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Tracking the coupling of two electroencephalogram series in the isoflurane and remifentanil anesthesia

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HIGHLIGHTS

- Through nonlinear model and surrogate analysis, the permutation cross-mutual information is a better method to estimate coupling of nonlinear systems.
- The permutation cross-mutual information can describe the coupling changes of EEG series under isoflurane and remifentanil anesthesia.
- Proposed permutation cross-mutual information has been proved to be a suitable measure to discriminate between the consciousness state and the anesthesia-induced unconsciousness state.

ABSTRACT

Objective: Coupling in multiple electroencephalogram (EEG) signals provides a perspective tool to understand the mechanism of brain communication. In this study, we propose a method based on permutation cross-mutual information (PCMI) to investigate whether or not the coupling between EEG series can be used to quantify the effect of specific anesthetic drugs (isoflurane and remifentanil) on brain activities.
Methods: A Rössler–Lorenz system and surrogate analysis was first employed to compare histogram-based mutual information (HMI) and PCMI for estimating the coupling of two nonlinear systems. Then, the HMI and the PCMI indices of EEG recordings from two sides of the forehead of 12 patients undergoing combined remifentanil and isoflurane anesthesia were demonstrated for tracking the effect of drug on the coupling of brain activities. Performance of all indices was assessed by the correlation coefficients (R_{ij}) and relative coefficient of variation (CV).
Results: The PCMI can track the coupling strength of two nonlinear systems, and it is sensitive to the phase change of the coupling systems. Compared to the HMI, the PCMI has a better correlation with the coupling strength in nonlinear systems. The PCMI could track the effect of anesthesia and distinguish the consciousness state from the unconsciousness state. Moreover, at the embedding dimension $m = 4$ and lag $\tau = 1$, the PCMI had a better performance than HMI in tracking the effect of anesthesia drugs on brain activities.
Conclusions: As a measure of coupling, the PCMI was able to reflect the state of consciousness from two EEG recordings.
Significance: The PCMI is a promising new coupling measure for estimating the effect of isoflurane and remifentanil anesthetic drugs on the brain activity.

1. Introduction

Monitoring the state of anesthesia is crucial in surgical operations. Light anesthesia may cause intra-operative awareness and postoperative recall. However, anesthesia overdose will result in

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hypotension, delayed recovery, or even the potential long-term mortality (Monk et al., 2005). In recent years, electroencephalogram (EEG) recordings have been used to reduce the risk due to overdose of anesthesia. As a reflection of cortical brain electrical activities, EEG provides a noninvasive approach to monitor the states of anesthesia. Although some commercial EEG-based monitors have been developed for identifying the patients' state of consciousness (Myles et al., 2003; Pritchett et al., 2010; Sackel, 2006), such as the bispectral index (BIS) monitor (Aspect Medical Systems, Newton, MA, USA) and the M-entropy module (GE Healthcare, Helsinki, Finland), these systems are based on one-channel EEG recording or focus on one brain area.

In anesthesia monitoring, the loss of consciousness (LOC) is a key issue. In John and Prichep (2005), the LOC induced from anesthesia was divided into six states. In these states, blockade of reverberations in cortical–thalamic–cortical loops, uncoupling of parietal–prefrontal cortical interactions and depression of the prefrontal cortex are three important mechanisms for functions of anesthesia. The impaired top-down processing with the anesthetic-induced unconsciousness can be observed by using EEG and functional magnetic resonance imaging (fMRI) (Jordan et al., 2013). It was also found that the propofol-induced unconsciousness occurs with abrupt, fragmented slow oscillations in local field potential across brain areas (Lewis et al., 2012). Further, Mashour proposed the "cognitive unbinding" to interpret the LOC (Mashour, 2013). Cognitive unbinding refers to the impaired synthesis of specialized cognitive activities in the brain. Temporal and spatial disruption of synchrony and convergence are two important tenets of the cognitive unbinding paradigm. And it is considered that information synthesis disrupting in areas, networks, or processes of brain is associated with anesthetic-induced unconsciousness (Mashour, 2013). Also, decrease of synchrony or loss of connectivity in functional areas are related to the anesthetized or sleep state (John et al., 2001; Massimini et al., 2005; Purdon et al., 2013). In the present study, we investigate whether the neural information integration of different functional areas can be used for tracking the effect of anesthesia on the brain actives.

To demonstrate the synchrony or convergence mechanism of anesthesia, a number of linear and nonlinear methods of time series analysis were proposed to estimate information coupling between EEG signals at different brain areas or spatial scales, such as coherence, phase–amplitude coupling, phase synchrony, and mutual information (MI) (Li et al., 2013; Pereda et al., 2005). Particularly, MI, a method for estimating information integration in time series, has been widely applied in EEG analysis (Abasolo et al., 2008; Hall and Sarkar, 2011). For example, the averaged cross-mutual information was employed to analyze the effect of total sleep deprivation on brain functional organization (Na et al., 2006) and to evaluate information integration capacity in propofol anesthesia (Lee et al., 2009). MI is based on the probability distribution of two time series. The simplest approach to estimate the probability distribution of their amplitude is calculating histograms with equal-sized bins, termed as the histogram-based mutual information (HMI). But the finite number of observations may induce systematic errors (Liang et al., 2013). Moreover, the calculation of the entropy with histograms is not accurate, and thus is not suited to describe nonlinear characteristics of EEG signals (Li and Ouyang, 2010). The kernel-based estimators and parametric methods are two other approaches proposed to calculate MI, but there are various restrictions in kernel optimization and parameter selection (François et al., 2007). Furthermore, HMI and kernel-based approaches are based on the amplitude estimate of the signals, and they are not very suitable for analyzing signals with nonlinear and nonstationary characteristics (Elbert et al., 1994; Vakorin et al., 2010).

The probability distribution analysis based on order pattern has been proposed for EEG analysis, and has been proved to be powerful in detecting abnormal information of a dynamical system (Olofsen et al., 2008). Among the order pattern methods, the permutation analysis is based on the order relations between the values of a time series and nonrelevant to the values themselves. The merit of the permutation analysis is its robustness, simplicity, and low computational complexity. Therefore, in this study we adapted the permutation cross-mutual information (PCMI) method to evaluate the information coupling of two-channel EEG signals from two sides of the forehead in anesthesia.

Although MI can describe the coupling of nonlinear systems, the inner dynamic properties of these systems are still unknown (Andrzejak et al., 2003). In addition, it is problematic to decide whether the PCMI reflects an underlying nonlinear deterministic dynamics or whether it is consistent with a linear stochastic model. In this study, a surrogate technique and a coupled Rössler–Lorenz nonlinear system are adopted to test the performance of PCMI to describe nonlinear coupling (Andrzejak et al., 2003).

This paper is structured as follows. Section 2 gives the details of the HMI and PCMI algorithms, the surrogate technique, as well as statistical analysis. In Section 3, a coupled Rössler–Lorenz nonlinear system is used to analyze the performance of PCMI and HMI with different parameters. In Section 4, EEG recordings, preprocessing, and parameter selection are introduced. The HMI and PCMI are applied to EEG data to detect the information coupling at the different anesthesia states. Finally, we discuss the PCMI results and speculated the neurophysiological interpretation of information coupling under anesthesia.

2. Methods

2.1. HMI and PCMI

The MI is a synchrony measure to calculate the shared information between two stochastic variables (Paluš, 1996). The HMI is the most widely used method for calculating MI. The HMI algorithm is described as follows:

Considering two random variables $x(t)$ and $y(t)$, $t = 1,\ldots,N$, given an origin ρ and a width h, the bins of histogram for two variables can be defined through the intervals $[\rho + mh,\ \rho + (m+1)h]$, $m = 0,\ldots, M$. Then, the values of each variable can be partitioned into M discrete bins λ_i. Define k_i and l_i as the number of measurements that lie within bin λ_i for $x(t)$ and $y(t)$. The probabilities $p(k_i)$ and $p(l_i)$ are the relative frequencies of occurrence for k_i and l_i. Meanwhile, define $p(kl_{ij})$ as the joint probability of $x(t)$ and $y(t)$. Then the MI based on Shannon entropy is defined by

$$\mathrm{MI}(x(t), y(t)) = H(x(t)) + H(y(t)) - H(x(t), y(t)) \tag{1}$$

where $H(x(t))$ and $H(y(t))$ are entropies, defined by

$$H(x(t)) = -\sum_{i=1}^{M} p(k_i)\log p(k_i), \quad H(y(t)) = -\sum_{i=1}^{M} p(l_i)\log p(l_i) \tag{2}$$

and the $H(x(t), y(t))$ is joint entropy (Palus and Stefanovska, 2003), defined by

$$H(x(t), y(t)) = -\sum_{j=1}^{M}\sum_{i=1}^{M} p(kl_{ij})\log(p(kl_{ij})) \tag{3}$$

In the histogram-based method, the parameters of M and h are first determined. However, the optimal number of bins depends on a strong assumption about the shape of the distribution; so far there is no best number of bins for practical time series (Li and Ouyang, 2010).