Epilepsy Research (2014) 108, 953—962

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

Drug-resistant focal sleep related epilepsy: Results and predictors of surgical outcome

Anna Losurdo[a], Paola Proserpio[b], Francesco Cardinale[b], Francesca Gozzo[b], Laura Tassi[b], Roberto Mai[b], Stefano Francione[b], Laura Castana[b], Giorgio Lo Russo[b], Giuseppe Casaceli[b], Ivana Sartori[b], Giacomo Della Marca[a], Massimo Cossu[b], Lino Nobili[b,c,*]

[a] *Institute of Neurology, Catholic University, Policlinico Universitario A. Gemelli, Rome, Italy*
[b] *''C. Munari'' Center of Epilepsy Surgery, Niguarda Hospital, Milan, Italy*
[c] *Institute of Bioimaging and Molecular Physiology, Genoa Unit, National Research Council, Genoa, Italy*

Received 25 July 2013; received in revised form 3 February 2014; accepted 28 February 2014
Available online 12 March 2014

KEYWORDS
Epilepsy;
Epilepsy surgery;
Sleep;
Sleep related epilepsy

Summary In this study we report the results of surgery in a large population of patients affected by drug-resistant focal sleep related epilepsy (SRE) and the identified prognostic factors. We conducted a retrospective analysis of a case series of 955 patients operated on for drug-resistant focal epilepsy from 1997 to 2009. Ninety-five patients with focal SRE and a follow-up of at least 2 years were identified. Presurgical, surgical and histopathological variables were analyzed. Risk of seizures recurrence was assessed by univariate and multivariate analysis. Mean age at epilepsy onset was 5.6 ± 4.9 years. MRI revealed a focal abnormality in 78.9% of cases. Sixty-two percent of patients required a Stereo-EEG investigation. The cortical resection involved the frontal lobe in 61.1% of cases, while in 38.9% an extrafrontal resection was performed. Focal cortical dysplasia (FCD) type II was the most frequent histopathological finding. Mean postoperative follow-up was 82.3 months. Seventy-three patients (76.8%) were in Engel's class I. At univariate analysis, variables associated with a favorable outcome were: absence of Stereo-EEG investigation; positive MRI; complete removal of the epileptogenic zone (EZ);

* Corresponding author at: Centre of Epilepsy Surgery ''C. Munari'', Center of Sleep Medicine, Niguarda Hospital, Piazza Ospedale Maggiore 2, 20162 Milan, Italy. Tel.: +39 0264447323; fax: +39 0264442874.
E-mail address: Lino.nobili@ospedaleniguarda.it (L. Nobili).

http://dx.doi.org/10.1016/j.eplepsyres.2014.02.016

presence of FCD type II and FCD type IIb. A diagnosis of FCD type I was associated with postoperative recurrence of seizures. Multivariate analysis identified the complete removal of the EZ and FCD type I as independent predictors of a favorable and unfavorable outcome respectively. SRE can frequently originate outside the frontal lobe and a favorable surgical outcome is achieved in three-fourths of cases independently from the location of the EZ.

Introduction

In patients with sleep related epilepsy (SRE), more than 90% of ictal events arise from sleep (Iber et al., 2007). The percentage of patients with epilepsy affected by focal SRE ranges from 7.5 to 45%, depending on the method of case ascertainment (Thomas et al., 2010). Focal SRE is considered a relatively benign clinical condition (D'Alessandro et al., 1983) because seizures occur almost exclusively during nocturnal sleep and in the majority of patients a good seizure control is achieved with pharmacological treatment. Nevertheless, a relatively high percentage of patients, mainly with a focal frontal epilepsy, is drug resistant (Bernasconi et al., 1998; Nobili et al., 2007; Provini et al., 1999). Sleep related seizures are a typical manifestation of Nocturnal Frontal Lobe Epilepsy (NFLE) (Nobili et al., 2007; Oldani et al., 1998; Provini et al., 1999; Scheffer et al., 1995); however, many studies have shown that, among drug resistant patients, sleep related seizures can originate in the temporal lobe (Bernasconi et al., 1998; Nobili et al., 2004; Tao et al., 2010), in the insular lobe (Dobesberger et al., 2008; Kaido et al., 2006; Proserpio et al., 2011b; Ryvlin et al., 2006; Zhang et al., 2008) and in the posterior cortical regions (Proserpio et al., 2011a).

Epilepsy surgery in NFLE has shown to be an effective treatment (Nobili et al., 2007); moreover, although limited to single cases or small groups of patients, good results seem to be achieved also in extra-frontal focal nocturnal seizures (Dobesberger et al., 2008; Elsharkawy et al., 2009; Mai et al., 2005; Proserpio et al., 2011a). The aim of our study is to report the results of surgery in a large population of patients affected by drug resistant focal SRE epilepsy and to point out possible presurgical and surgical prognostic factors.

Materials and methods

We have evaluated retrospectively a series of 955 patients operated on for drug-resistant focal epilepsy at ''C. Munari'' Epilepsy Surgery Centre from 1997 to 2009.

The selection criteria were:

1) Presence of sleep-related seizures. Patients were considered to be affected by sleep-related seizures if more than 90% of ictal events arose from sleep, referred to questioning of patients and their relatives. This distribution of seizures was confirmed by seizure diaries filled over a period for at least one year, and by subsequent long-term video-EEG recordings conducted both during sleep and wakefulness.
2) Post-operative follow-up period of at least 24 months.
3) Availability of a post-surgical MRI study (necessary for assessing the complete or incomplete removal of the epileptogenic zone; see ''surgery'').

The study was approved by the Ethic Committee of the Niguarda Hospital, Milan.

Presurgical evaluation

All patients underwent a presurgical investigation based on:

1. accurate analysis of personal and epileptic history;
2. scalp video-EEG (VEEG) monitoring, including at least one video-polysomnographic recording of nocturnal sleep;
3. MRI studies were performed according to the protocol proposed by Colombo et al. (2009, 2003), and they were customized with employment of appropriate sequences according to main electroclinical information (1.5-tesla ACS-NT unit; Philips Medical Systems, Best, The Netherlands). Intravenous contrast was injected when a neoplasm was suspected.
4. When non-invasive investigations failed to localize the epileptogenic zone (EZ; the brain region considered essential for inducing and maintaining the epileptic seizures), a stereo-electro-encephalography (SEEG) with stereotactically placed intracerebral electrodes was performed (Cossu et al., 2005). The arrangement of electrodes was tailored according to a predefined localization hypothesis based on non-invasive findings.

Surgery

Surgery aimed at resection of the EZ, whose identification was based on the anatomo-electro-clinical correlations. On these basis the area to be removed could be limited to a possible discrete lesion detected by MRI or be extended also to extralesional areas. In all the MRI-negative cases the resection area was defined on the basis of a SEEG investigation.

Surgical procedures were classified as complete or incomplete resection of the EZ. Resections were considered incomplete when: (1) the EZ was partly spared because it involved eloquent cortex (2) postoperative MRI revealed that surgical resection did not completely match the preoperative plan (3) the indications to surgery were based on data with residual uncertainties as to the actual limits of the EZ. In particular, the presurgical evaluation allowed the identification of a definite anatomical region to be removed; however it was not able to exclude with certainty the