Correlation between EEG rhythms during sleep: surface versus mediotemporal EEG

Annkathrin Poepel, Christoph Helmstaedter, Edgar Kockelmann, Nikolai Axmacher, Wieland Burr, Christian E. Elger and Juergen Fell

Department of Epileptology, University of Bonn, Bonn, Germany

Correspondence to Dr Juergen Fell, MA, PhD, Department of Epileptology, University of Bonn, Sigmund-Freud-Str. 25, D-53105 Bonn, Germany
Tel: +49 228 287 19343; fax: +49 228 287 16294; e-mail: juergen.fell@ukb.uni-bonn.de

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We compared surface and intracranial electroencephalogram recordings of mediotemporal structures. These structures are critically involved in declarative memory formation and memory consolidation during sleep. As memory processing is suggested to involve the interplay between fast and slow oscillations, we hypothesized different correlations between frequency bands in surface versus mediotemporal electroencephalogram recordings. Polysomnographic recordings obtained in 10 patients with unilateral temporal lobe epilepsy were analyzed. In accordance with earlier studies, we observed that power density in surface electroencephalogram is organized reciprocally between δ/θ and fast frequencies above 16 Hz during non–rapid-eye-movement sleep (negative correlations). In contrast, we found that within the hippocampus δ/θ power alternated in parallel with fast oscillations above 16 Hz during non–rapid-eye-movement sleep (positive correlations). *NeuroReport* 18:837–840 © 2007 Lippincott Williams & Wilkins.

Keywords: epilepsy, hippocampus, intracranial electroencephalogram, memory, non–rapid-eye-movement

Introduction

Surface sleep electroencephalogram (EEG) shows a characteristic fluctuation in different frequency bands over the night. Slow frequency bands ($\delta/\theta/\alpha$) are positively correlated with each other and reach maximum power values during non–rapid-eye-movement (non-REM) sleep [1]. High frequency bands (β/γ) are also positively correlated with each other, but arrive at a power maximum during REM sleep. Negative correlations of slow and fast frequency bands in surface EEG during sleep were observed in several investigations [1–5]. By differentiating between non-REM and REM sleep, it has been demonstrated that these negative correlations specifically occur during non-REM sleep, but not during REM sleep [6,7].

Mediotemporal brain structures have been shown to be crucial for the processing of declarative memories, that is, memories that are accessible to conscious recollection [8,9]. Intracranial recordings from the mediotemporal lobe in animals and humans exhibit characteristic interactions between slow and fast frequency bands, in particular between θ and γ oscillations [10,11]. Whereas, oscillations in a given frequency band are observed in different brain structures, they may be supported by completely different mechanisms [12]. For instance, hippocampal γ oscillations cooccurring with θ oscillations have been suggested to underlie memory encoding and retrieval [13]. Importantly, this interaction of hippocampal θ and γ oscillations might be due to a shared mechanism, which is independent of the state of vigilance. Neocortical γ oscillations, on the other hand, are characteristic of conscious stimulus processing [14–17], which is more often absent during non-REM sleep episodes that are dominated by slow oscillations.

We hypothesized, therefore, that the correlation between slow and fast oscillations within mediotemporal structures during non-REM sleep may exhibit different patterns compared with those observed in surface EEG. More specifically, the proposed relevance of a simultaneous activation of hippocampal slow and fast oscillations for the processing of declarative memories [13,18] would suggest a positive correlation of power values not only during waking state and REM sleep, but also during non-REM sleep. This contrasts with the well described negative correlation of slow and fast oscillations during non-REM sleep in the surface EEG [1,5,7]. To investigate this hypothesis, we analyzed intracranial EEG recordings in patients with pharmacoresistant focal epilepsy, who underwent presurgical evaluation for exact localization of the seizure-onset zone.

Materials

During presurgical evaluation, polysomnography and intracranial EEG were recorded from 10 patients (six women; mean age, 40.1 ± 22.6 years) with pharmacoresistant unilateral temporal-lobe epilepsy. Mean duration of epilepsy was 21.4 ± 11.3 years (see Table 1 for detailed clinical

information). All patients received anticonvulsive medication (for details see Table 1). During presurgical monitoring, doses were gradually reduced to facilitate the occurrence of seizures. Informed consent had been obtained from all patients and the study had been approved by the local institutional ethics committee. Surface EEG was recorded from positions Cz, C3, C4 and O1 (10–20 system). Electroocular activity was registered at the outer canthi of both eyes and submental electromyographic activity was acquired with electrodes attached to the skin. Surface and depth electroencephalograms were referenced to linked mastoids, bandpass-filtered [0.01 Hz (6 dB/octave)–70 Hz (12 dB/octave)], and recorded with a sampling rate of 200 Hz.

Multicontact depth electrodes had been implanted stereotactically along the longitudinal axis of each mediotemporal lobe [19]. The placement of electrode contacts within the hippocampus and the anterior parahippocampal gyrus, which is covered by rhinal cortex, was ascertained by magnetic resonance images in each patient. Magnetic resonance scans were acquired in sagittal, adjusted coronal (perpendicular to the longitudinal axis of the hippocampus) and axial (parallel to this axis) planes and contacts were mapped by transferring their positions from MRI to standardized anatomical drawings. Contacts were localized individually to contain at least one contact each in anterior parahippocampal gyrus (rhinal cortex, RC), anterior part of hippocampus (anterior third, AH) and posterior part of hippocampus (posterior third, PH). Only invasive EEG recordings of the mediotemporal lobe, contralateral to the zone of seizure origin, were analyzed. These data were compared with the central electrode of surface EEG (C3/C4) ipsilateral to the nonepileptic mediotemporal lobe.

Methods

Visual sleep-stage scoring was carried out for each 20-s epoch according to Rechtschaffen and Kales criteria [20] by two experienced raters (W.B. and J.F.). All EEG epochs were visually inspected for movement artefacts and epileptiform activity. Artefact segments were discarded irrespective of the duration of artefacts. Furthermore, all segments with power values above 50 μV^2 in the upper γ band (36–44 Hz) were discarded, to avoid high-frequency contamination, which may survive visual artefact rejection. In total, 53.0% of all EEG epochs were excluded from further analysis (45.1% based on step 1, 7.9% based on step 2).

Power spectra of all artefact-free epochs were calculated with a fast Fourier transform and the frequency range was divided into the following bands: δ (1–4 Hz), θ (4–8 Hz), α (8–12 Hz), $\beta 1$ (12–16 Hz), $\beta 2$ (16–20 Hz), $\gamma 1$ (20–28 Hz), $\gamma 2$ (28–36 Hz), and $\gamma 3$ (36–44 Hz). Pearson's correlations between power values for slow (δ, θ, α) and fast (β, γ) frequency ranges were calculated for surface EEG (C3/C4) and for all three locations of the mediotemporal depth electrodes. Correlation values between slow and fast frequency bands were Fisher *z*-transformed and group differences against zero were evaluated with two-tailed *t*-tests. Furthermore, differences of the correlation values between surface and mediotemporal EEG were analyzed by paired two-tailed *t*-test.

Table 2 Average correlations across patients between power densities of slow versus fast frequency bands during different sleep stages in surface EEG (C3/C4)

	Awake	Non-REM	REM
δ–$\beta 1$	0.213*	0.165	0.143
δ–$\beta 2$	0.117	−0.361***	0.007
δ–$\gamma 1$	0.123	−0.376***	−0.002
δ–$\gamma 2$	0.153	−0.298***	0.057
δ–$\gamma 3$	0.191*	−0.226*	0.072
θ–$\beta 1$	0.388**	0.292**	0.544***
θ–$\beta 2$	0.210**	−0.037	0.225**
θ–$\gamma 1$	0.029	−0.152	0.114
θ–$\gamma 2$	−0.026	−0.147*	0.135
θ–$\gamma 3$	−0.008	−0.106	0.186
α–$\beta 1$	0.512***	0.372***	0.661***
α–$\beta 2$	0.489***	0.192	0.318**
α–$\gamma 1$	0.180	0.089	0.173*
α–$\gamma 2$	0.069	0.284	0.023*
α–$\gamma 3$	0.715	0.297	0.015*

Correlation values have been Fisher *z*-transformed. Asterisks indicate the significance values for group *t*-tests (two-tailed) against zero.
EEG, electroencephalogram; REM, rapid eye movement.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Table 1 Patients' characteristics

Patient	Sex	Age (years)	Age of seizure onset (years)	Placement of electrodes	Seizure origin	Histopathological diagnosis	Medication (generic drug names)	Surgical procedure
P1	F	23	5	Bitemp 1,2,3	Left temporo-medial	HS	CZP, LTG, VPA	SAH (left)
P2	F	45	32	Bitemp	Left temporo-medial	HS	CBZ, LEV, TPM	SAH (left)
P3	M	42	8	Bitemp 1,4,5,6	Right temporo-basal and medial	HS	LEV	ATL (right)
P4	M	40	37	Bitemp	Right temporo-medial	HS	LEV, TPM, OXC	SAH (right)
P5	M	39	25	Bitemp 1,7	Left temporo-medial	Angio-blastoma	CBZ, PHT	Resection
P6	F	41	2	Bitemp	Right temporo-medial	HS	LTG	SAH (right)
P7	F	35	11	Bitemp	Left temporo-medial	HS	CBZ, PRM	No OP
P8	M	42	15	Bitemp 1,2,3,4,5,6	Right temporo-medial	HS	LEV, TPM, VPA	SAH (right)
P9	F	39	31	Bitemp 1,4,5,6	Left temporo-basal and medial	NH	LEV, OXC, PHT	ATL (left)
P10	F	55	22	Bitemp	Left temporo-medial	HS	GBP, LEV	SAH (left)

ATL, anterior temporal lobectomy; Bitemp, bitemporal hippocampal depth electrodes; CBZ, carbamazepin; CZP, clonazepam; GBP, gabapentin; HS, hippocampus sclerosis; LEV, levetiracetam; LTG, lamotrigin; NH, neuronal heterotopia and blurring of grey and white matter; OP, operation; OXC, oxcarbazepin; PHT, phenytoin; PRM, primidon; SAH, selective amygdala-hippocampectomy; TPM, topiramat; VPA, valproic acid; 1, temporo-basal stripes left; 2, frontal stripes left; 3, frontal stripes right; 4, temporo-basal stripes right; 5, temporo-lateral stripe left; 6, temporo-lateral stripe right; 7, left temporo-lateral grid.

Results

Surface EEG during the waking state revealed mainly positive correlations between the power fluctuations of slow and fast oscillations, which were statistically significant between α/θ and β bands, and between δ and $\beta 1$, and the $\gamma 3$ band (see Table 2). Similarly, we observed mainly positive correlations during REM sleep, which were significant between θ and β bands, and between α and β/γ bands. During non-REM sleep, however, negative correlations were found between δ/θ and $\beta 2$ and the γ bands (16–44 Hz). These negative correlations were statistically significant between δ and $\beta 2/\gamma$ bands, and between θ and $\gamma 2$ bands.

Table 3 Average correlations across patients of power densities between low and high frequency bands during non-REM sleep in mediotemporal depth electrodes: only those correlations are depicted that are significantly different from surface EEG (C3/C4)

	Rhinal cortex	Anterior hippocampus	Posterior hippocampus
δ–$\beta 1$		0.403* (>)	0.531** (>)
δ–$\beta 2$		0.208** (±)	0.396*** (±)
δ–$\gamma 1$		0.123* (±)	0.247** (±)
θ–$\beta 1$		0.602** (>)	0.582*** (>)
θ–$\beta 2$		0.287* (±)	0.519* (±)
θ–$\gamma 1$		0.200* (±)	0.334* (±)
α–$\beta 1$		0.817** (>)	0.770* (>)
α–$\beta 2$			0.679* (>)
α–$\gamma 1$	0.4237* (>)		

(>): Increased correlation values for mediotemporal lobe versus C3/C4.
(±): Increased correlation values for mediotemporal lobe versus C3/C4, the sign of the correlation changes from negative to positive.
Asterisks indicate the significance values for *t*-tests (two-tailed) against surface-EEG (C3/C4). REM, rapid eye movement.*$P<0.05$, **$P<0.01$, ***$P<0.001$.

Comparison of surface EEG and intracranial recordings of mediotemporal electrodes revealed no significant differences during waking state or during REM sleep. During non-REM sleep, however, correlations between slow and fast oscillations in the frequency range between 12 and 28 Hz shifted towards more positive values in the intracranial EEG compared with surface EEG (see Table 3).

Within the hippocampus, we found increasingly positive correlations between the slow oscillations ($\delta/\theta/\alpha$) and the lower β band (12–16 Hz). The correlations between δ/θ and $\beta 2/\gamma 1$ band (16–28 Hz) even changed from negative values at surface positions to positive values within the hippocampus. The average correlations between δ/θ and $\gamma 2/\gamma 3$ bands within the hippocampus also shifted towards more positive values compared with those of surface EEG, but these changes were not statistically significant.

The across-night dynamics of δ and $\gamma 1$ power densities in surface EEG and posterior hippocampal recordings are shown in Fig. 1 for one patient. In the surface EEG, δ and $\gamma 1$ power oscillate reciprocally, in particular during non-REM sleep, whereas, in hippocampal recordings, δ and $\gamma 1$ oscillations rather alternate in parallel.

Discussion

For surface EEG, our findings confirm the negative correlation between δ/θ and high-frequency ranges above 16 Hz during non-REM sleep, which has been reported in several earlier investigations [1,5–7]. The most remarkable finding of this study is that the inverse correlation of slow and fast frequency bands in surface EEG changes into a positive correlation in hippocampal recordings, particularly during non-REM sleep. Furthermore, correlations between slow oscillations and the sleep spindle range (12–16 Hz) are enhanced during non-REM sleep compared with waking state. These specific oscillatory patterns within the

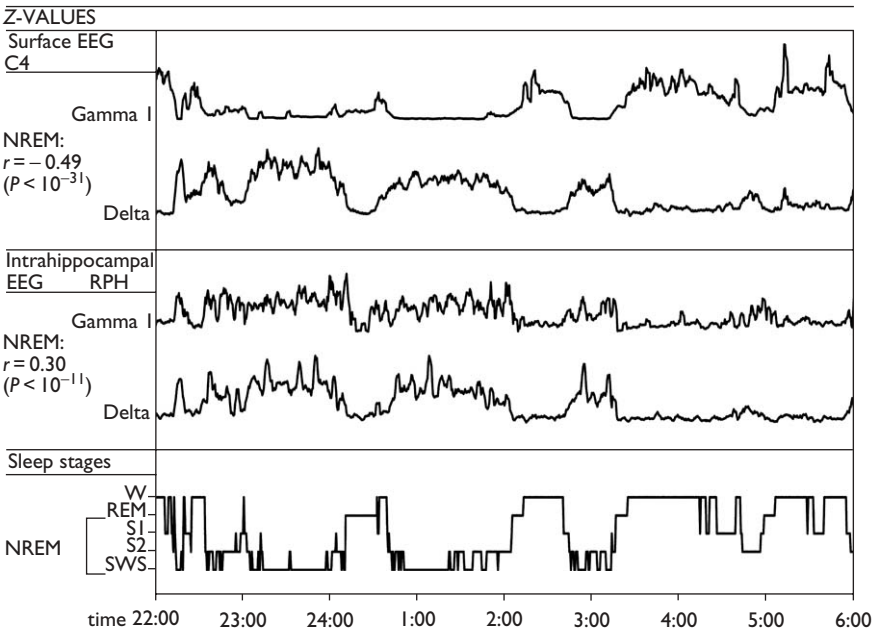

Fig. 1 Time course of δ and $\gamma 1$ bands in surface EEG and intrahippocampal EEG during the night, together with the hypnogram for one of the patients. Pearson's correlations between δ and $\gamma 1$ power across all non-REM (NREH) epochs are given together with the respective *P* values. EEG, electroencephalogram; REM, rapid eye movement; RPH, right posterior hippocampus; S1, light sleep stage 1; S2, light sleep stage 2; SWS, slow wave sleep (stage 3 and stage 4); W, state of wakefulness.

hippocampus might be related to the importance of cooccurring slow and fast hippocampal oscillations for the processing of declarative memories [13,18,21–23].

Taken together, we found that slow and fast oscillations were positively correlated in the human hippocampus, independent of whether patients are awake or whether they are in REM or non-REM sleep. In contrast, interaction between slow and fast oscillations in the neocortex showed a positive correlation during waking state and REM sleep, but a negative correlation during non-REM sleep. These results are in line with earlier data suggesting that the cooccurrence of γ and θ oscillations is relevant for memory processing in the hippocampus [13,18]. It has, for instance, been shown, that mentations can be recalled even after awakening from non-REM sleep with an average rate of about 50% [24]. At this time, however, there is no direct evidence for the hypothesis that the observed correlation of slow and fast oscillations within the hippocampus is indeed related to memory processes. In an earlier study, we investigated the electrophysiological correlates of successful memorization of dreams by awakening patients from REM sleep and requesting their dream reports [25]. A similar study addressing mentation recall from non-REM sleep could provide direct evidence for the idea that a positive correlation of slow and fast hippocampal oscillations supports memory processes.

Gamma oscillations in the neocortex, on the other hand, might correspond to conscious experiences, which are rather absent during slow-wave sleep [14–17]. Furthermore, our findings point towards the relevance of investigating the coupling of oscillations in different frequency bands rather than studying these oscillations themselves, as functional differences in brain activity might more directly map onto complex oscillatory patterns than onto specific oscillations in different frequency bands [26].

Conclusion

We observed that power density in surface EEG is organized reciprocally between δ/θ and fast frequencies above 16 Hz during non-REM sleep (negative correlations), a finding that is in agreement with earlier studies. In contrast, we found that, within the hippocampus, δ/θ power alternated in parallel with fast oscillations above 16 Hz during non-REM sleep (positive correlations). This specific pattern might be related to the interaction of hippocampal slow and fast oscillations and their suggested role in the representation of memory traces.

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