Epilepsy Research 122 (2016) 102–109

Contents lists available at www.sciencedirect.com

Epilepsy Research

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

Unfavorable surgical outcomes in partial epilepsy with secondary bilateral synchrony: Intracranial electroencephalography study

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ARTICLE INFO

Article history:
Received 12 September 2015
Received in revised form 26 February 2016
Accepted 12 March 2016
Available online 15 March 2016

Keywords:
Secondary bilateral synchrony
Epilepsy surgery
Intracranial electroencephalography
Surgical outcome

ABSTRACT

Objective: Secondary bilateral synchrony (SBS) indicates bilaterally synchronous epileptiform discharges arising from a focal cortical origin. The present study aims to investigate SBS in partial epilepsy with regard to surgical outcomes and intracranial EEG findings.
Methods: We retrospectively reviewed consecutive patients who underwent epilepsy surgery following extraoperative intracranial electroencephalography (EEG) study from 2008 to 2012. The presence of SBS was determined based upon the results of scalp EEG monitoring performed for presurgical evaluations. We reviewed scalp EEG, neuroimaging, intracranial EEG findings, and surgical outcomes in patients with SBS.
Results: We found 12 patients with SBS who were surgically treated for intractable partial epilepsy. Nine (75%) patients had lateralized ictal semiology and only two (16.6%) patients showed localized ictal onset in scalp EEG. Brain MRI showed epileptogenic lesion in three (25%) patients. Intracranial EEG demonstrated that ictal onset zone was widespread or non-localized in six (50%) patients. Low-voltage fast activity was the most common ictal onset EEG pattern. Rapid propagation of ictal onset was noted in 10 (83.3%) patients. Eleven patients underwent resective epilepsy surgery and only two patients (18.2%) achieved seizure-freedom (median follow-up 56 months). MRI-visible brain lesions were associated with favorable outcomes ($p = 0.024$). Patients with SBS, compared to frontal lobe epilepsy without SBS, showed lesser localization in ictal onset EEG ($p = 0.029$) and more rapid propagation during evolution of ictal rhythm ($p = 0.015$).
Conclusions: The present results suggested that resective surgery for partial epilepsy with SBS should be decided carefully, especially in case of nonlesional epilepsy. Poor localization and rapid spread of ictal onset were prominent in intracranial EEG, which might contribute to incomplete resection of the epileptogenic zone and poor surgical outcomes.

1. Introduction

Secondary bilateral synchrony (SBS) refers to bilaterally synchronous epileptiform discharges that originate from a unilateral cortical focus (Lombroso and Erba, 1970; Tukel and Jasper, 1952). It has been suggested that focal discharges from the epileptogenic focus involve the centrecephalic system to be projected to the bilateral hemispheres or interhemispheric connections to be transferred to the contralateral hemisphere (Aghakhani et al., 2006; Bancaud et al., 1974; Kobayashi et al., 1992; Yoshinaga et al., 1996). Regarding the location of its origin, SBS was initially reported to arise from medial frontal regions, but several studies found variable cortical regions including lateral frontal and extrafrontal lobes as epileptogenic foci of SBS (Blume and Pillay, 1985; Gabor and Marsan, 1969;

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http://dx.doi.org/10.1016/j.eplepsyres.2016.03.003
0920-1211/

Table 1
Summary of the presurgical evaluation.

Parameters	No. (%)
Video-EEG monitoring (n = 12)	
SBS morphology	
Generalized spike-and-wave complexes	8 (66.7)
Generalized polyspikes or polyspike-and-wave complexes	5 (41.7)
Bifrontal spike-and-wave complexes	3 (25)
Focal interictal spikes	10 (83.3)
Frontal	8 (66.7)
Temporal	7 (58.3)
Others	2 (16.7)
Focal slowing	5 (41.7)
Frontal	3 (25)
Temporal	2 (16.7)
Ictal EEG	
Localized onset	2 (16.7)
Diffuse onset	10 (83.3)
Lateralizing ictal semiology	9 (75)
Neuroimaging (n = 12)	
MRI-visible brain lesions	3 (25)
FDG-PET	
Any hypometabolism	9 (75)
Lateralized to the resection	5 (41.7)
Localized to the resection	2 (16.7)
Ictal SPECT (n = 10)	
Any hyperperfusion	9 (90)
Lateralized to the resection	6 (60)
Interictal SPECT (n = 7)	
Any hypoperfusion	3 (42.9)
Lateralized to the resection	2 (28.6)
Localized to the resection	1 (14.3)

Abbreviations: EEG, electroencephalography; MRI, magnetic resonance imaging; FDG-PET, ^{18}F-fluorodeoxyglucose-positron emission tomography; SPECT, single-photon emission computed tomography.

Jung et al., 2005). However, it is common that focal origins of generalized discharges are not apparent through the visual inspection of routine scalp recordings for several reasons: the limited cortex coverage by scalp electrodes; failure of low-voltage fast activity to penetrate the skull and scalp; and the rapid propagation of focal discharge (Blume and Pillay, 1985). Distinguishing SBS from primary bilateral synchronous discharges is important in terms of accurate diagnosis of epilepsy, appropriate medical treatment, and potential surgical candidacy. In this regard, investigators have sought to identify and analyze the focus of SBS by using other noninvasive methods, such as independent component analysis of electroencephalography (EEG), magnetic source imaging, interhemispheric time difference measurement, and combined EEG-functional magnetic resonance imaging (MRI) (Borelli et al., 2010; Chang et al., 2009; Jung et al., 2005; Kobayashi et al., 2000).

Despite modern advances in techniques for noninvasive evaluation, intracranial EEG still provides invaluable information in determining epileptogenic zone. It also enables us to explore epileptiform discharges with high sensitivity and spatial resolution. To the best of our knowledge, however, there has been little information in the literature regarding intracranial EEG study focusing on partial epilepsy with SBS and its association with surgical outcomes. Herein, we analyzed SBS in intractable focal epilepsy with regard to the surgical outcomes, preoperative investigations, and intracranial EEG findings and sought to identify predictors of favorable candidates for epilepsy surgery.

2. Materials and methods

2.1. Patient selection and noninvasive studies

We retrospectively reviewed the epilepsy surgery database of our institute and selected consecutive patients who underwent epilepsy surgery along with extraoperative intracranial EEG monitoring between 2008 and 2012. Excluded were those who were followed less than 2 years after surgery or had a previous history of epilepsy surgery. This study was approved by the institutional review board of Seoul National University Hospital (H-1508-063-094).

Twenty-one scalp electrodes were placed according to the international 10–20 system together with anterior temporal electrodes (T1 and T2). The EEG signals were sampled at 200 Hz and bandpass filtered between 1 and 70 Hz. The presence of SBS was decided based upon the results of scalp video-EEG monitoring which was performed for presurgical evaluation. We defined SBS as bilaterally synchronous or generalized epileptiform discharges occurring in the interictal periods (Tukel and Jasper, 1952). Because epilepsy surgery in this study was based on the premise that all patients had intractable partial epilepsy as suggested by presurgical investigations, we did not apply the additional EEG criteria to distinguish SBS from primary bilateral synchrony, such as the lead-in time of triggering spikes or the focal slow activity (Jung et al., 2005). We also reviewed other investigations including brain MRI, ^{18}F-fluorodeoxyglucose (FDG)-positron emission tomography (PET), and interictal and ictal single-photon emission computed tomography (SPECT). Brain MRI and functional neuroimaging were performed as previously described (Kim et al., 2009). Metabolism and perfusion abnormalities in functional neuroimaging were classified as localized or lateralized on the basis of agreement with the resection areas.

2.2. Intracranial EEG

Subdural electrodes were implanted according to the integrated results of noninvasive studies. Intracranial EEG was recorded by using a 128-channel digital video monitoring system (Grass Beehive Horizon, Grass Technologies, West Warwick, RI, USA). The sampling rate varied depending on the time of recording: 200 Hz until 2010 and 1600 Hz since 2011. We analyzed various EEG features including the lobar location, distribution, morphology, and propagation speed of ictal onset EEG. The ictal onset distribution was classified as focal (<5), regional (5–20), or widespread (>20) according to the number of adjacent electrodes affected. The ictal onset with simultaneous involvement of noncontiguous electrodes was defined as non-localized regardless of the number of affected electrodes. The ictal onset propagation was categorized as rapid ($\leq$1 s) or slow (>1 s) based on time lags between initial ictal discharges and spreading to adjacent electrodes 2 cm apart from the ictal onset zone.

2.3. Surgery, pathology and outcomes

The resection margin was primarily determined by the intracranial ictal onset zone. The area with persistent pathologic delta activities and frequent interictal spikes were also considered significant in designating the extent of resection, especially when the ictal onset zone was widespread or non-localized. Histopathology of focal cortical dysplasia was classified according to the International League Against Epilepsy (ILAE) classification system (Blumcke et al., 2011). We employed the Engel epilepsy surgery outcome scale to classify the seizure outcomes after surgery (Engel et al., 1993), which were divided as seizure free (class 1) or seizure persistent (class 2–4). In addition, we defined favorable outcomes as class 1 or 2 and unfavorable outcomes as class 3 or 4.

2.4. Statistical analysis

We compared various characteristics between two outcome groups by non-parametric analysis due to the small sample size. We performed Fisher's exact test for categorical variables and