SUMMARY

Early evidence described by a number of scholars worldwide suggests that neu-roCOVID-19 has both mild [e.g. loss of smell (anosmia), loss of taste (ageusia), neurological tics (heterophilia), visual disturbances, headaches, dizziness, disorientation] and more severe sequelae (e.g. cognitive impairment, seizures, delirium, psychosis, strokes). Long-term neurological problems or neurological deficits may also occur. The aim of this study was to describe the examination and neurotherapy of a boy following SARS-CoV-2 infection and NeuroCOVID-19 in whom neurological tics and motor automatisms as well as cognitive impairment, particularly attention deficit disorder, developed as a consequence.

We present a boy K.S., 7 years old, without any neurodevelopmental disorders, following a SARS-CoV-2 infection in May 2021 and the contraction of neuroCOVID-19 confirmed by a genetic test for the quantitative detection of neutralising antibodies (responsible for immunity) in the IgG class against SARS-CoV-2. The boy had relatively mild pseudomonal symptoms of the illness: temperature 38.5, runny nose, cough, muscle aches, headaches and general weakness. He was treated symptomatically and recovered after 2 weeks. Two months later, at the beginning of July 2021, neurological tics consisting of an upward turning of the eyeballs to the left appeared. These tics intensified in August 2021 and were accompanied by motor automatisms consisting of the left hand stiffening in salute-like position, while at the same time there was an inclination of the head to the left. In September 2021, after exertion in the swimming pool, an epileptic seizure occurred which caused the boy to start drowning. In the days that followed the above described tics and motor automatisms increased. He also developed sleep disorders, which consisted of him waking up several times during the night, during which time neurological tics and motor automatisms also appeared. Gradually, cognitive dysfunctions, especially attention deficits and behavioural changes, joined in, making it impossible for the boy to function independently at school and in many situations of daily life. Neurophysiological examination: qEEG, ERPs and sLORETA tomography performed on 11.09.2021 using automatic seizure activity detection software showed the presence of the neuromarker benign partial rolandic epilepsy (BPERS) and neurocognitive disturbances resembling the symptoms of attention deficit hyperactivity disorder (ADHD), compared with the neuromarkers of children with this condition (n=100) from the normative database of the Human Brain Index (HBI) in Switzerland. Detection of the neuromarker BPERS was helpful in selecting an individualised neurostimulation protocol. The patient participated in 20 neurofeedback sessions using (1) SMR reinforcement, theta inhibition; (2) theta inhibition, B1 reinforcement (15-18 Hz); (3) qEEG-guided neurofeedback. Neurostimulation with neurofeedback was conducted twice a week, for 15-20 minutes gradually increasing to 30-40 minutes per session. The patient also received individual goal-directed psychotherapy. After successive sessions of neurofeedback, a gradual reduction neurological symptoms was observed. By the end of neurotherapy, neurological tics, motor automatisms, neurocognitive disorders and behavioural disturbances had completely disappeared. The patient functions well in school and achieves very good results. HBI methodology was helpful in finding functional neuromarkers of benign partial Rolandic epilepsy and disturbed cognitive control. Therefore, it was possible to offer more effective neurorehabilitation of the disorders, which contribute to a better quality of life for the patient.

Key words: rolandic epilepsy, neurological tics, qEEG, ERPs, sLORETA
INTRODUCTION

Coronavirus (SARS-CoV-2), since the first confirmed case in Wuhan, China on December 31, 2019, has spread quickly throughout the world infecting 378 mln people, with more than 5.6 million child cases, as of the beginning of January 2022, and now constitutes a pandemic of note. Since this first detection, research has indicated that people contracting the virus may suffer neurological and mental disorders and deficits, in addition to the respiratory and other organ challenges caused by COVID-19 (Chen 2020; Pachalska et al. 2021). Specifically, early evidence suggests that COVID-19 has both mild (e.g., loss of smell (anosmia), loss of taste (ageusia), latent blinks (heterophila), headaches, dizziness, confusion) and more severe outcomes (e.g., cognitive impairments, seizures, delirium, psychosis, strokes). Longer-term neurological challenges or damage may also occur (Nikbakht et al. 2020; Aknin et al. 2021). If neurological symptoms occur following SARS-CoV-2 infection scholars speak of contracting NeuroCovid-19 (MacQueen & MacQueen 2021; Pachalska et al. 2021). It was observed that while children are as likely to contract COVID-19 as adults, they are less likely to become severely ill. Up to 50% of children and adolescents might have COVID-19 with no symptoms whatsoever.¹

What is the mechanism of neurological disorders, with particular emphasis on epilepsy after contracting NeuroCovid-19?

The neural pathway is a very important way for the SARS-CoV2 to enter into the central nervous system (Nikbakht et al. 2020). SARS-CoV2, as it was reported by Steardo (2020), like all six previous beta-coronaviruses, has the ability to enter the nervous system and causes neurological symptoms. The angiotensin-converting enzyme 2(ACE2) receptor provides the entry route for the coronavirus to infect human host cells. These receptors are mainly found in the brainstem and are responsible for regulating the cardiovascular and respiratory function. Like both the Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), NeuroCOVID-19 may also enter the brain directly through the olfactory tract without the need for ACE2 receptors. Wu (2020) has pointed out that these virus can travel into the central nervous system either by infecting sensory or motor neurons or by anterograde transport machinery, using kinesin and dynein. After the invasion, the virus triggers reactive astrogliosis and activates the microglia to induce a large inflammatory cascade. Huang (2020) has reported that virus entry into the central nervous system leads to the release of pro-inflammatory cytokines (IL-1B, IL-6, TNF-α), nitric oxide, prostaglandin E2, and free radicals, and causes chronic inflammation neural hyperexcitability, seizure, and death (see also Tufan et al. 2020)

Samuelsson (2006) find out that inflammatory cytokines exacerbate apoptosis and neuronal necrosis in the central nervous system, specifically in different parts

of the hippocampus, and these pro-inflammatory cytokines play a key role in epileptic pathogenesis. They also cause epilepsy by increasing glutamate and decreasing GABA in the cerebral cortex and hippocampus. One of the most harmful effects of these cytokines is the secretion of neurotoxic compounds through the autocrine/paracrine mechanisms. These cytokines increase the entry of calcium into neurons through AMPA and NMDA receptors, thereby increasing the neuronal hyper-excitability (see also Rana & Musto 2018; Nikbakht et al. 2020).

Neuropsychological studies reported in the subject literature have shown that acquired and usually transient cognitive and behavioral symptoms correlate in some children with epileptic activity on the EEG. Children with epilepsy tend to have normal intelligence but a higher percentage have attention deficit disorders and other deficits, learning problems, and school problems (language, visual-spatial, etc.) compared to controls (Pachalska et al. 2014, 2021). Many of these studies have shown abnormalities in categories similar to those of very well-known pathophysiological patterns in the population of children with ADHD, such as an increased theta-beta ratio lowering of the P3b component, and a lowering of the P3 component in the NOGO task.

If a child comes to the Clinic who was healthy prior to SARS-CoV-2 infection, and becomes ill after experiencing this infection and contracting NeuroCOVID-19 with benign Rolandic epilepsy we have to diagnose and treat him. As was stated by Aknin et al. (2021) the available knowledge should inform clinical guidelines, assessment, and public health planning while more systematic research using biological, clinical, and longitudinal methods provides further insights. One promising treatment used for children with this type of epilepsy is neurofeedback. The use of neurofeedback to reduce epileptic seizures has been the subject of considerable research for 40 years, starting with cats (Sterman 1982), monkeys (Sterman, Goodman, & Kovalesky, 1978), and humans (Sterman & Friar, 1972). Although EEG rhythm training is associated with clinical improvement, as well as electroencephalographic (EEG) normalization in patients with epileptic seizures (for review, see Sterman, 2000), few neurologists and epileptologists have adopted this approach for the treatment of seizure disorders.

The aim of this study was to describe the examination and neurotherapy of a boy following SARS-CoV-2 infection and NeuroCOVID-19 in whom neurological tics and motor automatisms as well as cognitive impairment, particularly attention deficit disorder, developed as a consequence.

**CASE STUDY**

A boy K.S., 7 years old, without neurodevelopmental disorders, after a SARS-CoV-2 infection in May 2021 and contraction of neuroCOVID-19 confirmed by a genetic test for the quantitative detection of neutralising antibodies (responsible for immunity) in the IgG class against SARS-CoV-2. The boy had relatively mild pseudomonal symptoms of the illness: temperature 38.5, runny nose, cough, muscle aches, headaches and general weakness.
He was treated symptomatically and recovered after 2 weeks. Two months later, at the beginning of July 2021, neurological tics consisting of an upward turning of the eyeballs to the left appeared. These tics intensified in August 2021 and were accompanied by motor automatisms consisting of the left hand stiffening in a salute-like position, while at the same time there was an inclination of the head to the left. In September 2021, after exertion in the swimming pool, an epileptic seizure occurred which caused the boy to start drowning. In the days that followed the above described tics and motor automatisms increased. He also developed sleep disorders, which consisted of him waking up several times during the night, during which time neurological tics and motor automatisms also appeared. Gradually, cognitive dysfunctions, especially attention deficits and behavioural changes, joined in, making it impossible for the boy to function independently at school and in many situations of daily life.

Fig. 1. Schematic representation of the two stimulus GO/NOGO task. From top to bottom: time dynamics of stimuli in four categories of trials. Abbreviations: the A, P, H stimuli are “Animals”, “Plants” and “Humans” respectively. GO trials are when A-A stimuli require the subject to press a button. NOGO trials are A-P stimuli, which require suppression of a prepared action. GO and NOGO trials represent “Continue set” in which subjects have to prepare for action after the first stimulus presentation (A). Ignore trials are stimuli pairs beginning with a P, which require no preparation for action. Novel trials are pairs requiring no action, with the presentation of a novel sound as the second stimuli. Ignore and Novel trials represent a “Discontinue set”, in which subjects do not need to prepare for action after the first stimulus presentation. Time intervals are depicted at the bottom.
Source: Pąchalska, Kaczmarek, Kropotov 2014, with permission.
A neurophysiological examination: qEEG, ERPs and sLORETA tomography performed on 11.09.2021 using automatic seizure activity detection software showed the presence of the neuromarker benign partial rolandic epilepsy (BPERS) and neurocognitive disturbances resembling symptoms of attention deficit hyperactivity disorder (ADHD), compared with neuromarkers of children with this condition (n=100) from the normative database of the Human Brain Index (HBI) in Switzerland. Detection of the neuromarker BPERS was helpful in selecting an individualised neurostimulation protocol.

The patient participated in 20 neurofeedback sessions using:
(1) SMR reinforcement, theta inhibition;
(2) theta inhibition, B1 reinforcement (15-18 Hz);
(3) qEEG-guided neurofeedback.

Neurostimulation with neurofeedback was conducted twice a week, for 15-20 minutes gradually increasing to 30-40 minutes per session. The patient also received individual goal-directed psychotherapy. After successive sessions of neurofeedback, a gradual reduction in seizures was observed. By the end of neurotherapy, the neurological tics, motor automatisms, neurocognitive disorders and behavioural disturbances had completely disappeared. The patient functions well in school and achieves very good academic results.

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 250 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, and 3) a modification of GO/NOO task (20 minutes).

The task consisted of 400 trials presented to the subject every 3 seconds. In the task we selected four categories of stimuli:
1) 20 different images of animals – referred to later as A,
2) 20 different images of plants – P,
3) 20 different images of humans presented together with an artificial sound – HS. Each sound was composed of four pure tones of 500, 800, 1100, 1400 Hz of 20 ms duration Trials consisted of the presentation of a pair of stimuli with an interstimulus interval of 1.1 sec.

Four categories of trials were selected: A-A, A-P, P-P, and P-HS. The trials were grouped into four sessions with one hundred trials each. In each session a unique set of five A stimuli, five P and five HS stimuli were selected. Each session consisted of a pseudo-random presentation of 100 pairs of stimuli with an equal probability for each category and each stimulus.

Absolute and relative magnitude spectra and coherences in all conditions computed and compared with the parameters of a corresponding age group from the Human Brain Index (HBI) reference database. The reference database includes the data of 1000 healthy people aged from 7 to 89 years.
The analysis consists of the following steps:

- **eye movement artifact correction and elimination**: a) using a spatial filtration technique based on zeroing the activation curves of the individual Independent Component Analysis (ICA) components corresponding to horizontal and vertical eye movements, as well as b) excluding epochs with excessive amplitude of EEG and excessive faster and slower frequency activity;
- **Fast-Fourier Transformation (FFT)** of the corrected EEG for extracting the EEG power and coherence for all 0.25 Hz bins in the frequency band from 0.5 to 30 Hz;
- **computation of event related potentials** by averaging EEG over trials for each category of trial and each channel with a time resolution of 4 ms;
- **decomposition of individual ERPs** into independent components by applying spatial filters extracted by means of the ICA from the collection of ERPs computed for the corresponding group of healthy subjects;
- **comparison of each extracted electrophysiological and behavioral variable** against the corresponding variable computed for a carefully constructed and statistically controlled age-regressed, normative database in which the variables have been transformed and confirmed for their Gaussian distribution.

**Automated spike detection**

A visual inspection of raw EEG was made 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 are defined on the basis of comparison spike detection by the program and by experienced experts on the data base of more than 300 EEG

![Fig. 2. The relative residual energy for dipole approximation of the detected spike is chosen less than 0.2 relative residual energy](image)
recordings in epileptic patients. There are three characteristics that define a spike or a sharp wave in EEG. They are paroxysmal character, high degree of sharpness and short duration (Pąchalska, Kaczmarek and Kropotov 2014). These parameters are presented in Fig. 2.

RESULTS

**Spikes/slow wave complexes**

For this patient the automatic spike detection was performed on EEG in the common average montage for both eyes open and eyes closed conditions. From 6 min of spontaneous EEG recording 86 spikes were detected. Average potentials for these spikes are presented in Fig. 3. As sLORETA images showed they are generated over left and right precentral gyri.

**Behavioral data**

The results of the patient’s comparison behavioral parameters in the GO/NOGO task are presented in Table 1. As one can see no statistically significant deviations in the subject’s the behavioral parameters are to be found.

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**Fig. 3.** Averaged spikes obtained in the subject by means of automatated spike detection. Top – waveforms of spikes at T3 at T4. X-axis time in ms, Y-axis – amplitude in μV. Middle – topographies. Bottom – sLORETA images.

**Table 1.** Behavioral parameters of the patient in the GO/NOGO task

<table>
<thead>
<tr>
<th>Objects</th>
<th>Omission</th>
<th>Commission</th>
<th>RT1</th>
<th>var(RT1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>14%</td>
<td>2%</td>
<td>430</td>
<td>12.2</td>
</tr>
<tr>
<td>Norms</td>
<td>6.3%</td>
<td>0.85%</td>
<td>480</td>
<td>13.2</td>
</tr>
<tr>
<td>P value</td>
<td>0.34</td>
<td>0.77</td>
<td>0.58</td>
<td>0.81</td>
</tr>
</tbody>
</table>
Deviations from normality in EEG spectra computed for 20 minutes of the GO/NOGO task are presented in Fig. 4. As one can see the EEG pattern is characterized by excessive slow activity over temporal areas (around 4.9 Hz) and the frontal areas (around 6.1 Hz). The last pattern appears to correspond to the frontal midline theta rhythm. This rhythm in the subject increases with the task load and has a similar frequency and spatial parameters to those found in healthy children of the same age. The slow content at the temporal areas appears to correspond to slow wave complexes and spikes in the temporal areas.

Event related potentials

The results of comparison of the ERPs independent components of our patient with the reference data of the Human Brain Index (HBI) at Chur, Switzerland are presented in Table 2. The number of such cases is not high and represents only 14% of GO trials.

As one can see the largest deviations are found in the conflict detection component. This component is generated in the anterior cingulate cortex in response to NOGO cues.

Neurotherapy

The patient participated in 20 neurofeedback sessions using (1) SMR reinforcement, theta inhibition; (2) theta inhibition, B1 reinforcement (15-18 Hz); (3) qEEG-guided neurofeedback. Neurostimulation with neurofeedback was conducted twice a week, for 15-20 minutes gradually increasing to 30-40 minutes per session. The patient also received individual goal-directed psychotherapy. After successive sessions of neurofeedback, a gradual reduction in neurological symptoms was observed. By the end of neurotherapy, the neurological tics, motor automatisms, neurocognitive disorders and behavioural disturbances had
Table 2. The results of comparison of the ERPs independent components of the patient with the reference data of the Human Brain Index (HBI) in Chur, Switzerland

<table>
<thead>
<tr>
<th>Component name and location</th>
<th>Functional meaning</th>
<th>2D map</th>
<th>3D s-LORETA image</th>
<th>Comparison to norms</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1/N1 visual wave Cuneous, occipital lobe</td>
<td>Reflects processing in the primary and secondary visual cortical areas. Corresponds to the P1/N1 visual wave.</td>
<td>![2D map image]</td>
<td>![3D s-LORETA image]</td>
<td>![Comparison to norms image]</td>
</tr>
<tr>
<td>Temporal P2 Angular gyrus and inferior temporal lobe</td>
<td>Reflects processing in the left visual ventral stream. Its sensitive to mismatch in the sensory domain when stimulus lated does not match the memory trace.</td>
<td>![2D map image]</td>
<td>![3D s-LORETA image]</td>
<td>![Comparison to norms image]</td>
</tr>
<tr>
<td>Temporal P2 Angular gyrus and inferior temporal lobe</td>
<td>Reflects processing in the right visual ventral stream.</td>
<td>![2D map image]</td>
<td>![3D s-LORETA image]</td>
<td>![Comparison to norms image]</td>
</tr>
<tr>
<td>P3 b P Superior parietal lobe</td>
<td>Reflects engagement operation of accumulation brain resources for performing action</td>
<td>![2D map image]</td>
<td>![3D s-LORETA image]</td>
<td>![Comparison to norms image]</td>
</tr>
<tr>
<td>P3 supression Supplementary motor cortex, frontal lobe</td>
<td>Reflects the operation of action inhibition when there is a need to suppress the ongoing activity in the case of an unpredicted event.</td>
<td>![2D map image]</td>
<td>![3D s-LORETA image]</td>
<td>![Comparison to norms image]</td>
</tr>
<tr>
<td>Anterior cingulate Frontal lobe</td>
<td>Reflects the operation of conflict detection and monitoring. Indicates that there is a conflict between two or several actions.</td>
<td>![2D map image]</td>
<td>![3D s-LORETA image]</td>
<td>![Comparison to norms image]</td>
</tr>
<tr>
<td>novelty Medial Prefrontal cortex</td>
<td>Corresponds to the Novelty P3a wave.</td>
<td>![2D map image]</td>
<td>![3D s-LORETA image]</td>
<td>![Comparison to norms image]</td>
</tr>
</tbody>
</table>
completely disappeared. The patient functions well in school and achieves very good results.

**DISCUSSION**

As the behavioral data show, the subject’s performance in the task does not differ statistically from the normative data. It should be noted here, that the ADHD population in this task is characterized by an excessive number of omission errors (index of inattention) and an excessive variance of response (index of inconsistency in responding) (Kropotov 2016).

EEG spectra abnormalities indicate an excessive frontal midline theta rhythm. This indicates a rare subtype of ADHD. People with such a dysfunction show hyperactivation of the anterior cingulate – the source of the Frontal midline theta. This hyperactivation effect (ceiling effect) is reflected in a decrease of the conflict monitoring component generated in the anterior cingulate cortex. The question still remains: how are interictal spikes associated with the observed physiological disturbances? (Pąchalska, Kaczmarek and Kropotov 2014).

**Can benign rolandic epilepsy occur after the contracting of NeuroCOVID-19?**

Benign rolandic epilepsy is characterized by twitching, numbness or tingling of the child’s face or tongue, and may interfere with speech and cause drooling. Seizures spread from one area of the brain and become generalized (Pąchalska, Kaczmarek & Kropotov 2014). Seizures associated with benign rolandic epilepsy are usually brief – no more than two minutes in duration. They tend to occur infrequently and most often at night. The child may maintain full awareness while the seizure is happening.

It should be stressed that epilepsy is a “family” of many different disorders that lead to seizures. Some children will have easily controlled seizures, have no other health problems, and become seizure-free on medications. Or they may have epilepsy with occasional seizures but no other health problems. Or they may have rare variants of epilepsy like benign Rolandic epilepsy. Benign Rolandic epilepsy or benign childhood epilepsy with centrotemporal spikes (BCECTS) is the most common epilepsy syndrome in childhood (Kramer, 2008). Most children will outgrow the syndrome (it starts around the age of 3-13 with a peak around 8-9 years and stops around the age 14-18), hence the label benign (Wirrel, 1998; Chahine, Mikati 2006; Pachalska et al. 2014). There is no subject literature available in the world where information can be found that Rolandic epilepsy occur after the contracting of NeuroCOVID-19. However, observations and clinical studies by Pąchalska et al. 2021 indicate that this is possible. It is highly likely that the mechanism for Rolandic epilepsy to occur after the contracting of NeuroCOVID-19 might be similar to the one described above.
CONCLUSIONS

HBI methodology was helpful in finding the functional neuromarkers of benign partial Rolandic epilepsy and disturbed cognitive control. Therefore, it was possible to offer more effective neurorehabilitation for the disorders, which contribute to a better quality of patient life.

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