G, Benabid A, Munari C. Perisylvian cortex involvement in seizures affecting the temporal lobe. In: Avanzini G, Beaumanoir C, Munari C, Avanzini G. *Limbic seizures in children*. Montrouge (France) : John Libbey Eurotext, 2001: 115-27.

Kalnins R, McIntosh A, Saling M, Berkovic S, Jackson G, Briellmann R. Subtle microscopic abnormalities in hippocampal sclerosis do not predict clinical features of temporal lobe epilepsy. *Epilepsia* 2004; 45: 940-7.

Lehe von M, Wellmer J, Urbach H, Schramm J, Elger C, Clusmann H. Insular lesionectomy for refractory epilepsy: management and outcome. *Brain* 2009; 132: 1048-56.

Lieb J, Dasheiff R, Engel J. Role of the frontal lobe in the propagation of medial temporal lobe seizures. *Epilepsia* 1991; 32: 822-37.

Mikuni N, Ikeda A, Terada K, *et al*. Frontopolar ictal epileptiform discharges on scalp electroencephalogram in temporal lobe epilepsy. *J Clin Neurophysiol* 1997; 14: 507-12.

O'Brien T, Kilpatrick C, Murrie V, Vogrin S, Cook M. Temporal lobe epilepsy caused my mesial temporal sclerosis and temporal neocortical lesions. *Brain* 1996; 119: 2133-41.

Pataraia E, Lurger S, Serles W, *et al*. Ictal scalp EEG in unilateral mesial temporal lobe epilepsy. *Epilepsia* 1998; 39: 608-14.

Pfander M, Arnold S, Henkel A, *et al*. Clinical features and EEG findings differentiating mesial from neocortical temporal lobe epilepsy. *Epileptic Disord* 2002; 4: 189-96.

Prayson R, Estes M, Morris H. Coexistence of neoplasia and cortical dysplasia in patients presenting with seizures. *Epilepsia* 1993; 34: 609-15.

Radhakrishnan K, So EL, Silbert PL, *et al*. Predictors of outcome of anterior temporal lobectomy for intractable epilepsy: a multivariate study. *Neurology* 1998; 51: 465-71.

Rheims S, Minotti L, Demarqay G, Hisrch E, Arzimanoglou A, Hoffmann D. Analysis of clinical patterns and underlying epileptogenic zones of hypermotor seizures. *Epilepsia* 2008; 49: 2030-40.

Sirven J, Malamut B, Liporace J, O'Connor M, Sperling M. Outcome after temporal lobectomy in bilateral temporal lobe epilepsy. *Ann Neurol* 1997; 42: 873-8.

So N, Olivier A, Andermann F, Gloor P, Quesnay P. Results of surgical treatment in patients with bitemporal epileptiform abnormalities. *Ann Neurol* 1989; 25: 432-9.

Srikijvilaikul T, Najm I, Hovinga C, Prayson R, Gonzales-Martinez A, Bingaman W. Seizure outcome after temporal lobectomy in temporal lobe cortical dysplasia. *Epilepsia* 2003; 44: 1420-4.

Steinhoff B, So N, Lim S, Lüders H. Ictal scalp EEG in temporal lobe epilepsy with unitemporal *versus* bitemporal interictal epileptiform discharges. *Neurology* 1995; 45: 889-96.

Tao J, Baldwin M, Ray A, Haws-Ebersole S, Ebersole J. The impact of cerebral source area and synchrony on recording scalp electroencephalography ictal patterns. *Epilepsia* 2007; 48: 2167-76.

Vaugier L, Aubert S, McConigal A, *et al*. Neural networks underlying hyperkinetic seizures of "temporal" lobe origin. *Epilepsy Res* 2009; 86: 200-8.

Wang L, Matthews G, Whetsell W, Abou-Khalil B. Hypermotor seizures in patients with temporal pole lesions. *Epilepsy Res* 2008; 82: 93-8.

Appendix 1. Supplementary figures

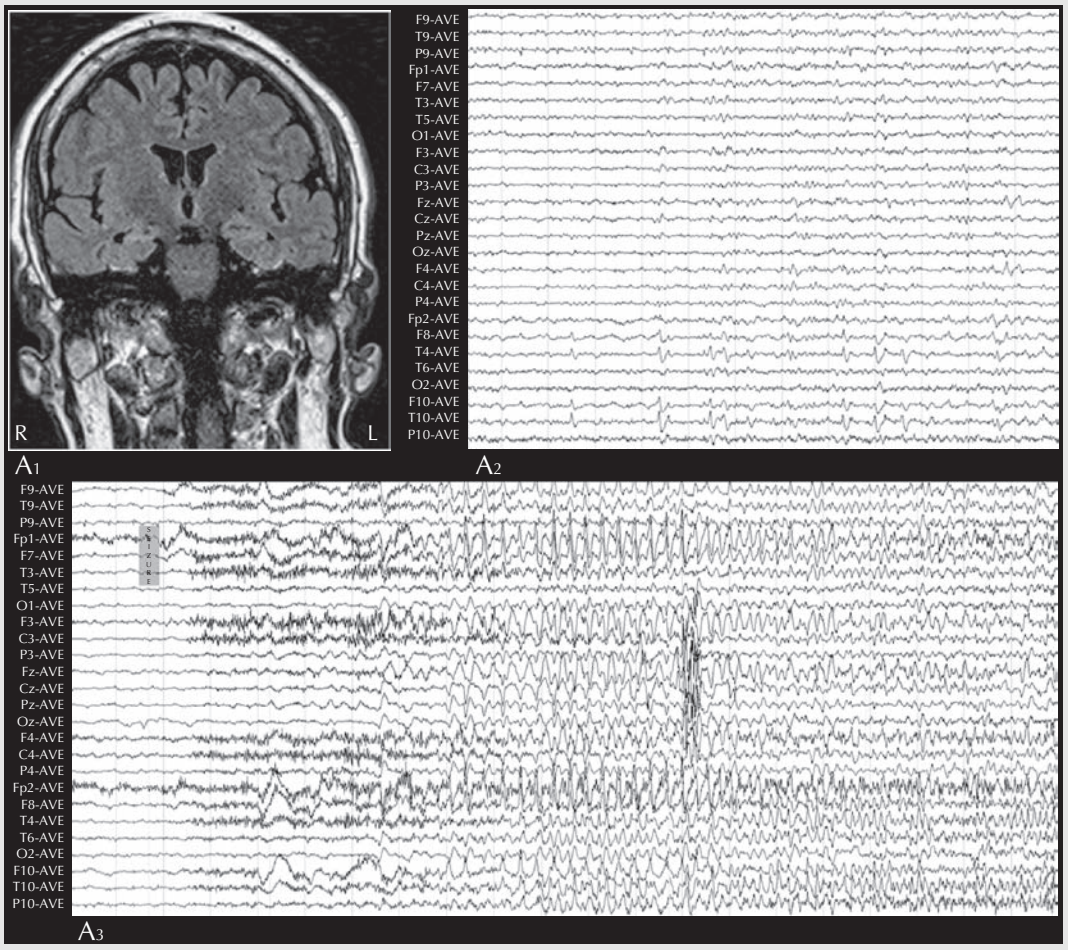

Figure S1. Patient 2. (A_1) MRI showing high intensity signal over the right medial temporal area. (A_2) Interictal EEG of a typical right anterior SW focus (F8/T4/F10/T10). (A_3) Ictal EEG presenting bilateral frontopolar-frontal repetitive SW activity (Fp2/F4/Fp1/F3), followed by a right temporal sustained and well-organised "theta/alpha" rhythm.

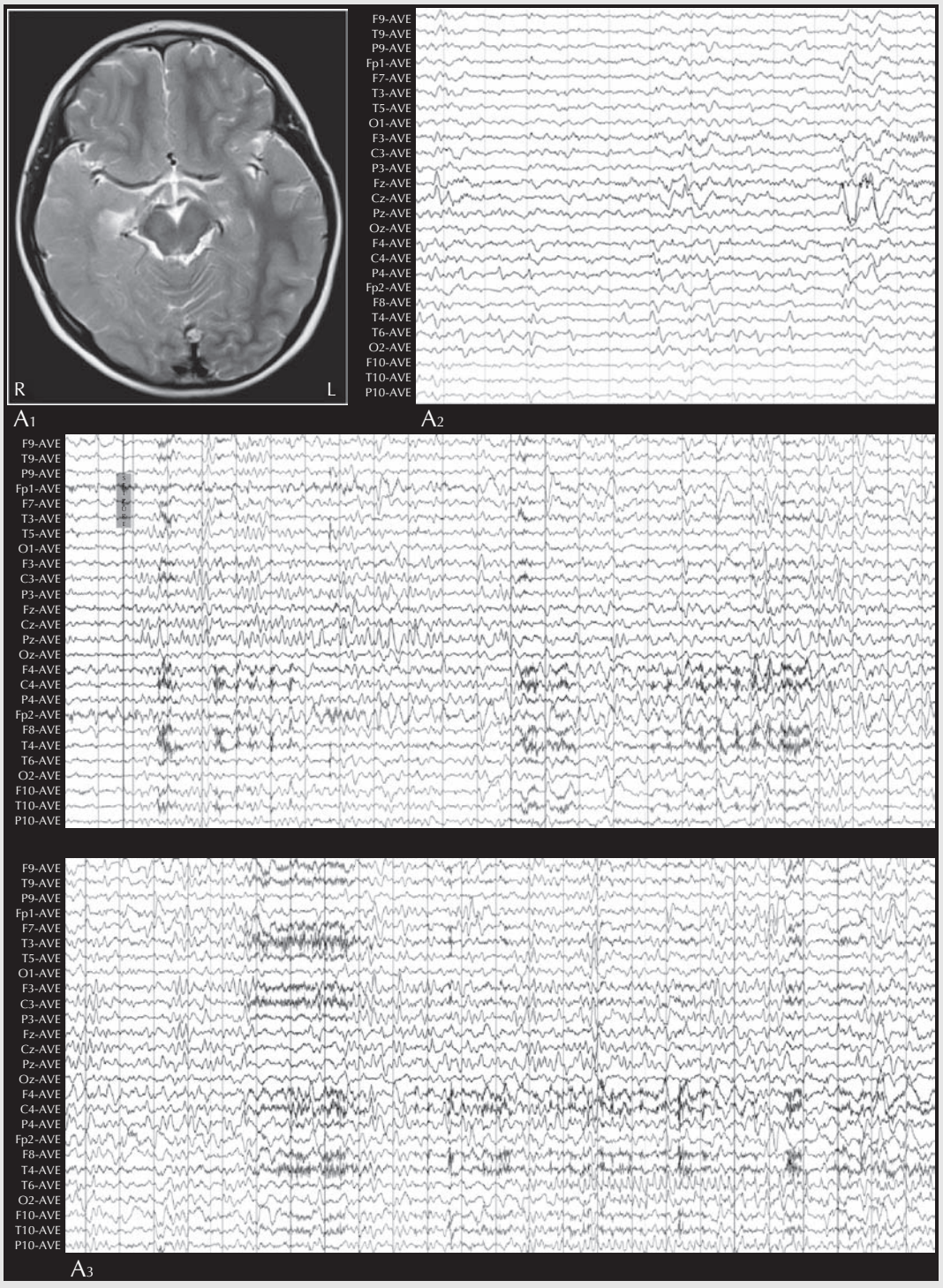

Figure S2. Patient 3. (A_1) MRI showing extensive right temporal lobe FCD, involving the pole, the medial-basal and lateral temporal neocortex, extending back towards the occipito-temporal junction. (A_2) Interictal EEG reveals a right mid-posterior temporal SW focus (T4/T6), occasionally extending to the anterior temporal region (F8/Fp2). (A_3) Ictal EEG shows a broadly distributed onset of semi-rhythmic "delta" pattern over the right frontal region and the anterior midline (Fp2/F4/Fz).

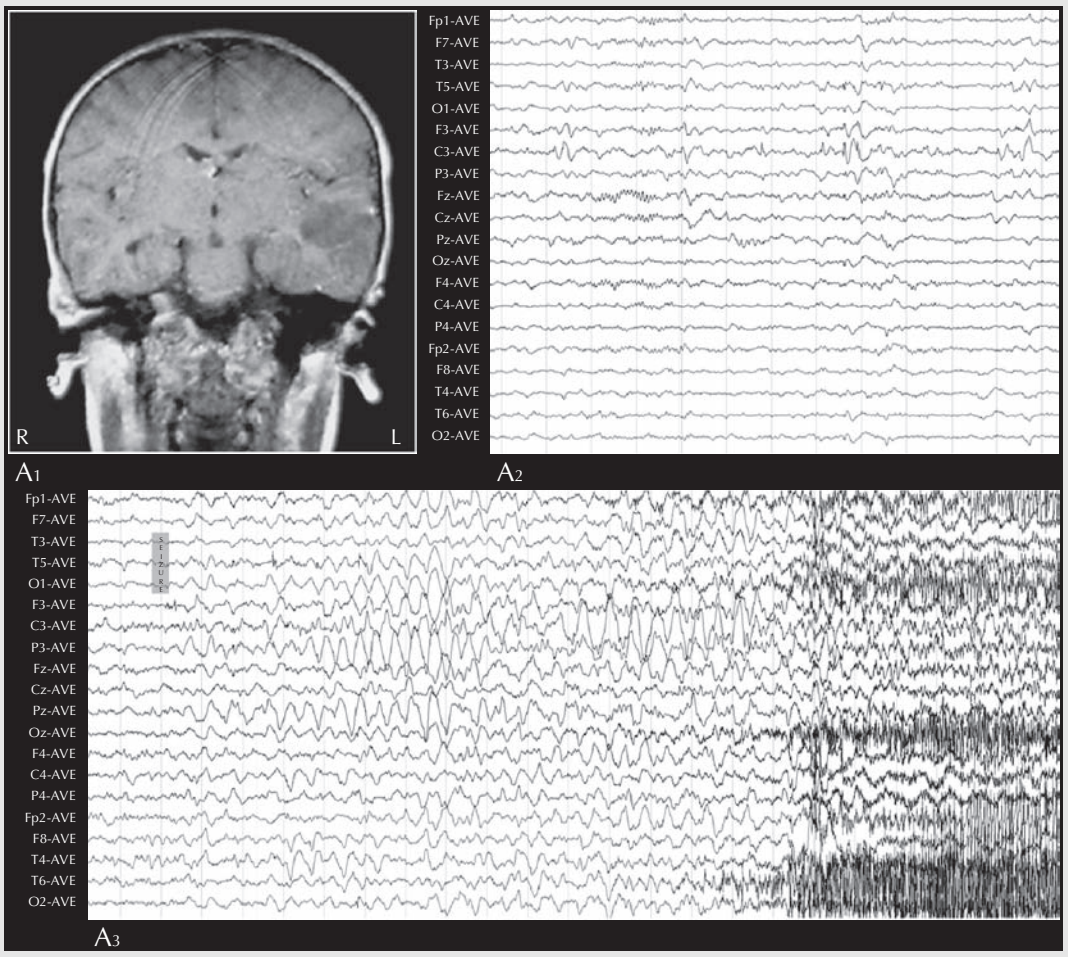

Figure S3. Patient 6. (A_1) MRI showing a left temporal lobe tumour invading the basal temporal and inferior lateral temporal neocortex. (A_2) Interictal EEG shows a well-localised SW focus over the left central region (C3). (A_3) Ictal EEG onset is broader, less well-organised, with a left-hemispheric rhythmic delta pattern, prominent over the parasagittal region (C3 and P3/Pz).

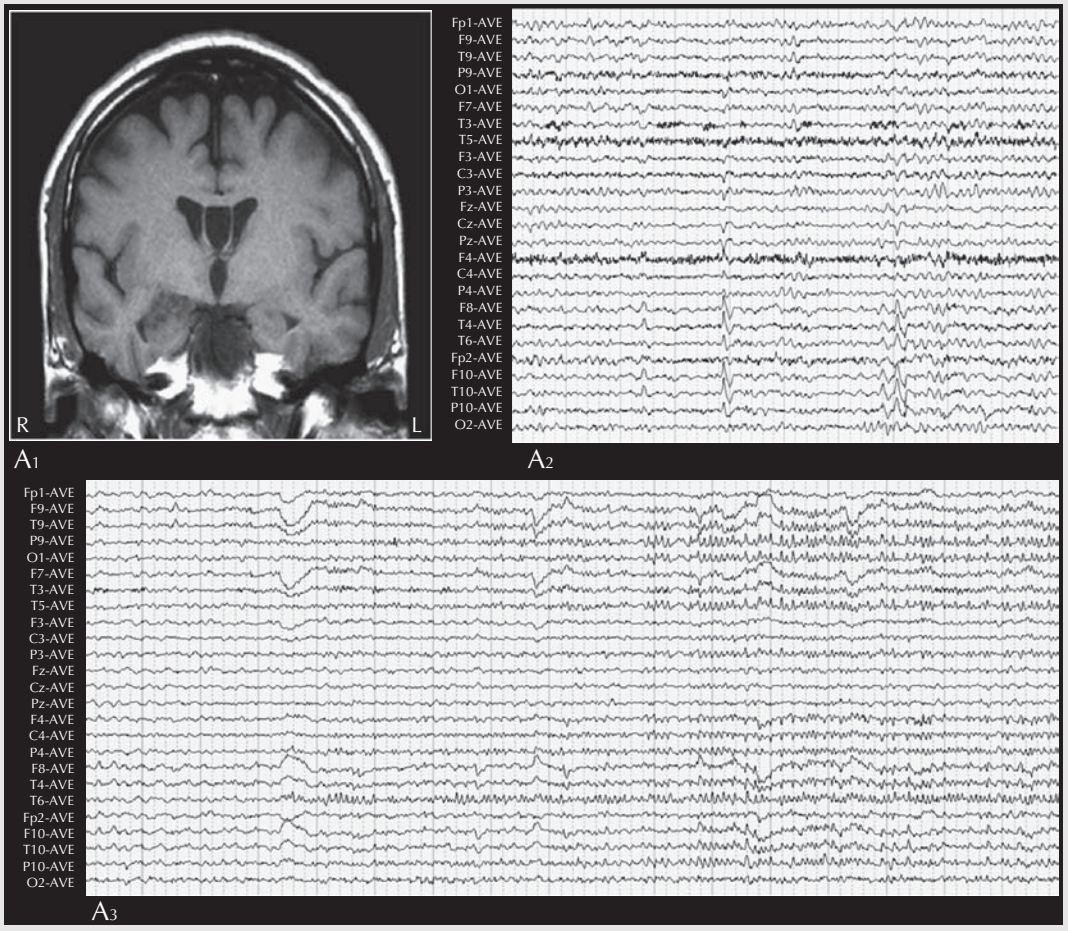

Figure S4. Patient 7. (A_1) MRI revealed a right medial temporal lobe mass lesion. (A_2) Interictal EEG shows a right anterior temporal interictal sharp wave focus (F8/F10 and T4/T10). (A_3) Ictal EEG demonstrates focal onsets of "alpha" activity from the posterior temporoparietal region (T6 to P4).