EVALUATION OF THE EFFECTIVENESS OF ELECTROENCEPHALOGRAPHIC TRAINING WITH NEUROFEEDBACK (EEG-NFB) FOR A PATIENT WITH DYSEXECUTIVE SYNDROME AFTER NEUROSURGERY OF TWO BRAIN ANEURYSMS DETECTED AFTER COVID-19 DISEASE

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SUMMARY
The purpose of this study is to evaluate the effectiveness of functional neuromarker-based electroencephalographic training with neurofeedback (EEG-NFB) for a patient with dysexecutive syndrome following neurosurgical operation of two brain aneurysms of the left and right middle cerebral artery (MCA) detected after COVID-19 disease. A right-handed, 56-years-old, not vaccinated, patient, became infected with SARS-CoV-2 and contracted COVID-19 with the manifestation of respiratory symptoms, high fever, dyspnea and low saturation of 79% SaO2. She was hospitalized at the Infectious Disease Unit, where a positive RT PCR test for COVID-19 was confirmed. The acute phase of COVID-19, during which oxygen therapy was administered, lasted two weeks and was complicated by brain fog and transient hypertension (175/100). There were no signs of focal damage to the central nervous system. She was discharged home in a good general and neurological condition. After returning home, the patient was unable to cope with daily functioning, as she said her brain fog continued to persist, manifesting itself as executive dysfunction. Eight weeks after the infection, the patient’s neuropsychiatric condition worsened. On CT and MRI examination of the cerebral vessels, she was diagnosed with the presence of two aneurysms located on the left and right middle cerebral arteries (MCA). She was operated on at the Department of Neurosurgery and Neurotraumatology, where a pterional craniotomy and clipping of both brain aneurysms was performed. The Yasargil titanium clip was placed on the aneurysm neck. During the surgery procedures, performed two months apart, there were no signs of a history of subarachnoid haemorrhage and the post-operative period was uneventful, except for a drooping right-eye eyelid (after the second surgery) with a tendency to improve. Each time, the patient was mobilized and walked independently and was discharged home in a good general condition, with no neurological symptoms, except for executive dysfunction. Approximately five months after the SARS-CoV-2 infection (four weeks after the second surgery), her executive dysfunction worsened. Neuropsychological testing using Mindstreams™ Interaction Computer Tests revealed moderate Dysexecutive Syndrome (DES), while neurophysiological testing using qEEGs, ERPs and sLORETA tomography, a functional neuromarker of frontotemporal area dysfunction. The EEG pattern was characterized by excessive, slow (about 6 Hz) activity in frontotemporal areas, which indicated the progressive loss of cognitive control over time. The patient was offered an electroencephalographic training protocol with neurofeedback (EEG-NFB) based on the detected functional neuromarker, which reduced DES. The improvement achieved during therapy was statistically significant [compared to the normative database (Human Brain Index, HBI)]. In effect, the patient’s quality of life improved, as she herself pointed out. Her symptoms of brain fog and DES disappeared and she returned to her previous work as a waitress. The Human Brain Index (HBI) methodology can be successfully used in the neuro-diagnosis and implementation of individualized electroencephalographic training with neurofeedback (EEG-NFT) for patients with executive dysfunction after contracting longCOVID.

Key words: brain fog, cerebral aneurysm clipping, executive dysfunction, HBI methodology
INTRODUCTION

Gaining knowledge about the nature of SARS-CoV-2 coronavirus infection and its short- and long-term consequences is still ongoing (Morga et al., 2023). This disease was first observed in the city of Wuhan in China’s Hubei province in early December 2019 and was announced to the world by China’s WHO office on December 31, 2019. Its causative agent, the SARS-CoV-2 coronavirus, was identified on January 7, 2020. COVID-19 is characterized by a multidimensionality (multiplicity and complexity) of symptoms, ones which continue to surprise (Pąchalska 2022; Li et al. 2023).

The health problems of patients who have become infected with SARS-CoV-2 and contract COVID-19 or NeuroCOVID-19 are discussed in many scientific papers (Greenhalgh et al. 2020; Huang et al. 2020; Aknin 2021; MacQueen & MacQueen 2021; Pąchalska 2022; Morga et al. 2023). Most infected patients fully recover within a few weeks but recent studies suggest that many symptoms do not fully resolve. Studied found that approximately 10-20% of patients had not fully recovered 3 weeks after the illness, while 1-3% complained of malaise after 12 weeks. However, multicenter surveys suggest higher percentage (Huang et al. 2020; Rymer 2021).

The UK’s National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), and the Royal College of General Practitioners (RCGP) proposed the first time clinical definitions for initial COVID-19 and longCOVID in October 30, 2020:

1. **acute COVID-19** – complaints and symptoms of COVID-19 lasting up to 4 weeks;
2. **long COVID-19** – complaints and symptoms of COVID-19 lasting 4 to 12 weeks;
3. **post-COVID-19 syndrome** – complaints and symptoms that develop during or after COVID-19 compatible infection and last >12 weeks and are not due to another diagnosis.

Since the beginning of the COVID-19 pandemic outbreak tens of thousands of scientific articles gave insight into the multifaceted (multiple and complex) symptomatology across multiple body systems: including the respiratory, osteoarticular, circulatory and gastrointestinal systems in patients who have experienced COVID-19 (Huang et al 2020; Sadeghi et al 2020; Gorbalenya et al 2020; Fiani et al 2021; Taquet et al 2021), as well as the central nervous system, dubbed NeuroCOVID-19 (Aknin et al 2021; MacQueen & MacQueen 2021; Pąchalska et al 2021).

Fiani et al (2021) divided the disorders found in NeuroCOVID-19 taking into account location of symptoms:

1. **central nervous system** (headache, dizziness, sensory disturbances, ataxia, encephalitis, stroke and seizures);
2. **peripheral nervous system** (skeletal muscle damage, peripheral nerve involvement, including hyposmia and hypogeusia).
These authors also note that in some individuals, neurological symptoms may precede typical respiratory symptoms (see also Helms et al 2020). Aknin et al (2021) after metaanalysis of an extensive literature review divided the neurological symptoms and complications that occur following SARS-CoV-2 infection and COVID-19 survival into:

1. **mild**, which include loss of smell (anosmia), loss of taste (ageusia), latent blinking (heterophila), headache and dizziness, disorientation, among others;
2. **severe** encompassing cognitive impairment, seizures, delirium, psychosis, strokes, etc.

Krasemann et al. (2022) found that NeuroCOVID resulted from dysregulation of the blood-brain barrier in individuals with COVID-19, which created entry route for SARS-CoV-2 in the CNS. Yet it is still unclear why a variety of neurological, neuropsychiatric and neurocognitive problems arise in NeuroCOVID and patients manifest so many different symptoms or syndromes (Almeria et al 2020; Taquet et al 2021; MacQueen & MacQueen 2021; Pachalska 2022; Goldberg et al 2020; Wu et al 2020; Mao et al 2020; Poyiadji et al 2020; Filatov et al 2020; Needham et al 2020; Pachalska et al 2021; Krasemann et al 2022).

NeuroCOVID sequelae also include postcovid brain aneurysms, which have only recently been discovered and described, as well as complications associated with their rupture (SAH) (Morga et al 2023). The aneurysms can occur both during the acute phase and longCOVID-19 (4 to 12 weeks), or post-COVID-19 syndrome, i.e., >12 weeks, but are not due to other other conditions (Morga et al 2023). Although the direct effect of COVID-19 on the formation and rupture of brain aneurysms (aSAH) is still not fully elucidated, an indirect link appears to be inflammatory processes (Dodd et al 2021). The mechanism of aneurysm formation following SARS-CoV-2 infection is partly explained in the subject literature and data on other similar inflammatory conditions in earlier viral diseases (SARS and MERS). The vascular damage found in these cases has illuminated several possible explanations for the changes that may explain the pathogenesis of cerebral aneurysms in COVID-19 (Kraseman 2022). It has been emphasized quite often that COVID-19-induced hypercytokinemia may degrade the integrity of cerebral vessels, which predisposes to the formation, malformation or rupture of brain aneurysms (aSAH). Much information in this regard is provided by reports of patients who developed brain aneurysm or aSAH after COVID-19 infection (Fiani et al 2021). We learn from them that these complications can occur both after a mild course of COVID-19 with pseudomembranous symptoms and after a severe course of pneumonia and acute respiratory distress syndrome (ARDS).

Neurocognitive symptoms, including executive functions, in patients with postcovid brain aneurysms treated with surgery are diverse. They depend of the course of SARS-CoV2 infection (pseudomonal and severe variants), the duration of hospitalization for COVID-19, the type of cerebral aneurysm treatment used (conservative, clipping, intravascular [coiling]), health status at hospital discharge.

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1 COVID-19 can involve persistence, sequelae, and other medical complications that last weeks to months after initial recovery (Lopez-Leon et al. 2021).

In relation to other cognitive processes in the brain, executive functions are on a higher level of processing, but they are not independent of the rest (Pąchalska 2007). The term “executive functions” is an umbrella term comprising a wide range of cognitive processes and behavioral competencies which include verbal reasoning, problem-solving, planning, sequencing, the ability to sustain attention, resistance to interference, utilization of feedback, multitasking, cognitive flexibility, and the ability to deal with novelty (Chan et al 2008). It should be borne in mind that executive functions are collectively referred to as cognitive control (Kolb & Whishaw 2003).

Executive functions enable the person to acquire feedback on her actions and to shape her own behavior in accordance with the situational demands (Busch et al. 2005). They represent a set of processes that are essential for cognitive control of behavior: selecting and effectively monitoring behaviors that facilitate the achievement of selected goals (Stuss & Knight 2013). Pąchalska (2007), based on many years of clinical study of patients with a variety of brain dysfunctions, argues that executive functions include:

1. **basic cognitive processes** such as attentional control, cognitive inhibition, inhibitory control, working memory and cognitive flexibility;

2. **higher-order executive functions**, which require simultaneous use of multiple basic executive functions and include planning and fluid intelligence (e.g., reasoning and problem solving).

Executive function deficits involve a reduction of an ability to self-regulate over time and inability to plan actions and achieve goals [Stuss et al 2000; Ardila et al 2007]. Training self-regulation strategies in brain-damaged patients is a way to improve their inhibitory control skills and cognitive flexibility. Also, these skills allow them to manage their emotional reactions. (Rolls & Grabenhorst 2008) These interventions include teaching how to plan and control the performance of various executive function tasks and how to implement them during training [Pąchalska 2007; 2008].

Dyssexecutive syndrome (DES) is one of the least understood (Godefroy et al 2010; Burgess et al 2017), yet a common sequel of SARS-CoV-2 infection and COVID-19 survival, including postcovid brain aneurysms (Morga et al 2023). The term “dysexecutive syndrome” was coined by Alan Baddeley (Baddeley & Wilson 1988) to describe a common pattern of disturbances in executive functions. DES consists of a group of symptoms (Halligan et al 2003), occurring as a result of a variety of damages to brain structure, including important neuronal circuits that provide monitoring and control of action (Kropotov 2016). DES is quite often associated, though not quite rightly, with frontal lobe dysfunction or pathology (Shallice et al 1989; Ardila et al 2007; Stuss & Knight 2013). Baddeley’s (1998) working memory system and the central executive system are thought to be the hypothesized systems impaired in DES [Wilson et al 1998]. The syndrome was once known as frontal lobe syndrome; however, the term DES is preferred because it emphasizes the functional pattern of deficits (symp-
toms) rather than the syndrome’s location in the frontal lobe, which is often not the only area affected [Wilson et al 1998; Halligan et al 2003; Katz et al 2007]. Individuals with DES have impaired orientation, attention control, planning, abstract thinking, flexibility, and behavioral control (Ardila 2019). The symptoms, which often occur together, we divided by Jurado & Rosselli (2007) into 3 categories:

1. **cognitive**, which primarily refer to dysfunctions in memory, ability to acquire new information, speech and reading with understanding. Deficits in this area cause many problems in making daily life decisions.

2. **emotional**, which refer to difficulties in inhibiting many types of emotions, such as anger, aggression, excitement, sadness or frustration. Higher levels of aggression or anger, are associated with a lack of skills related to behavioral control;

3. **behavioral**: which refer to loss of social skills due to impaired judgment and insight into what others may think, prompting behavioral changes in group situations and failure to comply with social norms. Difficulties with impulse control [Halligan et al 2003] leading to aggression and anger. There may also be perseveration: repetition of thoughts, behaviors or actions after they have occurred [Baxter et al 1989].

Various factors model the nature and depth of this syndrome. Most significant are brain aneurysm formation, the aftermath of a possible aneurysm rupture and the need for neurosurgery. Also, the short- and long-term consequences of SARS-CoV-2 infection and COVID-19 survival are of major importance (Aknin et al 2021). The specific features of DES depend on whether the brain aneurysm is silent or whether bleeding has occurred and urgent neurosurgical intervention has been required. Moreover, they involve the location covered by the bleeding area (e.g., left vs. right cerebral hemisphere, front vs. back of the brain), the aftermath of the bleeding and the side effects of neurosurgical intervention (Morga et al 2023).

Executive dysfunction, including DES, as a consequence of SARS-CoV-2 infection has not received adequate attention to date. Many papers report confusion and attention difficulties [Helms et al 2020; Wu et al 2020; Mao et al 2020; Poyiadji et al 2020] suggesting that this syndrome may be present in these patients. A detailed review of the literature on COVID-19 reveals at least one study of a group of 39 patients of whom 14 of (36%) developed DES [Helms et al 2020], however, encephalopathy is most commonly described [Filatov et al 2020; Needham et al 2020]. Encephalopathy is usually associated with generalized cognitive impairment, which fits into the clinical picture of DES [Sasannejad et al 2019].

It is worth recalling that executive functions are defined as higher-order cognitive processes that enable flexible configuration, regulation and monitoring of goal-directed behavior and thought by controlling lower-level cognitive operations, especially in novel or complex circumstances (Burgess 1997; Best et al 2009; Viviani & Vallesi, 2020). Hence, they play a significant role in human cognition and regulation of action and in daily life (Miyake & Friedman, 2012; Lee et
In the life of a person who suffers from dysexecutive syndrome, there is chaos, lack of planning and of action control, resulting in difficulties in coping with daily life and social dependence (Pąchalska 2022). There is a surprisingly small number of reports on programs that would offer help to these patients, especially using EEG-NFB (Enriquez-Geppert, Huster and Herrmann, 2013). Whereas electroencephalographic (EEG) training with neurofeedback (NFB) is a promising technique that supports individuals in learning how to modulate brain activity to achieve improvements in cognitive function and achieve cognitive and behavioral control. A review of articles provides promising evidence for the efficacy of EEG-NFT in improving executive function in healthy adults (Viviani & Vallesi 2021) and individuals with impaired executive function following a variety of brain injuries (Kropotov 2016) including those who were infected with SARS-CoV-2 and experienced COVID-19 (Needham et al 2020) and NeuroCOVID, longCOVID and postCOVID syndrome (Sasannejad et al 2019; Pąchalska 2022).

CASE STUDY

A right-handed, 56-year-old, not vaccinated, patient, previously untreated for any chronic diseases, with no genetic burden and no addictions, became infected with SARS-CoV-2 and contracted COVID-19 with manifestation of respiratory symptoms (sore throat, dry cough) and a high fever of 39.8°C. On the eighth day after infection, new symptoms (anorexia, weakness, locomotor difficulties and high lethargy) as well as shortness of breath and low saturation of 79% SaO2 were manifest. The patient was hospitalized in the Infectious Disease Unit, where a positive RT PCR test for COVID-19 was confirmed. The acute phase of COVID-19, during which oxygen therapy was administered, lasted two weeks. During treatment, there was transient hypertension (100/175), disorientation described as brain fog manifested by impaired attention, working memory, difficulties in planning, abstracting, behavioral control and orientation in time and space. There were no focal symptoms or cranial nerve deficits. Discharged home in good general condition, however, she continued to have brain fog manifested by cognitive impairment.

Eight weeks post infection, the patient’s condition worsened (ongoing symptomatic COVID-19). Laboratory tests showed no leukocytosis, the platelet count was 291 10e9/L. Blood electrolytes and coagulation tests were within normal limits except for D-dimers, which were elevated to 1.15 mg/L FEU. Neurological examination revealed motor instability, general weakness, disorientation and “brain fog” manifested by impaired self-awareness (the patient didn’t know who she was or what her name was), cognitive impairment (she didn’t recognize her own car or anything around her) and impaired executive functions (mainly difficulties in daily functioning). AngioCT of the cerebral vessels was performed to determine the cause of the severe headaches and dizziness, and the patient was found to have two aneurysms located in the left and right middle cerebral arteries. Her history revealed that she had no family history of aneurysms (her father had been operated on three years ago for critical carotid artery stenosis).
She also had no significant risk factors except, short-term hypertension, which she had developed after COVID-19.

The patient was qualified for emergency neurosurgery at the Department of Neurosurgery and Neurotraumatology at the University Hospital in Krakow. First, the aneurysm of the left middle cerebral artery (LMCA) was excluded from the cerebral circulation (Figure 1). A pterional craniotomy and clipping of brain aneurysm was performed. The Yasargil titanium clip was placed on the aneurysm neck. At the time of surgery, there were no signs of a history of subarachnoid hemorrhage. The post-operative period was uneventful. The patient was discharged home in good general and neurological condition on the 5th day after surgery.

After 2 months, the patient was admitted for a second neurosurgery at the Department of Neurosurgery and Neurotraumatology at the University Hospital.
in Krakow for clipping of a second brain aneurysm of the right middle cerebral artery (RMCA), which consequently was excluded from the cerebral circulation (Figure 2). A pterional craniotomy was performed on the right side and the brain aneurysm was clipped. At the time of surgery, there were no signs of a history of subarachnoid hemorrhage. The course after surgery was uncomplicated. The patient was mobilized and walked independently, with no neurological deterioration. She was discharged home in good general condition. The post-operative period was uneventful, except for a drooping right-eye eyelid (after the second surgery) with a tendency to improve.

Approximately five months after the SARS-CoV-2 infection (four weeks after the second surgery), the patient’s executive dysfunction intensified, causing difficulties in daily functioning. The patient was referred to the Reintegration and Training Center of the Polish Neuropsychological Society for further diagnosis and therapy.

**NEUROPHYSIOLOGICAL TESTING**

**Procedures of EEG recording and analysis**

EEG was recorded by means of the Mitsar (Mitsar, Ltd.) amplifier from 19 electrodes (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2 sites in the International 10-20 system) with 500 Hz sampling rate in 0.3-70 Hz frequency range in the following conditions: 1) eyes opened (EO) – at least 3 minutes, 2) eyes closed (EC) – at least 3 minutes. The data were stored on the hard disk in the linked ears reference montage and processed offline by means of WinEEG software. The software is based on the 30-years of experience obtained in laboratory work at the Human Brain Institute of the Russian Academy of Sciences (Kropotov 2016). Absolute and relative magnitude spectra and coherences in all conditions were computed and compared with the corresponding parameters from the Human Brain Institute (HBI) normative database. The normative database includes the data of about 1000 healthy people corresponding to the patient age (see: Kropotov 2016).

**SEARCH FOR PAROXYSMS**

Visual inspection of raw EEG was conducted in order to search for paroxysmal patterns that pop out of the background EEG. Besides the visual inspection an automated spike detection was performed. The method of automated spike detection is based on temporal parameters of spikes as well as on the spatial location of the corresponding spike dipole (Ktonas 1987). The amplitude-temporal parameters have been defined on the basis of comparison spike detection by the program and by experienced experts on the data base of more than 500 EEG recordings in epileptic patients. There are three characteristicsthat define a spike or a sharp wave in EEG: the paroxysmal character, high degree of sharpness, and short duration (Fig. 3).
The relative residual energy for dipole approximation of the detected spike is chosen less than 0.2. For this patient the automatic spike detection was performed on EEG in the common average montage for both eyes open and eyes closed conditions. No statistically and clinically significant spikes were observed.

**SPECTRA**

Deviations from the norm in EEG spectra calculated for 20 minutes of the GO/NOGO task before treatment are shown in Fig. 3 (on the left-hand side). As can be noted, the EEG pattern is characterized by excessive slow (about 6 Hz) activity in the frontotemporal areas, which increased significantly in the process of therapy. The resulting difference in this activity before and after therapy is statistically significant (Fig. 4, bottom).

*At the top:* the difference between the EEG spectrum in the pre-treatment state and the average norm.
A. map of the difference at 6.1 Hz.
B. Spectra difference with confidence levels under the graph (small vertical bar - P<0.05, medium vertical bar - P<0.01, Large vertical bar - P<0.001).

*Bottom:* the difference between EEG spectra after and before treatment.
C. map of the difference at 6.1 Hz.
D. difference in spectra with confidence levels below (small vertical bar - p<0.05, medium vertical strip - p<0.01, large vertical strip - p<0.001).

**EVENT RELATED POTENTIALS (ERPS)**

The results of the ERPs changes are presented in Figure 5. Dramatic changes in NOGO ERPs can be seen after the treatment with an increase in the NOGO potential over the Cz electrode and a decrease over the left temporal areas.

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2 The parameters are taken from the paper written by Ktonas (1987).
A. ERPs for GO condition calculated in Pz for pre (red line) and post (green line) treatment and ERPs difference wave post-pre treatment (blue line) with difference confidence levels below (small vertical bar – p<0.05, medium vertical bar – p<0.01, large vertical bar – p<0.001).

B. Difference wave map plotted at 300 ms (peak GO P3 wave latency).

C. ERPs for the NOGO condition calculated in Cz for the pre (red) and post (green) conditions and the ERPs difference waveform (post-pre) with confidence levels of the difference below (small vertical bar – p<0.05, medium vertical bar – p<0.01, large vertical bar – p<0.001).

D. Difference waveform map plotted at 400 ms (peak delay of NOGO P3 wave form).

**ELECTROENCEPHALOGRAPHIC TRAINING WITH NEUROFEEDBACK (EEG-NFT)**

The patient was offered an electroencephalographic training with neurofeedback (EEG-NFT) protocol modified to her needs. In its development, in accordance with world standards in this area, data obtained from QEEG and ERPs, including a functional neuromarker of cognitive control impairment, were used [cf. Kropotov 2016]. The goal of the treatment was to activate the frontal lobes. Electrodes were placed on Fz and Cz, and bipolar training of relative beta UP was introduced. Neurofeedback parameter = \((13-21 \text{ Hz})/(4-12 \text{ Hz})\). The patient was placed in front of a computer screen and asked to relax and watch therapy videos. When inappropriate brain work decreased slightly and appropriate brain work increased the image was clear and no objects obstructed the screen (e.g., people at the bottom of the screen), and the pleasant sound of music could also be heard [cf. Pąchalska, Kaczmarek & Kropotov 2021].
The training procedure was modified: a number of therapy videos were shown during one therapy meeting, adjusted to the patient’s capabilities (minimum 1 – maximum 5 videos). The videos used cognitive techniques aimed at improving cognitive control. A similar procedure, but without the combination with EEG-NBF, was previously used in behavioral training aimed at improving cognitive control in people awakened from long-term coma after brain injury with dysexecutive syndrome (cf. Pąchalska 2008).

**NEUROPSYCHOLOGICAL EXAMINATION**

We used the Mindstreams™ Interactive Computerized Tests to assess dysexecutive syndrome (Pąchalska et al 2010). These tests are standardized and count scores automatically without error. Also, they are easy to use (anyone can use such a test), quick and economical, have an accurate measure of reaction time, moreover, standards can be easily updated, and can be easily reapplied (follow up). In the patient under study, we assessed six scales of cognitive domains: attention, memory, visual-spatial functions, verbal functions, mobility and executive functions. The patient’s results for better illustration are shown in Table 1, and Fig. 6.

It can be noted that in exam. I (before therapy), the patient was found to have disorders that manifested themselves in all the cognitive domains examined: the

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**Table 1. Patient scores on six cognitive domain, including executive functions scales in Exam. I and II**

<table>
<thead>
<tr>
<th>Cognitive domain</th>
<th>Exam 1</th>
<th>Exam 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>47</td>
<td>89</td>
</tr>
<tr>
<td>Memory</td>
<td>51</td>
<td>91</td>
</tr>
<tr>
<td>Visual-spatial functions</td>
<td>67</td>
<td>91</td>
</tr>
<tr>
<td>Verbal functions</td>
<td>94</td>
<td>99</td>
</tr>
<tr>
<td>Mobility</td>
<td>91</td>
<td>99</td>
</tr>
<tr>
<td>Executive functions</td>
<td>42</td>
<td>94</td>
</tr>
</tbody>
</table>

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lowest score (42/100 points) was obtained by the patient in the area of executive functions which means the presence of increased dysexecutive syndrome (DES). There were also disorders of attention (47/100 points) and working memory (51/100 points). These scores improved in Exam. II (after therapy): large and statistically significant improvements in all domains tested, with the highest gains in executive functions (94/100 points).

In conclusion, it is worth noting that the proposed form of neurofeedback proved effective in reducing DES. The patient feels well, is happy that she no longer has “brain fog,” and performs everyday duties and tasks. She returned to her work as a waitress, with which she coped splendidly, and she functions well in society. Moreover, she again was enjoying everyday pleasures again.

DISCUSSION

Ongoing long-term independent epidemiological and clinical studies of the sequelae of SARS-CoV-2 infection and COVID-19 survivors have shown that the recovery process is not always easy. It is caused by a variety of both short-term and and long-term physiological, neurological and psychiatric deficits generally known as longCOVID or post-COVID syndrome [Sasannejad et al 2019; Wu et al 2020; Mao et al 2020; Stefanou et al 2022; Pąchalska 2022]. The multitude of symptoms that can occur in the acute phase of COVID-19, longCOVID and post-COVID syndrome require multispecialty diagnosis, especially if neurological, neurocognitive and psychiatric complications are present (Aknin et al 2021). One such complication is the formation and rupture of brain aneurysms, which require appropriate conservative treatment or neurosurgical intervention (Morga et al 2023).
What is the mechanism for the onset, long-term persistence and even aggravation of DES after SARS-CoV-2 infection in time?

In the patient we studied the occurrence of DES is significantly related to SARS-CoV-2 infection, COVID-19 and NeuroCOVID experience. This is supported by the fact that while still in hospital and immediately after leaving hospital, the patient complained of brain fog and difficulties in daily functioning. The worsening of these symptoms over time at 8 weeks and later at about 5 months after infection) suggests the development of long-COVID-19 in which complaints and symptoms develop during or after viral infection and last >12 weeks. This is consistent with studies by other authors, who report that patients with DES cannot control many cognitive processes, such as attention, working memory and social motivation (Ardila 2019), which impairs cognitive control and social functioning (Barkley 2012; Pąchalska, Kaczmarek & Kropoyov 2014).

The deterioration of DES symptoms four weeks after surgery is difficult to associate with neurosurgical intervention (clipping), although it may have caused perioperative trauma (Morga et al. 2023). Since cerebral aneurysm clipping is a type of microsurgery in which a metal surgical clip is used to close a brain aneurysm, it is still likely to destabilize the brain. The surgeon makes a small hole in the skull (craniotomy) to get to the brain and has to spread the brain tissues to dissect the brain vessel and brain aneurysm. He uses an operating microscope and micro-tools to perform this procedure, so there may be compression and ischemia of brain tissue, and thus destabilization of neuronal connections located in the frontal areas of the brain (adjacent to the Sylvian fissure). It is worth noting that in our patient it was the frontal areas of both hemispheres of the brain where the aneurysms were located. Accordingly, neurosurgical intervention, in addition to the sequelae of NeuroCOVID-19, may have contributed to a decrease in frontal cortex activity.

It is likely that the overlap of symptoms and complications associated with SARS-CoV-2 infection, COVID-19 survival, NeuroCOVID-19, and neurosurgical interventions (clipping of two aneurysms) caused an inhibitory effect on the executive and emotional systems through long inhibitory connections passing through the striatum. In consequence a weakening of dopaminergic brain activity that underlies the impaired executive system and activity impairment may have occurred. This primarily affects the dominant hemisphere and is reflected in the form of alpha asymmetry in the recording (greater activity on the left side) and by a reduction in ERPs components related to the executive system (Kropotov 2016). It is noteworthy, that no complications occurred in the early postoperative period following the surgical intervention, except for a drooping right eyelid (after the second surgery) with a tendency to improve, which completely disappear over a period of two months.

Unfortunately, there is a lack of studies of those who became infected with SARS-CoV-2, contracted COVID-19, NeuroCOVID-19, and at the same time who developed complications from the formation of two cerebral aneurysms, operated neurosurgically who additionally developed DES. Hence, a discussion
based on data from the subject literature is not possible. A report by Ravnik et al. (2006) describing patients with subarachnoid hemorrhage (SAH) covers similar issues. The study found that neither the site of craniotomy nor the time from the onset of subarachnoid hemorrhage to surgery had a major impact on postoperative cognitive performance. It was expected that patients with left-sided (dominant) craniotomy would perform badly on all neuropsychological tests. It turned out that the patients scored worse on several (rather than all) of the neuropsychological tests employed. Correlations between the time from the onset of subarachnoid hemorrhage to neurosurgery and neuropsychological test scores were not significant ($\rho$ range, -0.42 to 0.66). It suggests that the effect of neurosurgical intervention on DES scores or its individual components included in cognitive control is difficult to evaluate.

Despite growing knowledge on the process of overlapping short- and long-term symptoms of cognitive and emotional disorders in these patients, it is important to emphasize the need for multidimensional differential diagnosis, preferably based on functional neuromarkers. The Human Brain Index (HBI) methodology, as we have shown in this article, can be successfully used in the effective neurodiagnosis and introduction of individualized, functional neuromarker-based neurotherapy (tDCS, TMS or EEG-NFB) for patients with executive function disorders.

**EEG-NFB VS. EXECUTIVE FUNCTION THERAPY**

Since causal treatments for longCOVID-19" are currently unavailable, therapeutic approaches aimed at reducing symptoms in patients with long COVID-19 are proposed. There is also no cure for people with DES, but there are therapies to help them manage their symptoms (Barkley et al 2012). DES can affect many functions in the brain and vary from person to person (Friedman 2016). Because of this diversity of symptoms in DES, it has been suggested that the most effective therapy would involve multiple approaches (Halligan et al 2003). Indeed, it is necessary to improve a number of factors in executive functioning: strengthening self-awareness, goal setting, planning, self-initiation, self-control, self-inhibition, flexibility of action and strategic behavior. Our patient was offered a diagnostic and therapeutic algorithm based on HBI methodology(Kropotov 2016), which makes possible the identification and treat the underlying causes of neurocognitive symptoms that persist after the acute COVID-19. Functional neuromarker based EEG-NFB appropriately structured to the patient’s needs, which was used as a method of therapy, helped her to achieved the goal of treatment, that is reducing DES and minimizing difficulties in her social functioning.

It should be pointed out, that EEG-NFB is considered a new, non-invasive and promising training technique that allows trainees to learn to control and modulate their own brain activity (Angelakis et al, 2007; Doppelmayr & Weber, 2011; Gruzelier 2014; Enriquez-Geppert et al, 2017; Jirayucharoensak et al, 2019). A meta-analysis of multiple research papers by Viviani and Vallesi (2021) provides promising evidence for the effectiveness of EEG-NFB in enhancing executive function.
The EEG-NFB system estimates the state of specific neural parameters during the training process, and the computational interface provides real-time information about the patient’s physiological brain activity (e.g., using video and/or audio signals), requiring the patient to self-regulate neural parameters and providing feedback that indicates whether the training goal has been achieved or not (Corydon-Hammond et al., 2011; Campos da Paz et al., 2018; Enriquez-Geppert et al. 2013; Jirayucharoensak et al., 2019).

However, it is necessary to strictly follow the principles of training in order to achieve this effectiveness. Kropotov (2016) states that EEG-NFB training should be conducted based on the following three principles:

1. putting the dominant hemisphere into the Beta1 state and the non-dominant hemisphere into the SMR state with simultaneous inhibition of Theta and Beta2: this makes it possible to restore balance between the hemispheres and maintain internal homeostasis;
2. using the basic protocols in training, that is: SMR/Theta, SMR/Delta, and Beta1/Delta (we aim to inhibit slow waves: Delta, Theta, Beta2 and to stimulate waves: Alpha, SMR and Beta1).
3. using the relaxation protocol, that is Alpha/Theta wave training: this allows the trainee to enter a state of relaxation.

Different parameters (e.g., frequency and/or amplitude) can be trained in EEG-NFB (Egner & Gruzelier, 2004; Hanslmayr et al., 2005; Zoefel et al., 2011). Electroencephalographic (EEG) oscillations are related to cognitive functions and behavior. Groppe et al (2013), for example, characterized the most common oscillations in the electrocorticogram, providing evidence for their function. They suggested that:

1. alpha wave activity is related to sensory processing and attention;
2. theta wave activity has a general role in cortical processing (e.g., top-down processing);
3. beta wave activity is involved in sensorimotor functions.

The above presented data enable linking different EEG frequencies to different cognitive functions. This is known as frequency-to-function mapping (Fingelkurts & Fingelkurts, 2014). It is also worth mentioning that the theta and beta wave ratio illustrate the degree of activity of a particular brain area. Dynamic modulation of brain activity is possible because a properly trained person knows how to increase frequencies (e.g., their rhythm or amplitude) and stimulate target activities in specific areas of the brain, while inhibiting other target frequencies and inhibiting specific activities of different brain areas (Gruzelier 2014; Campos da Paz et al., 2018). Our patient’s training was conducted by a trained EEG-NFB therapist with a track record of more than 25,000 training sessions, so the patient could successfully learn to model her brain activity through operant conditioning and/or self-perception modification, with possible beneficial effects on behavioral outcomes (Egner & Gruzelier, 2004; Engelbregt et al., 2016).

The training effectiveness is ensured by stimulating games or videos used to promote and inhibit waves containing correctly adapted elements subordinated
to a specific direction of change. The description of the control is based on the range of brainwave frequencies and amplitudes, which are dependent on age and the clinical diagnosis established by the person performing the training. Preliminary tests are used to obtain quantitative EEG (qEEG) performed under open and closed eye conditions (Viviani and Vallesi 2021). In our patient’s, as presented above, we used therapeutic videos containing elements of cognitive training aimed at regaining cognitive control. However, in addition to the qEEG data, an additional factor allowing for proper training, we introduced a functional neuromarker performed not only based on qEEG studies, but also event-related potentials (EEPs) and sLORETA tomography (see also Kropotov 2016).

The cost of using the EEG-NFB technique is low. Hence, it has been the most widely used technique in recent years in the process of modulating brain functions, or in training various cognitive processes (Escolano et al., 2011). Based on the potential role of EEG-NFB in improving cognitive and behavioral functions, the approach is being used not only in the clinical field (cf. Kropotov 2016), but also amongst healthy individuals to increase their behavioral performance and cognitive functioning, defined as “optimal” or “peak performance” (Egner and Gruzelier 2004; Gruzelier, 2014; Vernon, 2005).

The EEG-NFB technique has proven effective in modulating various frequencies associated with various cognitive processes in healthy individuals (Enrique-Geppert et al., 2017; Gruzelier, 2014) and in reducing cognitive and executive dysfunction in individuals with various brain dysfunctions. Many studies have used EEG-NFB as a therapeutic tool in clinical populations suffering from neurological and psychiatric disorders to normalize abnormal electrical oscillatory activity underlying various types of cognitive disorders, such as attention (e.g., Arns et al, 2009; Lofthouse et al, 2012; Berger & Davelaar 2018; Yan et al, 2019), working memory (Wang & Hsieh 2013; Xiong et al 2014; Wei et al 2017), cognitive control (Mahjoory et al 2019) and executive function (Kropotov 2016).

**Why did the patient experience improvement?**

The EEG-NFB training offered to our patient is considered brain wave training with a qEEG assessment. It provides operant conditioning of neural oscillations, in which the brain is trained to gain control over specific EEG parameters through real-time visual or auditory feedback. Desired brain activity is reinforced and undesired activity is inhibited. All cognitive skills, including executive functions, can be coached and improved. The basis of various forms of therapy, including EEG-NFB, is neuroplasticity. The brain is made up of neurons that are interconnected by neuronal networks, and learning occurs by changing the strength of connections, through the process of adding or removing connections, or by adding new cells. Neuroplasticity refers to learning by adding cells, adding or removing connections, and changing the strength of connections associated with the repetition of information in the process of training (Pąchalska, Kaczmarek & Kropotov 2016).
MICROGENETIC MODEL IN THE INTERPRETATION OF THE SYMPTOMS OF THE PATIENT UNDER STUDY

In interpreting the accumulation of disorders in the patient we studied, a very important issue that requires separate analysis is the issue of time (4D dimension) and oscillation (pulsation) of mental states (5D dimension) (Pąchalska 2019). Consideration of the role of time allows to understand the dynamics of the formation of symptoms of executive function disorders. This parameter proved to be particularly important in her neuropsychological studies using Mindstreams™ Interactive Computer Tests (Pąchalska et al 2010) in which dysexecutive syndrome was detected, and in neurophysiological studies using qEEG, ERPs and sLORETA tomography, in which a functional neuromarker of frontotemporal area dysfunction resulting in progressive loss of cognitive control over time was detected. It is noteworthy, that the relationship of time to tasks testing executive functions becomes directly relevant only when cognitive and executive dysfunctions intensify (cf. Pąchalska, Kaczmarek and Kropotov 2014). This regularity is well explained by the microgenetic model depicting temporal temporal parameters of cognition (Figure 7).

We can see our patient’s temporal parameters of cognition also at the sensory level (S1). The study confirmed her dysfunctions related to criterion-related attention deficits (see also Fig. 6, cognitive domains). These problems modify the next stage, which is the transfer of information to memory (S2) and subsequent recall. An empirical example of such problems was demonstrated in ongoing studies by significant dysfunctions in people with executive function disorders, which occurred in isolated and co-occurring memory and retrieval material after a single exposure (Pąchalska, Kaczmarek and Kropotov 2014). Microgenetically, these disorders are associated with dysfunction of the pre-attentive buffer encoding information into working memory and recalling information from different...
types of memory (cf. Brown and Pąchalska 2003). Another critical moment is the action formation stage (S3). In the patient we studied, impulsive behavior was characteristic at this stage, associated with the tendency to give quick and thoughtless answers to the questions asked (see also Lipowska 2011). Although in this paper we presented only briefly the role of emotions in the clinical picture of the patient, they are very important in the proper course of executive functions and are confirmed by many empirical studies (cf. Pąchalska, Kaczmarek and Bednarek 2020). It is highly probable that the negative emotions felt by her in connection with the course of the entire disease and neurosurgical operation could have influenced DES. The next step is performance monitoring (S4). Problems in this area are particularly clearly highlighted in the neuropsychological concept of Barkley (2006). In the patient studied, they were particularly visible in tasks related to interference in both visual and auditory material, which caused her to develop disorders in the domain of executive functions (cf. Fig. 7, cognitive domains). The last stage in the microgenetic model, explaining the issues of the relationship between time (4D dimension) and oscillation (pulsation) of mental states (5D dimension) with executive functions, the ability to correct functioning under the influence of previous experience, is changing the operating mode (S5).

Only healthy brain might have appropriate activity of the motor and somatosensory cortex and properly organized afferents and efferents connections (which makes possible of input of sensory information, and output to other parts of brain) as well as integrative functions (see: Fig. 8) which can ensure an appropriate level of executive functioning (Pąchalska 2007; Kropotov 2009; Burgess et al 2017).

It is worth to remember that there are large individual differences in the activity of the brain, the motor and somatosensory dysfunctions, and consequently the organization of executive functions (Pąchalska 2007), executive dysfunctions

![Fig. 8. Activity in the motor and somatosensory cortex](source: elaboration of M. Pachalska)
(Friedman 2016), as well as after the process of different therapeutic approaches (Pałchalska 2008). From the above it follows that the microgenetic model of symptom formation perfectly explains the widespread making of the same mistakes by people with executive dysfunction, both on the cognitive and social level. This model also reflects the specificity of DES disorders in the patient, who has excessively slow (about 6 Hz) activity in the frontotemporal areas, lost integrative functions of the brain, and performs the tasks worse (lack of transfer from thinking to acting), as well as her test results obtained after EEG-NFB.

While searching for the mechanism, it should be emphasized that the formation of the DES symptom and the intensification of its individual components over time may be a bridge linking the symptoms of longCOVID with symptoms that may have been associated with two neurosurgical operations, or other factors related to the patient’s disease. The microgenetic model of symptom formation also explains the improvement achieved by the patient in the process of therapy using EEG-NFB. Better performance of tasks is ensured by normalization of activity in the frontotemporal cortex maintaining an appropriate level of attention and working memory, which means that executive dysfunctions disappear and the patient’s brain functions in a manner similar to that of a healthy person (Kropotov 2016).

It is worth mentioning that the examined patient showed an anti-vaccine attitude, which could have some impact on the course of the disease and the results obtained, especially in terms of executive functions. Executive functions are related, inter alia, to the ability to make risky decisions. A recent study by Roshchina et al. (2022) found that individuals’ risk attitudes predicted their intention to be vaccinated, and risk-favoring was positively associated with anti-COVID-19. In addition, the same study specified that people who are hesitant to the vaccine have high risk-favoring scores; in contrast, people who agree to be vaccinated show risk-averse attitudes. The results of these studies may explain the attitude of risk favoritism by our patient, because despite the fact that she did not get vaccinated and was seriously ill after the end of therapy and recovery, she returned to work as a waitress. This profession, as we know, is associated with a large number of social contacts and, therefore, the risk of getting sick again. However, we cannot say for sure, as other studies have shown that the decision-making process about vaccination is an attitude that can be influenced by various factors (MacDonald et al., 2015; Demirci et al. 2023).

**SUMING UP**

The case of a 56-year-old patient who contracted SARS-CoV-2 and contracted COVID-19 and NeuroCOVID-19 – the course of the disease, its consequences and complications, and the treatment applied – are instructive because she suffered from both longCOVID-19 and two aneurysms treated surgically. It posed both a diagnostic and therapeutic challenge because not all aspects of her illness were fully explainable and understandable.
The most important fact, however, is the patient’s recovery, which was possible primarily thanks to properly conducted diagnosis of SARS-CoV-2 infection and its consequences, neurosurgical intervention, monitoring after neurosurgery, which allowed detecting DES and setting goals and specific therapy methods, using the EEG-NFB developed for her needs. The restoration of the patient’s premorbid social activity was possible due to the use of control of cognitive disorders based on a functional neuromarker in EEG-NFB protocols. The issues presented in this article turned out to be broad, but they provided valuable clues on this patient difficulties (including complex and social activities), which should be taken into account in order to help such patients recover and reduce post-disease symptoms. It shows the need of conducting further research directed at providing further research evaluation of the potential of EEG-NFB as a method of treatment.

CONCLUSION

The Human Brain Index (HBI) methodology can be successfully used in neurodiagnosis and the introduction of individualized electroencephalographic training with neurofeedback (EEG-NFT) for patients with executive dysfunction and related difficulties in social functioning.

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