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The Application of Quantitative Electroencephalography (Spectral Edge Frequency 95) to Evaluate Sedation in Dogs

Min-Su Kim[1] and Tchi-Chou Nam

Department of Veterinary Surgery, College of Veterinary Medicine, Seoul National University

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Abstract : This study was performed to evaluate sedation with quantitative electroencephalography (EEG) analysis in dogs. EEG is used to evaluate objectively the effects of CNS acting with brain and behavioral changes. Especially, spectral edge frequency 95 (SEF 95) parameter is an effective method to determine the sedative status. The SEF 95 is the frequency below 95% of the total power. Twelve healthy intact male Miniature Schnauzer dogs, which did not show any neurological abnormalities and disease, were used for the study. EEG electrodes were inserted in subcutaneous tissue over the calvaria without entering adjacent muscles. The EEG data were acquired and analyzed by EEG raw wave and spectral edge frequency 95 analysis. After the administration of sedatives, the SEF 95 values were shown the significant changes compared with the normal state in all groups ($p<0.05$). It is suggested that SEF 95 analysis is useful method for assessing the state of sedation in dogs.

Key words **:** dogs, electroencephalography, sedation, spectral edge frequency.

Introduction

Sedation is a state characterized by central depression accompanied by drowsiness (5,12). In veterinary field, sedation needs to do muscle relaxation, anticonvulsant and behavior modification (12). The methods for assessing the sedation level are heart rate, respiratory rate, muscle relaxation, and ocular sign (7). However, the standard methods for clinical examination of sedation have been few reported. EEG can be a valuable tool in the evaluation of central nervous system activity (6). Electroencephalography (EEG) is a useful and noninvasive investigation tool for assessing the CNS activity and may be a more sensitive method than measurement of locomotor activity to assess sedation (1,2,6). In veterinary medicine, the EEG has been an important diagnostic method to aid in evaluation of many encephalopathies including brain tumors, seizure activity, and hydrocephalus (15). Moreover, effects of many drugs and anesthetics have been evaluated by routine inspection of canine EEG (13,14). Especially, the quantitative EEG such as relative band power analysis and spectral edge frequency analysis can be effective assistance in diagnosing various conditions affecting brain alternation (1). The SEF 95 is a frequency in the EEG determined by the 95% of the power spectral density, with lower values indicating a higher degree of sedation and hypnosis (10,11).

The present study was designed to evaluate sedation with the spectral edge frequency 95 analysis in dogs.

[1]Corresponding author.
E-mail : k7519@snu.ac.kr

Materials and Methods

Experimental animals

Twelve healthy intact male miniature schnauzer dogs (4.2-6.1 kg), which did not show any neurological abnormalities and disease, were used for the study. Food was withheld for at least 12 hours before the experiments. The experimental groups were divided 5 groups. Five groups were acepromazine group (n=10), butorphanol group (n=10), diazepam group (n=10), medetomidine group (n=10), and phenobarbital group (n=10), respectively. Dog were repeatedly used with a washout period of 2 weeks.

Experimental procedure

A calm environment was obtained and recording was started. After the electrodes were placed at appropriate sites, the first 30 min were spent allowing the dog to stay. Total experimental period were 30 min. In conscious condition, EEG recording was determined with intervals of 2 min in each group; the mean value was taken (a). Ten minutes after baseline recording, the sedative drugs were administered intravenously through the cephalic vein. During sedation, EEG recording were measured at intervals 4 min for duration of 20 min (b-f). Measurement was made at time point a-f (Fig 1).

Drugs

The experimental drugs used were: acepromazine (0.05 mg/kg; Sedaject®, Samu Median Co., Ltd, Korea), butorphanol (0.2 mg/kg; Butophan®, Myungmoon Pharm Co., Ltd., Korea), diazepam (0.5 mg/kg; Melode®, Dongwha Pharm. IND. Co.,

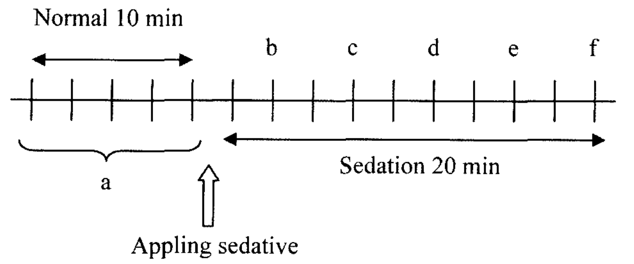

Fig 1. Experimental procedure. a: average of 5 times per every 2 min during 10 min in conscious condition, b-f: 5 times per every 4 min during 20 min in sedative condition.

Ltd. Korea), medetomidine (0.01 mg/kg; Domitor®, Orion Phama, Finland) and phenobarbital (5 m/kg; Luminal®, Daihan Pharm. Co. Ltd., Korea).

Electrode setting and EEG equipment

The electrode sites inserted for EEG recording in the skull & ears were clipped, and then 2% lidocain was subcutaneously administered at the sites. Five minutes after lidocain injection, the EEG electrodes were inserted in subcutaneous tissue over the calvaria without entering adjacent muscles. The electrodes, stainless-steel pins like type of a fish hook, were inserted underneath the skin. An eight-channel monopolar computerized EEG (Model: Quantitative EEG-8, LXE3208, Laxtha Inc., Korea) and needle electrodes were used (Fig 2). The electrode arrangement consisted of placing 8 electrodes on the head (frontal, parietal, and occipital area).

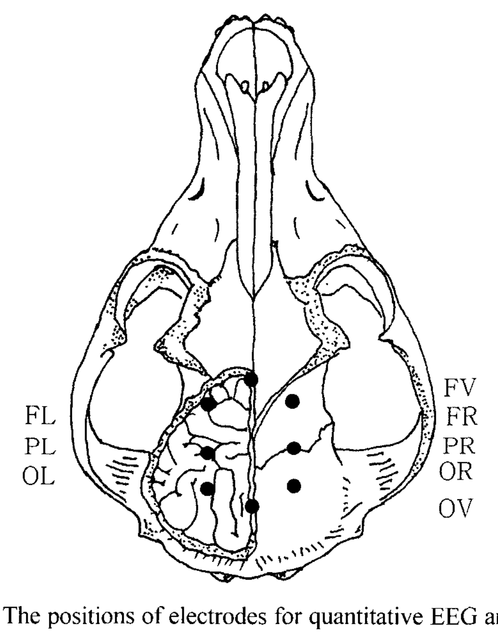

Fig 2. The positions of electrodes for quantitative EEG analysis in dog. The positions are drawn frontal, parietal, and occipital, respectively. Frontal vertex (FV) position was middle frontal electrode. Frontal right (FR) and frontal left (FL) position was right and left frontal electrodes, respectively. Parietal right (PR) and parietal left (PL) position was right and left parietal electrodes, respectively. Occipital right (OR) and occipital left (OL) position was right and left occipital electrodes, respectively. Occipital vertex (OV) position was middle occipital electrode.

EEG data processing

EEG analysis was performed with TeleScan version 2.0 software (LXE3208, Laxtha Inc, Korea). EEG data were filtered by a digital low-pass filter between 2 Hz low cut-off frequency and 50 Hz high cut-off. Quantitative EEG data were obtained by the Fast Fourier Transformation (FFT). FFT was used to obtain the frequency information of digitized EEG epochs. In this study, the quantitative EEG data were shown at the middle occipital electrode (OV) for evaluation of global cerebral activity.

Statistical analysis

Wilcoxon's signed rank test was used to compare the baseline values with sedative values of each group. For comparison of EEG values between groups the Kruskal-Wallis test was used. When a difference was found significant between groups, the Mann-Whitney U test was also performed. For each test, $p<0.05$ was considered significant.

Results

EEG waves of sedatives

The changes in the EEG wave before and after sedative administration are shown at Fig 3. In all groups it was shown that frequency and amplitude decreased compared with normal condition.

Spectral edge frequency (SEF) 95 analysis

The SEF95 values significantly decreased in all groups after administration of sedatives ($p<0.05$, Fig 4). Before administration, the baseline SEF95 values were 44.53±0.90 Hz (acepromazine), 43.80±1.03 Hz (butorphanol), 44.12±1.51 Hz (diazepam), 44.84±0.89 Hz (medetomidine), and 44.42±1.54 Hz (phenobarbital), respectively. Twelve minutes after administration, the SEF95 values were 39.75±3.66 Hz (acepromazine), 36.91±3.41 Hz (butorphanol), 41.41±3.33 Hz (diazepam), 42.28±1.11 Hz (medetomidine), and 38.12±5.94 Hz (phenobarbital), respectively. The SEF 95 values of butorphanol group were significantly different from other groups ($P<0.05$).

Discussion

It is important to judge the level of sedation or anesthesia in veterinary medicine. Many clinicians use clinical signs such as muscle relaxation, ocular signs, the heart rate & rhythm, and respiratory rate & rhythm to assess the sedation level in animals (7). In human, the verbal stress scale (VSS), which grades the patient's response to either verbal or physical stimuli, is often used (3). Although adequate in some situations, use of the VSS is not applicable to those incapable of responding. As the main site of action of sedative or anesthetic drugs is the CNS, there have been many studies on the

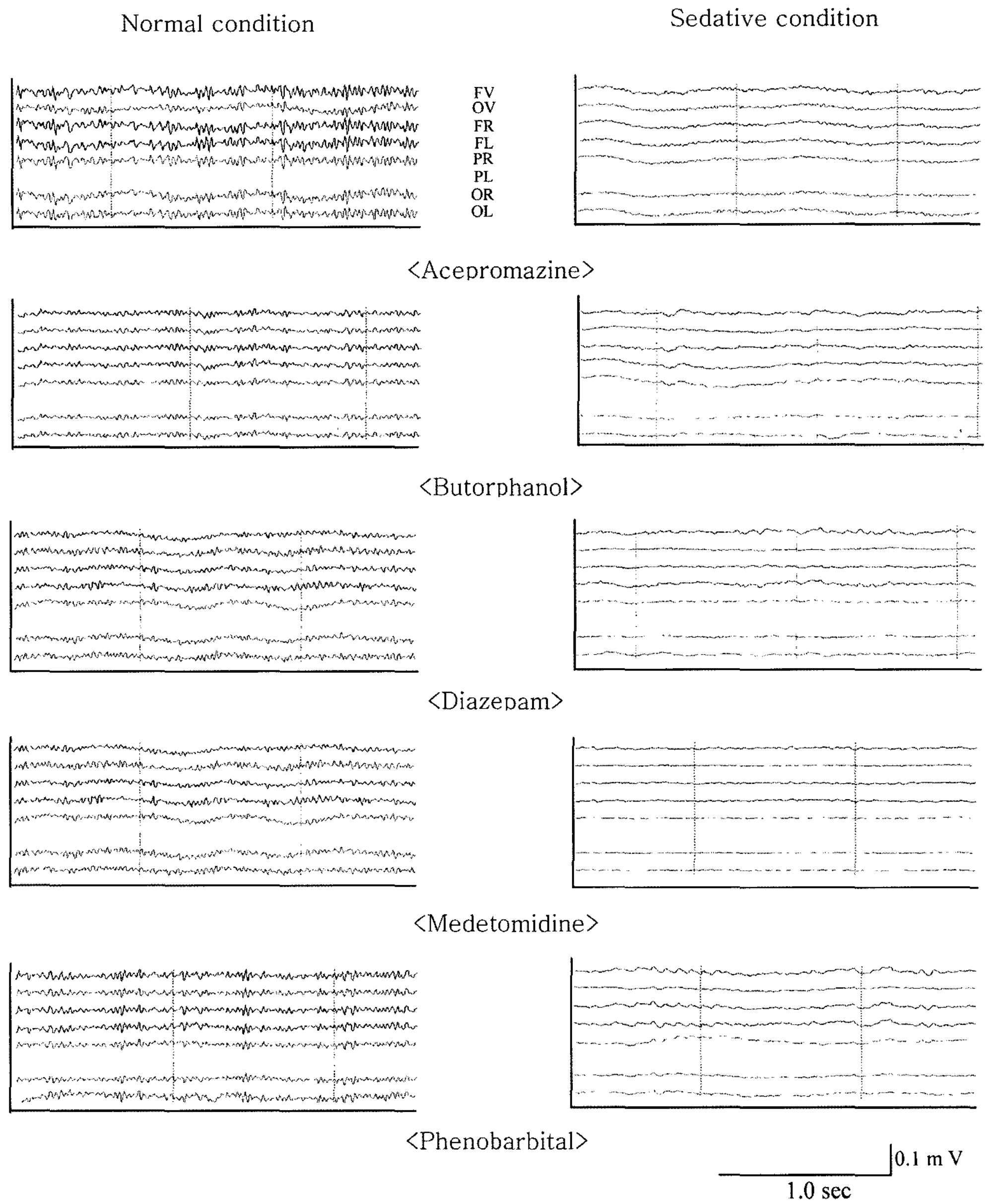

Fig 3. Change of the EEG raw wave before and after sedative administration in 5 groups. FV position is middle frontal electrode. OV position is middle occipital electrode. FR and FL position is right and left frontal electrodes, respectively. PR and PL position is right and left parietal electrodes, respectively. OR and OL position is right and left occipital electrodes, respectively.

relationship between sedation and the EEG. EEG monitoring is recommended for cerebrovascular surgery, cardiopulmonary bypass, and deliberate hypotension, as a measured method of anesthetic depth in human (9). In veterinary medicine, effects of many drugs and anesthetics have been evaluated by routine inspection of canine EEG. To evaluate the effect of sedative, it is important to examine the relationship between electrical activity in CNS and the effects of sedations drugs. Although the frequency and amplitude of EEG were shown the decrease pattern, the alteration of EEG raw wave was very difficult to interpret. Recently, computerized quantitative EEG has been used to study the level of sedation or anesthesia (7). Especially, quantitative EEG methods by the numerical parameters such as band power or spectral edge frequency have been used. Among the quantitative EEG parameters, SEF 95 analysis was used to assess sedation in this study. SEF 95 is the highest frequency of biologic origin present in the EEG signal. SEF analysis has been effectively used to describe the depth of sedation or anesthesia in dogs and horses. SEF has been also studied to correlate with the serum levels or inhaled concentrations of different anesthetics (8,13). In this study, it was shown that the SEF 95 values significantly reduced after administration of sedatives in all groups. Although the SEF 95 values of all groups significantly decreased, the SEF 95

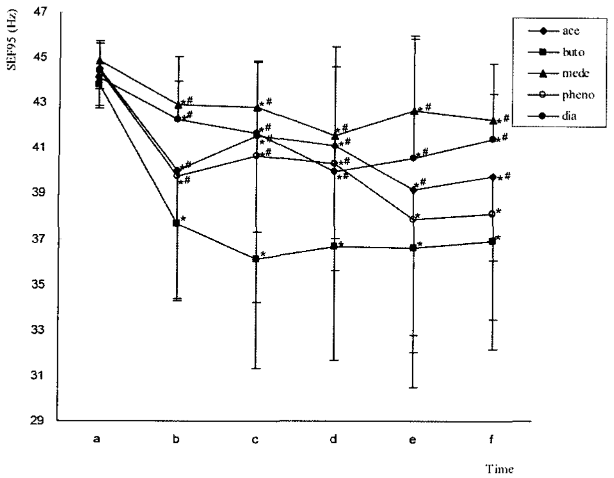

Fig 4. Te spectral edge frequency 95 analyses before (a) and during (b-f) sedation (cf. Fig. 1) recorded from the occipital electrode in each group (acepromazine, butorphanol, diazepam, medetomidine, and phenobarbital). *Significantly different from a ($p<0.05$), #Significantly different from butorphanol group ($p<0.05$).

values of butorphanol group showed the significant difference compared with other groups. This result shows that the opiate induces the deepest sedation as previous study (4).

Conclusion

In present study, quantitative EEG analysis was used for assessing the state of sedation induced by acepromazine, butorphanol, diazepam, medetomidine, and phenobarbital, respectively. We knew that SEF 95 values significantly decreased during sedation compared with these of normal baseline ($p<0.05$). The present result suggests that SEF 95 analysis is the useful methods for evaluation the state of sedation in dogs.

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개에서 진정 평가를 위한 정량적 뇌파검사의 적용

김민수[1] · 남치주

서울대학교 수의과대학

요 약 : 본 연구는 건강한 12마리의 슈나우저견에서 정량적 뇌파검사를 이용하여 진정을 평가한 것이다. 뇌파검사는 뇌나 행동의 변화와 관련된 중추신경계의 변화를 객관적으로 측정하는 데 사용이 된다. 특히 정량적 뇌파검사 방법인 spectral edge frequency 95 (SEF 95)는 진정의 상태를 평가하는 효과적인 방법이다. 본 실험에서 뇌파 전극은 8곳의 각각 다른 부위의 피하에 장착 하였으며 뇌파의 원래 파형과 SEF 95로 변환된 수치를 획득하여 분석하였다. 기전이 다른 5종의 진정제를 투여 한 후 측정된 모든 실험군의 SEF 95 값이 진정제 투여 전 상태와 비교하였을 때, 유의적으로 감소한다는 것을 확인하였다. 이상의 결과로 SEF 95의 정량적인 뇌파검사는 개에서 진정 상태를 평가하는 효과적인 방법이라고 생각된다.

주요어 : 개, 뇌파, 진정, SEF 95