Clinical Neurophysiology 127 (2016) 1170–1175

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

# Altered synchrony and loss of consciousness during frontal lobe seizures

Francesca Bonini [a,c], Isabelle Lambert [a], Fabrice Wendling [b], Aileen McGonigal [a,c], Fabrice Bartolomei [a,c,d,*]

[a] CHU Timone, Service de Neurophysiologie Clinique, Assistance Publique des Hôpitaux de Marseille, Marseille 13005, France
[b] INSERM, U642, Université Rennes 1, Rennes, France
[c] "Institut de Neurosciences des Systèmes, INSERM UMR 1106", France
[d] Hôpital Henri Gastaut/Centre Saint-Paul, CINAPSE, 300 Bd Sainte-Marguerite, 13009 Marseille, France

ARTICLE INFO

*Article history:*
Accepted 4 April 2015
Available online 15 April 2015

*Keywords:*
Consciousness
Frontal cortex
Synchrony
Focal epilepsy

HIGHLIGHTS

- This study investigated loss of consciousness in 52 frontal seizures.
- Interdependencies between signals were estimated by using non-linear regression analysis.
- Loss of consciousness appears to be related to changes in synchrony in prefrontal and parietal associative cortices.

ABSTRACT

*Objective:* Loss of consciousness (LOC) in frontal lobe epilepsy (FLE) has been rarely specifically studied until now. In this study we evaluated the LOC in a population of patients with FLE and studied the relationship between changes in synchrony and degree of LOC.
*Methods:* 24 patients undergoing stereoelectroencephalography (SEEG) during pre-surgical evaluation of FLE were studied. The LOC intensity was scored using the Consciousness Seizure Scale (CSS). For each studied seizure ($n = 52$), interdependencies between signals recorded from 5 brain regions were estimated as a function of time by using non-linear regression analysis ($h^2$ coefficient).
*Results:* Seizures were divided into 3 groups according to the CSS scale: group A (no LOC) with a score $\leqslant 2$, group B (intermediate or partial LOC) with a score ranging from 3 to 5, and group C (maximal LOC) with a score $\geqslant 6$. The majority of seizures in FLE patients disclosed significant LOC, particularly for patients with prefrontal lobe seizures. Mean correlation values were significantly different between groups A and C ($p < 0.001$), the maximal values of synchrony being observed in group C. Differences were significant for interaction affecting the external prefrontal cortex ($p = 0.004$) ($p = 0.01$) and the parietal cortex. In addition, a significant correlation was found between CSS scores and correlations values ($h^2$) of the prefrontal and the parietal region but not with the premotor cortex.
*Conclusions:* This study indicates that in FLE, prefrontal seizures frequently alter consciousness. As in other focal seizures, LOC appears to be related to changes in synchrony in prefrontal and parietal associative cortices.
*Significance:* LOC in FLE is frequent and as in other focal epilepsies is related to an alteration of prefrontal–parietal network.


## 1. Introduction

Loss of consciousness (LOC) is a serious clinical manifestation largely impacting the quality of life of patients with epilepsy (Cavanna and Monaco, 2009; Blumenfeld, 2011). A large body of evidence shows that LOC is associated with an increased risk of accidents and injury (Chen et al., 2014). During the last ten years, there has been a marked increase in the amount of studies in this field. In particular, the mechanisms by which focal seizures may alter consciousness have been subject of investigations based on neuroimaging or neurophysiological approaches. Most of these studies have focused on temporal lobe epilepsy (TLE) (Gloor et al., 1980; Munari et al., 1980; Lux et al., 2002; Blumenfeld et al., 2004a,b; Arthuis et al., 2009). It has been proposed that

* Corresponding author at: Service de Neurophysiologie Clinique, CHU Timone-264 Rue st Pierre, 13005 Marseille, France.
*E-mail address:* fabrice.bartolomei@ap-hm.fr (F. Bartolomei).

http://dx.doi.org/10.1016/j.clinph.2015.04.050
1388-2457/

LOC in TLE is linked to an involvement of fronto-parietal cortices being inhibited (Blumenfeld et al., 2004a,b) or abnormally over-synchronized (Arthuis et al., 2009) during complex partial seizures. Associative parietal and frontal cortices have been largely demonstrated to be necessary for normal awareness and their alteration is associated with specific alteration of awareness without impacting arousal (Di Perri et al., 2014).

A recent study from our group has stressed the role of parieto-frontal interaction in LOC associated with parietal seizures (Lambert et al., 2012). Excessive EEG synchrony was correlated with the degree of consciousness alteration. Until now, no specific study has investigated the LOC in frontal lobe seizures. This study thus aimed at studying LOC in frontal lobe seizures and at investigating the relationship between changes in synchrony and degree of LOC during this kind of seizures. Given the role of the interactions between prefrontal regions and the parietal associative cortex in the "consciousness workspace" (Laureys et al., 2005, 2007) we tested the hypothesis that consciousness alterations in frontal seizures are linked to prefrontal involvement and alterations of prefrontal–parietal synchronization.

## 2. Methods

### 2.1. Patients and SEEG recordings

24 patients undergoing pre-surgical evaluation of drug-resistant frontal lobe epilepsy (FLE) were selected from a series of patients in whom intracerebral recordings had been performed between 2001 and 2010 (Table 1). They were selected on the following basis: well defined frontal lobe seizures (epileptogenic zone well anatomically defined), at least one electrode explored the parietal lobe in addition with the frontal electrodes, and at least two seizures were useable for video analysis of LOC.

All patients underwent comprehensive evaluation including detailed history and neurological examination, neuropsychological testing, routine magnetic resonance imaging (MRI), surface electroencephalography (EEG) and stereoelectroencephalography (SEEG, depth electrodes).

SEEG exploration was carried out during long-term video-EEG monitoring. Recordings were performed using intracerebral multiple contact electrodes (10–15 contacts, length: 2 mm, diameter: 0.8 mm, 1.5 mm apart) placed according to Talairach's stereotactic method (Bartolomei et al., 2011) as illustrated in Fig. 1.

The anatomical targeting of electrodes was established in each patient according to available non-invasive information and hypotheses about the localization of the epileptogenic zone (for details see previous reports (Bartolomei et al., 2011). CT-scan/MRI data fusion was performed to accurately check the anatomical location of each contact along the electrode trajectory using MEDINRIA software (http://gforge.inria.fr/projects/medinria). In selected patients, several distinct functional regions of the frontal lobe were explored (Fig. 1). In the selected cases, electrodes sampling extrafrontal regions were also available. Signals were recorded on a 128 channel Deltamed/NATUS™ system. They were sampled at 512 Hz and recorded on a hard disk (16 bits/sample) using no digital filter. A high-pass filter (cut-off frequency equal to 0.16 Hz at −3 dB) was used to remove very slow variations that sometimes contaminate the baseline. Table 1 provides clinical information about the patients selected for the purpose of this study.

### 2.2. Determination of LOC during seizures: the Consciousness Seizure Scale (CSS)

One to three representative seizures from each patient were analyzed. Video stereotactic-EEG (SEEG) recordings were reviewed and LOC intensity was scored by two of the authors (FBo and IL, blinded to the EEG signal analysis) using an eight criteria scale (Consciousness Seizure Scale, CSS, Arthuis et al., 2009). This scale is detailed in the "Supplementary method" and has been validated in term of inter-rater reproductibility in our seminal paper (Arthuis et al., 2009). The mean of the two scores was retained for each analyzed seizure. Each seizure has been scored from 0 (no alteration of consciousness) to 9 (complete alteration of consciousness). This scale can be used provided that a good interaction and examination of the patient was performed during seizure. A standardized protocol assessing patients' responsiveness is used during video EEG recordings in our epilepsy unit (see the "Supplementary method"). Finally 52 video recorded seizures from those 24 patients were retained for analysis.

**Table 1**
General characteristics of patient population. *Abbreviations:* M: male; F: female; FCD: focal cortical dysplasia; R: right, L: left; preF: pre-frontal; preM: pre-motor; preC: pre-central.

| | Sex | Age at onset (*y*) | Age at recordings (*y*) | Epilepsy side | MRI/aetiology | Surgery | ILAE Class | Follow up (*y*) | EZ |
|---|---|---|---|---|---|---|---|---|---|
| P1 | F | 17 | 47 | L | Post-infective lesion | Refused | | | preF |
| P2 | F | 4 | 32 | L | Surgical scar | Radiosurgery | 2 | 4 | preC |
| P3 | F | 4 | 19 | L | FCD | Yes | 1 | 8 | preF |
| P4 | F | 12 | 34 | L | FCD | Yes | 1 | 4 | preF |
| P5 | F | 8 | 22 | R | Herpetic encephalitis | Yes | 3 | 2 | preF + T |
| P6 | M | 9 | 11 | R | FCD | Yes | 1 | 1.5 | preM |
| P7 | M | 6 | 30 | R | Cryptogenic | Yes | 1 | 10 | preF + T |
| P8 | M | 13 | 38 | R | Cryptogenic | Refused | | | preC/preM |
| P9 | M | 17 | 32 | R | Cryptogenic | Contraindicated | | | preF bilateral |
| P10 | F | 3 | 24 | L | FCD | Yes | 4 | 9 | preM |
| P11 | F | 1 | 14 | R | FCD | Awaited | | | preC/preM |
| P12 | M | 12 | 29 | R | FCD | Yes | 5 | 2 | preM |
| P13 | F | 11 | 25 | R | Cryptogenic | Radiosurgery | 4 | 4 | preC |
| P14 | M | 17 | 20 | Bilateral | Cryptogenic | Callosotomy | 5 | 6 | preF |
| P15 | F | 6 | 22 | R | Cryptogenic | Contraindicated | | | preF |
| P16 | M | 1 | 8 | R | FCD | Yes | 1 | 9 | preF |
| P17 | F | 18 | 26 | L | Post-traumatic | Yes | 1 | 1 | preF |
| P18 | M | 16 | 33 | R | FCD | Yes | 1 | 9 | preF |
| P19 | M | 12 | 30 | L | Cerebral abscess | Yes | 1 | 8 | preF |
| P20 | M | 5 | 29 | R | Cryptogenic | Refused | | | preF |
| P21 | F | 4 | 12 | L | FCD | Yes | 1 | 6 | preM |
| P22 | M | 1 | 34 | R | Cavernoma | Radiosurgery | 2 | 2 | preF |
| P23 | F | 3 | 19 | L | Cryptogenic | Contraindicated | | | preM/preF |
| P24 | F | 1 | 8 | R | Cryptogenic | Yes | 2 | 3 | preC |