The additional lateralising and localising value of the postictal EEG in frontal lobe epilepsy

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Highlights

- Our study revealed that 47/96 (49%) postictal periods contained lateralizing or localizing information.

- In 14/38 (39%) patients, at least one seizure with an unhelpful ictal EEG was followed by postictal EEG features that added new localising or lateralising information.

- A close examination of the postictal EEG can offer additional information which can contribute to the identification of a potentially resectable epileptogenic zone.

Abstract

Objective: The aim of this study was to describe the additional lateralising and localising value of the postictal EEG in frontal lobe epilepsy (FLE). The ictal EEG in FLE is frequently challenging to localise.

Methods: We identified patients investigated for epilepsy surgery with unilateral FLE based on consistent semiology, a clear lesion and/or with frontal onset on intracranial EEG. A one hour section of postictal EEG was analysed by two raters for new or activated EEG features and it was assessed whether these features offered additional information when compared to the ictal EEG. Postictal features assessed included asymmetrical return of the posterior dominant rhythm and potentiated lateralised or regional slowing, spikes or sharp waves.

Results: Thirty eight patients were included who had a combined total of ninety six seizures. 47/96 (49%) postictal periods contained lateralizing or localizing information. Further analysis showed that in 14/38 (39%) patients, at least one seizure with an unhelpful ictal EEG was followed by postictal EEG features that added new localising or lateralising information. A subgroup of 11 patients who were ≥1 year seizure-free (ILAE class 1) and thus classified as having a 'gold-standard' FLE diagnosis were analysed separately and it was found that 14/30 of their seizures (47%) had extra postictal information.

Conclusions: The new postictal information was always concordant with the ultimate diagnosis, except for asymmetric postictal return of background activity ipsilateral to the epileptogenic zone in three patients.

Significance: This study shows that a close examination of the postictal EEG can offer additional information which can contribute to the identification of a potentially resectable epileptogenic zone.

1. Introduction

The ictal and interictal EEG in frontal lobe epilepsy (FLE) is challenging and unreliable. The ictal EEG is localising in less than one third of patients (Laskowitz et al., 1995) and may otherwise be generalised, obscured by muscle and movement artefact or mislocalise to the temporal lobe or opposite hemisphere (Bagla and Skidmore., 2011). The interictal epileptiform abnormalities in FLE can be bilateral, multilobar or generalised (Laskowitz et al., 1995). This means that localising or lateralising features in the postictal EEG would be particularly helpful. However, no large study has explored the value of the postictal EEG in this patient group, although studies have explored its utility in temporal lobe epilepsy (TLE) (Jan et al., 2001; Kaibara and Blume, 1988; Gotman and Koffler, 1989). One study of 9 patients with FLE examined a ten minute postictal period and found regional activation of spikes in 1/9 patients (Bautista et al, 1998). However, as the average time interval for the EEG to return to baseline after FL seizures is 35 minutes (Arkiloa et al., 2013), assessing a longer period may provide further information.

This study was concerned with assessment of the post-ictal EEG in a well-defined FLE cohort to determine whether any changes observed add localizing or lateralizing value compared to the ictal EEG.

2. Methods

The telemetry database at the National Hospital for Neurology, a quaternary referral centre, was searched from 1st January 2008 to 21st December 2012. We included pre-surgical

patients with unilateral FLE based on consistent semiology and either a clear FL lesion and/or with intracranial proven frontal onset. All patients had been discussed in the pre-surgical multi-disciplinary team meeting and their imaging, neuropsychometry and other data were found to be concordant with the lobar classification of their epilepsy.

Up to five seizures were included for each patient with the longest seizures chosen first. Seizures had to be associated with objective clinical signs (loss of awareness and/or positive or negative motor signs). All seizures had to be followed by at least one hour of EEG without seizures. The last seizure of a cluster was included in some cases. Patients with previous craniotomy and a breach rhythm were included because the study only focused on additional postictal changes, when compared to the patient's EEG baseline. Seizures treated with a benzodiazepine were included in the analysis of all postictal features except for spike analysis because Diazepam significantly suppresses interictal spikes (Duncan, 1987).

Classification of the ictal EEG was based upon accepted criteria (Foldvary et al., 2001) with minor modifications:

1. Generalized / non-lateralized: activity involving multiple electrodes over both hemispheres equally; non-localisable and symmetrical bifronto-central patterns were also included in this category.

2. Lateralized: activity involving multiple electrodes over two or more lobes of a single hemisphere; frontotemporal patterns were included in this category.

3. Regional frontal: activity with a clear maximum in electrodes of one frontal lobe.

As this paper focuses on FLE, we added one additional category: regional vertex (i.e. non-lateralised) (Table 1). The addition of this 'regional vertex' category reflects the localising

(but not lateralising) value of a focal ictal pattern at the vertex which would otherwise have had to fall within the less localising category of 'bifrontocentral'. 'Regional vertex' is a descriptive terminology frequently used within our pre-surgical EEG telemetry reports. The classification of the ictal EEG was done by the consultant neurophysiologist (BD or TW) and confirmed at the pre-surgical multidisciplinary team meeting.

Visual and power spectrum analysis of one hour of postictal EEG was performed and presence of lateralising or localising information recorded (Figs. 1 and 2). Additional lateralising information included asymmetrical (amplitude difference more than 100%) return of the posterior dominant rhythm when symmetrical at baseline. In addition, new or potentiated features were recorded including: lateralised or regional slow (in theta or delta range); lateralised or regional epileptiform activity, including spikes and sharp waves. Potentiation was defined as >50% greater density when compared to the same state (e.g. wake or sleep) interictally. Lateralised slowing was defined as twofold the power compared to the contralateral homotopic region on a bipolar montage. We defined an activity as regional frontal if maximum voltage amplitudes occurred at frontal electrode positions of the 10-20 system F4 or F3, FP2 or FP1 electrodes. It was also recorded if a spike population had a change in voltage field distribution, such as a more restricted field post-ictally, with either greater lateralising or localising power.

The analysis was performed by KW (highly specialised clinical physiologist in video-EEG telemetry) and then by a second independent rater (SG, a certified electroencephalographer and neurologist), blinded to the patient's clinical information and to the ictal EEG. The postictal EEG was compared to one hour representative samples of seizure-free wake and

sleep periods. These periods were as shortly as possible before the analysed seizures occurred to control for the effects of drug reduction during admission. An interrater reliability analysis using the Kappa statistic was performed using IBM SPSS 19 to determine consistency among KW and SG when assessing additional lateralising information. In cases in which one rater believed that there was additional postictal information and the other rater disagreed, a consensus was reached on detailed review of the postictal EEG, blinded to the ictal EEG or the patient's clinical details.

3. Results

3.1 Patients

Thirty eight patients were included who had a combined total of ninety six seizures. The demographic details are listed in Table 1. Seizures with multiple semiological signs were classified by their most prominent or consistent feature (Lüders et al., 1999). All patients showed some EEG change with their seizures although in two seizures this was generalized suppression only. Fig. 3 gives details of pre-surgical work-up and presents ILAE outcome classifications for all patients who were resected on a scale from 1-6, where class 1 is entirely seizure free and subsequent classes reflect increasing seizure burden (Wieser et al., 2001).

3.2 Inter-rater agreement

There was moderate inter-rater agreement on the presence of additional lateralising value within the post-ictal EEG (.438 Cohen's Kappa; p = <.001; agreement on 72% of postictal EEGs). In no cases did the two raters identify lateralising information which implicated different hemispheres from one another.

3.3 Lateralising and localizing value of the post-ictal EEG

16/96 seizures had correctly lateralizing information (excluding 3 seizures with mislateralising asymmetrical return of alpha; see Table 2 and discussion). 31/96 seizures had unilateral localizing information. Seizures which contained a feature which lateralized (e.g. right hemisphere slowing) and a feature which localized (e.g. activation of right frontal spikes) were only counted once, in the localizing category, because the localizing information superseded the lateralizing information. In total, 47/96 (49%) seizures had postictal lateralizing or localizing information (Fig. 4). 22/47 seizures with postictal information had two or more lateralizing or localizing features and in none of these seizures was this mislateralising compared to the final diagnosis.

When analyzing by patient, 25/38 patients (66%) had at least one seizure with postictal lateralizing or localizing information (7 lateralising; 18 localizing), excluding those patients with mislateralising asymmetrical alpha.

Post-ictal information was classified as 'new' if it added entirely new localising or lateralising information not contained in the ictal EEG, as 'confirmatory' if it confirmed an asymmetry on a widespread ictal EEG pattern or 'concordant' in patients whose post-ictal period

contained the same lateralising or localising information already seen in the ictal EEG.

Altogether, new or confirmatory localising or lateralising information was obtained in 14

patients (see Fig. 4 for details).

3.4 Extra lateralising and localizing value of the post-ictal EEG in the 10 patients seizure-free

following resection

The eleven patients who were ≥1 year seizure-free (ILAE class 1) following resection were

taken as 'gold-standard' FLE and examined separately. The eleven patients had a combined

total of 30 seizures included in the study. 9/30 had postictal lateralizing signs and 5/30 had

postictal localizing signs. This gave a total of 14/30 seizures (47%) with extra postictal

information. 5/11 patients (45%) had additional information in their postictal EEG

supporting the initial hypothesis of the epileptogenic zone.

4. Discussion

On review of post-operative outcome of the patients within this series who were resected,

the majority of lesional cases became completely seizure free (11/18 ILAE class 1; 61%). In

line with the literature, non-lesional patients who were resected were less likely to achieve

seizure freedom; of just three who had reached 1 year follow-up, none were seizure-free

although all had >50% reduction of seizures (ILAE class 4 or better).

In this cohort there was a localizing ictal EEG pattern in 31/96 seizures (32%). This leaves a sizeable majority of non-localising seizure patterns, where detailed post-ictal EEG analysis has the potential to add information.

In our series, 47/96 (49%) seizures had additional lateralising or localizing information. However, the most important finding is that the postictal EEG adds new or confirmatory information which supplements an ill-defined ictal pattern in 27/96 seizures from 14 patients. Analysing the seizures from our eleven patients with a 'gold-standard' FLE diagnosis (seizure-free following resection) showed a similar percentage of postictal EEGs with additional features (47% vs. 49%) which supports the reliability of the data from our full cohort. Our data shows that the postictal EEG can be more helpful in FLE than a previous study suggested[6]. Our sample size was quadruple that of the earlier study and analysed a longer period of postictal EEG (1 hour vs. 10 minutes) which may explain this discrepancy.

All patients with post-ictally activated spikes showed lateralized or regional frontal spikes except for one patient who had activation of his interictal right temporal lobe spikes alongside activated right frontal slow. This patient has an area of abnormal cortical development involving the right orbitofrontal gyri. His ictal pattern in both seizures included was right inferior frontotemporal. In orbitofrontal epilepsies, spikes and ictal discharges can be seen exclusively in the temporal region (Bagla and Skidmore, 2011; Kriegel et al., 2012). This single case suggests that it is possible for mis-localising interictal spike populations to be activated following a seizure, echoing the findings of an intracranial study of eight TLE patients (Gotman and Koffler, 1989).

The asymmetrical return of the alpha rhythm was mislateralising, i.e. returned first to the side of seizure onset, in three seizures from two patients which showed no other postictal features. Both of these patients had EEG patterns that began or persisted without asymmetry and had bilateral spikes reflecting a widespread irritative zone. Both patients are seizure free suggesting that mislateralising alpha is not necessarily a poor prognostic indicator for post-surgical outcome. Regarding postictal slowing, we found no mislateralisation. This is in contrast to a study of TL seizures (Jan et al., 2001). In that study two of 46 postictal EEGs (from the same patient) showed mislateralising delta activity; subsequent subdural EEGs revealed seizures arising independently from each TL. In a different TL cohort, the 35 postictal periods with attenuation, activated slow activity or spikes lateralised correctly but this study did not assess the asymmetrical return of the alpha rhythm (Kaibara and Blume, 1988).

One limitation of this study is the moderate inter-rater concordance (Cohen's Kappa .438) with the two raters agreeing upon 72% of seizures analysed. In a study of postictal lateralised delta following TL seizures, an inter-rater agreement in 91% of 80 seizures was found (Jan et al., 2001). The lower inter-rater concordance found in our study likely relates to the greater variety of interictal abnormalities seen in FLE (Laskowitz et al., 1995) and the shorter post-ictal changes following FL seizures (Arkiloa et al., 2013). A study of postictal EEG following 51 seizures, mainly TL, described 'rare disagreements' among raters but did not give further details (Kaibara and Blume, 1988). A further limitation is that 32 of the 38 patients reported here have lesional FLE, which could influence postictal EEG changes and thus the findings may not be the same were a cohort of entirely non-lesional patients to be studied.

5. Conclusions

Overall, this study shows that the postictal EEG can offer new or confirmatory localising and lateralising information in an appreciable number of patients. We present postictal data analysis from a well-characterised FLE cohort with post-surgical follow-up available for half of the patients. The reliability of postictal information is most robust when two separate concordant features are seen in the post-ictal EEG. Asymmetrical return of the alpha rhythm was the only postictal feature which could mislateralise.

Conflicts of interest: none

Table 1: Demographic information

Patients (n=38)	
Age (mean)	36 years (range 17-59)
Gender	15 F; 23 M
Previous craniotomy	9/38
Lesion on MRI	32/38 FCD (17); DNET or other low grade tumour (8); vascular insult (4); cerebral contusion (1); cavernous haemangioma (1); abscess (1).
Intracranial investigation (proven unilateral FL onset)	27/38 (all 6 without a lesion and 21/32 with a lesion)
Seizures (n=96)	
Seizures treated with a benzodiazepine	5
Clinical seizure type	Complex motor (31); Tonic (25); Automotor (17); GTCS (9); Hypermotor (8); Clonic (2); Head versive (2); Dialeptic (2)*
Clinical seizure duration (median and range)[a]	35 seconds (range 6-676)
EEG seizure duration (median and range)[a]	40 seconds (range 6-1800)
Ictal EEG in the 96 seizures	Regional frontal (31); Lateralised (21); Generalised (24); Bifrontocentral with side emphasis (11); Regional vertex (9)

[a]In the case of post-ictal analysis of the last seizure of a cluster, clinical and EEG seizure duration reflects the duration from the first to the last seizure of the cluster; *Classified using semiological seizure classification (Lüders et al, 1999)

Table 2: Frequency of postictal features in all seizures analysed (n=96)

Asymmetrical return of posterior dominant rhythm	25/96 Mislateralised in 3/25 (these 3 were the only postictal periods which mislateralised)		
Lateralised slow	6/96		
Regional slow	22/96		
Lateralised spikes	4/96		
	3/4 activated in frequency	1/4 more lateralised field whereas widespread before	
Regional spikes	19/96		
	9/19 activated in frequency	9/19 more restricted frontal field (only lateralized before)	1/19 new frontal spike population
Any 1 feature	50/96		
2 or more features	22/96		

Fig. 1: Asymmetrical return of posterior dominant rhythm

Fig. 2: Activation of right frontal theta slowing

Fig. 3: Flow chart of pre-surgical work-up of patients

Fig. 4: Lateralising and localising information in the postictal EEG

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