Comparing EEG patterns in different age groups during general anesthesia with sevoflurane.

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Background

Analyzing the raw electroencephalography (EEG) waves during anesthesia is still challenging and has not been fully demonstrated. Alterations of consciousness are due to effects of anesthetic agents that act on the central nervous system, more precisely, on the brain. These alterations are major clinical endpoints of general anesthesia and can be analyzed and monitored throughout recordings of surface brain electrical activity, called electroencephalography (EEG). EEG is a powerful tool that refers to the recording of the brain's spontaneous electrical activity along the scalp and it can be used to measure voltage fluctuations which result from ionic current flows within neurons found in the brain. The electroencephalogram is increasingly used to measure anesthetic drug effect on the central nervous system. Since, analyzing the real-time raw electroencephalographic signal during anesthesia is difficult, several electroencephalographic monitors have been developed to extract and process information and to present the content in a continuous index from 0 to 100. Zero represents the deepest level of anesthesia (isoelectric encephalographic line), and 100 represents the awake state of a patient. The use of electroencephalographic monitors has been proven to decrease drug consumption during anesthesia and to lead to a faster recovery from anesthesia. Recently, the use of the Bispectral Index® (BIS®) monitor (Aspect Medical Systems, Newton, MA) has been shown to decrease the incidence of intraoperative awareness. Depth of anesthesia is frequently assessed using electroencephalogram processing systems, such as BIS and M-Entropy® (Datex-Ohmeda, Helsinki, Finland). The use of these monitors has been claimed to allow more accurate drug administration which has the theoretical benefit of avoiding phases of too light or too profound anesthesia and the associated risks of hemodynamic instability. Inadequate general anesthesia caused by under dosage causes intraoperative awareness whereas prolonged anesthesia increases the risk of postoperative complications because of over dosage. The most important factor that contributes to the inadequate general anesthesia is the current limited ability to determine the level of awareness. In this study, we want to analyze the raw EEG waves under general anesthesia using sevoflurane of MAC 1.0 for different age groups from 0 to 80 years old.

Like other organ systems, the nervous system is functionally immature at birth, myelination is rapid during the first 2 years and completed by 7 years of age.[i] Therefore, the BIS algorithm cannot automatically be extrapolated to young children. Some investigations suggest that BIS may be valid in children older than 2 years of age.[ii] Only one study, as far as we know, evaluated prospectively the correlation of BIS with end-tidal sevoflurane concentration in children. Regarding the effect of age on BIS values, there have been reports comparing the BIS between infants and children or between children and adults[iii] but there have been no reports comparing the raw EEG waves in all age groups (0-80 years old) under sevoflurane of 1.0 MAC. Minimal alveolar concentration (MAC) was introduced to compare the potencies of inhalation anesthetic agents. Sevoflurane is a commonly used inhalation anesthesia agent today. However, the relation between concentration of 1.0 MAC sevoflurane and raw EEG states in different age groups is relatively unstudied. In this prospective randomized study we want to know if there is any correlation of brain waves under general anesthesia in different age groups. It is therefore of neuroscientific interest to assess whether the electroencephalographic correlates of sevoflurane-induced unconsciousness have different or similar frequency range among the age groups.

General anesthetic and sedative agents induce highly structured oscillations in the EEG.[iv] There is growing evidence that these oscillations relate directly to the systems-level mechanisms by which anesthetics produce altered states of consciousness. During normal brain function, oscillations regulate the timing and coordination of brain activity within and between functional systems and circuits. Anesthesia induced oscillations are thought to disrupt this coordinated activity, producing different states of altered arousal depending upon the receptors and circuits upon which the drugs act.[v] General anesthesia with sevoflurane is characterized in the EEG by frontally coherent alpha (8–12 Hz), delta (1–4 Hz), and high amplitude slow (0.1–1Hz) oscillations.[vi] This pattern, observed when adult patients are sufficiently anaesthetized to conduct surgery, is similar to that observed under propofol-induced general anesthesia and suggests a common systems-level mechanism of action.[vii] Given that the brain rapidly develops and undergoes significant changes from childbirth into adulthood, anesthesia induced EEG oscillations in children might differ from those of adults, and could vary significantly with age. Characterizing the structure of the EEG in relation to age would help establish the foundations for age-appropriate monitoring of brain states during general anesthesia and sedation in children. We aimed to examine the effects of age on the EEG during general anesthesia, with sevoflurane as the sole hypnotic agent. The EEG is typically described in terms of rhythmic activity and transients. The rhythmic activity is divided into bands by frequency (figure 1 and figure 3).

Objective

Aim:

This study is designed to evaluate the correlation of raw EEG patterns and age under 1.0 MAC sevoflurane.

Study design and purpose

This study is being conducted to evaluate and assess the electroencephalography wave patterns in different age patients undergoing surgery under general anesthesia. The aim of our study is to compare the raw EEG waves in different age patients and analyze any changes in these patterns among various age groups and which of these groups will have the EEG signal of high-frequency waves or low frequency waves. Previous studies have shown that light sedation is often accompanied by decreasing posterior alpha waves and increasing the intensity of frontal/central beta waves.

Sample size: 120

Based on 6 different age groups from infants to elderly (0-80 years old), we are recruiting 120 patients with an American Society of Anesthesiology score (ASA) I or II, scheduled for elective surgery under general anesthesia lasting less than 2 hours. Each group will have 20 cases.

Methods:

A sample of 120 healthy patients from the Second Affiliated Hospital of Wenzhou Medical University with American Society of Anesthesiologists (ASA) physical status I or II will be randomly selected and included in this study. After obtaining ethical approval and written informed consent, we will enroll 120 patients (ASA I and II), aged 0-80 years of either gender undergoing minor elective surgery. The selected patients will be divided into 6 different groups according to their age (figure 2). The surgeries will last less than two hours each and will be performed under general anesthesia which is an indispensable part of surgery. Depth of anesthesia and electrical brain activity will be monitored using Bispectral index monitoring system. However, these are based on the underlying changes in the features of an EEG signal as the signals vary with the level of anesthesia. We will compare the different EEG waves (alpha, delta, theta and gamma) for all age patients while maintaining 1.0 MAC sevoflurane. Data related to non-invasive blood pressure, heart rate, respiration rate, oxygen saturation, EEG waves frequencies, end tidal volume of sevoflurane and BIS values will be recorded. These data will be analyzed every 1 min for the first 10mins during maintenance of anesthesia with 1.0 MAC sevoflurane. Data collection will be first recorded after tracheal intubation. The raw EEG wave will be recorded by means of a Universal Serial Bus (USB) which will later be analyzed and processed offline.

120 patients undergoing minor elective surgeries will be allocated in 6 age groups: 1month-1 year old (infant period), 1-3 years old (toddler period), 3-6 years old (preschool age period), 7-18 years old (school age period), 18-65 years old (adults) and 65-80 years old (elderly). After arrival in the operating room, an intravenous line will be inserted into a large forearm vein, and standard monitors will be applied. Each patient will be continuously monitored by a 3-lead electrocardiogram, noninvasive arterial pressure, pulse oximetry, and end-tidal carbon dioxide concentration. In addition to the standard conventional monitors, BIS electrodes will be placed before induction on each patient. The electroencephalogram will be recorded continuously over a period of 10 minutes using the Aspect A-2000 BIS®monitor (version XP). All the 120 patients enrolled in this study will be studied for 10 minutes after induction and tracheal intubation without any surgical stimulus. After the skin of the forehead had been prepared and cleaned with

alcohol, the BIS® (BIS-XP sensor) and BIS electrodes will be positioned as recommended by the manufacturers. Anesthesia will be induced by sevoflurane inhalation only with a tight-fitting facemask and a 4-l airflow of 100% oxygen. As spontaneous breathing diminishes, patients will be manually assisted and with cessation of spontaneous breathing, will be mechanically ventilated via the facemask to an end-tidal carbon dioxide of 35 mmHg. The induction of anesthesia will be the same in all age groups and will consist of sufentanil 0.2-0.3mcg/kg or fentanyl 1-2 mcg/kg before intubation and 0.2 mg/kg cisatracurium to facilitate intubation. Sevoflurane inhalation will be adjusted in all age groups to maintain 1.0 MAC concentration. After tracheal intubation, patients will be ventilated with a tidal volume of 6-8 ml/kg and the respiratory rate will be adapted to obtain an end-tidal carbon dioxide concentration of 30–35 mmHg. After intubation, sevoflurane will be titrated to generate an end-tidal concentration (ETsevo) of 2.0, 3.0, and 4.0% in a stepwise increase or decrease pattern in each age group to maintain 1.0 MAC concentration.

All patients will be ventilated using an Ohmeda-Datex anesthetic machine with soda lime (CO_2 absorber). Hypotension, defined as a decrease in blood pressure by 25% from baseline, will be treated with intravenous fluid or phenyl ephedrine (20 microgram bolus). Raw EEG data, BIS values and end target expiratory concentration of sevoflurane will be recorded every one minute for a period of 10 mins after induction and intubation. Raw EEG data (figure4-patient of 80 years old), will be analyzed and processed using the pdf screenshot from the BIS vista monitor. The pdf screenshots of the raw EEG will be recorded by means of a Universal Serial Bus (USB). The pdf screenshots will be taken twice during the 10 minutes of recording to minimize any loss of data.

Inclusion Criteria:

Patients age between 0 to 80 years old, ASA I or II scheduled for minor surgeries under general anesthesia lasting less than 2 hours each.

Exclusion Criteria:

Potential subjects with any neurologic or psychiatric disease, relative or absolute contraindication to sevoflurane including pregnancy by patient self-report, and any recent prescription or illicit medication use will be excluded. Patients with a history of any disabling central nervous or cerebrovascular disease and patients who had received central nervous system–active drugs will be excluded from the study. We will exclude patients with poor quality data, most likely because of poor electrode contact.

Potential benefits

The advantages of this study are to help the anesthesiologist have a better understanding of the brain waves under general anesthesia. EEG monitoring provides assessment of brain perfusion during state of general anesthesia. Brain death during anesthesia can be assessed and prevented with the use of raw EEG patterns.

EEG waves monitoring is a key aspect in preventing brain damage and ensuring the level of anesthesia is within the required range.

Maintaining the required range of deep anesthesia (BIS value of 40 to 60) helps avoid the incidence of awareness with recall in adults during general anesthesia and sedation.

Potential risks

There are no risks and complications associated with this study. However, mild redness may appear on the forehead in some patients from the BIS electrodes.

Statistics:

Statistical analyses will be performed with a statistical package (SPSS version 21.0; SPSS, Chicago, IL) and Microsoft excel. All data will be presented as mean±sd. Demographic data will be compared by using standard t-tests; comparison of incidence data between groups performed by using Fisher's exact tests. A P value < 0.05 will be considered significant.

Study duration:

We are estimating that the entire study will require one year, including patient recruitment, data collection, data analysis and report writing.

Co-Investigators:

Name	Department	Role
Beekoo Deepti	Anesthesiology, The second affiliated hospital of Wenzhou Medical University.	Principal Investigator
Shangguan Wangning	Anesthesiology, The second affiliated hospital of Wenzhou Medical University.	Co-Clinical Investigator

Payment:

There is no financial benefit or any reimbursement for participation in this study.

Figure 1:

Band	Frequency (Hz)
Delta	< 4
Theta	≥ 4 and < 8
Alpha	≥ 8 and < 14
Beta	≥ 14

Figure 2:

Groups	Age
1- Infant period	1month-1 year old
2- Toddler period	1-3 years old
3- Preschool age period	3-6 years old
4- School age period	7-18 years old
5- Adults	18-65 years old
6- Elderly	65-80 years old

Figure 3:

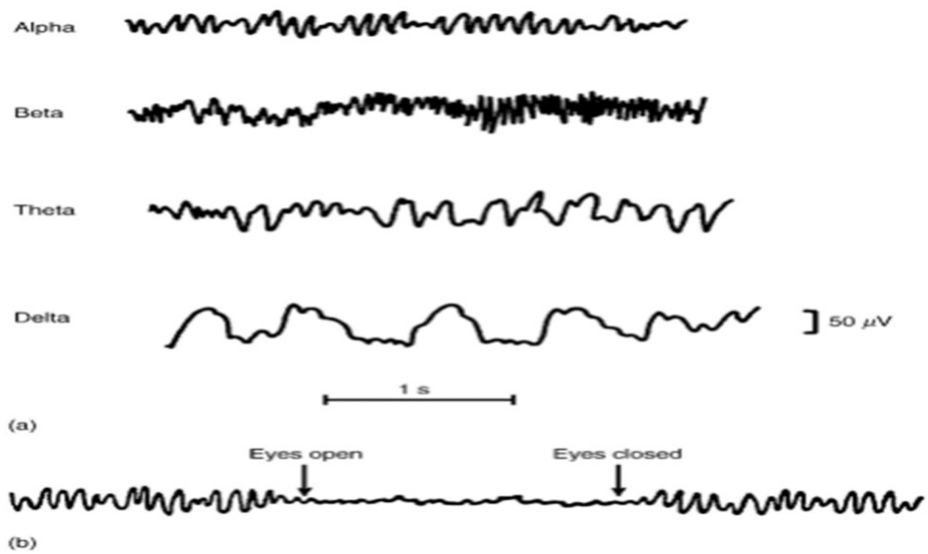
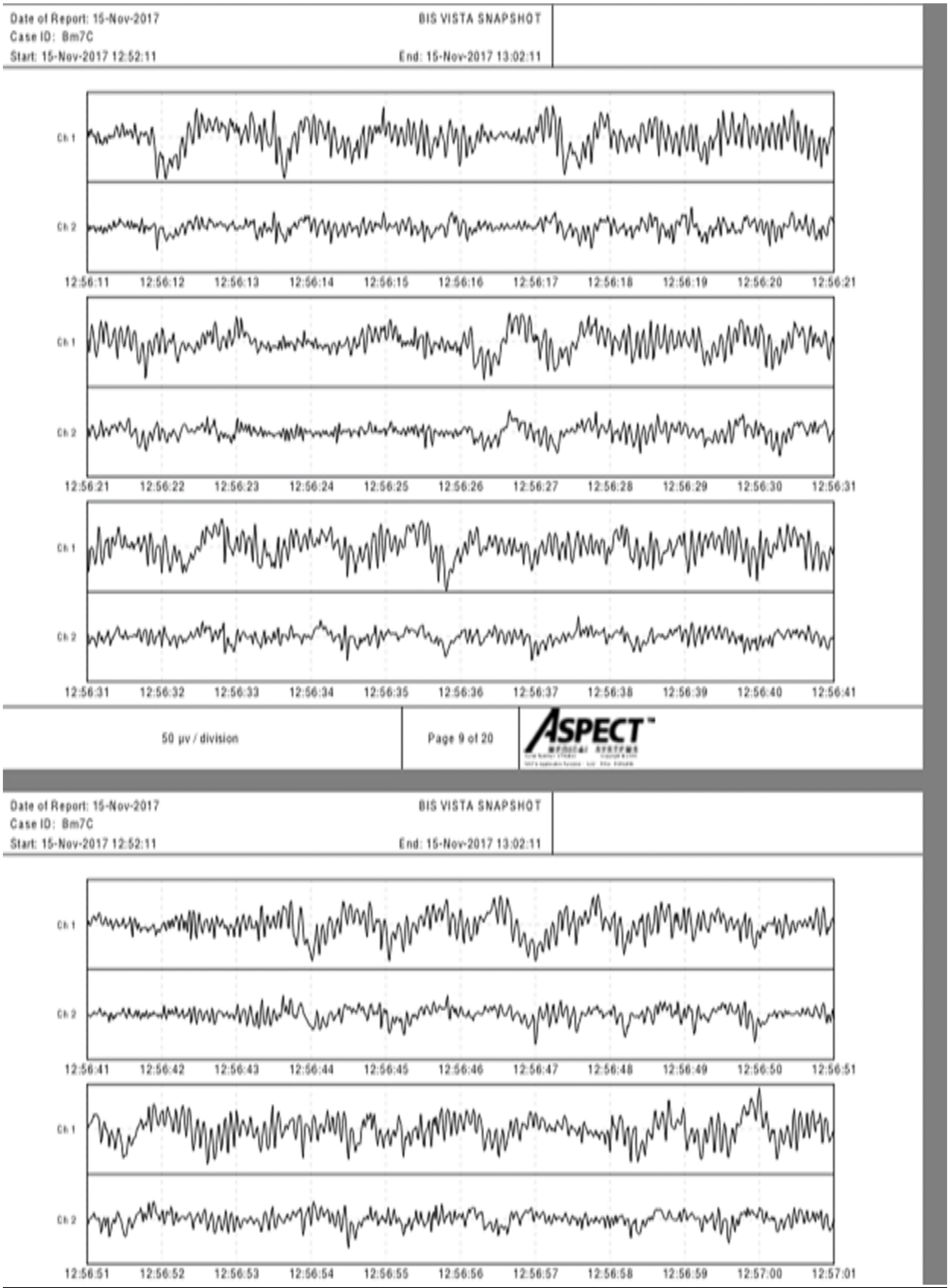

Alpha
Beta
Theta
Delta
50 μV
1 s
(a)
Eyes open
Eyes closed
(b)

Figure 4:


Date of Report: 15-Nov-2017
Case ID: Bm7C
Start: 15-Nov-2017 12:52:11
BIS VISTA SNAPSHOT
End: 15-Nov-2017 13:02:11
Ch 1
Ch 2
12:56:11 12:56:12 12:56:13 12:56:14 12:56:15 12:56:16 12:56:17 12:56:18 12:56:19 12:56:20 12:56:21
12:56:21 12:56:22 12:56:23 12:56:24 12:56:25 12:56:26 12:56:27 12:56:28 12:56:29 12:56:30 12:56:31
12:56:31 12:56:32 12:56:33 12:56:34 12:56:35 12:56:36 12:56:37 12:56:38 12:56:39 12:56:40 12:56:41
50 µv / division
Page 9 of 20
ASPECT
Date of Report: 15-Nov-2017
Case ID: Bm7C
Start: 15-Nov-2017 12:52:11
BIS VISTA SNAPSHOT
End: 15-Nov-2017 13:02:11
12:56:41 12:56:42 12:56:43 12:56:44 12:56:45 12:56:46 12:56:47 12:56:48 12:56:49 12:56:50 12:56:51
12:56:51 12:56:52 12:56:53 12:56:54 12:56:55 12:56:56 12:56:57 12:56:58 12:56:59 12:57:00 12:57:01

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