CASE STUDY

ACTA Vol. 13, No. 4, 2015, 395-403
NEUROPSYCHOLOGICA

Received: 11.06.2015
Accepted: 28.12.2015

A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

DOI:10.5604/17307503.1193831

NEUROMARKERS OF ANXIETY IN A PATIENT WITH SUSPECTED SCHIZOPHRENIA AND TIA: THE EFFECT OF INDIVIDUALLY-TAILORED NEUROFEEDBACK

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SUMMARY

Background: The aim of the study was to evaluate the effectiveness of individually tailored neurofeedback protocol for the reduction of anxiety which was diagnosed in a patient with suspected schizophrenia and TIA. The neuromarkers in Quantitative EEG (QEEG) and Event-related potentials (ERPs) were utilized in the construction of the protocol and the evaluation of the effectiveness of neurofeedback.

Case study: A 54-year-old patient, experienced a Transient Ischemic Attack (TIA) of the left brain hemisphere. He had been treated previously for more than 30 years for schizophrenia. After the episode of TIA, he suffered mild anomia, intensification in the severity of headaches, muscular tension, difficulties with sleeping as well as an inability to continue work in his given profession. Neuropsychological tests showed the presence of anxiety. The QEEG/ERP assessment of the patient did not find any ERPs neuromarkers of schizophrenia but instead there we found a neuromarker of anxiety. It is expressed by excessive central high beta rhythmicity. A suppression beta protocol of neurofeedback was suggested. After 20 sessions of neurofeedback found in the QEEG/ERP assessment a decrease of the central high beta activity without any significant changes in ERPs. Finally, the patient returned to work.

Conclusions: The QEEG/ERP assessment provides a powerful tool for diagnosing the leading brain dysfunction and for constructing an individually tailored neurofeedback protocol. Presented above case study confirms the need for administering new neurotechnologies in the diagnosis of mental disorders with particular emphasis put on the schizophrenia spectrum. For a patients with cognitive problems the differential diagnosis should include carotid artery stenosis in which the Doppler Ultrasound (DUS) examination is gold standard.

Key words: TIA, carotid artery, anxiety, neuromarkers, neurotherapy

The way that the phenomena of the major psychoses have been classified and conceptualized has fluctuated markedly during the past 30 years. Kępiński's formulation of it in Poland (1974) has been clinically influential and scientifically fruitful although alternative models of diagnosis have been always available. The negative symptoms, for example, are well known to neurologists in the form of akinetic mutism, catatonia and abulia (Wright 2008). They occur, according to Wing (1990), in a wide range of psychiatric conditions, including dementia, the autistic spectrum disorder, in an approximate dimention and severity. However, the positive symptoms appear clinically to be near the top of an approximate hierarchy (Kępiński 1974; Wing 1990; Kropotov 2009; Kolb, Whishaw 2007). Diagnosis of these patients is even harder since the symptoms of conditions laiddown such as affective psychosis and neurosis, are commonly associated (Wing, 1990). Therefore, the heterogeneity of symptoms observed in this wide range of psychotic symptoms including schizophrenia spectrum, affective psychosis and neurosis, and creates considerable difficulties in putting together a differential diagnosis of mental disorders (Lewis and Levitt 2002).

The classification rules in the 10th edition of the International Classification of Diseases should be used as a general standard of comparison but it is important to apply all sets of rules to a clinical database, which allows for a flexible approach to the investigation of co-morbidity. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM 5), published on the 18 May 2013, the evaluation should be performed during the course of an illness. Hence, taking into account the behavioral criteria leads to many diagnostics problems. This situation creates real diagnostics difficulties, which results in an inability to apply an effective treatment.

Those difficulties can be overcome with the use of brain imaging, and QEEG in particular (Kropotov 2009). It makes possible the performing of detailed analysis of the gathered data and delineating independent components of ERPs, which may serve as neuromarkers of schizophrenia (Kropotov 2016). It was stated that the P3b ERPs wave is a significant marker of schizophrenia, since it is significantly lowered in the schizophrenic patients both treated and untreated (Harrison, Weinberger 2005; Boutros et al. 2009; Seeman et al. 2014;). Hence, component P3 is considered to be an endophenotype of schizophrenia, therefore its presence is also believed to be a predictor of psychosis (Pąchalska, Kaczmarek, Kropotov 2014). At the same time, neurophysiological studies make planning the course of a therapeutic procedure possible, e.g. neurofeedback. Moreover, neurofeedback is a very effective form of treatment along with pharmacological treatment (Kropotov 2009) and psychotherapy (Kolb, Whishaw 2007) or neurotherapy (Pąchalska, Kaczmarek, Kropotov 2014; Kropotov 2016).

The aim of the study was to evaluate the effectiveness of an individually tailored neurofeedback protocol for the reduction of anxiety which was diagnosed in the patient with suspected schizophrenia and TIA. The neuromarkers in QEEG and ERPs were utilized in the construction of the protocol and evaluation of the effectiveness of the neurofeedback.

CASE STUDY

A 54-year-old patient was treated with antipsychotic drugs for over 30 years after being diagnosed with schizophrenia at the age of 21. It is worth pointing out that he was a type of misantrope starting with adolescence and he used to withdraw from social contacts. Most pronounced was considerable slowness, especially pronounced in his verbal expressions. Yet, his social functioning was fairly good and he was able to finish his education. Unfortunately, his slowness turned into such a level of intensification of dysfluency of speech that it was misdiagnosed as having mutism within the course of time. Therefore, his parents decided to look for help in medical institutions. A psychiatrist diagnosed schizophrenia and the patient was put in the mental illness hospital. He was given psychotic drugs, which produced hallucinations.

After being discharged from the hospital the patient started to work as a vocational therapist, and was leading courses of art therapy. He was very efficient as an art therapist, because his slowness, especially in speech, made his contact with aphasic patients easier. They were able to understand what they are supposed to do, since they were given much more time for understanding. In order to improve his artistic skills the patient undertook studies at the Academy of Fine Arts, and finished them with success.

The real cause of disorders observed in our patient was explained due to a Transient Ischemic Attack (TIA) of the left brain hemisphere at the age of 54. This TIA was manifested with mild anomia, intensification in the severity of headaches, muscular tension, difficulties with sleeping. Those symptoms were aggravated during first hour and had been completely resolved by 24 hours from their onset.

The data gained during functional brain examination [QEEG, ERPs, sLoreta tomography of the brain] points to attention disorders, impulsivity, and difficulties in right reactions to GO/NOGO stimuli, which is characteristic for an anxiety disorder, and might have increased after the TIA.

It should be stressed, however, that we did not find any interruption in the blood flow to the brain which can result in a stroke or TIA. The data obtained from the carotid Doppler Ultrasoud examination (DUS), a very useful diagnostic tool for assessing carotid artery blood flow, did not show any signs of pathology of those vessls (e.g., thrombosis, arteriosclerotic plaque, post-inflamatory narrowing), so the blood inflow to the brain on both sides was normal. Despite the fact that a large percentage of strokes are due to embolisation from the heart in the course of atrial fibrillation or from the post-infarction scars, but ECG excluded such a disorder at the time of examination. This fact does not preclude a single occurrence of atrial fibrillation with microembolisation.

NEUROPHYSIOLOGICAL RESULTS

Quantitative electroencelography EEG (QEEG)

A 5 sec. EEG fragment recorded in the current source density montage during eyes closed condition in the first recording is presented in Fig. 1. One can see

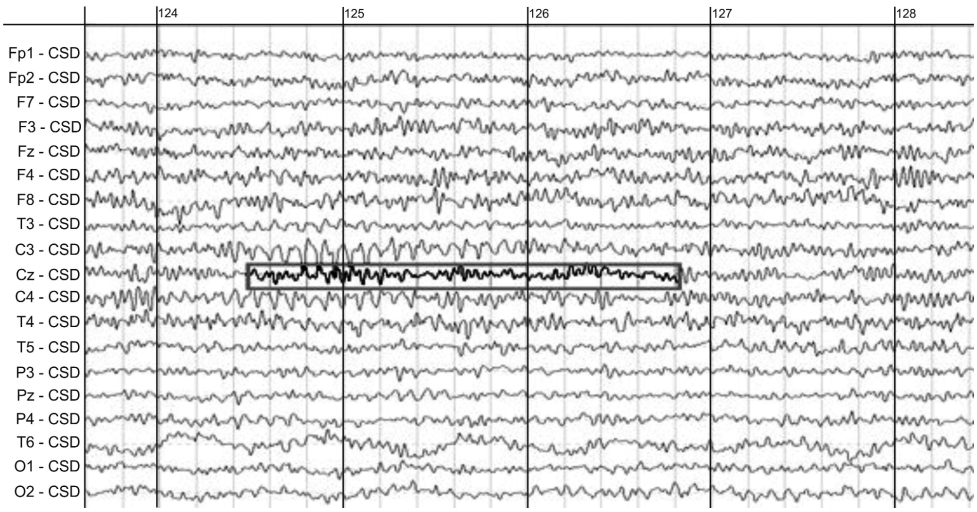

Fig. 1. A 5 sec. EEG fragment in the current source density montage during eyes closed condition for the subject under study. Horizontal line at the top represents seconds of recording. The black box shows central beta activity which is present simultaneously with mu-rhythms at C3 and C4

persistent beta rhythm at the Cz point, which is not suppressed during a burst of mu-rhythms.

Fig. 2 demonstrates EEG spectra for the task condition during the first and second recordings in comparison to the averaged EEG spectra for the group of healthy controls (N=80). Note the excess of central beta rhythms in the first recording and the normalization of this activity in the second recording.

Neurofeedback protocol

On the basis of the QEEG assessment during the first recording a neurofeedback protocol was suggested. The protocol included suppression of high beta activity (20-30 Hz) at Cz point. Fig. 2 demonstrates also a decrease of the beta activity after 20 sessions of neurofeedback.

Event related potentials (ERPs)

Figure 3 demonstrates ERP dynamics before and after 20 neurofeedback sessions. It should be noted here that we were testing the working hypothesis of schizophrenia in this patient. According to the HBI (Human Brain Indexes) studies the representative group (N=100) of schizophrenic patients is characterized by a substantial decrease of the NOGO-GO ERP difference wave recorded in the cued GO/NOGO task. The size of this decrease was about 1.0 suggesting a high level of sensitivity and specificity. No decrease of the NOGO-GO ERP difference wave was observed in this patient (Fig. 3). The 20 sessions of neurofeedback did not change this parameter (Fig. 3).

Neuropsychological assessment

In the neuropsychological examination with the use of standard tests of brain work assessment the following disturbances were noted:

- In examination 1:
  1. attention deficits (– III; WMS-III =9/24 attention items,

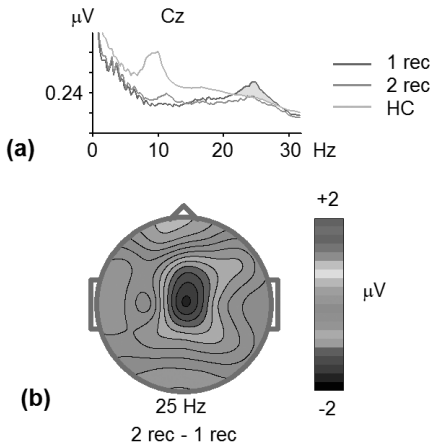

Fig. 2. Excess of the central beta activity in the subject during the first recording and its decrease after 20 sessions of neurofeedback. (a) EEG amplitude spectra for the subject during the cued GO/NOGO task in the first and second recordings (1 rec and 2 rec) in comparison to the spectra computed for a large group (N=80) of healthy subjects (HC) of the corresponding age, that is 54-years old men. (b) the difference (2 rec – 1 rec) amplitude map at 25 Hz

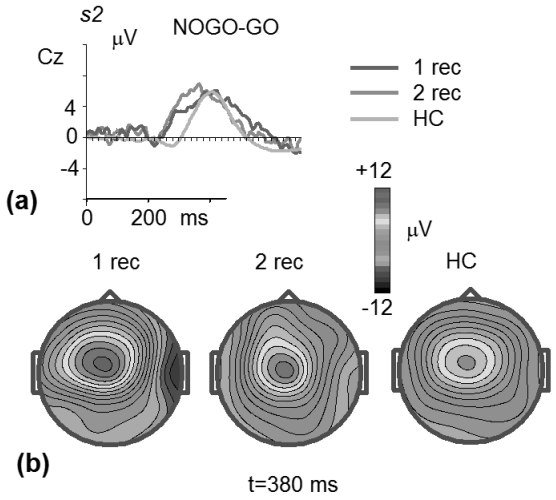

Fig. 3. No signs of abnormality in ERPs in the GO/NOGO task and no changes after 20 sessions of neurofeedback. (a) The NOGO/GO difference ERP waves before (1 rec) and after (2 rec) 20 sessions of neurofeedback in comparison to the corresponding ERP difference wave computed for the group of healthy controls of the corresponding age. (b) Maps of the difference waves at 380 ms for the 1 and 2 recordings in comparison to the healthy control group

2. memory deficits (Wechsler Memory Scale – III; WMS-III = 6/24 memory items),
3. mild disorders in naming of a amnestic aphasia type (Boston Naming Test; BNT = 48/60 correct names).

- In examination 2:
  4. attention deficits (– III; WMS-III =23/24 attention items,
  5. memory deficits (Wechsler Memory Scale – III; WMS-III = 22/24 memory items),
  6. mild disorders in naming of an amnestic aphasia type (Boston Naming Test; BNT = 59/60 correct names).

A considerable improvement in all examined parameters can be noted in the second examination. At the same time, observation of the patient revealed that he did not initiate any spontaneous conversation. He reacts only to the questions put by an examiner, and it takes him some time, too. Yet, he did give correct answers in almost all tests during the second examination, and no signs of disorders were noted.

It was assumed that the patient's difficulties may result from speech disfluency. Therefore, the patient was given the Thurston Test of Speech Fluency, which showed:

In examination 1:

1. 6 words out of 24 for a norm
2. In examination 2:
3. 10 words out of 24 for a norm

The small improvement of results in the second examination shows that the dysfluency of speech is very persistent in\the patient. It allows one to draw the conclusion that speech dysfluency was the main reason for conducting the former diagnosis of mutism.

Anxiety was measured on the adapted 100-millimeter Visual Analog Anxiety Scale, and a Sad-Happy Face Scale (Fig. 4).

We found, that in the first examination he marked 98 mm which is very high level of anxiety, and in the second examination 13 mm, which represents no anxiety at all. This is large improvement in the results, which might be connected with the neurofeedback treatment.

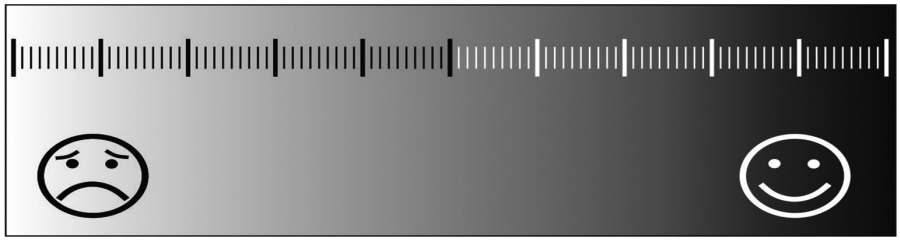

Fig. 4. The adapted 100-millimeter Visual Analog Anxiety Scale, and a Sad-Happy Face Scale: 0 millimetres on the scale represented a lack of anxiety, while 100 millimetres on the scale – severe anxiety. Source: own study

DISCUSSION

It is worth considering the reasons for the misdiagnosing of schizophrenia. The main reason was the traditional approach to the diagnosis of schizophrenia in which the most conventionally were considered, first in terms of the positive and negative symptoms separately and then in terms of the relationship between them at different cross-sectional levels (Wing 1990). The various ways in which schizophrenia can be formulated as a category, and the overlap with other symptoms (Brown i Pąchalska 2003), can then be identified and used with an alternative hypothesis concerning causes, pathology, treatment and course. In addition, misdiagnosed schizophrenia might be due to a symptoms profile similar to the axial symptoms of schizophrenia, such as mutism, emotional disorders recalling affect blunting as well as vegetative symptoms. It turned out, however, that the above mentioned symptoms resulted mainly from the slowness of cognitive functions (Lisman et al. 2008); de Manzano et al 2010;). It was manifested by the slow performing of all motor action and by limited verbal expression connected with dysfunctions of speech fluency. Those lead to his withdrawal from verbal contact with his family, which was mistaken for mutism.

Moreover, the patient did not express his feelings, which in combination with the limitation of facial expressions was interpreted as an emotional blunting. That last feature, as learned from the interview, was the familiar feature. Both his mother and his father were aloof persons who considered expressing emotions to be the sign of a lack of culture and low intelligence levels.

The incident of TIA of the left brain hemisphere forced the patient to take part in various diagnostic and therapeutic procedures, including vascular surgeon, to exclude internal carotid artery narrowing by arteriosclerotic plaque and secondary thrombotic embolisation.

A DUS did not show any signs of pathology of the common and internal carotid artery. Even though, a large percentage of strokes are due to embolisation from the heart in the course of atrial fibrillation or from the post-infarction scars, but the ECG excluded such a disorder at the time of the examination. This fact does not preclude a single occurrence of atrial fibrillation with microembolisation.

The stress connected with the illness itself, as well as with the process of diagnosis caused the feeling of disability. In consequence, he was not able to do his job and worried about a possibility to secure a family (wife and three children). He lost his prior feeling of security, and experienced fits of panic, which disabled undertaking any action,. Those increased his motor slowness, and his speech dysfluency in particular.

Neurophysiological examination including the QEEG/ERP assessment of the patient did not find any ERPs neuromarkers of schizophrenia (see: Kropotv 2016) but we observed a neuromarker of anxiety instead. The neuromarker of anxiety is expressed in excessive centrally high beta rhythmicity. A suppression beta protocol of neurofeedback was suggested. Taking into account the opinion of a psychiatrist it was decided to put off antipsychotic drugs and to administer anxiolytics.

The diagnosis was also confirmed by the neuropsychological assessment. It is highly probable that the score of the first examination could have been interpreted as mild anomia. Yet, the observed difficulties might have been the result of the long latency of the patient's utterances. He needed more time to find a given name than it is expected in the Boston Naming Test. Additional confirmation for that hypothesis provide low scores in the Thurston Speech Fluency Test, and their considerable stability.

The QEEG/ERPs assessment after 20 sessions of neurofeedback found a decrease of the central high beta activity without any significant changes in ERPs.

After a period of 3 months the patient had recovered. The values of standard neuropsychological test also normalized to a considerable degree. It is worth pointing out that the patient returned to his work, and he is able to perform his daily activities and to function well in his social environment.

Summarizing, it should be stressed that a 54-year-old patient, with suspected schizophrenia, experienced a TIA of the left brain hemisphere, showed that the diagnosis of psychotic disorders is a very complicated process due to the overlap of symptoms (Pąchalska, Kaczmarek, Kropotov 2014). In consequence, the patient was misdiagnosed with schizophrenia. His behavior provoked the negative reactions of others leading to an enhancement of his difficulties (Pąchalska, Kaczmarek, Kropotov 2014). In accordance with the microgenetic theory of symptom it is the manifestation of a complex process of unfolding sensory, motor, and emotional functions (Brown i Pąchalska 2003; Brown 2005; Frith 2007; Pachalska et al. 2015). This is a reason for many diagnostics problems. The best solution is the delineation of the neuromarkers of individual disorders. Yet, it is a very complex task, and requires performing interdisciplinary studies, in which representatives of all the neurosciences, and not only one, would have to take part. A very important role in proper diagnosis of this case was also performed by the vascular surgeon.

This is one more example of the need to apply new neurotechnologies in the diagnosis of mental disorders, and within the schizophrenia spectrum in particular.

CONCLUSIONS

New diagnostic neurotechnologies administered in the case of the patient treated for schizophrenia for over 20 years have proved to be very useful. Of particular significance was the QEEG recorded during the performing of the tasks that make possible the measurement of ERPs.

In consequence, use of diagnostic tools results in:

- withrawal of earlier diagnosis of schizophrenia, since the neuromarker of schizophrenia was absent,
- revealing of the neuromarker of anxiety.

Applyed neuroterapy (nurofeeback) resulted in :

- a reduction of anxiety symptoms,
- a return to work.

Presented above case study confirms the need for administering new neurotechnologies in the diagnosis of mental disorders with particular emphasis put on the schizophrenia spectrum.

For a patients with cognitive problems the differential diagnosis should include carotid artery stenosis in which the Doppler Ultrasound (DUS) examination is gold standard.

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