33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Spectral Features of Electroencephalogram in Characterizing Various Brain States Under Anesthesia

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Abstract— **The administration of the anesthetic agents is known to alter the electroencephalogram (EEG) signal significantly with the brain being their primary target. In this study, we analyzed the EEG recorded from six ASA I/II patients undergoing a 1-2 hour surgery. The EEG was collected before and during induction, maintenance and recovery of anesthesia using the 10/20 lead-system. A combination of fentanyl and propofol (±rocuronium) was used for induction and a Sevoflurane in air/O_2 mixture was administered through an endotracheal tube to achieve the steady minimum alveolar concentration (MAC). This study showed that 0 to 4 Hz signal power was most sensitive to the changes associated with induction of anesthesia whereas the 4 to 12 Hz power was important in classifying states during maintenance of anesthesia. Anesthesia also promoted heightened phase coherence in 8 to 16 Hz and 16 to 30 Hz ranges during maintenance and induction of anesthesia, respectively. Additionally, strong cross-frequency coupling between 7 to 20 Hz and 10 to 40 Hz was observed during anesthesia suggesting alteration of neural coding.**

I. Introduction

THE main goal of anesthesia is to maintain the patients at a level of unconsciousness deep enough to enable patients to undergo surgery without recall or pain, while at the same time ensuring dosage is not excessive. Because this task involves a fine control of the amount of the administered anesthetics, a reliable measure of the depth of anesthesia (DoA) can be helpful. The bispectral index (BIS) and the middle latency auditory evoked response (MLAER) are some of the DoA monitoring technologies available today but their effectiveness is still debatable due to their lack of selectivity, sensitivity and reliability [2], [6], [7], [8], [12]. The effort to improve on the monitoring of DoA is ongoing, and in particular, researchers have started to look at the interaction of brain rhythms to understand neural coding and/or its disruption during anesthesia. For example, Imas et al., in two separate studies involving rats, have suggested that anesthetics disrupt the frontal-posterior information transfer at gamma frequencies (20 - 60 Hz) as well as 5 - 25 Hz [4],[5]. In addition, delta waves (0 - 4 Hz) have been shown to modulate alpha (8 - 13 Hz) [10] as well as theta (3.5 - 7.5 Hz) [11]. Furthermore, using a conductance-based model, Ching et al. have demonstrated that propofol appears to induce synchronous alpha (10 - 13) rhythms in cortical networks by facilitating cortico-thalamic synaptic connections [1]. These findings suggest that the interactions between neuronal populations are indeed altered during anesthesia and therefore should be taken into consideration in making DoA monitoring more effective.

In this present study, we explore time-frequency features that may better characterize the various brain states during anesthesia. In particular, the interaction of neuronal populations was investigated from the EEG by examining phase coupling between different regions of the brain and across multiple frequencies, to elucidate changes in neural coding implicated in anesthesia.

II. Methods and Materials

A. Electroencephalogram Acquisition

Digitized scalp EEG signals were sampled at 1024 Hz using disposable silver/silver-chloride electrodes 9 mm in diameter (XLTEK, Oakville, Ont.). Electrode placement followed the international standard 10-20 system recommended by the International Federation of Societies for Electroencephalography and Clinical Neurophysiology (IFSECN). EEG signals were recorded from 6 patients undergoing surgical procedures requiring general anesthesia lasting approximately 1 hour in duration. The patients were screened such that they were not being prescribed central nervous system (CNS) medications and did not have a diagnosed CNS pathology. EEG signals were recorded continuously just prior to and during anesthesia and surgery and during the immediate recovery period afterwards. The bispectral index was simultaneously recorded using the BIS monitor (Aspect, Massachusetts, USA).

Manuscript received April 15, 2011. This work was supported in part by the National Science and Engineering Research Council of Canada (NSERC) and Canadian Institute of Health Research (CIHR).

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B. General Anesthesia Protocol

General anesthesia was induced with fentanyl (2-3 mcg/kg) propofol (2.5 mg/kg) and rocuronium (0.7 mg/kg) followed by propofol infusion (140 mcg/kg/min) to maintain an anesthetic plasma level of propofol at 6 mcg/ml for 5 minutes to allow for EEG and BIS recordings at steady state. When the loss of the eyelash reflex was noted, patients were subsequently intubated. During the induction of anesthesia, patients were routinely ventilated to keep SaO_2 at more than 97%. During the maintenance phase of anesthesia, patients received a volatile anesthetic Sevoflurane, air/O_2 (1:1), to achieve a steady MAC value of 1.2, as well as supplemental doses of fentanyl as required. This was maintained for the duration of surgery. Additionally, rocuronium IV boluses (0.3 mg/kg) were given to achieve full muscle relaxation as indicated by the peripheral nerve stimulator in 4 out of the 6 patients.

C. Wavelet Phase Coherence

The method for obtaining a nonstationary phase coherence measure from the continuous wavelet transform follows from the work of Hoke et al. [3], Tass et al.[13], and Li et al. [9]. To begin, we calculated the continuous wavelet transform (CWT) of a signal, $x(t)$, yielding the complex-valued wavelet coefficient matrix $W(\sigma,\tau) = w(\sigma,\tau) + i\tilde{w}(\sigma,\tau)$ over scales σ and time shifts τ. The relative phase difference between two signals is expressed by the relationship:

$$\Delta\phi(t) = \arctan\frac{\tilde{y}_1(t)y_2(t) - y_1(t)\tilde{y}_2(t)}{y_1(t)y_2(t) + \tilde{y}_1(t)\tilde{y}_2(t)}. \quad (1)$$

Therefore, the relative phase difference between the complex wavelet coefficients of two signals, $W_1(\sigma,\tau)$ and $W_2(\sigma,\tau)$, can be written as

$$\Delta\phi(\sigma,\tau) = \arctan\frac{\tilde{w}_1(\sigma,\tau)w_2(\sigma,\tau) - w_1(\sigma,\tau)\tilde{w}_2(\sigma,\tau)}{w_1(\sigma,\tau)w_2(\sigma,\tau) + \tilde{w}_1(\sigma,\tau)\tilde{w}_2(\sigma,\tau)}. \quad (2)$$

The relative phase coherence, $0 \le \rho \le 1$, between two signals for a given scale (~ 1/frequency) and time segment, $T = [\tau - \Delta\tau, \tau + \Delta\tau]$, is the following:

$$\rho(\sigma,T) = \left|\left\langle \exp(i\Delta\phi(\sigma,T))\right\rangle\right| \quad (3)$$

where the angled brackets denotes the time-average.

D. Wavelet Bicoherence

The wavelet bicoherence allows for estimation of higher-order coupling between different frequency parings. The XYX wavelet cross-bispectrum is defined as

$$B_{xyx}(\sigma_1,\sigma_2,T) = \int_T W_X(\sigma_1,\tau)W_Y(\sigma_2,\tau)W_X^*(\sigma,\tau)d\tau \quad (4)$$

where $1/\sigma = 1/\sigma_1 + 1/\sigma_2$ and the asterisk denotes the complex conjugate. Therefore, the XYX bicoherence is the cross-bispectrum normalized in power to the range 0 to 1:

$$b_{xyx}(\sigma_1,\sigma_2,T) = \frac{|B_{xyx}(\sigma_1,\sigma_2,T)|}{\sqrt{\int_T |W_X(\sigma_1,\tau)W_Y(\sigma_2,\tau)|^2 \int_T |W_X(\sigma,\tau)|^2 d\tau}}. \quad (5)$$

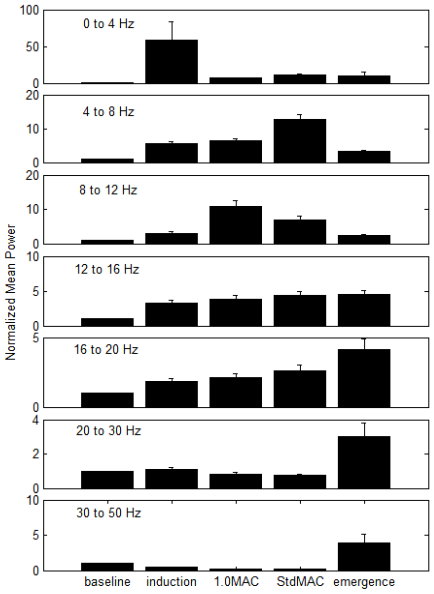

Fig. 1. Normalized mean power of various frequency components of the EEG before, during and after anesthesia.

III. Results

A. Localized Spectral Features of the EEG

EEG recordings were acquired following the standard 10/20 lead system with a common reference electrode located between Cz and Fz. Then differences of the neighboring electrode pairs were obtained to analyze EEG signals locally. Electrode pairs included in the following analysis are F3-Fz, C3-Cz, P3-Pz, F4-Fz, C4-Cz, and P4-Pz. All of these paired EEG signals showed distinct high-frequency complex activity during the awake condition, then shifted to lower-frequency, more rhythmic activity under anesthesia. Time-frequency analysis using the wavelet transform revealed that the power of EEG signals above 20 Hz was high during the awake condition, then drastically diminished with administration of anesthetics, whereas the components below 20 Hz exhibited the opposite trend.

To quantify the changes associated with specific states of the brain undergoing anesthesia, EEG signals were decomposed into band-limited signals using a finite impulse response (FIR) filter of order 5000. Various bandwidths were explored according to their ability to discriminate states by power, and the final choice of bands was 0 to 4 Hz, 4 to 8 Hz, 8 to 12 Hz, 12 to 16 Hz, 16 to 20 Hz, 20 to 30 Hz, 30 to 50 Hz, and 50 to 80 Hz. The five significant anesthetic states categorized in this study are "baseline", "induction", "1.0 MAC", "steady MAC", and "emergence". Baseline represents the recordings from awake patients before administration of any anesthetics; induction comprises the data taken from 30 to 60 seconds after administration of a combination of fentanyl and propofol, and represents the state en route to sedation; 1.0 MAC and steady MAC correspond to the maintenance phase of anesthesia achieved by the inhalant anesthetic,

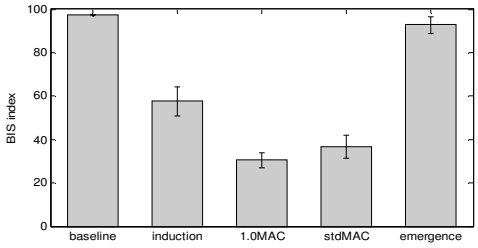

Fig. 2. Average Bispectral Index (BIS^{TM}) at the various states of anesthesia for all six patients.

Sevofluorane, where the latter represents a deep-enough anesthetic state for surgical stimulus and the former represents a transitional state towards the steady state; emergence represents a transitional state of awakening with some responsiveness to commands but not full consciousness.

The average power of the decomposed frequency signals of the aforementioned bandwidths was computed for each of the five states and normalized to the power of the baseline for each patient. The mean of the normalized power for each state and frequency band was calculated and is shown in Fig. 1. Besides the lower frequencies (< 20 Hz) being enhanced and higher frequencies (> 20 Hz) being reduced under anesthesia, each of the frequency components exhibited unique patterns during the course of anesthesia. All frequencies were sensitive to the changes occurring during induction, with 0 to 4 Hz being most sensitive and exhibiting a hundred-fold increase compared to the baseline. However this large enhancement of power in 0 to 4 Hz was short-lived and diminished quickly. On the other hand, the power in 4 to 8 Hz gradually increased throughout anesthesia until the steady anesthetized state was reached – as noted by the steady MAC level – then started to recover during emergence. 8 to 12 Hz power also increased with administration of anesthetics but peaked during 1.0 MAC before reaching steady state. Powers of 30 to 50 Hz were diminished with induction and reduced further with Sevoflurane, but the power during emergence surpassed that of baseline. The power of 12 to 20 Hz did not show significant changes during the course of anesthesia other than the initial increase during induction. By comparison, as seen in Fig. 2, the BIS index recorded during baseline was close to 100, dropping quickly to around 60 (57.6+/- 13.2) during induction. The BIS index after the loss of eyelash reflex but before the start of sevoflurane was significantly smaller at 37.42+/-7.19. Administration of sevoflurane only slightly decreased the BIS index to around 30 (33.44 +/- 10.11) compared to prior to its administration, and remained much the same throughout anesthesia subsequently. During emergence from anesthesia, the BIS index recovered to close to the baseline level.

B. Neuronal Communication Between Different Brain Regions

Communication between neuronal ensembles lies at the heart of information coding and binding in the brain. One way of characterizing this is to measure phase-to-phase coupling between signals of various regions. Phase coherence

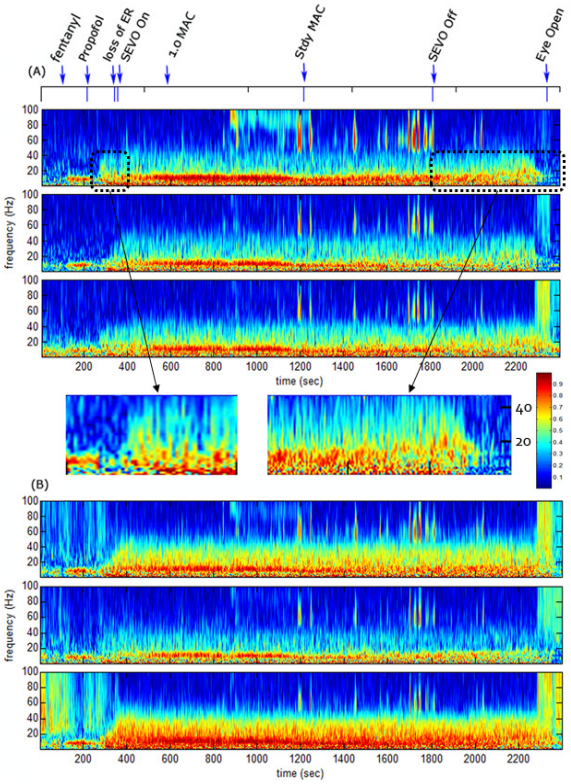

Fig. 3. Phase coherence of EEG signals (A) lateral pairs: F3-F7 & F8-F4, T3-C3 & T4-C4, T5-P3 & T6-P4 (B) frontal-posterior pairs: F8-F4 & T4-C4, F8-F4 & T6-P4, T4-C4 & T6-P4

quantifies the relative degree of phase coordination between two signals and provides a good indication of phase-to-phase coupling. Phase coherence was computed from the CWT for various pairs of electrodes, including bilateral electrode pairs (F3-F7 & F8-F4, T3-C3 & T4-C4 and T5-P3 & T6-P4) and anterior-posterior pairs of the right hemisphere (F8-F4 & T4-C4, F8-F4 & T6-P4, T4-C4 & T6-P4) as shown in Fig. 3. While the patients were awake, phase coherence of frequencies above 10 Hz was low (< 0.2) in bilateral pairs but was significantly higher in the anterior-posterior pairs. Interestingly, as patients were waking up, phase coherence of the same frequency range appeared high in the bilateral pairings as well as the anterior-posterior pairings. During the maintenance phase of anesthesia, a large bandwidth consistently showed high phase coherence, especially in the frequency range of 8 to 16 Hz. The transition into (induction) and out of (emergence) of anesthesia was accompanied by an increased phase coherence in the 16 to 25 Hz range, as shown in the insets of Fig. 3A.

Phase-to-phase coupling between different frequencies was quantified by the wavelet bicoherence, as described in the Methods and Materials section above. The wavelet bicoherence was computed for various combinations of electrode pairings. As before, the differential electrode configuration was utilized. The computed pairings included the bilateral frontal electrodes (F7-F3 vs. F8-F4), bilateral central electrodes (T3-C3 vs. T4-C4), ipsilateral frontal to central electrodes (F8-F4 vs. T4-C4), and ipsilateral central to

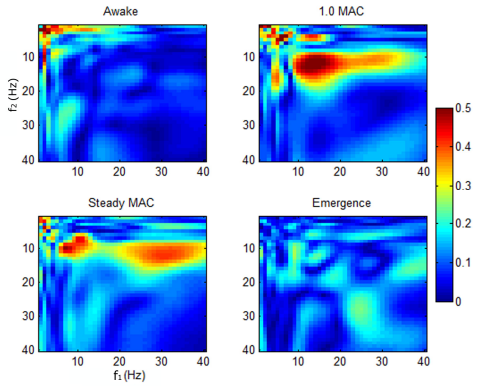

Fig. 4. Example wavelet bicoherence of EEG signals corresponding to different anesthetic states for the bilateral frontal pairings (F3-F7 vs F8-F4). During 1.0 MAC and Steady MAC, a high coherence region was observed for f_1: 10 to 40 Hz and f_2: 10 to 20 Hz.

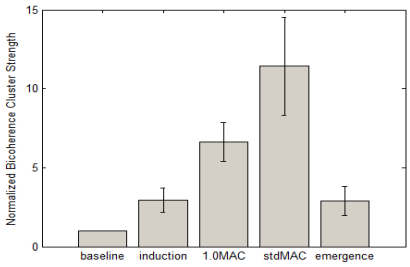

Fig. 5. Wavelet bicoherence mean cluster strength for the different anesthetic states.

posterior electrodes (T4-C4 vs. T6-P4). Fig. 4 shows example wavelet bicoherence plots for the various states of anesthesia. By visual inspection of these bicoherence plots for all patients, significant bicoherence between 10 to 40 Hz and 8 to 18 Hz emerged as the anesthesia was initiated. An image clustering technique using an 8-connected neighbor search was implemented to identify the significant bicoherence clusters in this frequency region of interest and the time-varying strength of the clusters computed. The mean bicoherence strength of the clusters in this region corresponding to each of the five states defined earlier (i.e. baseline, induction, 1.0 MAC, steady MAC and emergence) is plotted in Fig. 5. The results show a monotonically increasing trend in the bicoherence until steady MAC is reached, and then the bicoherence subsides with emergence.

IV. Discussion

In this study, we have extracted several features that maybe sensitive to the changes associated with different states of anesthesia. Patients typically reach a state of unconsciousness within minutes of the administration of intravenous or inhalational induction agents. These rapid changes correlate with the sudden changes in power in low-frequency EEG signals (especially in < 4 Hz). Switching over to maintenance of anesthesia using agents such as Sevoflurane does not manifest in outwardly-observable clinical signs, although the action is affecting brain electrical activity. Without the ability to communicate with patients under anesthesia, the precise mechanisms during the maintenance phase are difficult to ascertain. Therefore, additional features that can characterize and distinguish the various states of anesthesia, and that are derived from specialized signal-processing techniques, are likely to be clinically relevant. We have shown that the spectral power of various frequencies show trends throughout the maintenance phase (i.e. 4 to 8 Hz increases and 8 to 12 Hz decreases, Fig. 1). Moreover, phase-to-phase coupling measures revealed that the theta-to-gamma frequency neural coding changes as a result of anesthesia. Abnormally elevated values of wavelet bicoherence between 7 to 20 Hz and 10 to 40 Hz were observed. Features derived from spectral power, phase coherence and wavelet bicoherence might prove useful in designing and implementing a classifier better able to distinguish anesthetic states and their transitions for purposes of monitoring DoA.

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