



Effect of partial drug withdrawal on the lateralization of interictal epileptiform discharges and its relationship to surgical outcome in patients with hippocampal sclerosis

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Summary

Objective: To assess changes in the relative lateralization of interictal epileptiform discharges (IEDs) and interictal EEG prognostic value in terms of surgical outcome between periods with full medication (FMP) and reduced medication (RMP) in patients with temporal lobe epilepsy (TLE) associated with hippocampal sclerosis (HS).

Methods: Interictal scalp EEGs of 43 patients were evaluated for the presence of IEDs separately in a waking state (WS) and sleeping state (SS) during FMP and RMP. In each period, patients were categorized as having unitemporal or bitemporal IEDs. Surgical outcome was classified at year 1 after surgery and at last follow-up visit as Engel I or Engel II–IV; and alternatively as completely seizure-free or not seizure-free.

Results: There were significant changes in relative IED lateralization between FMP and RMP during SS. The representation of patients with unitemporal IEDs declined from 37 (86%) in FMP during SS to 25 (58%) in RMP during SS ($p=0.003$). At year 1 after surgery, the relative IED lateralization is a predictive factor for surgical outcome defined as Engel I vs. Engel II–IV in

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both FMP during WS ($p=0.037$) and during SS ($p=0.007$), and for surgical outcome defined as completely seizure-free vs. not seizure-free in FMP during SS ($p=0.042$). At last follow up visit, the relative IED lateralization is a predictor for outcome defined as Engel I vs. Engel II–IV in FMP during SS ($p=0.020$), and for outcome defined as completely seizure-free vs. not seizure-free in both FMP during WS ($p=0.043$) and in FMP during SS ($p=0.015$). When stepwise logistic regression analysis was applied, only FMP during SS was found to be an independent predictor for surgical outcome at year 1 after surgery (completely seizure-free vs. not seizure-free $p=0.032$, Engel I vs. Engel II–IV $p=0.006$) and at last follow-up visit (completely seizure-free vs. not seizure-free $p=0.024$, Engel I vs. Engel II–IV $p=0.017$). Gender was found to be independent predictor for surgical efficacy at year 1 if the outcome was defined as completely seizure-free vs. not seizure-free ($p=0.036$).

Conclusion: The predictive value of relative IED lateralization with respect to surgical outcome in interictal EEG is present only during FMP; the predictive value decreases with the reduction of AEDs caused by the change of relative IED lateralization.

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Introduction

Temporal lobe epilepsy (TLE) is the most common form of drug-resistant epilepsy (Wiebe et al., 2001). Surgery was proved to be an effective therapeutic method in cases where pharmacological treatment failed (Williamson, 1998). In approximately two-thirds of patients, surgery leads to seizure freedom (Engel, 1996; Janszky et al., 2005a).

Many investigators focused on the evaluation of interictal EEG and its significance in predicting post-surgical outcome. In general, in patients with TLE, the relative lateralization of interictal epileptiform discharges (IEDs), i.e. the lateralization ratio of interictal spikes between the two hemispheres (unitemporal or bitemporal), appears to have prognostic value. Unitemporal IEDs are thought to be a favorable prognostic factor, while bitemporal IEDs are associated with worse outcomes (Chung et al., 1991; Radhakrishnan et al., 1998; Villanueva et al., 2004). This division fails in the subgroup of patients with mesial TLE associated with unilateral HS proved by histopathological examination or unilateral hippocampal atrophy on magnetic resonance imaging (MRI). Three studies focused on this subgroup proved no differences in surgical outcome between patients with unitemporal and bitemporal IEDs (Hardy et al., 2003; Janszky et al., 2005b; Krendl et al., 2008). Schulz et al. (2000) proved significant differences in outcome between these two groups, but their study included both mesial TLE associated with HS and non-lesional cases. Aull-Watschinger et al. (2008) found the relative IED lateralization to be a predictive factor for short-term (at year 1 and 2 after surgery) outcomes where an excellent outcome was defined as no seizures, with or without nondisabling auras, during the 12 month-period prior to the assessment, but there were no statistically significant differences between patients with unitemporal and bitemporal IED if the excellent outcome was defined as complete seizure freedom at any time after surgery.

Antiepileptic drug (AED) reduction influences neither the frequency of IEDs nor the localization of seizure origin, but the influence of AED reduction on relative IED lateralization has not yet been systematically studied (Gotman and Marciani, 1985; Gotman and Koffler, 1989; Marciani and Gotman, 1986; So and Gotman, 1990; Spencer et al., 1981).

The main goal of our study was to determine if there is a change in relative IED lateralization and/or interictal EEG prognostic value related to the surgical outcome caused by AED reduction and the effect of sleep in patients with mesial TLE associated with unilateral HS.

Methods

Patient selection

This retrospective study included all the patients with unilateral HS who had surgery at the Brno Epilepsy Center of St. Anne's University Hospital between 2005 and 2011 and who reached at least 1 year follow-up after the surgery. All included patients had unilateral HS on MRI, the presence of which was subsequently proven by histopathological evaluation. We excluded patients with other possible epileptogenic lesion than HS present on MRI, except blurring of border between gray and white matter in temporal pole and subsequently detected focal cortical dysplasia (FCD) in histopathological specimen of resected tissue of temporal pole. These criteria were applied because it seems that FCD in the temporal pole does not influence surgical outcome and because standard anteromedial temporal lobe resection was performed in all patients (Kuba et al., 2012).

We analyzed interictal EEG during semi-invasive video-EEG monitoring (scalp EEG + sphenoidal electrodes) in both waking state (WS) and sleeping state (SS). The SS analysis was performed in the non-rapid eye movement (non-REM) sleep stage II–III in two periods. These two periods were defined by AED daily dosage, as a full medication period (FMP) and a reduced medication period (RMP). Only patients with both WS and SS recordings during FMP as well as during RMP were included in this study (see below—EEG criteria) (Fig. 1).

Patient demographic data (age at seizure onset, epilepsy duration, age at time of surgery, time after surgery), other characteristics [number of habitual seizures per month, occurrence of habitual generalized tonic–clonic seizures (GTCS) in two years preceding surgery], and data describing semi-invasive EEG monitoring (duration and number of seizures) were assessed by reviewing patient charts.

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