ELECTROPHYSIOLOGICAL EVALUATION OF THE EFFECTIVENESS OF NEUROFEEDBACK IN AMELIORATING CHRONIC POST-TRAUMATIC STRESS DISORDER

Rafał Morga[1(A,B,D,E,F)], **Dariusz Adamek**[2(A,B,D)],
Weronika MacQueen[3(A,B,E)], **Bruce Duncan MacQueen**[4(A,D,F)],
Jolanta Góral-Półrola[5(A,B,D,E,F)], **Joanna Bitner-Szulc**[6(A,B,E)],
Juri D. Kropotov[7(A,B,C,D,E,F)], **Maria Pąchalska**[3)A,B,D,E,F,G)]

[1] The Department of Neurosurgery and Neurotraumatology, CMUJ, Kraków, Poland
[2] Department of Clinical and Experimental Pathomorphology, CMUJ, Kraków, Poland
[3] Chair of Neuropsychology and Neurorehabilitation, Andrzej Frycz Modrzewski Cracow University, Kraków, Poland
[4] University of Tulsa, Tulsa, Oklahoma, USA
[5] Old Polish University, Kielce, Poland
[6] Department of Human Development, Institute of Psychology, Kazimierz Wielki University, Bydgoszcz, Poland
[7] Laboratory for the Neurobiology of Action Programming, Russian Academy of Sciences, Institute of the Human Brain, St. Petersburg, Russia

SUMMARY

Background: The aim of our research was to evaluate the effectiveness of neurofeedback in reducing the symptoms of chronic Post Traumatic Stress Disorder (PTSD) in a patient who had developed the syndrome following a recurrence of sphenoid wing meningioma (SOM). EEG spectra and event-related potentials (ERPs) were used to construct an individual neurofeedback protocol and to provide objective monitoring of treatment efficacy.

Case study: The patient, a 34-year-old female, was diagnosed with a sphenoid wing meningioma (SOM), which had been successfully operated. Three years later, however, the SOM had overgrown at the optic foramen and extended into the optic canal, and the patient had developed blurred vision. She was repeatedly operated, and recovered well. However, due to the recurrence she developed flashbacks, anxiety and sleep difficulties, such that she was unable to continue working in her profession. The symptoms had been occurring for 4 months. ERPs in a cued NOGO task, along with EEG spectra in the resting state and during task performance were used to assess brain functioning, providing the basis for a neurofeedback protocol. Twenty sessions of individually tailored neurofeedback were performed. The patient experienced a reduction of symptoms, accompanied by normalization of ERPs parameters.

Conclusions: The results obtained in this case point to the possible benefits of individually tailored neurofeedback protocols in the treatment of PTSD.

Key words: Post-traumatic stress disorder (PTSD),
cued GO/NOGO task, P3 NOGO, neurofeedback

INTRODUCTION

Post-Traumatic Stress Disorder (PTSD) is a syndrome of emotional, cognitive, and neurobehavioral symptoms triggered by the memory of a traumatic event: that is, an emotionally-charged experience that leaves a lasting negative impact on the individual's mental state. In previous editions of the *Diagnostic and Statistical Manual* (DSM), the "traumatic event" was defined as a catastrophic occurrence that was "outside ordinary human experience": war, natural disaster, violent crime, and the like. Historically, the syndrome now called PTSD was first observed clinically in soldiers fighting in the trenches in World War I, under constant artillery bombardment, and was called "shell shock" (Jones, 2010; Leys, 2000). By the Second World War, the term "shell shock" had been replaced by "combat fatigue" or "battle fatigue" (Jones, 2006). After the war ended, symptoms similar to combat fatigue were observed in persons who had survived confinement in concentration camps, or, in some cases, prisoner of war camps, which produced the term "concentration camp syndrome" (Leys, 2000; Pąchalska, Kaczmarek & Kropotov 2014). This finally led to the development of the concept of PTSD, now familiar both to clinicians and to the general public.

The original assumption, then, was that PTSD would usually be diagnosed only if there was a history of traumatic wartime experience, though major natural disasters were also included. Over the years, however, the category of events that are understood to be possible causes of PTSD has expanded considerably, so that the fifth edition of the DSM (APA, 2013) mentions "exposure to actual or threatened death, serious injury or sexual violation." Thus a serious illness that could possibly cause death or serious disability now very clearly falls within the definition.

It would seem obvious, then, that the diagnosis of a malignant tumor could easily be a "traumatic event" capable of inducing the symptoms of PTSD. Indeed, the American Society of Clinical Oncology patient information website recently published an article that explains some of the cancer-related triggers of PTSD symptoms (American Society of Clinical Oncology, 2016). The diagnosis of "cancer in the brain" is especially life-shattering for most patients: the initial diagnosis disrupts the course of ordinary life, and the prospect of debilitating changes to mental functioning and finally death produces fear, worry, anxiety and dread. The fight against cancer becomes the entire focus of the person's mental and physical strength. Not surprisingly, some patients develop clinical symptoms that justify the diagnosis of PTSD.

DSM-5 lists four diagnostic clusters of symptoms for PTSD:

1. Re-experiencing: the patient experiences flashbacks (spontaneous recollection of the traumatic event, often with the inability to recognize that this is a memory and not an actual event), intrusive recollections, or recurrent dreams;
2. Avoidance: the patient consistently avoids contact with people, places or things associated with the traumatic event;
3. Negative cognitions and moods: the patient has persistent and significant feelings of guilt, blame, estrangement, or loss of interest in daily activities;

4. Arousal: the patient exhibits aggressive, reckless or self-destructive behavior, sleep disorders, hypervigilance, or other signs of excessive reactivity to threats, real or imagined.

In this paper we present the case study of a patient who developed PTSD symptoms, apparently triggered by the recurrence of a cancer she had thought to have been successively excised. Her brain functioning was tested with QEEG/ERP methodology, and an individually tailored neurofeedback protocol was suggested. After 20 sessions of neurofeedback, her brain functioning was objectively improved, accompanied by a reduction of clinical PTSD symptoms.

CASE STUDY

A 34-year-old female, trained as a teacher in health sciences, developed a sphenoid wing meningioma (SOM), which was successfully neurosurgically operated. Three years later, however, the SOM had recurred: it was overgrown at the optic foramen and extended into the optic canal, and the patient had developed blurred vision. She was again operated neurosurgically. MRI studies showed a partially enhancing sclerotic lesion in the sphenoid wing region on the left side, compressing the left visual canal and the left optic nerve (Fig. 1). The morphology of the tumor suggested type III medial sphenoid wing meningioma.

Histopathological findings revealed a relatively large clump of tumor cells separated by strands of fibrous tissue (see Fig. 4). What is noteworthy here is that meningiomas in the orbital region frequently do not only form one separated tumoral mass, but grow dispersively in sometimes very small cell clusters (see the description of Fig. 4). In the reported case here, the tumor showed this feature, which sometimes, if the sample of a tissue sent for neuropathological examination is too small, may conceal the presence of a tumor, or the meningioma cells may even be overlooked. However, the crucial problem is that it is quite often practically impossible in the orbit for the pathologist to unequivocally declare (or confirm) the radicality of tumor removal. It is always essential in this location to exclude the presence of an intracranial part of the tumor.
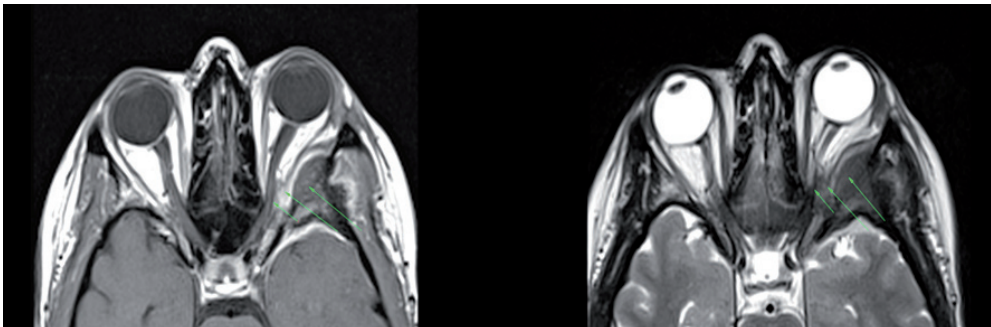

Fig. 1. MRI of the orbits: A/ FSET1 + CM sequence, B/ frFSET2 sequence, axial plane: Compressed visual canal (small arrow), intraorbital enhancing part of tumor (middle arrow), sclerotic intraosseus part of meningioma/enlarged sphenoid wing (long arrow)
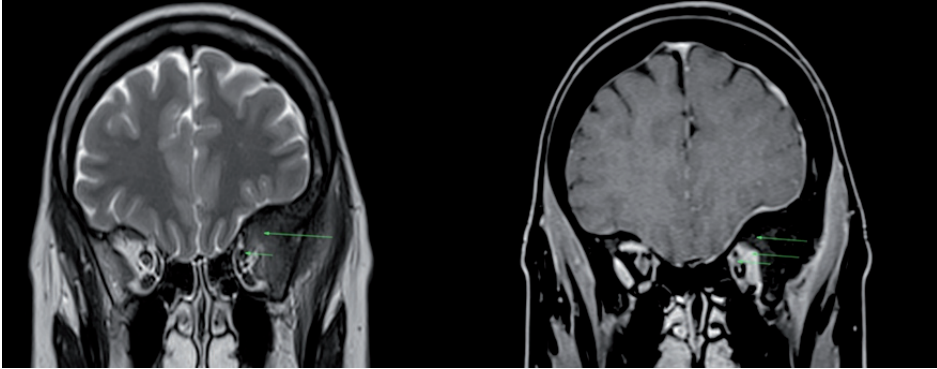
Fig. 2. MRI of the orbits: A/ frFSET2 sequence, B/ FSET1fs + CM sequence, coronal plane: Compressed optic nerve (small arrow), intraorbital enhancing part of tumor (middle arrow), sclerotic intraosseus part of meningioma/enlarged sphenoid wing (long arrow)
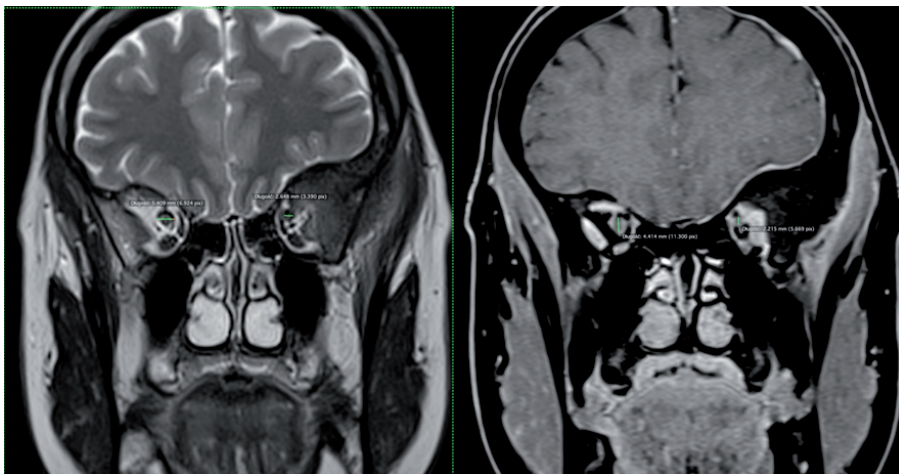

Fig. 3. MRI: of the orbits A/ frFSET2 sequence, B/ FSET1fs + CM sequence, coronal plane: measurements of the right (normal) and left (compressed) optic nerve diameter

Despite the severity of the lesions, the patient recovered successfully after the second operation. However, after learning that she again had meningothelial meningioma of the orbit, the patient developed severe symptoms: arrhythmia, rapid breathing, muscle pain, increased arousal such as difficulty sleeping and concentrating, nervousness, and a tendency to irritation and anger. She re-experienced flashbacks, in which she saw and heard the doctor telling her the diagnosis, and recurrent nightmares. She avoided contact with places and people (including doctors) associated with the traumatic events. Finally, she lost interest in daily activities, which rendered her unable to continue work in her given profession. These symptoms lasted for 4 months, until she decided to ask for help in receiving an accurate diagnosis and neurofeedback treatment.
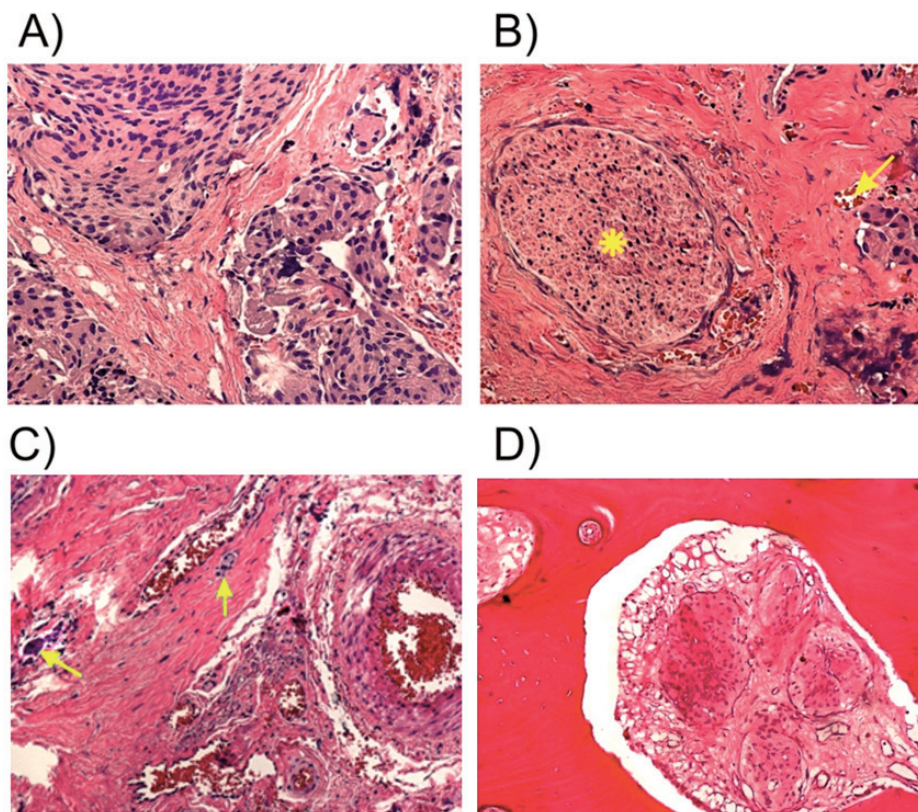
Fig. 4. Meningothelial meningioma of the orbit. Microphotographs a, b and c are from the resected material during first surgery of the tumor of the orbit, photo d - from the second surgery. All slides were stained with hematoxylin-eosin.

A) a relatively large clump of tumor cells separated by strands of fibrous tissue
B) a nerve bundle (asterisk) of one of the oculomotor nerves and a small group of meningioma cells in its vicinity indicated by arrow
C) a small artery and some more tiny tumor cell grouping scattered within a conspicuous fibrous tissue (arrows)
D) invasion of the bone by meningioma

Quantitative EEG and event-related potentials

The methods of quantitative EEG and event-related potentials were used for diagnostic purposes. The patient participated in a cued GO/NOGO task (Kropotov, 2009) with 19-channel EEG recording. The EEG spectra were computed in the resting state (eyes open, eyes closed) and during task performance, while event-related potentials were recorded in the cued GO/NOGO task, and compared with the Human Brain Index database (Kropotov 2008, 2016; https://www.hbimed.com/).

The task consisted of 400 trials, sequentially presented to the subject at 3-second intervals. Three categories of visual stimuli were used:
1. 20 different images of animals – referred to hereinafter as A,
2. 20 different images of plants - P,

3. 20 different images of people of different professions (presented together with an artificial "novel" sound) referred to as H.

The trials consisted of the presentation of pairs of stimuli with inter-stimulus intervals of 1 s. Th duration of stimuli presentation was 100 ms. Four categories of trials were used: A-A, A-P, P-P, and P-H. In the trails with A-A and P-P pairs the first and the second stimuli were identical. The trials were grouped into four sessions with one hundred trials in each. In each session a unique set of five A stimuli, five P and five H stimuli was selected. Each session consisted of a pseudo-random presentation of 100 pairs of stimuli with equal probability for each category and each trial category (Kropotov, 2008).

The task was to press a button with the right hand to all A-A pairs as fast as possible and to withhold from pressing in response to any other pairs. The participants performed 10 trials without recording to see if they understood the instruction. They rested for a few minutes after completing 100 trials. Stimuli occupied about 3.8° of the visual field around the centre of the screen. Visual stimuli (were selected to have) had similar 2D sizes and luminosities.

Eye blink artefacts were corrected by zeroing the activation curves of individual independent components corresponding to eye blinks. These components were obtained by the application of Independent Component Analysis (ICA) to the raw EEG fragments (Kropotov, 2008). Epochs with excessive amplitude of filtered EEG and/or excessive faster and/or slower frequency activity were automatically marked and excluded from further analysis. The exclusion thresholds were set as follows: (1) 100 µV for non-filtered EEG; (2) 50 µV for slow waves in 0–1 Hz band; and (3) 35 µV for fast waves filtered in the band 20–35 Hz. In addition, we visually inspected the recordings and excluded any remaining artefacts.

EEG spectra, pre-treatment

For computing pre-treatment EEG spectra, artifact-free fragments of EEG were divided into 4 sec epochs with a 50% overlap. The Hanning time window was used. The EEG spectra were computed for each epoch and averaged. The mean value and standard deviations for each 0.25 Hz bin were computed. In Eyes Open, Eyes Closed and GO/NOGO task, a decrease of the relative EEG power was found in the alpha frequency band (8-13 Hz), accompanied by an increase of the relative EEG power in the high beta frequency band (21-30 Hz) (Fig. 5).

ERPs, pre-treatment

The behavioral parameters in the cued GO/NOGO task during the pretreatment recording are presented in Table 1.

As one can see, the subject is slow and inconsistent in response, which appears to indicate a specific impairment in cognitive control.

The NOGO ERP waves as electrophysiological indices of cognitive control in comparison to those of healthy subjects are presented in Fig. 6.

The QEEG data demonstrate the state of hyper-activation of the somatosensory cortex indexed by decrease of the mu-rhythm and increase of the relative high beta rhythm (Fig. 5).
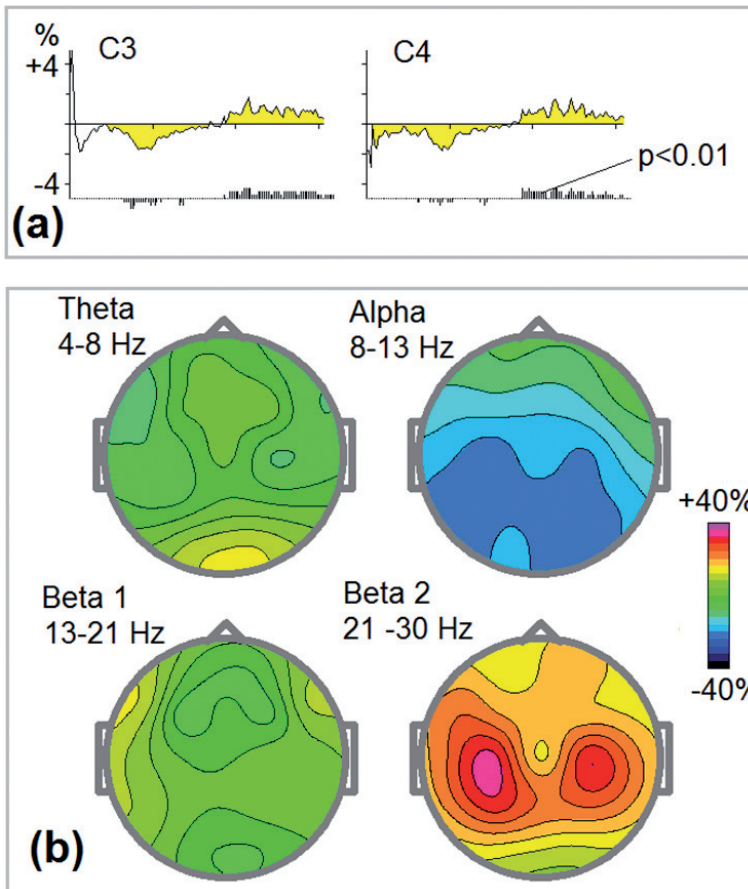

Fig. 5. Deviations of the relative EEG spectra recorded in the subject in the eyes open condition from the normative data in the first recording (pretreatment). (a) Relative EEG spectra differences ("Subject" minus "Grand average of Healthy Controls") with p-values of statistical significance below the curves. Y-axis – %, X-axis – frequency. At the bottom, p-values of the confidence of the difference (small bars – p<0.05, medium bars – p<0.01, large bars – p<0.001). (b) Maps of the relative EEG spectra deviations from the reference in four frequency bands

Table 1. Behavioral parameters of the subject in GO/NOGO task (Pretreatment)

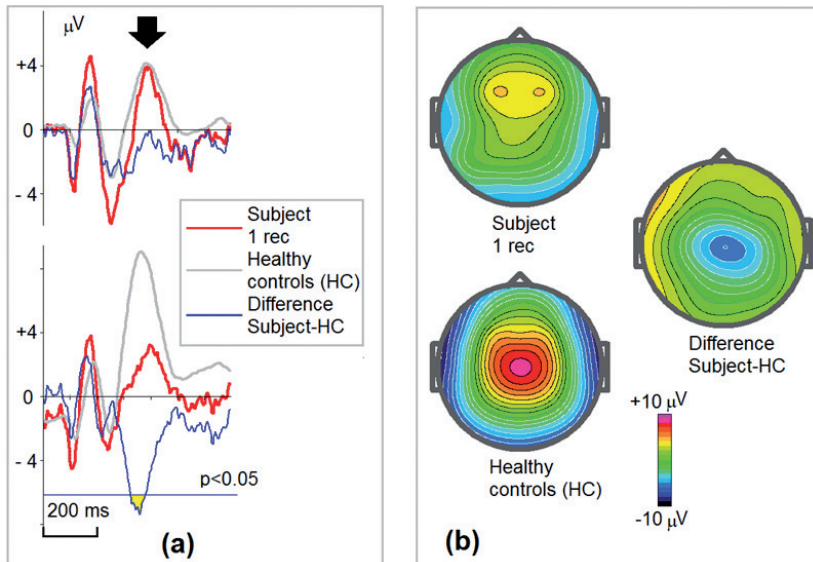| Factors	Omission	Commission	RT	var(RT)
Pretreatment	3%	0%	580	12.7
Norms	2.5%	0.7%	377	7.8
p-value of the difference (subject-healthy controls)	0.88	0.52	0.002	0.04

Fig. 6. NOGO ERPs and their maps in the cued GO/NOGO task for the subject in comparison to healthy controls. (a) ERPs for Fz and Cz electrodes for the subject (red lines) in comparison to the grand average of a group of healthy controls (N=23) (gray lines), their difference waves (blue lines), with p-values reflecting the confidence level of the difference. Y-axis – potential in micro-volts, X-axis – the post second stimulus time in ms. (b) maps of the corresponding ERPs and ERP difference waves take at time indicated by arrow at (a)

Neurofeedback protocol

Based on the data, a protocol of neurofeedback (NF) was suggested, with the goal of deactivating the somatosensory cortex (Kropotov 2018). The protocol includes training mu-rhythm up with simultaneous inhibition of the high beta rhythm (see Pachalska, Kaczmarek & Kropotov, 2014). NF sessions were conducted by experienced NF clinicians, who completed a session fidelity checklist designed to mirror the specific components of each session, which involved rating the full, partial or unsuccessful implementation of each component, any factors that impeded protocol adherence, and any modifications to protocol that seemed to be necessary. Changes to the starting protocol, such as frequency adjustments, were automatically recorded by the NF software (Pachalska, Kaczmarek & Kropotov, 2014). A clinician met weekly with the supervisor to review the specifics of each NF session, session fidelity checklists, and protocol adjustments, as suggested by van der Kolk, Hodgdon, Gapen et al. (2010). Twenty sessions of the NF were performed for 7 weeks, with 3 sessions per week. The results are presented below.

ERPs, post-treatment

The behavioral parameters in the GO/NOGO task after treatment in comparison to the group of healthy controls, indicating normalization of the reaction time and the variance of response. In line with behavioral data, the ERP correlates of cognitive control are also normalized (Fig. 7).
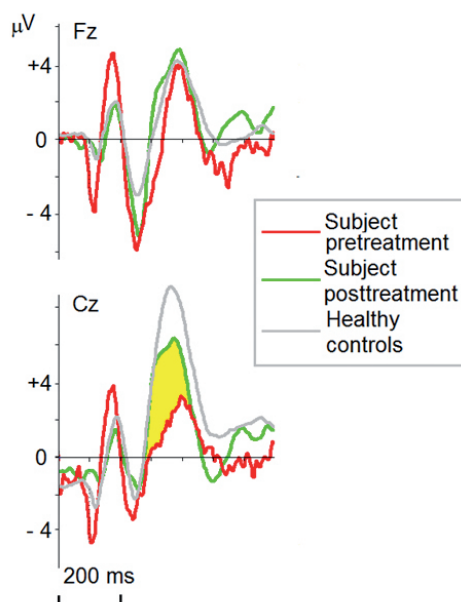
Fig. 7. Normalization of NOGO ERPs in the cued GO/NOGO task for the subject after 20 sessions of the neurofeedback protocol. ERPs for Fz and Cz electrodes for the subject for the post-treatment recording (green lines) in comparison to ERPs of pre-treatment recording (red lines) and the grand average of the group of healthy controls (N=23) (gray lines). Y-axis – potential in micro-volts, X-axis – the post second stimulus time in ms

The patient stated that her health related quality of life (HRQoL) after treatment improved significantly.

DISCUSSION

The results of the present study show that QEEG/ERP assessments provided some important information regarding the behavioral features in the patient described here, who developed PTSD symptoms in response to a second cancer diagnosis (sphenoid wing meningioma). The QEEG spectra recorded prior to treatment (before neurofeedback) showed hyper-activation of the somatosensory cortex, associated with symptoms of hyper-arousal (including anxiety, fear, and insomnia). The QEEG pattern was accompanied by a decrease in the ERP component, associated with impaired cognitive control in the subject. A protocol of neurofeedback treatment was suggested, with the primary goal being to deactivate the somatosensory cortex.

The results we observed indicate a positive effect of the individually tailored neurofeedback on the patient's PTSD symptoms. This is consistent with other studies that have found similar positive effects of neurofeedback training on symptoms of PTSD in other groups of patients (Graap & Freides, 1988; Gapen et al., 2016; Chrapusta, Kropotov & Pąchalska, 2017; Kropotov 2018; Askovic et al., 2019).

Questions regarding the similarity of cancer-related PTSD to PTSD subsequent to other traumas, along with questions regarding its etiology and appropriate treatment, must be addressed by future research.

CONCLUSIONS

A program of neurofeedback, tailored to the individual's particular needs on the basis of data provided by EEG and ERP studies, can help to reduce the symptoms of PTSD in an individual affected by an adverse medical diagnosis.

REFERENCES

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. Arlington, VA, USA: American Psychiatric Association.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition. Arlington, VA, USA: American Psychiatric Association.

American Society of Clinical Oncology. (2016). *Post-Traumatic Stress Disorder and cancer*. Retrieved from: http://www.cancer.net/survivorship/life-after-cancer/post-traumatic-stress-disorder-and-cancer.

Askovic, M., Watters, A.J., Coello, M., Aroche, J., Harris, A.W.F. & Kropotov, J. (2019). Evaluation of neurofeedback for Posttraumatic Stress Disorder related to refugee experiences using self-report and cognitive ERP measures. *Clinical EEG & Neuroscience, 1-8*. doi: 10.1177/1550059419849170.

Chrapusta, A., Kropotov, J.D., Pąchalska, M. (2017). Neuromarkers of Post-Traumatic Stress Disorder (PTSD) in a patient after bilateral hand amputation – ERP case study. *Ann Agric Environ Med*, *24*(2), 265-270. DOI: 10.26444/aaem/74597.

Gapen, M., van der Kolk, B.A., Hamlin, E., Hirshberg, L., Suvak, M. & Spinazzola, J. (2016). A pilot study of neurofeedback for chronic PTSD. *Applied Psychophysiological Biofeedback*, *41*, 251-261.

Graap, K. & Freides, D. (1998). Regarding the database for the Peniston alpha-theta EEG biofeedback protocol. *Applied Psychophysiological Biofeedback, 23,* 265-272.

Jones, E. (2006). Historical approaches to post-combat disorders. *Philosophical Transactions of the Royal Society of London, B: Biological Sciences, 361*(1468), 533–542.

Jones, E. (2010). Shell Shock at Maghull and the Maudsley: the origins of psychological medicine. *Journal of the History of Medicine & Allied Sciences, 65*, 368–395.

Kropotov, J.D. (2009). *QEEG, Event-related potentials and Neurotherapy*. Amsterdam: Elsevier Academic Press.

Kropotov, J.D. (2016). *Functional neuromarkers for psychiatry*. Amsterdam: Elsevier Academic Press.

Kropotov J.D. (2018). Functional neuromarkers for neuropsychology. *Acta Neuropsychologica 16*(1): 1-7. DOI: 10.5604/01.3001.0011.6504

Leys, R. (2000). *Trauma, a genealogy*. Chicago: Chicago University Press.

Pąchalska M., Kaczmarek, B. & Kropotov, J.D. (2014). *Neuropsychologia kliniczna od teorii do praktyki*. (Clinical neuropsychology: from theory to practice). Warsaw: WN PWN.

van der Kolk, B. A., Hodgdon, H., Gapen, M., Musicaro, R., Suvak, M. K., Hamlin, E., & Spinazzola, J. (2016). A randomized controlled study of neurofeedback for chronic PTSD. *PloS one*, *11*(12), e0166752. doi:10.1371/journal.pone.0166752.

Address for correspondence:
Prof. Maria Pachalska, MD. PhD.
Chair of Neuropsychology and Neurorehabilitation
Andrzej Frycz Modrzewski Krakow University,
Andrzeja Herlinga-Grudzińskiego 1
30-750 Krakow, Poland
e-mail: neuropsychologia23@o2.pl