Clinical Neurophysiology 125 (2014) 194–201

Contents lists available at SciVerse ScienceDirect

Clinical Neurophysiology

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

Simultaneous bicoherence analysis of occipital and frontal electroencephalograms in awake and anesthetized subjects

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ARTICLE INFO

Article history:
Accepted 22 June 2013
Available online 12 July 2013

Keywords:
Alpha wave
Consciousness
Nonlinear analysis
Thalamocortical network
Bicoherence
Occipital electroencephalogram
Anesthesia depth

HIGHLIGHTS

- A prominent α rhythm accompanying high bicoherence growth is often seen in occipital awake EEGs in younger persons.
- With the induction of anesthesia, the occipital α bicoherence peak disappears and a frontal α bicoherence peak appears.
- The occipital neural network is spatially differently modulated from the frontal EEG in the regulation of consciousness and anesthesia.

ABSTRACT

Objective: Occipital electroencephalogram (EEG) activity is known to be different from the frontal EEG during wakefulness and anesthesia. However, less is known about occipital non-linear dynamics analyzed by EEG-bicoherence, which can reflect the oscillatory features that are dependent on thalamocortical modulation.

Methods: Forty patients were anesthetized using sevoflurane (1% or 3%) combined with remifentanil. Frontal and occipital EEGs were simultaneously collected, and bicoherence was analyzed before and after induction of anesthesia.

Results: Occipital awake EEGs often demonstrate a bicoherence α peak, differing from frontal awake EEGs in the absence of bicoherence growth. With 1% sevoflurane, occipital α bicoherence disappeared and frontal α bicoherence peaks appeared. Although 3% sevoflurane caused an increase in occipital δ-θ normalized power, similar to the frontal region (peak relative δ-θ power, 13.1 ± 2.2% vs. 12.2 ± 2.7%, $p > 0.05$), occipital bicoherence showed no growth in any frequency area, contrasting with the frontal bicoherence spectrum with a conspicuous peak in the δ-θ area (19.8 ± 8.9 vs. 43.6 ± 13.8, $p < 0.05$).

Conclusions: The occipital bicoherence spectrum in the peri-anesthesia period is quite different from the frontal bicoherence spectrum, which is not usually obvious in the power spectrum.

Significance: Nonlinear regulation of the occipital EEG is different from the frontal EEG during every stage of anesthesia.

1. Introduction

Electroencephalographic activity is spatially heterogeneous, depending on the conditions of wakefulness and unconsciousness (Cimenser et al., 2011; Lee et al., 2009; Alkire et al., 2008). With loss of consciousness, prefrontal areas play a leading role in the propagation of synchronized signals at low frequencies (Bertini et al., 2007; Boveroux et al., 2010; De Gennaro et al., 2004, 2005; Gugino et al., 2001; Lee et al., 2010). Interestingly, the increase in α activity during unconsciousness is more evident in frontal electroencephalograms (EEG) than in the occipital region. Conversely, α-wave predominance is more prominent in occipital than frontal EEGs in awake, relaxed individuals with their eyes closed. Thus, the coordinated α activity in the occipital and frontal regions differs between conscious and unconscious states.

In the frontal cortex, general anesthesia causes α- and δ-θ-activity, such as spindle waves, associated with modulation of neural network regulation, including resonance of the thalamocortical and corticothalamic axons (Llinás and Steriade, 2006; Alkire et al.,

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http://dx.doi.org/10.1016/j.clinph.2013.06.024

2008; Buzsáki, 2006; Vyazovskiy et al., 2007; Ching et al., 2010; Feige et al., 2005; Schneider and Kochs, 2007). Such frontal thalamocortical regulation is reflected by synchronization and the increase in quadratic phase coupling in the frontal EEG (Hagihira et al., 2002; Hayashi et al., 2008a,b). These synchronizations also correlate with unconscious states, by impeding responsiveness to external stimuli (Ching et al., 2010; Hayashi et al., 2010; Buzsáki, 2006). While frontal thalamocortical regulation is thus important for reflection of neural regulation during anesthesia and unconsciousness, the occipital region is also thought to play a notable role in consciousness (Cantero et al., 2000; Lörincz et al., 2008). Although the physiology of the awake occipital α rhythm is naturally different from the unconscious frontal α rhythm, some reports suggest that positive feedback regulation in the thalamus contributes to the appearance of the occipital α wave, as well as the reverberating regulations in frontal α rhythm (Hughes et al., 2008, 2011).

In nonlinear modulation, such as that seen in a reverberating system, the output signal from the reverberating circuit is expected to reenter the system as the input signal, causing the self-modulated characteristics, namely the components of intermodulation products (IMP: a signal component produced by multiplication of input signal components). This results in quadratic phase coupling between the wave components in a signal. The re-entrant loops thus result in IMP and the increase of quadratic phase coupling in the EEG, reflecting the reverberating regulation between the cortex and thalamus. However, the synchronous and reverberating features of the occipital EEG, reflecting quadratic phase-coupling, have not yet been elucidated. Moreover, the spatial difference of nonlinear EEG dynamics between frontal and occipital parts of the brain has also not been examined.

As described in a previous report (Hagihira et al., 2002; Hayashi et al., 2008a,b; Sigl and Chamoun, 1994; Rampil, 1998), bicoherence is a signal-processing technique capable of tracking changes in any reentry system, quantifying IMP and the quadratic phase coupling between two wave components with frequencies f_1 and f_2 in a signal, by introducing the third wave component with frequency ($f_1 + f_2$). Adoption of the third wave component with frequency ($f_1 + f_2$) is beneficial in detecting the IMP, because each phase angle of the original two wave components is inherited to create the phase angle of the generated third wave component in the quadratic nonlinear system (Appendix).

Electroencephalographic bicoherence, a normalized power-independent measure of bispectral analysis, can thus assess reverberating features, including the thalamocortical network, using a single-channel EEG wave (Hayashi et al., 2008a,b; Hagihira et al., 2002); hence, bicoherence analysis can provide some perspective concerning occipital EEGs in relation to the thalamus. The present study therefore examined changes in occipital EEGs, particularly bicoherence changes, compared to frontal EEGs, before and during anesthesia, to investigate the non-linear oscillatory features of the occipital EEG related to anesthesia.

2. Methods

2.1. Protocol

The review board for human experiments at Nantan General Hospital approved the protocol of the current study. Written informed consent was obtained from all patients prior to participation. Subjects comprised 40 patients (12 men, 28 women) with a mean age of 50.8 ± 17.4 years (range, 20–79 years) and an American Society of Anesthesiologists physical status of I or II who were scheduled to undergo non-cranial surgery. None of the patients had any neurological diseases. Patients were not premedicated before induction of anesthesia, in accordance with routine procedure at our institution. In the operating room, a bispectral index (BIS) sensor (Quatro sensor; Aspect Medical Systems, Natick, MA) consisting of four electroencephalographic electrodes was mounted on the forehead according to the guidelines provided by the manufacturer. Another Quatro sensor was mounted ipsilaterally in the occipital region as proposed by Shiraishi and Dahaba, using conductive EEG Paste (Dahaba et al., 2010; Shiraishi et al., 2004). The corresponding sites according to the international ten-twenty system for frontal and occipital BIS recording are Fp1 and O1, respectively, with the reference site at A1. These Quatro sensors were connected to two A-2000 BIS® monitors (version 4.0; Aspect Medical Systems) and raw EEGs were continuously collected for off-line analysis, in addition to BIS. BIS is the number that is partly empirically derived using bispectral analysis, but is not the bispectral analysis-derived parameter itself. BIS ranges from 0 (equivalent to EEG silence) to 100 (equivalent to fully awake and alert), based on the multivariate statistical model using bispectral and other variables, such as power spectra derived parameters.

With patients calmly lying with their eyes closed, anesthesia was induced using propofol (2 mg/kg) combined with a continuous infusion of remifentanil (0.5 μg kg^{-1} min^{-1}), facilitated by 1 mg/kg rocuronium, and maintained using sevoflurane (1–3%) and oxygen 35%, combined with remifentanil at 0.3 μg kg^{-1} min^{-1}. Mechanical ventilation was adjusted to maintain normocapnia. Rocuronium was administered to obtain sufficient muscle relaxation during surgery. Mean arterial blood pressure and heart rate were maintained at >60 mmHg and >50 beats/min, respectively, using phenylephrine and atropine as required. The concentration of expired sevoflurane was continuously monitored and end-tidal concentration of sevoflurane was deliberately kept at the target concentration (1% or 3%) for 30 min to achieve a steady state for analysis.

2.2. Data acquisition and analysis

Electrode impedance was checked every 10 min and was maintained at $\leqslant$5 kΩ throughout the study using the A-2000®. Raw EEG signals through A-2000® (converted from analog to digital at 128 Hz) were collected using BSA version 3.22B2 software (Bispectrum Analyzer for A-2000 BIS® monitor) *via* an RS232 interface on a personal computer (CFW2; Panasonic, Osaka, Japan). Signals less than 0.5 Hz or greater than 50 Hz were excluded. BIS values were monitored with the A-2000® from the preceding 1-min period of EEG, then extracted to a personal computer directly from the A-2000®. Spectral edge frequency (SEF95; the frequency below which 95% of the power in the spectrum resides) was calculated using BSA software as the mean over 1 min. Bicoherence values were defined as the normalized values (ranging from 0% to 100%), and were computed offline in all pairs of frequencies between 1.5 and 20 Hz at 0.5-Hz intervals from 3 consecutive minutes of artifact-free signals, similar to the calculation method described in our previous studies (Hayashi et al., 2008a,b; Hayashi et al., 2010; Hagihira et al., 2002). Signals were divided into a series of 2-s epochs, with each epoch overlapping by 75%. After applying the Blackman window function, the Fourier transform of each epoch was computed. Bicoherence values were calculated using the following equations:

$$\text{Triple product}: \mathrm{TP}_j(f_1, f_2) = X_j(f_1)X_j(f_2)X_j^*(f_1 + f_2)$$

$$\text{Bispectrum}: B(f_1, f_2) = \left|\sum_j \mathrm{TP}_j(f_1, f_2)\right|$$

$$\text{Bicoherence}: \mathrm{BIC}(f_1, f_2) = \frac{B(f_1, f_2)}{\sum_j |\mathrm{TP}_j(f_1 f_2)|} \cdot 100$$

with j referring to epoch number, X_j (f_1) representing a complex value calculated by Fourier transformation of the jth epoch, and $X_j^*(f_1)$