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Interictal estimation of intracranial seizure onset in temporal lobe epilepsy

Antonio Valentín [a,b,*,1], Gonzalo Alarcón [a,b,d,*,1], Sally F. Barrington [c], Jorge J. García Seoane [d], María C. Martín-Miguel [e], Richard P. Selway [f], Michalis Koutroumanidis [a,g]

[a] Department of Clinical Neuroscience, King's College London, Institute of Psychiatry, UK
[b] Department of Clinical Neurophysiology, King's College Hospital, London, UK
[c] Clinical PET centre, Guy's and St Thomas' NHS Trust, King's College London, London, UK
[d] Departamento de Fisiología, Facultad de Medicina, Universidad Complutense, Madrid, Spain
[e] Departamento de Neurofisiología, Hospital Gregorio Marañón, Madrid, Spain
[f] Department of Neurosurgery, King's College Hospital, London, UK
[g] Department of Clinical Neurophysiology and Epilepsies, Guy's and St Thomas' NHS Trust, London, UK

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HIGHLIGHTS

- Interictal intracranial tests such as focal slow activity (IFSA), single pulse electrical stimulation (SPES) and ^{18}FDG PET can successfully complement ictal recordings.
- When lateralized to the same side, intracranial IFSA and SPES reliably predicted the side and site (mesial or lateral temporal) of seizure onset.
- IFSA and SPES are simple, fast and inexpensive. If performed early in the telemetry period they have the potential to reduce telemetry time, and the associated risks and costs.

ABSTRACT

Objectives: To evaluate the lateralizing and localizing values of interictal focal slow activity (IFSA), single pulse electrical stimulation (SPES) and ^{18}FDG PET, in order to estimate their potential to complement ictal intracranial recordings and reduce prolonged monitoring in patients with temporal lobe epilepsy.
Methods: The study includes 30 consecutive patients with bilateral temporal subdural electrodes and focal seizure onset. IFSA, SPES and ^{18}FDG PET when available, were visually assessed and their combined lateralization was based on the majority of the individual lateralizing tests.
Results: In the 18 patients who had all three tests, lateralization was congruent with seizure onset areas in 15 (83%). When lateralized (15 patients), ^{18}FDG PET was always congruent with intracranial seizure onset. In all 12 patients without ^{18}FDG PET, lateralization combining IFSA and SPES was congruent with seizure onset, including two with bilateral independent seizure onset on subdural monitoring. 22 out of the 23 patients who had surgery enjoyed favorable outcome (Engel I or II).
Conclusion: Intracranial IFSA and SPES can reliably predict the side and site (mesial versus lateral temporal) of seizure onset when they lateralize to the same side.
Significance: ^{18}FDG PET can be useful in planning electrode implantation. During intracranial recordings, IFSA and SPES have the potential to reduce telemetry time, risks and costs.

1. Introduction

Successful outcome of resective epilepsy surgery depends on the correct localization of functionally and structurally abnormal cortex that generates seizures (Tellez-Zenteno et al., 2010). Despite the continuing advances of non-invasive techniques, particularly imaging, identification of epileptogenic cortex and the study of cortical function may still require intracranial EEG. The decision for, and the type of intracranial EEG evaluation depends on the underlying epilepsy and the expertise of the individual center (Zumsteg and Wieser, 2000; Nair et al., 2008), but usually, a number of spontaneous habitual seizures must be captured before epilepsy surgery can be decided upon. Intracranial recordings may last for

* Corresponding authors. Address: Department of Clinical Neuroscience, P.O. Box 43, Institute of Psychiatry, King's College London, De Crespigny Park, London SE5 8AF, UK. Tel.: +44 207 848 5161; fax: +44 207 848 0988 (A. Valentín).
E-mail address: antonio.valentin@kcl.ac.uk (A. Valentín).
[1] These authors are joint first authors.

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several days and bear costs and risks proportional to the duration of the study (Rose et al., 2003; Noe and Drazkowski, 2009; Nair et al., 2008). Consequently, techniques that contribute to the identification of epileptogenic cortex during the *interictal* state and shorten the telemetry period could be of substantial clinical value (Henry and Roman, 2011; Tito et al., 2010; Ayala et al., 2011).

Spontaneous interictal epileptiform discharges are often evaluated in patients with intracranial recordings for the assessment of temporal lobe epilepsy, but their value is limited because they are often bilateral and independent (Alarcon et al., 1994; Fernandez Torre et al., 1999), even in patients with a single unilateral seizure focus (Blume et al., 2001; Chung et al., 1991; So et al., 1989). Consequently, the value of interictal discharges in presurgical assessment is unclear (Asano et al., 2009; Hufnagel et al., 2000). In the present work, we evaluate the role of alternative interictal findings from intracranial recordings in TLE.

Stimulation with brief electrical pulses through implanted electrodes has been used for the study of cortical excitability in human epilepsy (Wilson et al., 1991; Wilson and Engel, 1993; Klooster et al., 2011; Enatsu et al., 2012a,b). Our group has shown that late responses to single pulse electrical stimulation (SPES) of the cortex through subdural electrodes relate to the seizure-onset zone and the removal of epileptogenic cortex identified using SPES predicts good surgical outcome (Flanagan et al., 2009; Valentin et al., 2005b; Alarcon and Valentin, 2012). We have also demonstrated that in temporal lobe epilepsy (TLE), interictal focal slow activity (IFSA) correlates with temporal lobe hypometabolism on interictal ^{18}FDG PET (Koutroumanidis et al., 1998). This observation was recently confirmed by Tao et al. (2011), who used subdural EEG recordings to demonstrate high correlation of interictal slow activity with the irritative and seizure onset zones in lateral neocortical, but not in mesial, TLE.

In search of a battery of interictal tests that could reliably complement ictal intracranial recordings, we investigated the lateralizing and localizing value of IFSA, SPES and ^{18}FDG PET and compared it with the gold standard of focal seizure onset. IFSA and SPES are assessable during intracranial telemetry while ^{18}FDG PET is increasingly used during preoperative investigation of patients who are likely to later undergo invasive EEG studies (O'Brien et al., 2008).

2. Patients and methods

The study includes 30 consecutive patients with medically intractable TLE (9 men, 21 women; median age 37 years; range 14–59 years) who had intracranial video-EEG telemetry at King's College Hospital, London, UK between 1999 and 2009, following inconclusive non-invasive assessment that included imaging, neuropsychology (Akanuma et al., 2003) and scalp EEG and video telemetry recorded with the Maudsley System of electrode positioning (Kissani et al., 2001; Alarcon et al., 2001). The need for intracranial recordings and the implantation strategy was based on a consensus decision made by a multidisciplinary team consisting of neurosurgeons, neurologists, neuroradiologists, neurophysiologists, neuropsychologists and neuropaediatricians. The general criteria leading to intracranial recordings have been described in detail elsewhere (Alarcon et al., 2006, 2012). In essence, patients undergoing intracranial recordings were those patients: (a) with normal structural imaging; or (b) with inconsistencies between positive findings from structural neuroimaging, seizure onset on scalp EEG telemetry, seizure semiology, distribution of abnormalities in the interictal scalp EEG, ^{18}FDG PET or neuropsychological findings. ^{18}FDG PET was not obtained in underage patients or in those where the question was lateral versus medial or anterior versus posterior temporal. As the recruitment period was extensive, covering over 10 years, the clinical indications for the use of ^{18}FDG PET in presurgical assessment of epilepsy evolved over this period. Consequently, some of the patients who were assessed without PET in the past would have been candidates for ^{18}FDG PET in recent years.

The specific criteria for inclusion in the present study were: (a) bilateral subdural electrode (AdTech Medical Instruments Corp., WI, USA) recording from both temporal lobes, with the deepest contacts close to the subiculum, as confirmed by X-ray and CT imaging, and (b) focal seizure onset localized within the temporal areas and restricted to less than 3 electrode contacts. All patients had at least one 8-contact subdural strip on each temporal lobe, while seven had additional frontal, parietal or occipital subdural strips or mats. Exclusion criteria were: (a) past history of significant head injury or acute or chronic neurological illness other than epilepsy at the time of the intracranial EEG recordings, as these conditions could generate non-specific EEG slowing, maybe resembling IFSA; (b) previous brain surgery, including telemetry with intracranial electrodes; (c) intra-axial space-occupying lesions on magnetic resonance imaging (MRI) and (d) MRI evidence suggestive of bilateral mesial temporal sclerosis (MTS), as these patients are not straightforward surgical candidates. Patients with suboptimal mesial temporal positioning of the deepest contacts of the subdural electrodes and those with diffuse or regional seizure onset affecting four or more consecutive electrode contacts were also excluded. This study has been approved by King's College Hospital, Neuroscience Audit Committee.

2.1. Single pulse electrical stimulation (SPES)

SPES was applied in all 30 patients, between adjacent electrodes with a constant-current neurostimulator (Medelec ST10 Sensor, Oxford Instruments). The clinical protocol for SPES and evaluation of responses has been described previously. Essentially, all contacts implanted were used for stimulation with at least 10 single pulses (1 ms pulse duration, 4–6 mA, 0.2 Hz), and responses to SPES were recorded from all remaining contacts. Delayed responses to SPES appear to be a marker for epileptogenesis in TLE (Flanagan et al., 2009; Lacruz et al., 2007; Valentin et al., 2002, 2005a, 2005b, Alarcon and Valentin, 2012).

2.2. Interictal ^{18}FDG PET

Eighteen patients had interictal ^{18}FDG PET scan using an ECAT 951R scanner (Siemens CTI, Knoxville, TN) or ^{18}FDG PET – CT scans using a Discovery VCT or DST (General Electric, Milwaukee, WI). Our ^{18}FDG PET protocol has been described elsewhere (Barrington et al., 1998). Scans were anonymised and were visually analyzed in terms of topography, degree and laterality of hypometabolism by two investigators (SB and MK), who were blind to patients' identities, with any difference resolved by consensus. Bitemporal hypometabolism was assessed by means of a specific protocol detailed elsewhere (Koutroumanidis et al., 2000).

2.3. Intracranial EEG analysis and identification of interictal focal slow activity (IFSA)

Four 20-min artifact-free interictal intracranial EEG epochs from two different days were selected for each patient during wakefulness (2 epochs) and light sleep (2 epochs). Twenty minutes during wakefulness and 20 min during light sleep for two consecutive days is a sufficiently reliable sample, as regional slow activity in focal epilepsy is not subjected to significant day to day changes (Gotman and Koffler, 1989). Only EEGs recorded at least 24 h before and after seizures were considered for the study. No changes in patients' habitual medication were carried out before obtaining