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Monitoring the depth of anesthesia using entropy features and an artificial neural network

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HIGHLIGHTS

- A comprehensive set of features is proposed to assess the effect of anesthetic.
- Sample entropy and permutation entropy features quantify the amount of complexity in EEG data.
- The proposed method classifies EEG data into awake, light, general and deep anesthetized states.
- An Artificial Neural Network is used to classify the EEG into different anesthetized states.
- We propose a novel method to estimate depth of anesthesia in a quick and accurate manner.

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ABSTRACT

Monitoring the depth of anesthesia using an electroencephalogram (EEG) is a major ongoing challenge for anesthetists. The EEG is a recording of brain electrical activity, and it contains valuable information related to the different physiological states of the brain. This study proposes a novel automated method consisting of two steps for assessing anesthesia depth. Initially, the sample entropy and permutation entropy features were extracted from the EEG signal. Because EEG-derived parameters represent different aspects of the EEG features, it would be reasonable to use multiple parameters to assess the effect of the anesthetic. The sample entropy and permutation entropy features quantified the amount of complexity or irregularity in the EEG data and were conceptually simple, computationally efficient and artifact-resistant. Next, the extracted features were used as input for an artificial neural network, which was a data processing system based on the structure of a biological nervous system. The experimental results indicated that an overall accuracy of 88% could be obtained during sevoflurane anesthesia in 17 patients to classify the EEG data into awake, light, general and deep anesthetized states. In addition, this method yielded a classification accuracy of 92.4% to distinguish between awake and general anesthesia in an independent database of propofol and desflurane anesthesia in 129 patients. Considering the high accuracy of this method, a new EEG monitoring system could be developed to assist the anesthesiologist in estimating the depth of anesthesia in a rapid and accurate manner.

1. Introduction

Monitoring the depth of anesthesia has been a challenge in anesthetic research. Intraoperative awareness resulting from an inadequate depth of anesthesia may cause psychological effects on patients (Sebel et al., 2004). Clinical indices such as blood pressure, heart rate, sweating or limb movements have been used to assess the depth of anesthesia. However, these traditional methods may vary from patient to patient depending on the type of surgery. In addition, the use of other drugs such as muscle relaxants and vasodilators make the analysis of these signs difficult and unreliable.

Investigators have focused on finding reliable noninvasive ways to monitor the depth of anesthesia over the last several decades. Researchers have turned their attention toward the analysis of brain activity using the electroencephalogram (EEG) because the central nervous system is a target of anesthetic drugs (Gugino et al., 2001). Because EEG signals contain valuable information for the

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understanding of anesthesia, the EEG is considered a useful tool in the study and assessment of the depth of anesthesia in clinical applications.

During the past two decades, a number of EEG-based methods such as the 95% spectral edge frequency, median frequency (Schwender et al., 1998) and bispectral index (Rampil, 1998) (BIS, Aspect Medical Systems Inc., Newton, MA) have been proposed to assess the level of consciousness during general anesthesia. However, these methods are sensitive to artifacts and run the risk of time delays in response to EEG changes (Pilge et al., 2006).

Nonlinearity can also be observed in many dynamic systems found in nature, including the brain (Fell et al., 2000; Elbert et al., 1994). Nonlinearity in the brain is important even at the cellular level because threshold and saturation phenomena control the dynamic behavior of individual neurons (Elbert et al., 1994). Moreover, many studies have shown that nonlinear analyses can be applied to the EEG for different medical applications (Chouvarda et al., 2010; Nguyen-Ky et al., 2010; Ferents et al., 2006; Shalbaf et al., 2012a,b). These analyses provide information that cannot be obtained using traditional EEG spectral-band analyses (Fell et al., 1996). Therefore, it is reasonable to apply methods from the theory of nonlinear dynamics and information theory, such as entropy, to brain signals for an estimation of the depth of anesthesia.

The first entropy introduced was Shannon entropy, which is based on the probability distribution of the recorded values (Shannon and Weaver, 1964; Bruhn et al., 2001). Because the Shannon entropy of the EEG signal has little information regarding EEG dynamics and also tends to increase inaccurately with deepening anesthesia, it is not reliable for clinical use. This obstacle was overcome by the use of spectral entropy, which is represented by the Shannon entropy formula properly normalized and applied to the power spectral density of the EEG recording (Vanluchene et al., 2004). A monitoring system based on spectral entropy using an indicator known as Response Entropy (RE) (M-Entropy Module, Datex-Ohmeda, Finland) has been recently developed for clinical practice (Viertio-Oja et al., 2004). In this system, the RE is obtained across the frequency band 0.8–47 Hz and includes electromyogram-dominated frequencies.

Recently, two nonlinear parameters, namely, sample entropy (SampEn) (Richman and Moorman, 2000; Shalbaf et al., 2012a,b; Yum et al., 2008; Alcaraz and Rieta, 2010) and permutation entropy (PermEn), have been developed to explore the structure of EEG recordings (Bandt and Pompe, 2002; Cao et al., 2004; Li et al., 2010; Olofsen et al., 2008). SampEn is a favorable method used to address the predictability of a dynamic system (Richman and Moorman, 2000). It estimates the probability that the sequences in a dataset, which are initially closely related, remain closely related, within a given tolerance, on the next incremental comparison. SampEn properly tracks the dynamics of brain activity in anesthesia, particularly at high doses of anesthetics, but it requires long and noiseless EEG data (Shalbaf et al., 2012a,b). PermEn is another complexity measure that explores the local order structure of a dynamic time series (Bandt and Pompe, 2002). Its calculation is based on mapping the time series onto a symbolic sequence to quantify the probability of the different symbols (Cao et al., 2004). PermEn is conceptually simple, computationally efficient and artifact-resistant, but it does not work at a very deeply anesthetized state, mainly due to the high-frequency waves during the suppression period (Li et al., 2010; Olofsen et al., 2008).

The method of calculating the effect of an anesthetic drug on the EEG using just one mathematical measure involves the idea that the EEG signal property changes monotonically when the anesthetic level changes continuously (Kortelainen et al., 2011). However, anesthetic agents express a continuum of neurophysiological changes, which results in the complexity of the EEG. Thus, measuring this complexity with a single parameter is unreasonable and does not work well all of the time. However, a comprehensive set of features is required to adequately describe the transition from awake to deep anesthesia using the EEG (Kortelainen et al., 2011). This challenge opens new possibilities for future researchers.

In this paper, a novel automated method for assessing the anesthetic depth level is proposed. The proposed method consists of two steps. The SampEn and PermEn features are initially extracted from the EEG signal. Next, the extracted features are used as the input to an artificial neural network (ANN) (Bose and Liang, 1996) to classify the EEG into different anesthetized states. ANN was developed on the basis of biological nervous systems and exhibits a parallel highly interconnected structure that generates its computations as rapidly as possible. The capability of this method to classify the EEG into awake, lightly anesthetized, general anesthetized and deeply anesthetized states were investigated compared to the RE, as determined using the M-Entropy Module during sevoflurane anesthesia. Furthermore, the adequacy of the new method to classify independent datasets was also examined. The performance of the proposed scheme was evaluated for sensitivity and classification accuracy.

2. Materials and methods

2.1. Subjects and data acquisition

2.1.1. Sevoflurane database

We studied 17 patients (age 18–63 years, American Society of Anesthesiologists (ASA) physical status I or II) who were scheduled for elective general, orthopedic or gynecological surgery. These details have been previously described (Mckay et al., 2006). All of the subjects were recruited from Waikato Hospital, Hamilton, New Zealand. All of the patients gave their written informed consent and the protocols used in this study were approved by the Waikato Hospital Ethics Committee.

A composite electrode, which consisted of a self-adhering flexible band holding three electrodes, was used to record the EEG between the forehead and temple. A plug-in M-Entropy Module (Datex-Ohmeda) was used to measure the RE, which was sampled at 0.2 Hz. A sampling rate of EEG data were 100/s. In this module, the band pass filters with low and high cut-off frequencies were set at 0.5 and 47 Hz, respectively, and the notch filter was set at 50 Hz. Segments with a maximum amplitude greater than 200 μV were rejected as artifacts. Inspired and expired sevoflurane concentrations were measured at the mouth and sampled at 100/s.

Patients were connected via a facemask to a closed anesthetic breathing circuit, and fresh gas flow was set at 4 L/min. The patients were preoxygenated under the supervision of the anesthesiologist. Next, the following anesthetic protocol was performed (cycle 1). Sevoflurane was delivered using a vaporizer at 3% inspiration for 2 min, followed immediately by a 7% inspired concentration. The RE was simultaneously recorded. The specific time at which the RE decreased to 20 or less was noted and 7% sevoflurane was continued for a further 2 min. The sevoflurane was then turned off until the RE returned to a value of 70. This was the end of the first anesthetic cycle. No supplemental medications were administered during the first cycle and no attempt was made to rouse the subjects. Loss of consciousness (LOC) was assessed based on the loss of the response to a verbal command from the anesthesiologist. Subsequently (cycle 2), the anesthesia was re-deepened, and a laryngeal airway or endotracheal tube was inserted. The elective surgery commenced during the equilibrium phase of anesthesia. During the second anesthetic cycle, supplemental medications, including fentanyl, and muscle relaxants were administered at the discretion of the anesthesiologist. Data collection was discontinued