Source localisation in the clinical practice: spontaneous EEG examinations with LORETA

Ph.D. thesis

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I. Introduction

Electroencephalography (EEG) is a low-cost method, representing summarized neuronal electric activity. EEG can be safely performed even in the case of clasutrophobia, pacemaker or ferromagnetic implants. The major difficulty in clinical utilization of EEG-analysis is the so-called "inverse solution problem" (how to find the sources of a given scalp EEG potential). In the past, research for the source of a given scalp EEG potential was based on the "dipole theory" and resulted in controversial conclusions. In the last decade, novel source localization methods were developed based on current source density computing, like low resolution electromagnetic tomography (LORETA). LORETA computes a physically existing dimension, current density (CD, Amper/meters squared) for 2394 voxels (with 7 mm spatial resolution) within the cortical gray matter and hippocampus. For the sake of brevity, this is called "activity" here. The method can be used for the three-dimensional localization of the neuronal generators of a given EEG frequency band. The method determines current density at 2,394 voxels (with claimed 7 mm spatial resolution) of the cortical gray matter and hippocampus, based on the "smoothness" assumption (neighboring neuronal generators show highly correlated activity), finally describing it on the Talairach human brain atlas. The method is able to assess electrical activity and to localize electrical generators in 3 dimensions in seven frequency domains [regarding to: delta (1.5–6 Hz), theta (6.5–8 Hz), alpha1 (8.5–10 Hz), alpha2 (10.5–12 Hz), beta1 (12.5–18 Hz), beta2 (18.5–21 Hz) and beta3 (21.5–30 Hz). LORETA computes a physically existing dimension, current density (CD, Amper/meters squared) for each voxel.

II. Study 1: Diurnal Alterations of Brain Electrical Activity in Healthy Adults: A LORETA Study

II. 1. Aim

The main goal of our study was to detect diurnal regional changes in the background EEG activity in healthy subjects during wakefulness with closed eyes, and assess the possible changes during regular daylight activity.

II. 2. Subjects

Fourteen healthy young male right-handed postgraduate medical students participated in the study (mean age: 23.6 years, SD = 1.7). Our purpose was to examine such a coherent group which is most preferred in a typical running EEG- or pharmaco-EEG study. All of the volunteers had not had any CNS-affecting items in their medical history, recent complaint or disease, drug use or abuse; they had negative neurological examination; their routine blood parameters (haematology, chemistry, liver and kidney function) were normal.

II. 3. Procedure and Material

The EEG recordings were done at the EP-EEG Laboratory of the Neurology Department, University of Pe´cs. EEG recording sessions were performed at 8 a.m., at 2 p.m., at 8 p.m. and on the next day at 2 p.m. All of the EEG recordings were organized on working days (Monday, Tuesday, Wednesday, and Thursday). The subjects were asked to live their normal life (learning, shopping, reading, etc.). The probands were asked 7 days before the experiment to drink no alcohol or coffee, not participate in any parties, and to sleep normally (7–8 h a night). They slept 7–8 h 7 nights before the experiment. All of the probands slept in the ward at Department of Neurology in the night between the 3rd and 4th EEG session, they all were

awakened next morning at 7 a.m. Before the first EEG-session, they were also waken up at 7 a.m. All of the persons had fasted 3 h before each EEG session to avoid post-lunch dip. All EEG recordings were done in October in the same acoustically and electromagnetically semi-isolated room, with the same equipment (Brain Quick System 98, Micromed, Italy) by experienced personnel, according to the recommended standards for qEEG studies. The EEG signals were recorded in 19 channels from electrodes placed after the international 10–20 system (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, O1, O2, T3, T4, T5, T6); linked ears electrodes served as recording reference. Eye movements and EMG activity were also recorded from 4 electrodes for post hoc artifact detection. Spontaneous EEG was recorded for 10 min with a sampling rate of 128 Hz and with A/D conversion of 12 bits. The subject laid in a relaxed position with closed eyes. The vigilance of the patients was tested by means of simple questions during the recording. Off-line, all recorded data were carefully reviewed for technical and biological artifacts; artifact epochs were excluded. All EEG data were digitally bandpassed to 1.0–30 Hz and then we made LORETA analysis.
For LORETA, statistical differences between pairs of conditions were computed as images of t-values. To assess the possible diurnal changes in background EEG activity, voxel-by-voxel dependent t-tests were computed using log transformed and not normalized data set. The t-statistic images were examined to locate regions showing statistically significant effects, as previously described, using a non-parametric approach thresholded at the conventional 5% probability level.

II. 4. Results

Comparison 1.: 2 p.m. versus 8 a.m

Significantly increased activity was detected in theta, alpha2 and all of beta bands. In theta frequency band, there was a bilateral increase of activity in the frontal midline structures: anterior cingulate, superior and medial frontal gyri. An unilateral increase of activity was detected in the left dorsolateral prefrontal lobe. In the alpha2 frequency band, a bilateral increase of activity was observed in the major part of mesial regions. An unilateral increase of activity was found in the left premotor-prefrontal region, and over the right temporooccipital areas.
In the beta1 frequency band, a bilateral increase of activity in the basal temporal areas, mesial frontal and parietal cortex, and an unilateral increase of activity was seen in the left insula, left frontal lobe, and in the right temporo-occipital cortices and right hippocampus.
In the beta2 frequency band, a bilateral increase of activity in the basal temporal areas, mesial frontal and parietal cortex and also the convex part of frontal lobe, and an unilateral increase of activity was detected in the left premotor-prefrontal cortex, right hippocampus and right temporo-parietal cortex.
In the beta3 frequency band, a bilateral increase of activity in the posterior mesial areas, and an unilateral increase of activity was found in the left prefrontal region, right hippocampus and right temporo-parieto-occipital cortex.

Comparison 2.: 8 p.m. versus 8 a.m

Significantly increased activity was seen in theta, alpha2 and all of beta bands. In theta frequency band, there was an unilateral increase of activity in the left dorsolateral prefontal lobe.
In the alpha2 frequency band, a diffuse unilateral increase of activity was found in the left hemisphere, also including the left hippocampus.
In the beta1 frequency band, a bilateral increase of activity was observed over the whole cerebral cortex (including both hippocampi) with the exceptions of right middle frontal gyrus and inferior parietal lobule.

In the beta2 frequency band, a bilateral increase of activity was seen over the whole cerebral cortex (including both hippocampi) with the exception of left temporo-parietal cortical area.
In the beta3 frequency band, a bilateral increase of activity in the basal temporal and mesial areas including both hippocampi and an unilateral increase of activity was found in the left prefrontal region and right temporo-parieto-occipital cortex.

Comparison 3.: Next Day, 2 p.m. versus First Day, 2 p.m.
Analyzing all of the conventional frequency bands, no significant changes were found.

II.5. Conclusion

The results of the present study show that there were notable changes in the EEG background activity during a 24-h period, while the 24-h control did not show any change. Characteristic distribution of increased activity of cortex (no change in delta band, and massive changes in the upper frequency bands) may mirror increasing activation of reticular formation and thus evoked thalamocortical feedback mechanisms as an important neurophysiological part of maintenance of arousal.

III. Study 2: Characteristic Changes in Brain Electrical Activity Due to Chronic Hypoxia in Patients with Obstructive Sleep Apnea Syndrome (OSAS): A Combined EEG Study Using LORETA and Omega Complexity

III. 1. Aim

This study was designed to detect existing neurophysiological differences between apneic patients and normal controls to examine the noxious effects of chronic intermittent hypoxia on the cerebral cortex. For this purpose, we used LORETA, providing detailed information on intracerebral distribution of EEG generators for separate frequency components. We analyzed spontaneous brain electrical activity during wakefulness, before nocturnal sleep; sleep EEG, sleep architecture or parameters describing sleep stages were not examined in this study.

III. 2. Subjects

Twenty-five patients with newly diagnosed OSAS participated in the study (mean age: 50.2 years, SD = 11.9; 2 female, 23 male). All patients had negative neurological examination. Diagnosis of OSAS was made after international guidelines. The mean of apnea-hypopnea index of the patients was 53.6 (SD = 26.7).
Fourteen non-paid healthy persons (mean age: 49.2 years, SD = 10.9; 3 female, 11 male) served as normal controls in the study; they were recruited from the medical staff, relatives and friends of the staff. Control persons had no reported events possibly affecting CNS in their medical history, recent complaint or disease, drug use (except oral contraceptives) or abuse.

III. 3. Procedure and Material

The EEG recordings were performed at the EP-EEG Laboratory of the Neurology Department, University of Pécs. All OSAS patients as well as all control persons had the EEG recording sessions 9 p.m. All the consecutive part (epoch selection, statistics, LORETA analysis) of this study was done like in the case of diurnal study.

III. 4. Results

An increased activity in alpha2 frequency band was detected bilaterally in the precuneus, paracentral and posterior cingulate cortex comparing apneic patients to normal controls.

III. 5. Conclusions

Chronic disturbances of oxygen supply of brain tissues might cause multiple changes in brain electrical activity, particularly in regions involved in emotional perception, long-term memory storage and retrieval and the default mode network.

IV. Publications related to the thesis

M. Toth, A. Kiss, P. Kosztolanyi, I. Kondakor: Diurnal alterations of brain electrical activity in healthy adults: a LORETA study. Brain Topography (2007) 20:63-76. Impact faktor: 1.256.

M. Toth, B. Faludi, J. Wackermann, J. Czopf, I. Kondakor: Characteristic changes in brain electrical activity due to chronic hypoxia in patients with obstructive sleep apnea syndrome (OSAS): a combined EEG study using LORETA and Omega complexity. Brain Topography (2009) 22:185-190. Impact faktor: 2.080.

Cumulative impact factor: 3.336.

VI. Publications not related to to the thesis

M. Toth: „The epsilon theory: a novel synthesis of the underlying molecular and electrophysiological mechanisms of primary generalized epilepsy and the possible mechanism of action of valproate." Medical Hypotheses (2005) 64, 267-272. Impact faktor: 0.91.

I. Kondakor, **M. Toth,** J. Wackermann, C. Gyimesi, J. Czopf, B. Clemens: "Distribution of spatial complexity of EEG in idiopathic generalized epilepsy and its change after chronic valproate therapy". Brain Topography (2005) 18(2):115-23. Impact faktor: 1.34.

B. Clemens, M. Bessenyei, P. Piros, **M. Toth**, L. Seress, I. Kondakor: „Characteristic distribution of interictal brain electrical activity in idiopathic generalized epilepsy". Epilepsia (2007) 48(5):941–949. Impact faktor: 3.54.

B. Clemens, M. Bessenyei, **M. Toth**, I. Kondakor: „Valproate selectively reduces EEG activity in anterior parts of the cortex in patients with idiopathic generalized epilepsy. A low resolution electromagnetic tomography (LORETA) study". Epilepsy Research (2007) 75:186-191. Impact faktor: 2.377.

B. Clemens, J. Bank, P. Piros, M. Bessenyei, S. Vető, **M. Toth**, I. Kondakor: „Three-dimensional localization of abnormal EEG activity in migraine: A low resolution electromagnetic tomography (LORETA) study of migraine patients in the pain-free interval". Brain Topography (2008) 21(1):36-42. Impact faktor: 1.41.

B. Clemens, P. Piros, M. Bessenyei, **M. Toth**, K. Hollody, I. Kondakor: „Imaging the cortical effect of lamotrigine in patients with idiopathic generalized epilepsy: A low resolution electromagnetic tomography (LORETA) study". Epilepsy Research (2008) 81(2-3):204-10. Impact faktor: 2.377.

B. Clemens, M. Bessenyei, I. Fekete, S. Puskas, I. Kondakor, **M. Toth**, K. Hollody. „Theta EEG source localization using LORETA in partial epilepsy patients with and without medication." Clin Neurophysiology (2010) 121:848-858. Impact faktor: 2.972.

Cumulative impact factor: 14.926.

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