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3D EEG and Clinical Evidence of Brain Dying. Preliminary Report

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Summary

Determination of brain dying means reversible or irreversible injury to the brain, including the brainstem. Current guidelines rely on clinical examination including the proof of coma, absent brain stem reflexes, and apnoea test. Neurophysiological testing using electroencephalography and evoked potentials — somatosensory evoked potentials and brainstem auditory evoked potential could have been helpful in the final diagnostic brain death conclusion, but the diagnostic accuracy of these methods in the last years has revealed controversies. Here, we present data on quantitative EEG signal evaluation (qEEG) by a 3-dimensional brain mapping (3D BM) as developing tool to clarify whether the transverse and anterior posterior coherences such as connectivity indices may demonstrate connection in transversal or anterior posterior dimensions with «wavelet transformation» and if the 3D BM visualization of the of representative EEG signals may improve informative value of EEG signals quantification when evaluating the brain dying.

The purpose of our work is to provide an update on the evidence and controversies on the use of EEG for determining brain dying and raise discussion on EEG applications to improve the transplantation program.

Results. We analyzed the EEG records of 10 patients admitted for cardiopulmonary resuscitation (CPR) during September, 2017 — August, 2018. Data from one patient, ŽM, 33 years old, after haemorrhagic shock (August 2018) were analyzed in details. Quantitative EEG dynamics by images and clinical course of brain dying were monitored prior and after the amantadine sulfate intravenous administration for brain revival. Data demonstrated the ability of brain to survive; the cause of final brain death was heart failure.

Conclusion. Data confirm the hope for survival of the brain in a coma and demonstrate brain capability to keep functionally optimal state as a potential for a good social adaptation.

Keywords: electroencephalography; brain dying; quantitative EEG; 3D brain mapping, longitudinal and transversal coherencies, wavelet transformation, resuscitation

Conflict of interest. The authors declare no conflict of interest.

3D ЭЭГ и клинические признаки смерти мозга. Предварительное сообщение

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Резюме

Под смертью мозга понимается обратимое или необратимое повреждение головного мозга, включая его ствол. Современные рекомендации по диагностике смерти мозга опираются на данные клинического обследования, включающие объективные признаки комы, отсутствие стволовых рефлексов и положительный тест на апноэ. Нейрофизиологическое тестирование с использованием электроэнцефалографии (ЭЭГ) и вызванных потенциалов (соматосенсорных и слуховых стволовых) могло бы помочь в окончательном диагностическом заключении о смерти мозга, но диагностическая точность указанных методов в последние годы является предметом многочисленных обсуждений. В данной статье представили результаты количественной оценки сигналов ЭЭГ с помощью трехмерного картирования мозга (3D КМ) как нового инструмента выяснения взаимосвязи между коэффи-

циентами когерентности при поперечном и передне-заднем сканировании и «вейвлет-преобразовании», а также поставили вопрос о том, может ли визуализация репрезентативных сигналов ЭЭГ с помощью 3D КМ улучшить информативность количественной оценки сигналов ЭЭГ при определении смерти мозга.

Цель работы — предоставить последнюю информацию об имеющихся доказательных данных и нерешенных вопросах в отношении использования ЭЭГ для определения смерти мозга и инициировать дискуссию о применении ЭЭГ для повышения эффективности стратегий трансплантации.

Результаты. Проанализировали записи ЭЭГ 10 пациентов, поступивших для проведения сердечно-легочной реанимации в период с сентября 2017 г. по август 2018 г. Данные пациентки, Ж. М., 33 лет, перенесшей геморрагический шок (август 2018 г.), проанализировали подробно. Оценили динамику количественных показателей ЭЭГ по изображениям и изменения клинической картины смерти мозга до и после внутривенного введения амантадина сульфата, который применяли для оживления головного мозга. Результаты продемонстрировали способность мозга к сохранению жизнеспособности, при этом причиной биологической смерти мозга стала сердечная недостаточность.

Заключение. Получили обнадеживающие данные, позволяющие предполагать возможность выживания мозга при коме и демонстрирующие способность мозга сохранять такое функциональное состояние, которое может явиться основой для успешной социальной адаптации.

Ключевые слова: электроэнцефалография; смерть мозга; количественная ЭЭГ; 3D картирование мозга, коэффициент когерентности при продольном и поперечном сканировании; вейвлет-преобразование; реанимация

Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.

Introduction

The brain stem controls the essential functions necessary for survival, such as breathing, blood pressure, and heart rate. Currently, despite the differences in clinical practice in individual countries [1] the standard diagnosis of brain dying depends on three cardinal neurological features: coma, lack of brain stem reflexes, and apnoea [2].

Brain dying, briefly speaking, is referred to the incompletely reversible state leading to complete, irreversible, and permanent loss of all brain and brainstem functions. Brain dying implements also the possible termination of a human's life; correspondingly, the diagnosis of the dynamic process «brain dying» resulting in brain death is very important (Ad hoc committee of the Harvard medical school to examine the definition of brain death, 1968). However, some social disagreements or different diagnosis criteria in clinical practice are still remain around the world. Some standard tests to determine the brain death are widely used, such as the apnoea test or brainstem function examination [1]. Notably, it is commonly agreed that EEG might serve as an auxiliary and useful aid in the confirmatory tests common for adults and children [3–5]. Typically, isoelectric EEG recording is required for the brain death condition at least 30 min and may last 3–24 h [1]; the positive response of EEG tests suggests functioning of the brain. Consequently, the patient in deep coma — «brain dying» condition — might show some EEG electro-activity, while the brain-dead patient will not. It is not known what to do with a quantitatively positive EEG signal test such as a three-dimensional brain mapping (3D BM) exhibiting the presence of oscillations in many cases, where the classic isoelectric EEG long lasting registrations are not visually seen. Are the 3D BM signals real? Whether this problem represents a fairy tale lasting for many years, or an imaginable phantasy of our innate intelligent soul in the era of a computer intelligence? It seems to be a crucial challenge for neuroscience in the 21st century. A quantitative evaluation of «qualia», the internal and subjective component of sense perceptions from stimulation of senses by the computer intelligence, in our case, might become a main goal for current neuroscience.

Novadays, the evaluation of EEG patterns by means of a power spectral analysis has become a major challenge for predicting enhanced or nonchangeable neurological status beside the discharge of the patient from cardio-pulmonary resuscitation (CPR). EEG is employed to measure electrical potentials at the surface of the scalp to detect cortical activity that commonly refer as «brain waves». The analysis of the quantitative EEG (qEEG) in a digital format is considered as a «Brain Mapping». The qEEG is an extension of the analysis of the visual EEG interpretation, which may assist and even augment our understanding of the EEG and brain function. the procedure of qEEG records EEG activity using a multi-electrode recording with the aid of a computer. Multi-channel EEG data are processed using various algorithms, such as the classic «Fourier» algorithm, or in a more modern format as a cross-spectral «wavelet» analysis. The digital data are statistically analyzed, sometimes comparing values with «normative» database reference values. The processed EEG data are usually converted into color maps of the functioning brain called «Brain maps». EEG information and derived qEEG data can be interpreted and used by experts as a clinical tool to monitor and evaluate the brain function changes following various interventions such as neurofeedback or medications, as well as survival-dying or brain death data.

Various analytic approaches include commercial databases or database-free methodology, such as EEG phenotype analysis, or classic EEG Vigilance model (Bente, 1964) [6] are used in modern clinical application of the EEG/qEEG. The use of advanced techniques such as Independent Component Analysis (ICA) and neuro-imaging techniques such as Low Resolution Electro-magnetic Tomography (LORETA) can map the actual sources of the cortical rhythms.

The purpose of our work is to provide an update on the evidence and controversies on the use of EEG for determining brain dying and raise discussion on EEG applications to improve the transplantation program.

Oscillations coming of ECG signal, natural respiration pacing signal, and blood pressure are interpreted as an important natural oscillations that affect the EEG signal generation by «cross-coupling» mechanism modulating EEG signal frequency, amplitude and even the phase.

Interpreting EEG with a high sensitivity required for the diagnosis of brain dying and brain death, can pose a diagnostic challenge. Furthermore, EEG is frequently affected by physiologic variables and drugs. However, no consensus exists for minimal requirements for blood pressure, oxygen saturation, body temperature during the EEG recording, minimal time for observation after the brain injury or rewarming from hypothermia, and determining the brain death when the findings of electro-cerebral inactivity (ECI) is equivocal. Therefore, there is a strong need in establishing detailed guidelines for performing EEG to determine brain dying [7].

We would like to clarify, in which functional module, or in which of basic functional modules, the oscillator of individual frequency bands is situated as a sign of possible spontaneous or provoked activity using functional restoration with amantadine sulphate (by intravenous (IV) administration at a dose of 200 mg, 5 injections), and whether these quantitative indicators of brain vital basic function e.g. consciousness (carriers of lucidity, vigilance, aware cognition, aware consciousness) are present [8].

ECI is required to confirm cessation of brain function, but this does not ensure either the irreversibility or loss of whole brain function.

If sedative medication used before the diagnosis of brain dying-brain death, the French guidelines recommend using the techniques based on the study of intra-cerebral blood flow such as cerebral angiography, which was not influenced by the medications.

The cause of sufficiency of a single EEG described in the American EEG guidelines is that no patients survived for more than a short period after an EEG showed ECI, excluding the cases, which were due to overdosing with CNS depressants. Therefore, single EEG demonstrates that ECI is a highly reliable tool for determining cortical dying and death.

Materials and Methods

In the Clinic of Anaesthesiology and Intensive Medicine we analyzed the EEG records of 10 patients admitted for cardiopulmonary resuscitation (CPR) during September, 2017 — August, 2018. Data from one patient, ŽM, 33 years old, after haemorrhagic shock (August 2018) were analyzed in details. For detection of EEG signal we used NEURON SPECTRUM AM with specialized software. By processing EEG signals, we evaluated the classic EEG line signal in reference, transversal and longitudinal montages. Data recording were performed during 20–30 minutes. After that, the analysis of EEG line signal was continued by means of classic visual evaluation, rapid Fourier´s transform, cross-spectral analysis, and 3D BM in colors. Our aim was to exclude the current wave within the frequency frame of 0.1–40 Hz with an amplitude below 2μV that represented a classic criterion for definition of «brain death» by EEG signal. Brain dying resulted in appearance of a flat EEG curve with an amplitude above 2μV but with a progressive decrease in power measured by the amplitude. We consider this pattern as that demonstrating the ECH electro-cerebral hypoactivity.

The EEG/qEEG procedure was performed twice or trice as a standard advance for diagnosing brain dying and brain death.

Many natural oscillation as determined by ECG, BP, pacing respiration could serve as the secondary natural sources of EEG signal transforming to its frame through cross-coupling of frequency, amplitude and even a phase of both particular EEG band oscillations and extra-cerebral biological rhythms [9, 10].

Brain Mapping (BM-pEEG). The map shows the amplitude distribution of the EEG signal frequency band potentials. The essence of the BM consists of coding the numerical values of the signals into the color scale and its iterative interpolation, even for the areas where the signal values have not been really measured. The goal of interpolation is to obtain spatial image (raster) from a discrete image [11].

The procedure of 3D BM. These data constituted a 19-channel EEG recording in accordance with the international 10–20 system, referenced to the Cz electrode, sampled at 500 Hz and band-pass filtered at 0.5–45 Hz. After the visual evaluation, we designated an optimal 5–8 s section of the EEG signal that was a subject of a further digital power cross-spectral analysis, the results of which we iteratively interpolated to the color sperctrum and obtained a spatial 3D image (raster) from a discrete image.

Case report. Patient Ž. M., woman, 33 years old, was admitted to the Clinic of Anaesthesiology and Intensive Medicine on August, 7, 2018 and hospitalized untill

August, 24, 2018. The patient was transferred from the District Hospital after Caesarean section and unexpected womb bleeding, after which she was underwent cardiopulmonary resuscitation. During August 02–07, 2018 patient was treated because of post-Cesarian section hemorrhagic shock in the District Hospital.

Neurologic examination done in the August, 7, 2018 at 5.00 p.m. states: the patient does not respond to the nociceptive stimulus, comatose state GCS 3 points, insufficient spontaneous breathing activity and cough reflex are present, photoreaction bilaterally is absent, ciliospinal dilatation of the pupils is revealed, after the illumination of the eyes, a moderate mydriasis appears, corneal reflex is bilaterally positive but significantly weakened, masseter reflex is absent. Gag-reflex, tendon-jerk reflexes (C8-S2 responses) are absent. Skeletal muscles are flaccid, pathologic exteroceptive reflexes absent, and limbs are passively situated along the somatic trunk. Sclerae are light icteric, conjunctiva is pale, eyeballs are in a middle position and motionless, nystagmus is absent. Blood pressure 70/50 mmHg, HR 85/min. Continuous medication: catecholamine (Noradrenaline) and Terlipressin (Remestyp). Peripheral oxygen saturation 99%. Continuous administration of anti-arrhythmic drug Amiodarone and orotracheal intubation are performed. The urinary catheter drains concentrated, thick, deep yellow-colored urine.

On the day of admission, the patient was after the fourth hemodialysis. The abdominal wound after the cesarian section was covered, not overflowed, the intestine and the stomach peristalsis was audible.

The following day, August 8, 2018, the consecutive neurologic and nephrologic examinations, EEG investigation, CT-scan of the brain and + 3D reconstruction were performed. Diagnosis: coma. State after bleeding shock, CNS structures with no sign of intracranial middle line shift. Ventricular system and SA without signs of extension, without convincing pathological changes supratentorial and infra-tentorial. No signs of intracranial haemorrhage, without fresh focal ischemic changes. No evidence for a malignant brain edema.

Neurological examination on August 9, 2018: Hypoxemic-anoxic multiorgan damage in severe post-haemorrhagic shock, hepato-renal syndrome. Brain stem reflexes are absent, GCS 3. Tracheostomy in August 09. 2018 was performed, it was revised in August 14. 2018. Laparoscopic cholecystectomy performed in August 23, 2018 concluded: thick-walled gall bladder with gangrene of the mucosa. According to the anaesthesist's report, surgery with no any anaesthesia complication. During the entire ICU stay, the patient was monitored daily by a gynaecologist, neurologist, surgeon, cardiologist, dialysis physician, and endocrinology specialist. The course of the entire hospitalization and the treatment was conducted and managed according to all current laboratory parameters (biochemistry, hematology) of the patient's clinical condition and recommendations of all consultants. Due to the variability of the clinical neurological state (undulating state of consciousness, GCS 5–7 after amantadine sulphate administration), the patient gradually disconnected from the ventilator (weaning) intermittently fixed her gaze, primitively responded to a simple verbal challenge and responded by face flushing on arrival of her husband. This neurological condition persisted until 24.08.2018, when early in the morning hemodynamic and cardiac instability progressed, and the doses of drugs with vasoactive support were increased.

That day, starting from 1.30 p.m. and transfer to haemodialysis, the vital functions failed, and widespread CPR was initiated. ECG demonstrated ventricular fibrillation, and defibrillation was performed. ECG monitoring showed asystole, and significantly pale skin color and anemic conjunctiva appeared. The advanced life support continued. Subsequently, the rhythm changed again to asystole and at 2.15 p.m. due to the length of CPR (45 minutes) and general condition of the patient, the CPR was terminated.

Results

EEG evaluation (investigation) during the hospitalization.

Neurologic examination revealed coma GCS 3 on admission, extinction of brain stem reflexes, tendon-jerk areflexia, skeletal muscles flaccidity. Between 08.08.2018 — 14. 08.2018 EEG investigations revealed the following patterns shown in Figures 1–6.

August 14, 2018: Following the 5th administration of amantadine sulphate, 200 mg, i. v. GCS increased from 3–4 to 5–7 scores. The patient was able to perform simple motor tasks: close and open her eyes, even on command, gaze a person near the bed. She reacted very vividly to the presence of her husband, tendon-jerk reflexes were present in a range of C8-S1, light reaction and abdominal reflexes were assessed.

The autopsy material of the brain neuropil and myocardial tissue (Fig. 7).

Excerpt from the autopsy protocol (a macroprint of the brain):

The brain mass is 1.582 g, it is enlarged compared to the norm, the entire brain tissue is soft, dough like, disintegrating by hand (the respiratory brain in the initial stage?). The sulci are smooth, the gyri are flattened, the border of the grey and the white matter can be distinguished on the cut, the tissue is aqueous and adherent to the knife. The brain ventricles are almost extinct, filled with a small amount of clear cerebrospinal fluid, the lining of the ventricles is fine, glossy, the choroid plexus are of a purple color.

Brain stem structures — conus compressions: The pons, the cerebellum and the medulla are intact with no changes in the anatomical integration, soft dough-like consistency. The frontal, temporal, and occipital herniations are highlighted — aqueous brain.

Brain microscopic features: in the cortex, the evidence of a vacuola degeneration of the pyramidal cells, a resorption reaction around the cells due to

granular cells and the microglia multiplication. Peri-capillary and peri-neurocytes swelling. Thalamus: necrobiotic changes and neural cell necrosis, presence of granular (resorption making) cells, peri-capillary swelling.

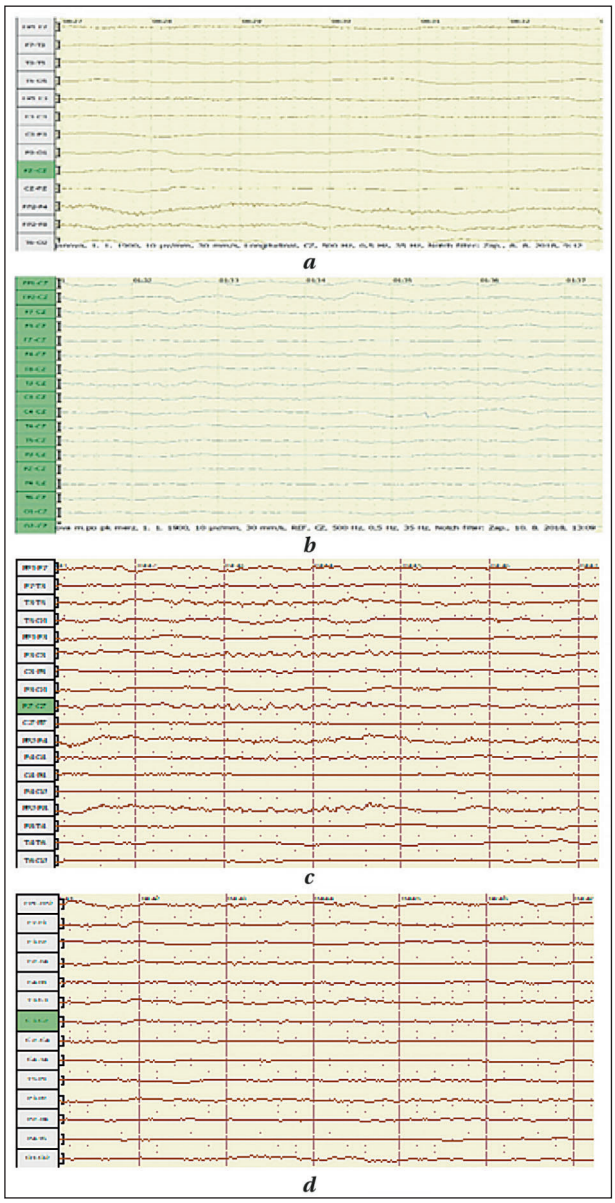

Fig. 1. Ž M, 33 years, EEG.
***a* — 08.08.2018,** without amantadine sulphate. Longitudinal montage of EEG signal, sensitivity 10 μV/mm, 6 seconds lasting EEG. Here and in b and c: cross-spectral analysis of the signal followed by 3D BM color-scale quantification of particular EEG frequency bands was performed. Flat EEG show low voltage activity in rare grids above 2μV of amplitude (AP), with rare higher voltage, demonstrating «brain dying» pattern.
***b* — 10.08.2018,** here and in c and d: following the amantadine sulphate, 200 mg each dose, IV administered. EEG signal, sensitivity 10μV/mm, 6.5 seconds lasting EEG sample. Clinical state: coma; GCS values: 3–4 scores. EEG signal is flat with a low voltage activity (slightly above 2μV).
***c* — 14.08.2018,** EEG signal at a frequency of 8 Hz in a longitudinal montage. The alpha frequency was situated in six channels of frontal regions showing distinct arousal effect with an AP increase up to 20 μV. GCS values at that time increased to 5–7 scores.
***d* — 14.08.2018,** Transversal montage illustrates arousal effect namely in frontal region as not continual but dispersed alpha waves with AP approximately 10–20 μV.

Discussion

Decreasing delta rhythm performance (disinhibition, «pacemaker» activity transmission into the EEG signal) over both hemispheres, and namely over the left hemisphere under the influence of amantadine sulphate as observed on August 10, 2018, demonstrated disinhibition of delta frequency band, e. g. the first electric prodromal sign of incoming arousal performance in aware conscious regulating brain structures.

There were no changes of EEG gamma band output over the entire neurocranium on August 10, 2018. It probably correlated with disconnection over the cingulate gyres as the decisive part of default mode resting state network, DMRSN [12].

There was no change in the alpha and theta output on August 10, 2018 after the IV administration of a 5th dose of amantadine sulphate, 200 mg per dose, that showed strong extinction of occipital and hippocampal allo-cortical oscillation activities in 3D BM, which were evident around 10μV in a basic EEG signal. That patterns were completely changed in August 14, 2018, when the AP of alpha rhythm increased in prevailing grids to 10–20μV/mm in a basic EEG signal and oscillators of alpha and theta rhythms created in 3D BM (Figure 4, *j*, *k*) images of powerful signal. The same situation was observed with beta-LF and beta-HF (Figure 4, *l*). The gamma

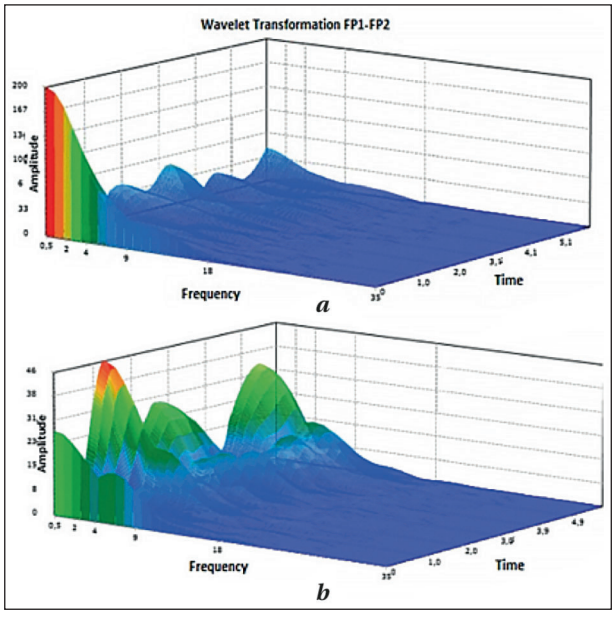

Fig. 2. Wavelet transformation of EEG signal.
Note. *a* — 10.08.2018: wavelet transform from transversal montage following amantadine sulphate administration, leading electrodes FP1-FP2 in 6 seconds lasting window.
***b* — 14.08.2018:** following the 5th dose of amantadine sulphate, 200 mg each dose, IV administration. Wavelet transformation of EEG signal from Fig. 1, *d*.

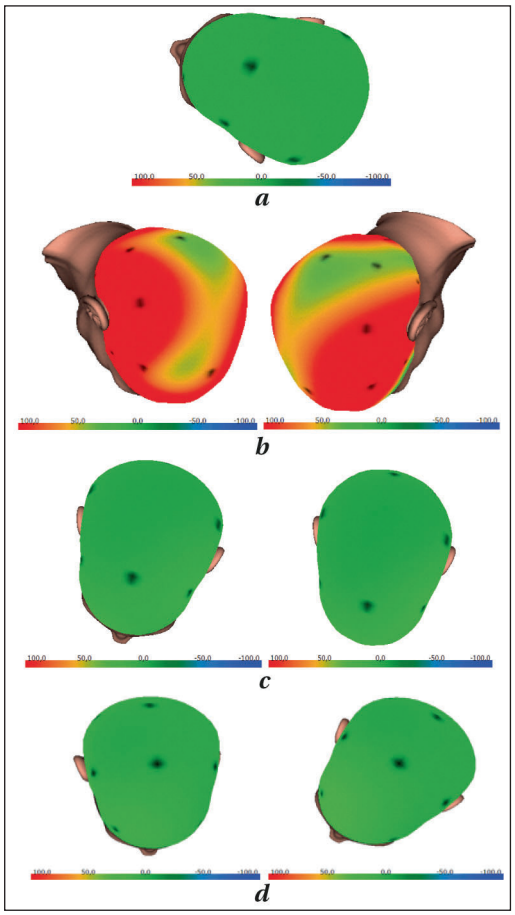

Fig. 3. Ž M, 33 years, 08.08.2018, without amantadine sulphate.
a — gamma frequency band BM in a longitudinal montage with a power value of 0.0 μV/mm.
b — delta frequency; longitudinal montage of powerful bilateral temporo-frontal oscillations and without power in occipital and parieto-centromotor parasagital regions. It means a presence of a «pacemaker activity» in brain structures.
c — Beta-LF to the left, beta-HF to the right BM in a longitudinal montage. No any power oscillation over the whole neurocranium means unconsciousness without any motor and mental performances.
d — Theta rhythm left, alpha rhythm right BM with 0.0 μV AP power; longitudinal montage.

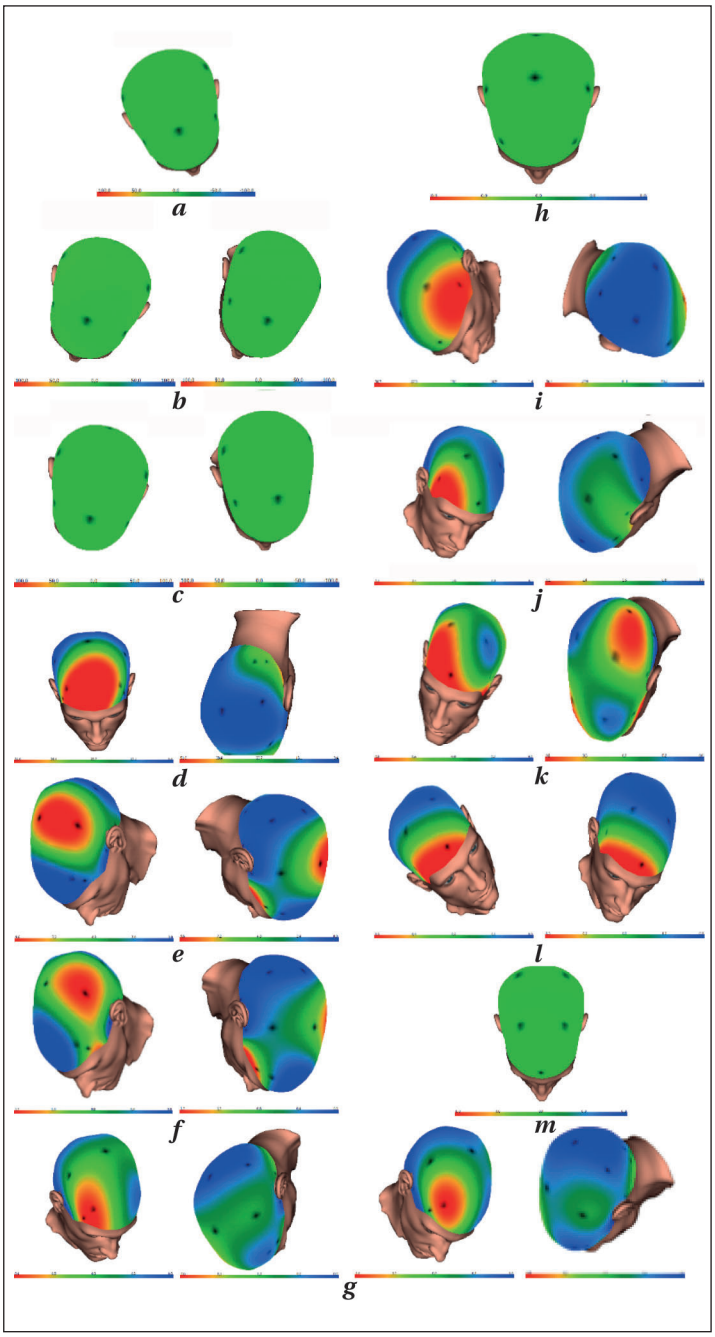

Fig. 4. Ž M, 33 years, following the amantadine sulphate administrations on 10.08.2018 and 14.08.2018.
10.08.2018, with amantadine sulphate, 200 mg, IV administration:
a — gamma rhythm is without any arousal effect without any power in reference montage;
b — without any signs of arousal in theta rhythm left, and alpha rhythm right 3D BM — reference montage;
c — without any signs of arousal effect in EEG signal – beta-LF left, beta-HF right 3D BM — reference montage.
14. 08.2018, after the 5th dose of amantadine sulphate, 200 mg each dose, IV administration:
d — delta frequency in a longitudinal montage; 3D BM shows very intense delta oscillations in bifrontal-prefrontal-central-motor regions;
e — theta frequency in a longitudinal montage; 3D BM shows very intense oscillations in central-motor-parietal-left with covering vertex region and lightly right parasagittal prefrontal-central-motor and parietal regions;
f — alpha frequency oscillator-raster picture is situated in parietal left covering partial parietal vertex region, and frontal-prefrontal opercular left regions;
g — Beta-LF(two pictures left), beta-HF (two pictures right). Both oscillations pictures are situated in similar positions;
h — gamma rhythm without any change in performance showing 0.0 power value;
i — delta rhythm oscillations in left frontal-prefrontal-anterior-temporal regions — transversal montage;
j — strong theta rhythm oscillations located to the frontal-prefrontal regions (right) and light theta rhythm oscillations located to the temporal-parietal regions and parietal-occipital boundary (left); transversal montage;
k — ehere are two strong alpha oscillations: frontal-prefrontal — central motor regions (right) and occipital-parietal regions (left). Possible our-self interpretation: Right hemisphere is working with decreased lucidity and vigilance, vice versa the left hemisphere works with high lucidity and vigilance — functional dissociation of quantitative parameters in consciousness – transversal montage;
l — beta-LF oscillations (to the left) and beta-HF oscillations (to the right) are only slightly different in location, size, power and shape due to 3D BM raster; transversal montage;
m — gamma frequency oscillator does not exist because of 0.0 power; transversal montage.

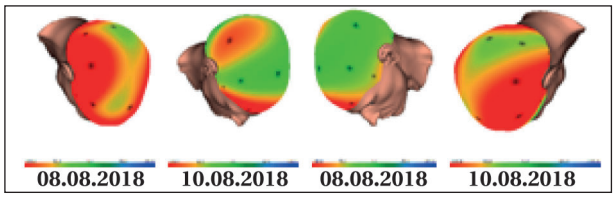

Fig. 5. Ž M, 33 years old, no amantadine (8.08.2018) versus amantadine sulphate, 200 mg, IV administration (10.08.2018).
Note. Comparison of 3D BM delta frequency power with arousal effect on August 10 in delta frequency power as resulted from delta band disinhibition. Substantial reduction of delta power inhibitory rhythm over the left and the right hemispheres. It is arousal positive due to disinhibition; reference montage.

rhythm was not detected as the last one during the period of progressive worsening of the comatose state and during general anaesthesia [12]. However, we did not see any gamma rhythm changes because we did not use the eLORETA program, which is capable to detect EEG signals from low resolution area, the cingulate gyrus, for technical reasons.

The images of the above-mentioned oscillators, except for the gamma frequency band, were not displayed due to the low power of the EEG signal from August 8, 2018 untill August 14, 2018. When the arousal

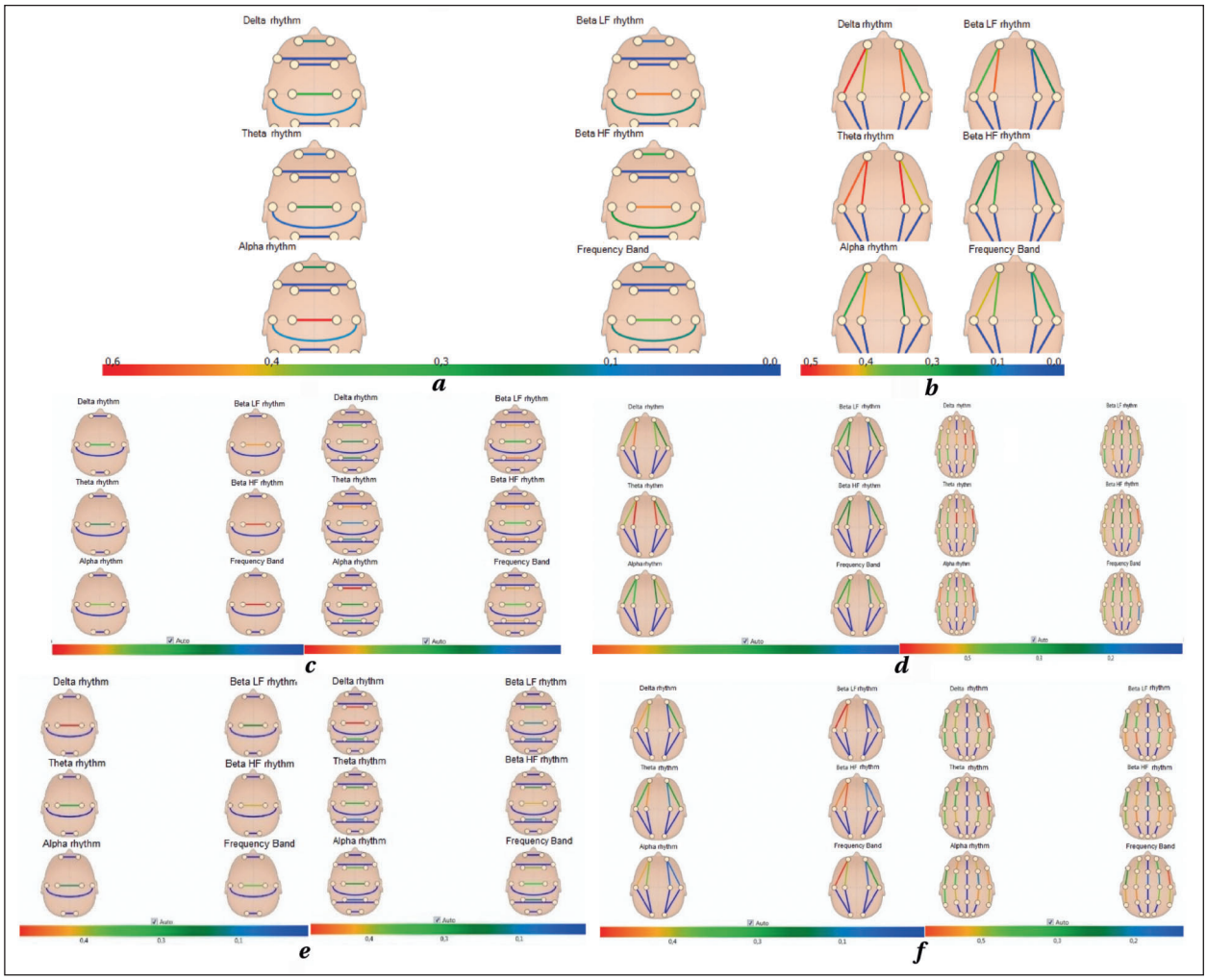

Fig. 6. Brain maps.
a — Brain maps of interhemispheric coherencies-indexes of connectivity in particular frequency bands show frontal and occipital split brain condition, only central-motor connectivity in alpha, beta-LF, and beta-HF is preserved; transversal montage.
b — Brain maps of the anterior-posterior coherencies-indexes of connectivity in particular frequency bands show total posterior hemispheric part disconnection and only some anterior hemispheric regions are connected in delta, theta, alfa bands and partially in beta LF, and beta HF; longitudinal montage.
Ž M, 33 years old:
c — 10.08.2018: following amantadine sulphate, 200 mg, IV administration. Brain maps of inter-hemispheric coherencies, indexes of connectivity in particular frequency bands show in 4 and 8 channel registrations frontal and occipital split-brain situation. Notice: the long distance of registration electrodes false-interrupts bi-prefrontal, bi-temporal, and bi-occipital connections; transversal montage.
d — 14.08.2018: after the 5th dose of amantadine sulphate, 200 mg each dose, IV administration. Brain maps in anterior-posterior direction show in color the coherencies – indexes of connectivity in 8 and 16 channels dispersion split, namely in bi-parietal-occipital regions; longitudinal montage.
e — 14.08.2018: after the 5th dose of amantadine sulphate, 200 mg each dose, IV administration. Brain maps in transversal direction.
f — 14.08.2018: after the 5th dose of amantadine sulphate, 200 mg each dose, IV administration. Brain maps in longitudinal montage. Disconnection in 4 vertex bipolar montages of 16 channel mode presumably means decisive disconnections in cingulate gyrus supporting/generating the aware human consciousness as a product of default mode network [12].

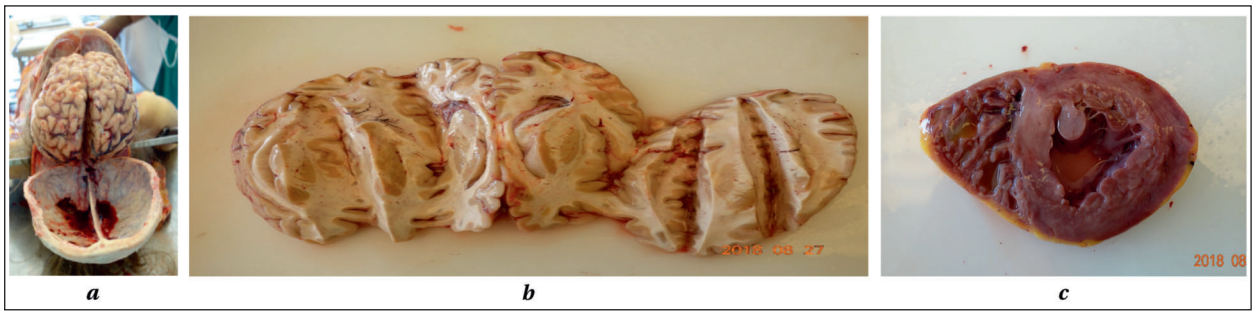

Fig. 7. Convexity of both hemispheres. Aqueous brain flows out of the intracranial space (*a*). Sagittal cuts through brain hemispheres (*b*). Crossed heart section. Dilation of the left heart ventricle with wall hypertrophy, acute cardiomyopathy (*c*).

reaction to the 5th dose of amantadine sulphate supported brain electrogenesis in AP of EEG signal, it increased from lightly below 10 μV/mm to predominantly 10–20 μV/mm. Then, the 3D BM revealed in a raster mode high oscillator performance in these regions that meant functional neuronal adequacy for starting lucid consciousness. The 3D BM raster pictures from August 14, 2018, correlated with pupil light-reaction, brain stem reflexes revitalization, behavioral activation, and a sign of gazing observation, an attention.

From August 8 to August 10, 2018 the patient exhibited patterns of a brain dying process according to clinical picture and pEEG, extinction of the brainstem reflexes, tendon-jerk areflexia and pacing of heart and respiration decrease. However, after the 5th administration of amantadine sulphate at a dose of 200 mg the surprising revitalization was observed that lasted from August 14, 2018, until the August 28, 2018, when the secondary post-ischemic lesions (due to excitotoxicity resulted form kidney failure) and brain stem alterations were added to the primary ischemic neocortex and allocortex lesions as illustrated by pEEG and completed total brain destruction. Since August 14, 2018, brain neuropil tissue showed signs of competence to renew the complete human aware consciousness, and also the highest mental, emotional, and social levels of aware human consciousness that we repeatedly observed in similar cases in the past [8].

Brain dying but not brain death as demonstrated by basic EEG signal and some pEEG tools was correlated with the clinical extinction of brain stem functions and reflexes as revealed during period from August, 8 to August 10, 2018. This feature followed by surprising revitalization in basic visual mode — joint attention, behavioural samples, brain stem reflexes, and pEEG. The observed revitalization occurred in brain stem functions - mesencephalon, pons, medulla, brain stem reflexes, but 18 days later the heart pacemaker and breathing pacing failed. Whether the subsequent, post-ischemic brain tissue lesions due to excitotoxicity resulted in a unfavourable fate of our female patient? No! It was the myocardial destruction due to heart arrest that led to a secondary death of the brain. Clinical restoration of stem reflexes and lucid and vigilant consciousness, revival of visual contacts (attention to nursing staff and especially to her husband after the administration of the 5th dose of amantadine sulphate at a dose of 200 mg) provided a prerequisite for optimistic definitive exit from brain dying toward functional adjustment of mental and psychomotor functions. The brain was capable of revitalization because it retained delta activity that had been recognized as a sign of vital performances (blood pressure, ventilation rhythm, ECG oscillating at a <0.10Hz frequency band, transformed in one constant segment as illustrated by 3D BM and wavelet transformation). There is a well-known classical principle in the evaluation of EEG signal in the diagnosis of brain death, which states that if there is only one frequency band of the EEG signal, the brain cannot be considered dead. A number of EEG and fMRI studies in mammals have demonstrated that spontaneous low frequency oscillations in cerebral activity at <0.1 Hz represent a fundamental component of brain activity [13, 14]. Areas involved in this intrinsic activity including the posterior cingulate cortex/praecuneus, medial prefrontal cortex, and bilateral temporoparietal junction are known as the «default mode resting state network, DMRSN» [15].

The DMRSN is a resting state network that is active during passive moments and deactivated when one engages in a mental task [16]. However, the majority of energy utilized in the brain can be attributed to DMRSN activity [17]. The decrease in connectivity levels measured by mean squared of coherences in the gamma frequency band above DMRSN is considered a robust measure of decreased lucidity of consciousness during general anaesthesia as an example to surpass the brain death model [12, 18, 19].

From August 8 to August 10, 2018, and until the outcome on August 28, 2018, the secondary post-ischemic brain stem lesions along with the primary ischemic neocortex and allocortex lesions as shown by pEEG have completed the total brain destruction exhibiting dough-like aqueous brain structure on a postmortem investigation. It was only a matter of time when heart pacemaker and breathing pacing would disappear due to multiple inner organs failure after exsanguination due to massive hemorrhage occurred in the patient.

Finally, our data warrant the opening a discussion on weather the 3 DM BM in color might be well suited to monitoring dying and definitive brain death. We suggest that it's worth to explore the 3D BM informative value — with optimistic expectations.

Conclusions

The 3D brain mapping is a promising, up-to-date electrophysiologic and dynamic quantitative method employing automatic PC-aided statistic programs for dynamic evaluation of digital signals of dying brain that may impact the intensive care medicine.

To determine brain dying, electro-cerebral hypoactivity (ECH) should be demonstrated on scalp EEG, which is recorded considering the following criteria:

(a) sensitivity of 10μV/mm; The arbitrarily accepted electrologic life-death threshold is AP value 2 μV of EEG waves registered from the skull surface;

(b) inter-electrode distances less than 10 cm;

(c) covering over all major brain areas including midline area;

(d) recording for at least 30 minutes;

(e) during the application of amantadine sulphate as five i. v. administrations at a dose of 200 mg each, there was a revival of the EEG signal in the baseline curve and in the 3D BM, associated with the revival of brain stem reflexes including the light reaction.

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