Epilepsy & Behavior 58 (2016) 69–75

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Visual and semiautomated evaluation of epileptogenicity in focal cortical dysplasias — An intracranial EEG study

Stephanie Gollwitzer [a,c,*], Ivan Valente [a], Roman Rodionov [a,b], Catherine Scott [a], Laura Mantoan Ritter [h], Tim Wehner [a], Hajo M. Hamer [c], Fabrice Bartolomei [d,e,f,g], Beate Diehl [a]

[a] NIHR University College London Hospitals Biomedical Research Centre, UCL Institute of Neurology & National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, United Kingdom
[b] Epilepsy Society, Chalfont St Peter, SL9 0RJ, United Kingdom
[c] Epilepsy Center, Department of Neurology, University Hospital Erlangen, Erlangen, Germany
[d] Service de Neurophysiologie Clinique, APHM, Hôpital de la Timone, 13005 Marseille, France
[e] INSERM UMR 1106, INS, 27 Bd Jean Moulin, 13385 Marseille, France
[f] Aix Marseille Université, Faculté de Médecine, Marseille, France
[g] Hôpital Henri Gastaut, Etablissement Hospitalier Spécialisé dans le traitement des Epilepsies, 300 Boulevard de Sainte-Marguerite, 13009 Marseille, France
[h] Clinical Neurosciences Department, King's College, NHS Foundation Trust, Denmark Hill, London SE5 9RS, United Kingdom

ARTICLE INFO

Article history:
Received 10 January 2016
Revised 6 March 2016
Accepted 7 March 2016
Available online xxxx

Keywords:
Focal epilepsy
Epileptogenicity Index
Epilepsy surgery
SEEG

ABSTRACT

Introduction: The aim of the study was the evaluation of the added value of depth to subdural electrodes in delineating epileptogenicity of focal cortical dysplasias (FCDs) and to test the Epileptogenicity Index (EI) in this setting.
Material and methods: Fifteen patients with FCD underwent iEEG with subdural and depth electrodes. Visual/EI analysis was performed in up to three habitual seizures per patient.
Results: Visual analysis: Grid onset seizures (n = 10) started in electrodes overlying the lesion in 7 and remote from it in 3 cases. Depth onset seizures (n = 7) affected only intralesional contacts in 4, intra- and extralesional in 2, and exclusively extralesional in 1 patient. Seizures started in depth and grid contacts simultaneously in 2 cases.
EI analysis: The EI completely confirmed visual localization of seizure onset in 8 cases and depicted ictal onset-time accurately in 13. Beta/gamma ictal patterns were most reliably captured.
Impact on surgical decision: Resection outline differed from MRI lesion in 7 patients based on grid and in three based on depth electrode information.
Discussion: In FCD, seizures can be generated within gyral/deep tissue appearing normal on imaging.
Conclusion: Investigating FCD with subdural and depth electrodes is efficient to outline the seizure onset zone. The EI is a helpful additional tool to quantify epileptogenicity. Specific ictal patterns are prerequisite for reliable results.

1. Introduction

Focal cortical dysplasia (FCD) is increasingly recognized as one of the most common causes of early onset intractable focal epilepsy in both adults and children [1,2]. Although favorable outcomes after focal resections with up to 60% of patients being rendered seizure-free have been reported [3–5], presurgical evaluation of the epileptogenic zone (EZ) is still challenging. This is, in part, due to the fact that even high resolution MRI does not always detect the pathology and especially mild type I FCD is missed on imaging in 35 to 63% of patients [6,7]. Moreover, boundaries of the lesion are often difficult to delineate as dysplastic areas can be more extensive than apparent on MRI [3,8]. In addition, scalp EEG can correctly localize the ictal onset zone in only 40–70% of cases [6,9]. As complete resection of the epileptic lesion, incorporating both MRI pathology and EEG ictal onset zone, is the best predictor of good postoperative seizure outcome, intracranial EEG (iEEG) recordings are often necessary in order to develop a surgical strategy [4,10–13].

No consensus on the design of an intracranial EEG study optimal for both definition of the ictal onset zone and differentiation from eloquent cortex has been reached. While subdural grid and strip electrodes provide excellent spatial resolution on the gyral surface and allow for detailed mapping of cortical function, sampling is restricted to cortex immediately beneath the convexity and cerebral tissue radial to the plane of the grid or strip [14]. Multiple depth electrodes (stereo-EEG; SEEG), in contrast, enable sampling from deep cortical tissue and regions nonaccessible by subdural electrodes, e.g., depth of sulci or opercular areas. They can also provide direct intralesional recording. Information gained from depth electrodes, however, can be fragmentary as sampling is limited to tissue in the immediate vicinity of electrode

* Corresponding author at: Epilepsy Center, Department of Neurology, University Hospital Erlangen, Schwabachanlage 6, 91054 Erlangen, Germany. Tel.: +49 9131 8544525; fax: +49 9131 85 36469.
E-mail address: Stephanie.gollwitzer@uk-erlangen.de (S. Gollwitzer).

http://dx.doi.org/10.1016/j.yebeh.2016.03.009
1525-5050/

contacts, and traditionally SEEG implantation schemes are designed to sample from a wider network rather than a lesional and perilesional volume. In order to develop a comprehensive understanding of the three-dimensional ictal onset zone and eloquent cortex, a combined approach appears reasonable.

We retrospectively audited our experience on 15 patients who underwent invasive EEG with both subdural and additional depth electrodes and evaluated the impact of the different modalities on the proposed shape of the epileptogenic zone and the proposed resection margins.

In addition to visual analysis, we calculated the Epileptogenicity Index (EI), a quantitative measure designed for the automated analysis of depth EEG recordings and evaluated in mesial temporal lobe epilepsies and focal epilepsies in the context of focal cortical dysplasias and neurodevelopmental tumors [13,15]. Although shown to be reliable in different subtypes of focal epilepsies studied with multiple depth electrodes, the EI has not been systematically tested in a subdural or combined intracranial EEG approach before.

2. Material and methods

2.1. Patients

Fifteen consecutive patients (8 male, 7 female, mean age 35.2 years, age at epilepsy onset 8.3 years) with intractable focal epilepsy due to suspected focal cortical dysplasia most likely IIB according to MRI criteria [16,17], who underwent iEEG recordings with subdural grid and/or strip electrodes and additional depth electrodes inserted through the grid at the National Hospital for Neurology and Neurosurgery, London, between 2009 and 2013 were included and retrospectively reviewed. The FCD was located in the frontal lobe in ten, in the parietal lobe in four, and in the occipital lobe in one patient. In all cases, a scalp EEG video telemetry, 3 Tesla MRI, and functional MRI for the localization of language, motor, or sensory areas were performed prior to iEEG. Additionally, some patients underwent ictal SPECT, FDG PET, or MEG (Table 1). The study was approved as retrospective audit into efficacy and safety of intracranial EEG implantations by the hospital.

2.2. Intracranial EEG

The implantation scheme was based on the hypothesis of the epileptogenic zone derived from semiology and presurgical assessment. Prior to implantation, each case was discussed in a multidisciplinary team meeting. Individual targets for depth electrode insertion were defined on a case-by-case basis, aiming to target the center of the migration disorder based on MRI appearance and, ideally, also informing anterior/posterior and rostrocaudal extent of epileptogenicity intracortically and in the depth. Electrodes were inserted into the center of the cortical thickening based on T1-weighted MRI; the T2 hyperintensity and, if present, a transmantle sign were also targeted. In the case of the bottom of sulcus dysplasias, sampling of the lesion was attempted, respecting pial boundaries. The exact target within the MRI abnormality was also guided by semiology, noninvasive diagnostics, and anatomical considerations. If, for example, the seizure onset zone was expected in the anterior portion of the visible lesion, an electrode was inserted anteriorly into the center of the lesion. Thus, a tailored implantation scheme was designed for each patient.

An average number of 75 subdural and 15 depth electrode contacts were inserted in each patient. After implantation, CT scans were performed, and images coregistered with preimplantation MRI. Thus, electrode maps were generated on 3D brain surface rendering allowing for localization of electrodes with respect to anatomical structures and lesional boundaries as outlined on MRI. This approach leads to a specific coregistration error caused by brainshift and is dependent on the size of the craniotomy. In order to minimize this effect, each coregistered scan was visually reviewed and manually corrected.

The EEG monitoring was maintained for 6 days on average.

The EEG data were recorded with the standard clinical video-EEG system (Nicolet One) sampled at 500 Hz per channel, with bandpass filtering between 0.5 Hz and 1/4 sampling rate. Cortical stimulation for functional mapping was performed in all patients, using bipolar stimulation of adjacent electrodes [18].

Table 1
Demographics, noninvasive presurgical diagnostics, and implantation scheme.

Patient	Age	Sex	Age at onset	Lobe	Side	Diagnostics	Subdural electrode contacts	Depth electrodes contacts
1	39	M	6	F	R	fMRI, MEG	54	10
2	49	F	5	F	L	fMRI	70	22
3	34	F	7	F	L	fMRI, PET	80	24
4	38	M	9	F	L	fMRI, PET	124	12
5	28	M	12	F	L	fMRI, PET, SPECT	80	8
6[a]	24	F	1	F	L	fMRI, SPECT	60	8
7	27	M	14	F	L	fMRI	80	8
8	33	F	1	P	L	fMRI	56	14
9	25	F	11	P	L	fMRI	66	12
10[a]	21	M	2	F	R	fMRI	64	18
11	28	M	7	P	R	fMRI	64	16
12[a]	43	F	11	O	L	fMRI, MEG, PET, SPECT	104	20
13	54	M	8	F	L	fMRI	64	32
14	25	M	6	P	L	fMRI, MEG	80	10
15	60	F	25	F	L	fMRI	86	12

M: male, F: female; affected lobe: P: parietal, F: frontal, O: occipital; affected hemisphere: R: right, L: left; fMRI: functional MRI, MEG: magnetencephalography, PET: positron emission tomography, SPECT: single photon emission computed tomography.
[a] Patient with one analyzed seizure only.

2.3. Visual analysis

In 12 patients, three consecutive habitual seizures were reviewed by a certified electroencephalographer (SG); in three patients (patients 6, 10, and 12), only one seizure occurred during the recording and was analyzed. We defined the ictal onset for each seizure as the time of first appearance of the ictal pattern, characterized by rapid discharges, an amplitude decrement, or repetitive spike wave or sharp wave discharges. We then identified the electrodes bearing the ictal onset and assigned the ictal onset zone to an anatomical region, which was either on the cortical surface, represented by the grid or the two most lateral depth electrode contacts, or in the cortical depth represented by the mesial depth electrode contacts. For each patient, we analyzed the overlap between the three-dimensional EEG ictal onset zone and the lesion visible on MRI. We also reviewed the resection margins proposed on the basis of the visual analysis of iEEG as documented by the physician reporting the study, as is routine practice for clinical care. Surgical outcome was evaluated according to the ILAE classification [19].

2.4. EI

The EI was calculated according to the methods previously described [15] to obtain a quantification of epileptogenicity. In brief, it is an algorithm that takes two factors into account: first, the propensity of brain tissue to generate rapid discharges, mirrored by a shift of the spectral energy ratio (ER) between high (beta and gamma) and low (delta, alpha, and theta) frequencies and, second, the delay of involvement of every regarded structure in relation to the first structure involved. The seizure onset is characterized by a dramatic increase in the ER derived from a Fast Fourier Transform using a sliding window technique. In order to increase sensitivity and specificity for the detection of onset time, two parameters can be adjusted manually: bias $_{v}$ refers to the amount of power fluctuations regarded as “normal” and threshold λ marks a significant ER change. When the seizure onset time has been noted for electrodes involved, the energy ratio averaged over time