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## **Estimation of the propagation direction and spectral properties of the EEG signals registered during sevoflurane anaesthesia using Directed Transfer Function method**

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The aim of this study was to estimate spectral properties and propagation of the EEG signals registered during sevoflurane anaesthesia between individual EEG recording channels. The intensities of activity flows were calculated for delta, theta, alpha and beta waves using the Directed Transfer Function integration procedure. It was found that delta waves played the dominant role in the EEG signal propagation during anaesthesia and it was suggested that theta and alpha waves propagation could be related to the processes participating in the wakefulness control. Data obtained with DTF method were compared with data received from the analysis of cerebral blood flow with the use of PET in other laboratory. This study showed that analysis of the EEG signal propagation is useful for better understanding and thus safer induction of anaesthesia procedure.

**Key words:** EEG signal, volatile anaesthesia, fluorinated inhalation anaesthetics, sevoflurane, Directed Transfer Function method

## Introduction

Studies of the anaesthesia impact on the EEG activity are very important for the understanding of anaesthesia mechanisms and side effects. Such studies should encompass search for the appearance of atypical patterns in EEG signal as well as the analysis of signal spectral properties and propagation between individual EEG recording channels.

Spectral properties of the EEG–signal registered during anaesthesia induced by propofol and maintained by fluorinated inhalation anaesthetics (isoflurane, desflurane and sevoflurane) were analyzed in our previous studies [4, 5]. However, this analysis has been performed only for four EEG channels.

The first topographic studies of EEG patterns during sevoflurane anesthesia with the use of standard 10/20 system were performed by Sonkajarvi et al. [7]. Their analysis was based on mapping of signal amplitudes and spectral power in given frequency bands. However, such maps represented only the spatial distribution of EEG activity but did not give information about propagation directions of the EEG signals between individual channels.

The problem of propagation of the EEG-signals registered during anaesthesia has not been studied before. Therefore, in this study we present such results obtained with the use of Directed Transfer Function (DTF) method [2].

## Materials and methods

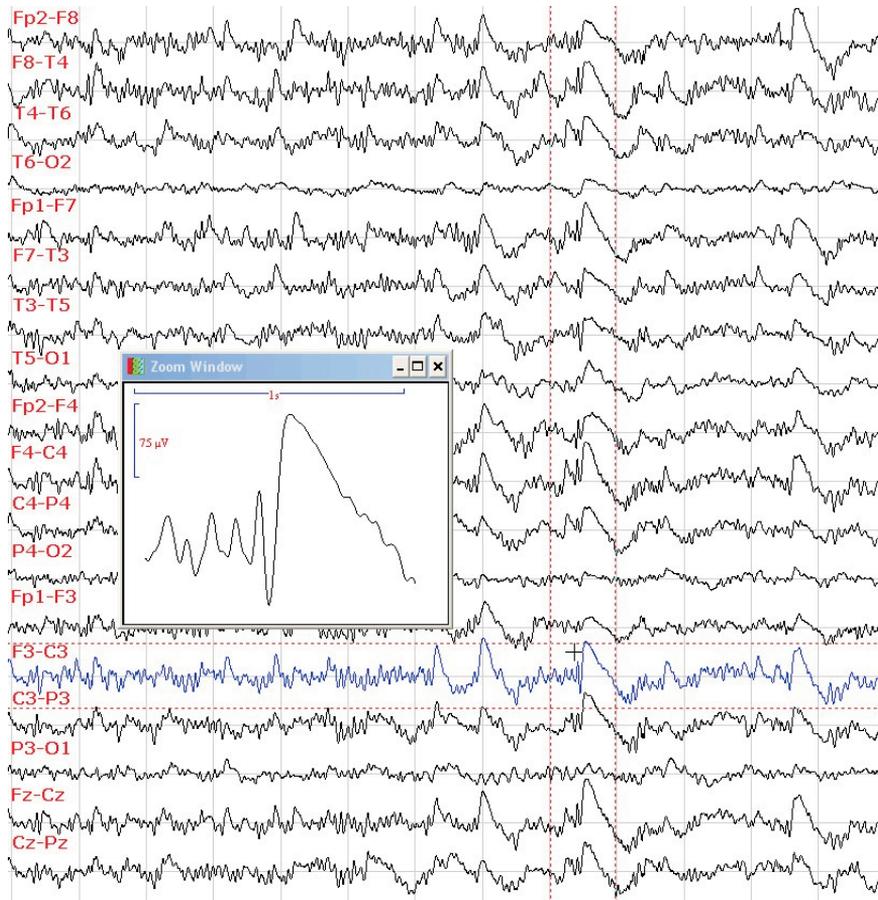
### Anaesthesiological procedure

The data were taken from two adult patients undergoing surgery under general anaesthesia in the Department of Anesthesiology, Intensive Therapy and Emergency Medicine, Medical University of Silesia. The both patients were normal, healthy subjects with no prior neurological deficit. The study was approved by the Ethical Committee of the Medical University of Silesia and written informed consent was obtained from all of patients involved.

Patients were anaesthetised with sevoflurane. Before induction of anesthesia EEG control recording was performed. In order to avoid opioids and N<sub>2</sub>O effect on central nervous system, an epidural catheter was placed in the lumbar space to obtain adequate

analgesia via the introduction of 0.5% bupivacaine in saline solution. Anesthesia was induced with the propofol 2–2.5 mg/kg, and vecuronium (Norcuron, Organon) 0.08–0.10 mg/kg. After laryngeal mask insertion the lungs were ventilated to obtain the normoventilation of 35–37 mmHg and anesthesia was maintained with mixture of air/oxygen with sevoflurane. The administration of volatile anaesthetic was started after a waiting time needed to eliminate the effect of intravenous induction.

Two different methods of volatile anaesthetic administration were applied, each for one patient. In the first original, authors' method, named as the slow administration method, was proposed the anaesthetic concentration was increased gradually by



**Figure 1.** An example of EEG record with the characteristic sharp wave–slow wave patterns like that presented in the zoom window.

0.2 MAC (Minimal Alveolar Concentration) every 5 minutes up to the maximal concentration 1.6 MAC. Then the concentration of anaesthetic agent was subsequently decreased by 0.2 MAC every 5 minutes until the end of surgery, return of consciousness and the laryngeal mask removal. In the second method — rapid administration method — the maximal concentration value was elicited at the initial phase of anaesthesia and then it was decreased slowly.

### EEG registration

The EEG-signal was registered by DigiTrack Data Acquisition System (ELMIKO, Warsaw, Poland) with sampling frequency of 250 Hz. Signals was obtained from unipolar derivations according to the international 10/20 system of electrode placement. The reference electrode was placed at the nose (patient 1) or at the ears (patient 2). An example of EEG record with the sharp wave-slow wave patterns, characteristic for volatile anaesthesia, is shown on Figure 1.

### DTF method

The Directed Transfer Function method was introduced by Kaminski and Blinowska in 1991 [2]. DTF is defined in the framework of multivariate autoregressive model (MVAR) transformed to the frequency domain and offers a measure of signal transmission between all the sources represented by individual channels in applied recording apparatus.

At the first step of the procedure a multivariate autoregressive (MVAR) model is fitted to the data. Data from all the channels were considered as one process and were analyzed simultaneously. The vector of data  $X_t$  at a time  $t$ , expressed in samples, is a sum of a weighted sum of  $p$  preceding data values plus a random component  $E_t$ :

$$X_t = \sum_{i=1}^p A_i X_{t-i} + E_t \quad (1)$$

where  $A_i$  are the MVAR model parameters.

Thus, in time domain model is described by equation:

$$E_t = \sum_{i=0}^p A_i X_{t-i} \quad (2)$$

or in frequency domain by equation:

$$\mathbf{E}(f) = \mathbf{A}(f)\mathbf{X}(f) \quad (3)$$

which can be presented as:

$$\mathbf{X}(f) = \mathbf{A}^{-1}(f)\mathbf{E}(f) = \mathbf{H}(f)\mathbf{E}(f) \quad (4)$$

Equation (3) shows that MVAR can be treated as a black-box model with noise  $\mathbf{E}(f)$  at the input and the signal  $\mathbf{X}(f)$  at the output. All the information about the spectral properties and interrelation between channels is contained in the transfer matrix,  $\mathbf{H}(f)$ , of the model.

This model may be presented in the non-normalized version for all inflows to channel  $i$ :

$$\Theta_{ij}^2(f) = |\mathbf{H}_{ij}(f)|^2 \quad (5)$$

or in normalized version:

$$\gamma_{ij}^2(f) = \frac{|\mathbf{H}_{ij}(f)|^2}{\sum_{m=1}^k |\mathbf{H}_{im}(f)|^2} \quad (6)$$

Formulas 4 and 5 determine transmission from channel  $j$  to channel  $i$ . Low values of  $\gamma_{ij}^2(f)$  and  $\Theta_{ij}^2(f)$  correspond to weak transmission whereas high values correspond to strong one.

The number of MVAR model coefficients and the number of the data points should satisfy condition:

$$\frac{\text{number of MVAR coefficients}}{\text{number of data points}} = \frac{k^2 p}{kN} = \frac{kp}{N} < 0.1 \quad (7)$$

where:  $k$  – number of channels;  $p$  – model order;  $N$  – number of data points.

In the current study 5-minutes long epochs (75000 samples) were used for MVAR estimations. The optimal model order was set to 7 for all epochs. In the case of

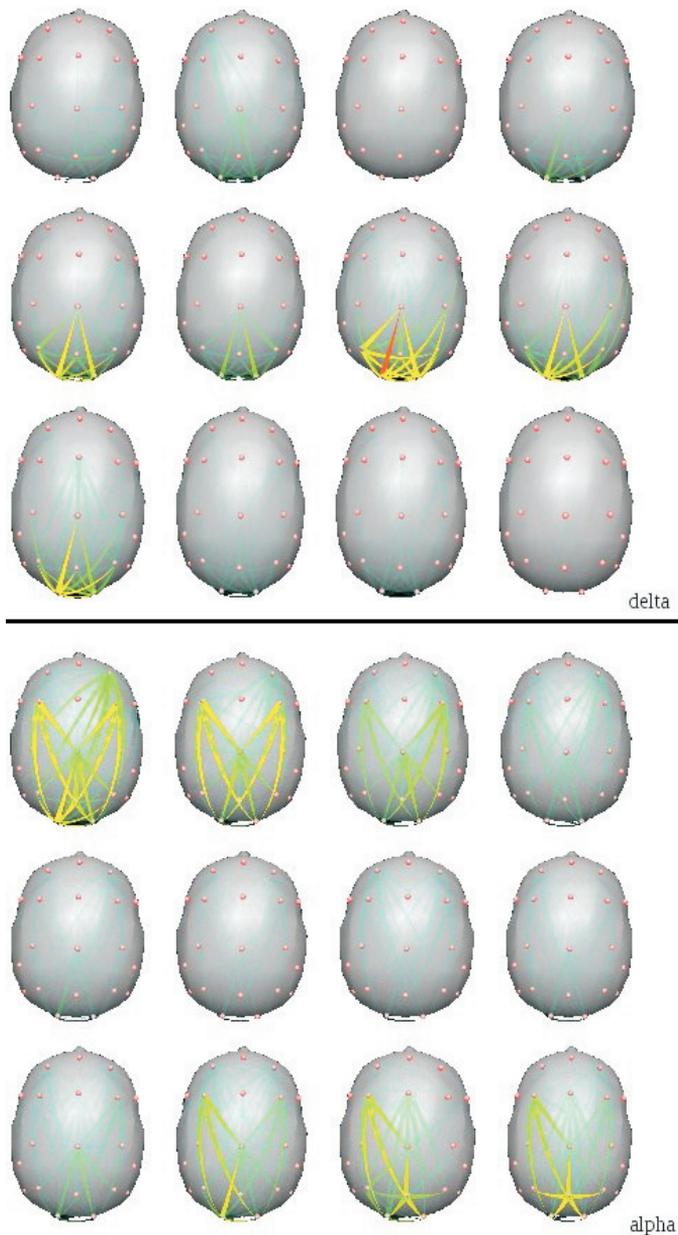
calculations for delta frequency band, in order to emphasize the signal in that range, the data were low-pass filtered and 8 times down-sampled before MVAR calculations (the model order was set to 4 in that case). The statistical thresholds for DTF values were estimated by means of repeated surrogate data calculations and set at the  $\alpha = 0.95$ .

## Results

All the results presented in this paper were obtained using the non-normalized Directed Transfer Function. The non-normalized version facilitates comparison of flows values for different EEG measurements. The flow intensities were calculated separately for delta (0.1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz) and beta (12–30 Hz) waves using the Directed Transfer Function integration procedure in the corresponding frequency ranges.

The intensities of flows were integrated over frequency ranges to make the quantitative comparison easier. The values integrated in delta and alpha ranges are presented in Figure 2 in the form of arrows. The flow intensity is coded by color — the color/intensity scale is common for all groups of each figure and sharp ends of arrows show direction of flows. The DTFs were calculated for 5-minutes long segments corresponding to the individual anaesthetic concentrations. The successive diagrams on Figure 2 show flows calculated for increasing and for decreasing branch of concentrations from 0.8 to 1.6 and from 1.6 to 0.4 MAC for delta and alpha waves, respectively. The level of 1.6 MAC lasted 10 minutes whereas the remaining ones lasted 5 minutes.

The biggest intensities were observed for delta waves. Change of sevoflurane concentration from 0.8 to 1 MAC evoked the appearance of the delta waves propagation from the occipital derivations (mainly O1) to the temporal ones (T5 and T6). The maximal values of the flow intensity were reached at 1.4 MAC for decreasing branch of concentration (Figure 2). On the other hand, the maximal values of alpha waves intensities were associated mainly with propagation from the midline derivations: Fz, Cz, to the occipital lobe: P3, Pz, P4, O1, O2 (Figure 2). The intensity of alpha waves flow was decreased and that of slow waves (delta and theta) was increased with the anaesthesia deepening what is consistent with our previous findings [5].



**Figure 2.** Significant flows for delta and alpha waves for increasing branch of concentrations from 0.8 to 1.6 (the 1<sup>st</sup> row of maps) and for decreasing branch of concentrations from 1.6 to 0.4 (the 2<sup>nd</sup> and the 3<sup>th</sup> row of maps). The concentration was changed every 0.2 MAC.

## Discussion

Directed Transfer Function method allowed the estimation of the propagation directions and spectral properties of the EEG signals registered during sevoflurane anaesthesia using presented before two methods: slow and rapid administration. Obtained results showed that with the anaesthesia deepening the intensity of alpha waves flow was decreased and that of slow waves (delta and theta) increased what was consistent with our previous findings [5]. All together these data showed for the main role of delta waves in the EEG signal propagation. The participation of delta waves in signal propagation depended on the anaesthetic concentration. Change of sevoflurane concentration from 0.4 to 1 MAC evoked the appearance of the delta waves propagation from the occipital derivations (mainly O1) to the temporal ones (T5 and T6).

The problem of brain activity propagation during anaesthesia has not been studied before with the use of EEG. Therefore we compared our results with those obtained by other authors using the analysis of regional cerebral blood flow (rCBF) to obtain data on the activity in the individual brain structures during anaesthesia.

Our data on the propagation of delta waves are generally consistent with data concerning the effect of anesthetic administration on rCBF obtained by Shlunzen et al. with use of PET [6] showing that the decrease in rCBF in the occipital regions (posterior, lingual gyrus, precuneus and cerebellum) was associated with rCBF increase in the insula and superior temporal cortex.

Obtained results showed also that theta and alpha waves propagated mainly from the midline derivations: Fz, Cz, to the parietal and occipital lobe: P3, Pz, P4, O1, O2. The values of theta waves flows were maximal for the concentrations of 1.6 MAC, whereas, those of alpha waves for the concentration from 0.4 to 0.8 MAC.

Although the EEG signals in our study were analyzed in only two patients, the results were consistent in both cases despite differences in anaesthetic protocol. Comparison with results from other modalities, such as PET, suggests that these flows can be related to the rCBF decrease and increase observed by Schlunzen et al. [6] in such brain structures involved in the wakefulness regulation as thalamus and the lingual gyrus. These arguments would support the hypothesis of Alkire et al. [1] that the thalamus is the structure involved in consciousness control. It is worth to note that the topographic analysis of coherence and propagation direction of EEG activity during sleep performed by Kaminski et al. [3] has demonstrated the propagation of EEG activity

from the frontocentral region to the occipital one, and the range of this interaction was highest during deep sleep.

The topography of spikes and other EEG patterns appearing during sevoflurane anaesthesia was recently studied by Sonkajarvi et al [7]. They showed that rapid induction of anaesthesia produced multifocal spikes and polyspikes in the frequency range of delta waves with the maximal amplitude in frontal cortex. In some subjects periodic epileptic discharges (PED) were observed synchronously over the whole cortex. This finding is consistent with our results. In this study we have observed the maximal amplitude of sharp wave — slow wave patterns at the frontal derivations for sevoflurane concentrations greater than 1 MAC.

## Conclusions

The performed preliminary analysis of the EEGsignal propagation during sevoflurane anaesthesia showed that further studies of sevoflurane anaesthesia effects on the central nervous system activity using simultaneously the EEG and functional MRI registrations which could be possibly useful to shed light on the mechanism of generation of the sharp wave — slow wave patterns. Moreover an explanation of the relations between such patterns observed during volatile anaesthesia, during sleep and in epilepsy could result in better understanding of the anaesthesia side effects and thus safer induction of anaesthesia.

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