

Could the wavelet synchrony of resting-state EEG discriminate between vegetative state and akinetik mutism in patients with severe brain injury?

Introduction

Accurate assessment of current functional state of patients in vegetative state or other unconscious states, such as akinetik mutism is very important for correct treatment strategy and rehabilitation activities especially in cases when the difference between those states is not clinically obvious.¹⁻³ This requires searching rigorous methods of functional state assessment.

Brain responses for simple tones⁴⁻⁶ and naturalistic stimuli could be used to estimate event-related brain activity^{7,8} whereas the analyses of resting-state EEG could reveal neuronal networking providing a background for responses to stimuli.⁹ Supposedly, the study of resting-state neuronal activity could help to search individual stimuli to bring brain activity to the level where the purposeful activity of patients is possible.

This pilot study is dedicated to revealing features of resting-state wavelet synchrony in unconscious patients with severe brain injury. We suppose that revealed features could help in assessment of a current state and selection of efficient rehabilitation activity.

Methods

Brain activity of 9 in-patients with severe brain injury (TBI) treated in Burdenko National Medical Research Center of Neurosurgery was analyzed in the study. The experimental protocol was approved by the

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Oknina LB,¹ Zigmantovich AS,¹ Zaitsev OS,² Masherov EL,² Sharova EV¹

¹Institute of Higher Nervous Activity and Neurophysiology of the RAS, Russia

²Burdenko National Medical Research Center of Neurosurgery, Russia

Correspondence: Oknina LB, Institute of Higher Nervous Activity and Neurophysiology of the RAS, Russia, Email lelia@yandex.ru

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local Ethics Committee (Burdenko Neurosurgery Institute Research Center of Neurosurgery). Taking into account that all patients were in unconscious state the written informed consent was obtained from patients' relatives. Prior the experiment relatives of patients received complete information about the methods and goals of research.

Patients' age varied from 15 to 72 (33,8±18,3 years). The total of 22 studies was analyzed. Follow up was from 6 months to 8 years. Characteristics of patients, their functional state during the first EEG-record after TBI and outcome are presented in Table 1.

Table 1 Characteristics of patients, their functional state during the first EEG-record after TBI and outcome and the features of synchrony mapping in resting-state EEG

Patient	Gender	Age (years)	Follow up (years)	Functional state during the first EEG	outcome	Maximal wavelet synchrony, hemisphere	Maximal wavelet-synchrony, area
1	M	34	8	AM	Cons.*	d	F-C
2	F	72	5	VS	VS	s	C-P
3	M	20	5	AM	AM	d	F-C-T
4	F	63	4	AM	Cons.	d	F-C-T, P-C
5	M	56	0,5	VS	Cons.	s	F-C, P-C
6	F	35	0,5	AM	Cons.	s	F-C-P
7	M	37	1,2	VS	VS/death	s	F-C
8	M	23	3	AM	Cons.	s	C-P, O
9	F	21	5	VS	Cons.	d	P-T

*-consciousness recovery in 7 years after TBI, outcome—death due to cardiac arrest.

M, male; F, female; VS, vegetative state; AM, akinetik mutism; Cons., consciousness recovery; F, frontal; C, central; P, parietal; O, occipital; T, temporal; d, right hemisphere; s, left hemisphere.

The control group consisted of 30 healthy subjects aged 18 to 59 (mean age 30 ± 13).¹⁰ Brain activity was recorded on the equipment Neurobotics (Russia) from 32 sites. Vertical and horizontal electro-oculograms were recorded from the right supra-orbital margin and outside corner of the eye fissure for monitoring blinking and eye movement and further off-line artifact correction ($>50\text{mV}$). EEG was recorded with common ear electrodes. Impedance was less than $5\text{k}\Omega$ and the range from 0.1 to 100Hz, the 16-bit amplifier was used. Discretization was 1024Hz.

Data analysis. 3 minute EEG without artifacts was used to analyze wavelet synchrony. 30 points were randomly sited on EEG. Wavelet synchrony was calculated in intervals including 800ms after the point and averaged. For wavelet synchrony calculation¹¹ maternal wavelet-Morlet with parameters $F_b=1$ and $F_c=1$ was used. The values of synchrony were calculated for all pairs of sites. Calculation of

synchrony was made in the range 1-15Hz. The range was determined by the fact that 1Hz filter rejects slow artifacts due to oculogram and 15Hz border allows to exclude from calculation high-frequency miographyoscillations. To calculate a repeated measures effect, the permutation test was used.¹²

Results

Although wavelet-connectivity detected in unconscious patients varied, it was possible to reveal some features typical for patients in vegetative state and akinetik mutism.

The lesser value of wavelet synchrony was detected in patients with chronic vegetative state in comparison to the norm or patients in mutism. The dependence of resting-state wavelet synchrony from current state and outcome according to variance analysis (ANOVA) is presented in Figure 1.

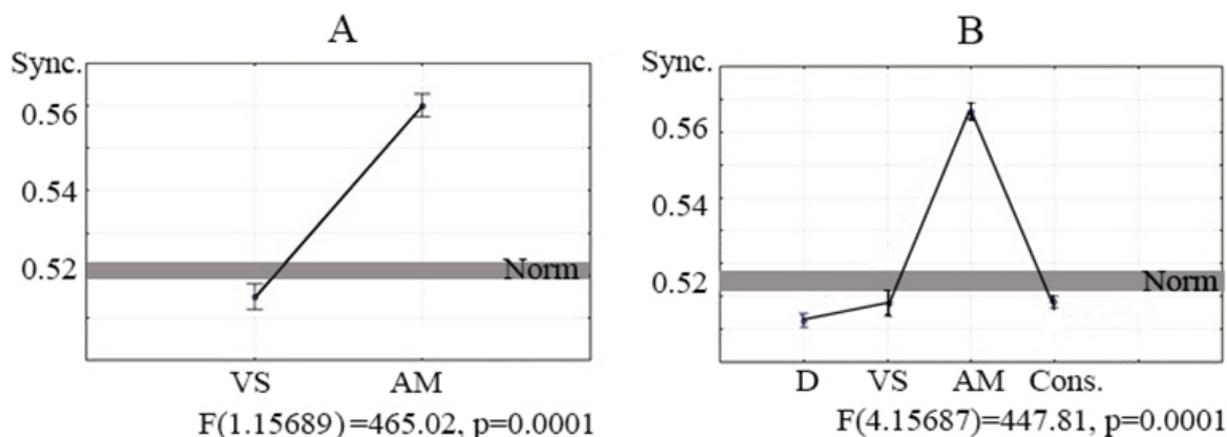


Figure 1 Dependence of wavelet synchrony from A, current state; B, outcome; VS, vegetative state; AM, akinetik mutism; D, death; Cons., consciousness recovery.

In case of the most favorable outcome of VS, the maximum of wavelet synchrony was mapped in the posterior areas (parietal area), in comparison to cases of VS reversible in a lesser degree, when stronger wavelet synchrony leaned towards the inferior area (frontal and central areas).

Discussion

The increased value of wavelet synchrony in posterior areas, detected in patients with good recovery could reflect stronger brainstem influence essential for reaching the “right” background activation level that allows passing the threshold needed for involving other structures in activation processes. This correlates with the published data on the functional role of brainstem in processes of consciousness recovery.¹³ It is crucial that similarly increased wavelet synchrony was not detected in patients with chronic vegetative state.

The resting-state wavelet synchrony in patients in mutism has a significantly higher value in comparison to both the norm and vegetative state. Supposedly, the individual stimuli could be selected to decrease the level of activation.

A low level of synchrony is due to be increased up to a certain activation level for stabilization of many chaotically appearing combinations of brain neuronal activity needed to involve patients in voluntary processes.

Study limitation

Although the features of wavelet synchrony in vegetative state and mutism are distinct enough, the data obtained do not allow us to make a reliable prognosis of consciousness recovery due to the limited number of patients.

Conclusion

Wavelet synchrony could be used to discriminate between vegetative state and mutism: patients in vegetative state have a lower value of wavelet synchrony in comparison to norm, whereas patients in mutism, a significantly higher.

Acknowledgements

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Conflict of interest

The author declares no conflict of interest.

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