Chapter

Therapeutic Effect of Infra-Low-Frequency Neurofeedback Training on Children and Adolescents with ADHD

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Abstract

In this observational study the outcomes of an EEG-based infra-low-frequency (ILF) neurofeedback intervention on patients with attention deficit (hyperactivity) disorder (ADHD) are presented. The question is addressed whether this computer-aided treatment, which uses a brain-computer-interface to alleviate the clinical symptoms of mental disorders, is an effective non-pharmaceutical therapy for ADHD in childhood and adolescence. In a period of about 15 weeks 196 ADHD patients were treated with about 30 sessions of ILF neurofeedback in an ambulant setting. Besides regular evaluation of the severity of clinical symptoms, a continuous performance test (CPT) for parameters of attention and impulse control was conducted before and after the neurofeedback treatment. During and after the therapy, the patients did not only experience a substantial reduction in the severity of their ADHD-typical clinical symptoms, but also their performance in a continuous test procedure was significantly improved for all examined parameters of attention and impulse control, like response time, variability of reaction time, omission errors and commission errors. In a post neurofeedback intervention assessment 97% of patients reported improvement in symptoms of inattention, hyperactivity or impulsivity. Only 3% of the patients claimed no noticeable alleviation of ADHD-related symptoms. These results suggest that ILF neurofeedback is a clinically effective method that can be considered as a treatment option for ADHD and might help reducing or even avoiding psychotropic medication.

Keywords: Infra-low frequency (ILF) neurofeedback, ADHD, therapy, continuous performance test, clinical study

1. Introduction

Hyperkinetic disorder, also known as attention deficit disorder (ADD) or attention deficit hyperactivity disorder, is a disorder that typically occurs in childhood. The core symptoms include increased inattention and/or hyperactivity and impulsivity as well as lack of emotional self-control and motivation. ADHD is a complex psychiatric and neurologically based disorder that usually is comorbid with other conditions: over one-half of children with ADHD have accessory symptoms like learning disabilities, conduct disorders, poor coordination, depression, anxiety, obsessive–compulsive disorders and bipolar disorders [1, 2]. Accordingly, the pathophysiological causes of ADHD are to be found in the central nervous system (CNS). Corresponding studies on ADHD patients show changes in dopaminergic and noradrenergic neurotransmission [3–6] as well as a (presumably related) developmental delay of the cortex, especially in the prefrontal region relevant for executive functions, attention and motor control [7]. In addition to these functional changes in defined brain areas, functional imaging studies in ADHD patients also have demonstrated changes in neuronal networks, e.g., in frontostriatal, frontoparietal and ventral attention networks [8, 9] and in the default mode network (DMN) [10].

According to current estimations about five percent of children worldwide meet the diagnostic criteria of ADHD [11] and if left untreated, symptoms may persist into adulthood. Therefore, innovative and effective treatment methods that show long-lasting effectivity without the accompanying unwanted side effects of psychotropic drugs are of great relevance. Neurofeedback has been proven to be a treatment method that offers comparable effects in the therapy of ADHD like the use of pharmacological substances such as methylphenidate [12–17]. Follow-up studies and meta-analyses six, 12 or even 24 months after neurofeedback treatment show a sustained improvement of ADHD core symptoms [18, 19].

Neurofeedback is a computer-aided therapy method for clinical use, mainly as a treatment for mental disorders with the aim to improve self-regulation processes of the brain using a brain-computer interface (BCI). During a neurofeedback session selected parameters of the patient's electroencephalogram (EEG) are extracted according to their frequency and power density, processed, transformed into audio-visual feedback signals which then are being made perceptible for the patient's sensory organs by computer animations. By utilizing specific frequency components of the continuously measured full band EEG, the corresponding cerebral activities and their dynamics are reported back (feedback) to the central nervous system from where they originate. Due to the high performance of today's modern EEG and computer systems, electrical potential fluctuations of cerebral origin can continously be recorded from the skull with a high dynamic range. Furthermore, the neurofeedback-specific processing up to the generation and visual and acoustic presentation of the feedback signals can take place almost in real time, so that there is a minimal time delay only between the brain's generation of electrical activity, its electroencephalographical measurement and the presentation and perception of the EEG-derived audio-visual feedback signals. As a result, the brain can interact with the perceptual audio-visual "echo" of parts of its own activity, by improvement of its self-regulatory abilities [20, 21].

It has been known for a long time that brain functions can be influenced by feedback mechanisms [22], but neurofeedback was only developed in the late 1960s – without its clinical potential being recognized at first. A few years later, the first clinical studies showed particularly good therapeutic success using this technique in patients with severe epilepsy [23–26]. It was later shown that the effects remained even ten years after the end of the neurofeedback treatment [27]. Since self-regulation is an essential and fundamental function of the brain, the clinical treatment spectrum of neurofeedback is broad. Thus, in addition to epilepsy and the already mentioned hyperkinetic disorder, neurofeedback has also been shown to be an appropriate treatment for many other neurological disorders involving brain dysregulation, such as autism spectrum disorder (ASD) [28–33], migraine [34, 35], post-traumatic stress disorder (PTSD) [36–40], schizophrenia [20] and several others.

The various neurofeedback methods used typically differ in the extraction of the frequency components of the measured EEG that are used to calculate and control the feedback signals. In so-called frequency band training, the focus is on conventional frequency ranges of the human EEG between 1 and 40 Hz. Brain activities in this range usually dominate the EEG due to their clearly visible wave-like characters. It has long been confirmed in clinical studies that neurofeedback training in these frequency ranges, namely 4–8 Hz (theta range), 12–15 Hz (sensorimotor rhythm, SMR), and 16–20 Hz (beta range), can be an appropriate and effective treatment for children with ADHD [40–42]. However, the full band EEG also contains long-lasting potential shifts that are assigned to slow activities of the frequency range below 0.1 Hz. Such potential fluctuations typically are created by cortical neurons in preparation for sensomotoric tasks as well as for motor or cognitive behavior and events [16, 43]. According to their functional significance, these voltage signals are either classified as readiness potentials or, according to their time course, referred as slow cortical potentials (SCPs). It is assumed that slow surface negative potentials of cortical neurons represent a measure for the excitability of cortical neurons, while positive defections of such SCPs in the EEG signify a widespread absence of facilitation [43–45]. By influencing SCPs with weak external direct current voltage stimuli applied to the head, it could be shown that slow cortical negativity in certain cortical areas leads to better performance in sensorimotor tasks [16]. Abnormalities in SCP size seem to affect behavior and it has, for instance, been shown that children with ADHD show EEG abnormalities in the frequency range of SCPs [46, 47]. Children with attention deficits show smaller negative SCPs during the anticipation phase of a task in comparison to children without attention problems [16]. The two neurofeedback training methods that utilize such slow potentials in the EEG are ILF- and SCP-neurofeedback. Various studies document SCP neurofeedback training as an effective form of therapy for ADHD [18, 48, 49].

ILF neurofeedback was primarily developed empirically based on clinical observations from the frequency band and SCP methods. It utilizes the conventional frequencies between 1 and 40 Hz within nine fixed bands and transforms any dynamic progression of their spectral power above individual thresholds into a certain set of feedback signals ("Inhibits"). By this mechanism, the brain receives feedback about sudden changes in spectral power densities, which are linked directly to the respective brain activity components in the EEG. At the same time, the amplitudes and dynamics of the very slow cortical potentials of the "infra-low" frequency range of <0.1 Hz are determined in the EEG and, after setting an individual gain factor via a lowpass filter cutoff frequency by the therapist, transferred as a second set of feedback signals ("Signal"). The ILF neurofeedback protocol determines that the EEG is recorded in a bipolar montage. Thus, not the dynamically changing brain activity underneath each two electrodes is the targeted signal but their ratio and consequently, ILF neurofeedback represents a coherence training.

Other essential and standalone elements of the ILF neurofeedback protocol are that neither specific frequencies of brain activity in the EEG are actively promoted or suppressed via the feedback process, nor is the patient supposed to produce brain activity of specific frequencies voluntarily. Rather, the therapeutic work in ILF neurofeedback is based on the assumption that the symptoms of the patient indicate over- or under-excitation in certain multiple association areas of the brain [50].

By placing the EEG electrodes above such multiple association areas on the head of the patient, the brain receives continuous feedback on its internal states. This happens via up to 15 different computer-generated audio-visual feedback signal parameters to trigger neurophysiological modulation on an unconscious level.

The patient may become aware of the feedback-induced cerebral changes through the conscious perception of temporary positive sensations, like relaxation, increased concentration or motoric calmness or a reduced level of alertness. However, such temporary sensations could also be mild sensations of fatigue, headaches, increased motor activity or dizziness and thus, unwanted effects. The therapist is therefore encouraged, to always observe the patient for signs of relaxation, stress, comfort or discomfort and to also inquire at regular intervals about perceived feelings. In case of positive observations or reports from the patient the therapist will proceed with the actual settings of the training parameters or change them to eliminate unwanted effects.

In addition to these partly subjective effects of the training, there were recently also reports published that demonstrate defined neurophysiological changes in the brain which can be attributed to the use of ILF neurofeedback. A quantitative analysis of 19-channel EEG recordings before and after 20 sessions of ILF neurofeedback training shows a significant increase in spectral power in the 0.5 Hz frequency band [51, 52]. The general increase in spectral power of the ILF component of the EEG indicates that ILF neurofeedback training induces a modified baseline brain state. Another study using functional magnetic resonance imaging (fMRI) shows that even a single session of ILF neurofeedback leads to significant changes in connectivity in the brain [53].

While SCP and frequency band training have been used for many years to treat ADHD, there are only a few studies in which ILF neurofeedback has been used as a treatment method [54]. ILF neurofeedback could represent a particularly effective treatment method for pathologies in which the brain is dysregulated. It combines the above-mentioned components that characterize the procedure with the methodological immanence for the therapist to adapt the treatment to the patient's individual symptomatology. In consequence, the natural question arises concerning the evidence-based level of ILF neurofeedback therapy. The present study therefore aims to clarify the question whether ILF neurofeedback is an effective therapy for children and adolescents with ADHD. In addition, little research has been done on the effectiveness of neurofeedback for ADHD in everyday life, so the present study tracks the individual symptom profiles. This examines if the effect of ILF neurofeedback leads to an improvement in life quality of those affected.

2. Methods

2.1 Study operator and therapists

The present study was conducted as a pilot project of a network of five practices for child and adolescent psychiatry in Germany. It is in accordance with the declaration of Helsinki. All interventions mentioned in this study were carried out by a total of 25 specialist therapists who had qualified in a certified training course of ILF neurofeedback lasting several days.

The data of the present observational study was collected by the participating practices in the course of treatment of their patients. A declaration of consent for the anonymized collection and processing of the data in the sense of an observational study with a pilot character was enclosed with the treatment contract, which the patients received before the start of the therapy, and which was signed by the patients or, in the case of minors, by the parents.

2.2 Participants

Participants in this study were recruited from children and adolescents who visited one of the participating practices due to ADHD-related symptoms or already diagnosed ADHD. Some of them were already under drug treatment with methylphenidate medication at the beginning of the study. In addition to age and informed consent, the clinically validated diagnosis of attention deficit (hyperactivity) disorder was another inclusion criterion for study participation. **Figure 1** shows the inclusion criteria for the study.

A total of 251 patients participated in the data collection and received therapy in the form of ILF neurofeedback treatment. On average, these patients had an age of 12.1 years (SD: 2.8, interval: 7.3–21.5), with 82% belonging to the age group 7–14 years and 18% to the age group 15–21 years. The gender distribution of the participants shows a majority of 79% males and 21% females.

2.3 Study design

In the present observational study, a symptom tracking procedure was used to measure subjectively perceived expression and severity of ADHD-typical symptoms before the start (T_0) and at the end (T_2) of ILF neurofeedback therapy. A QIKtest device was used for continuous performance tests to measure for attention, sustained attention, and impulse control at T_0 and T_2. For each participant the therapy consisted

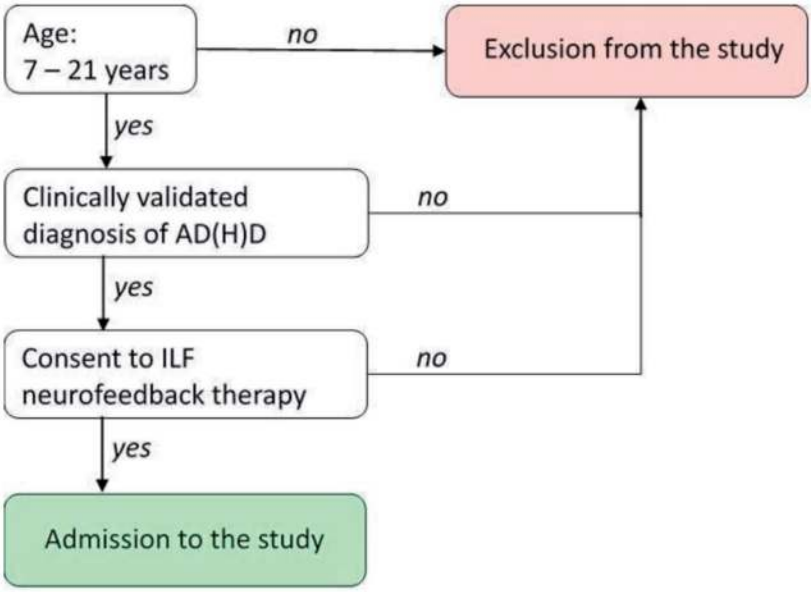

Figure 1.
Inclusion and exclusion criteria of this observational study. Included into the study were children and adolescents with an age between 7 and 21 years, a diagnosed hyperkinetic disorder and a signed consent for a ILF neurofeedback therapy.

of approximately 30 ILF neurofeedback sessions, each lasting up to 50 minutes, with about two sessions every week and thus, a therapy period of about 15 weeks (see **Figure 2**).

2.4 Electrophysiology and software

The ILF neurofeedback interventions were performed with neurofeedback systems from BEE Medic Inc. (Germany), that consist of a 2-channel EEG differential amplifier EEG NeuroAmp® II (Corscience Inc., Germany) with full bandwidth (DC to 100 Hz), 32 bit resolution, a sampling rate of 500 sps and integrated impedance meter (impedance range 0–140 kOhm) as well as the software Cygnet® (BEE Medic Inc., Germany).

Before applying the electrodes, the skin at the electrode positions was treated with an abrasive cleaning paste (Nuprep®, Weaver and Company, USA) and then Ag/AgCl electrodes were applied using conductive paste (Ten20®; Weaver and Company, USA) to ensure a proper conductivity.

2.5 ILF neurofeedback protocol

The used neurofeedback-method was according to the ILF neurofeedback protocol and followed the description of Susan Othmer [55]. It consists of a 2-channel EEG that was recorded from the scalp of a patient using a bipolar montage and electrode placement sites in accordance with the international 10–20 EEG system. Electrodes were placed individually according to the protocol guide [55], with starting placements at T3-T4 or T4-P4 electrode sites.

The neurofeedback process and the audio visual feedback was controlled and applied using Cygnet® software. During continuous EEG recording, features of the EEG were extracted in near real time to build two different dynamically changing components of the feedback process: “Inhibits” and “Signal”.

To calculate the “Inhibits” component, the supra-threshold EEG power densities of nine filter blocks in fixed frequency steps in the range between 1 and 40 Hz were summed up. The thresholds of the nine frequency bands were individually and dynamically set and adjusted to maintain the actual EEG power density of a frequency band to be sub-threshold for about 95% of the time. Due to this calculation method of dynamically adapting threshold values, a sudden increase in power density in an EEG frequency band instantly leads to suprathreshold values and thus immediately to an increase in the “inhibits” component.

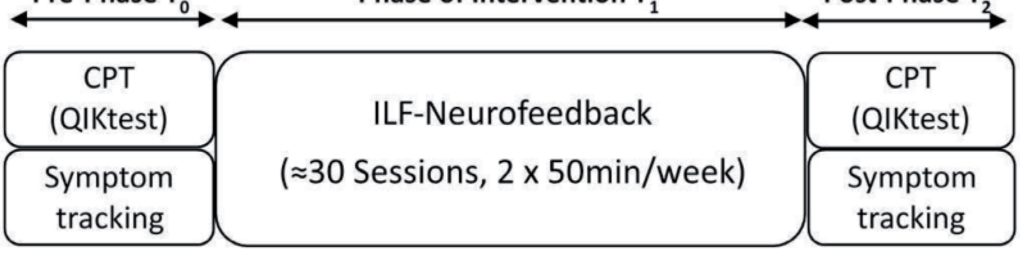

Figure 2.
Study design showing the different phases.

To calculate for the “Signal” component the EEG power density of a “infra-slow” frequency band was extracted and determined. In the neurofeedback protocol used “infra-slow” frequencies are defined as frequencies below 0.1 Hz. Accordingly, the therapist is required to set the cut-off frequency of a low-pass filter in the millihertz frequency range via the software in order to extract the “infra-slow” “signal” component from the EEG and to continuously determine its signal strength.

One of the core features of the ILF neurofeedback is the subsequent transformation of the continuously determined “inhibit” as well as “signal” components into animated audio-visual feedback signals, which are presented to the patient on a separate computer screen. Typically, this is done via an animated computer game in which certain acoustic and visual parameters are directly coupled to either the “inhibit” or “signal” component or their ratio. Various feedback “games” were available to the ADHD patients for free selection and their common feature was that the calculated “inhibit” component modulated the volume of the underlying music and determined the color contrast and brightness of the animated environment. The simultaneous modulatory effects of the “Signal” component concerned the speed of the animated game character and the volume of its sounds.

The promotion of CNS stability is the first objective of brain training [37]. Because brain stability is an individual feature, an individualized training strategy, in which the reinforcement “infra-slow” frequency is optimized for each individual, is a mandatory element of the ILF neurofeedback protocol [55]. According to the protocol, the “signal” frequency has to be adjusted by the therapist during the first sessions to the state in which the person is maximally calm, attentive and as euthymic as the nervous system is capable of being at that moment. The fine-tuning of the optimal reinforcement frequency (ORF) then is done on the basis of reports from the patient on their own status or observations of the therapist. In this study, the ORF for the infra-low signal was determined individually during the first 1–3 sessions based on the report of the patient or from observing behavioral signs of stress, alertness, wellbeing or relaxation on the patient by the therapist. Thereafter, the ILF neurofeedback therapy was proceeded with the “signal” frequency set to the patient’s individual ORF.

2.6 Continuous performance test (CPT)

In order to measure changes in attention, sustained attention and impulse control, a CPT with the QIKtest device (BEE Medic Inc., Germany) was carried out before the start and at the end of neurofeedback therapy. The QIKtest is a mobile, stand-alone test display/input device with a standardized test procedure that is used in particular to record selective attention, sustained attention and impulsive behavior. The CPT of the QIKtests consist of displaying “GO/NO GO “tasks for 21 minutes. The test is divided into five phases, in which the occurrence, incidence and intervals of “GO” tasks differ to measure four parameters of attention: average reaction time (RT), variability of reaction time (VAR), omission errors (OM) and commission errors (CO).

During the CPT, two simple visual conditions (“target”/“GO” and “non-target”/“NOGO”) are presented once every two seconds to the patients on the screen of the QIKtest device via nine luminous fields: “GO” when all fields except the middle field light up and “NO-GO” when all nine fields light up.

In a period of 2 seconds, in a seemingly (for the patient) random fashion one of the two stimulus conditions lights up for a duration of 100 milliseconds. The subject’s task is to press a button on the QIKtest device as quickly as possible only when the “GO” condition appears. This results in two possible types of errors: Omission errors, when the required reaction to the "GO" condition failed to appear, and commission errors, when the reaction button on the QIKtest device was pressed after a "NO-GO" signal was displayed. In addition, the QIKtest device measures the reaction time for each correct reaction with a measurement accuracy of 0.1 milliseconds and calculates RT and VAR.

The statistical evaluation of the test results was carried out using PSPP (GNU project, open source), version 1.2.0.

In order to qualitatively classify changes in the investigated attention parameters and those of impulse control, the CPT database of EEG Expert (EEG Expert Limited, Ankara, Turkey) was used. The "equivalent mental age", derived from the mean result of a reference group for the specific age, was determined for RT, VAR, OM and CO from the corresponding norm curves. The CPT database contains >50,000 records of individuals of both sexes aged 6–70 years in 40 age groups, with at least 500 records per age group.

2.7 Symptom tracking

To assess symptom changes through ILF neurofeedback therapy, patients were asked to track their individual symptoms out of a catalog of 137 ADHD-specific and other symptoms from the categories of sleep, attention and learning behavior, sensory and perception, behavior, emotions, physical symptoms and pain, before (T_0) and after the ILF neurofeedback intervention (T_2). Between the two points of measurement (T_0 = Pre and T_2 = post) was the phase of neurofeedback intervention (T_1) (see **Figure 2**). Participating patients could indicate a severity level between 0 (symptom does not apply at all) and 10 (symptom occurs very frequently or is maximal pronounced) for each of the 137 given symptoms.

The statistical evaluation of the symptom survey was done using the software PSPP, version 1.2.0.

3. Results

Of the 251 ADHD patients treated with ILF neurofeedback during the entire data collection period, only 196 had pre-post QIKtest data collected. The average duration of therapy in terms of neurofeedback sessions was 38.5 (SD = 21.6), three participants dropped out of therapy.

3.1 Continuous performance test

The pre-post data at T_0 and T_2 of 196 participants were included in the evaluation of the continuous performance test using the QIKtest device. Changes in four variables were analyzed: average reaction time (RT), variability of reaction time (VAR), omission errors (OM) and commission errors (CO). The averaged RT of the patients improved during the duration of the ILF neurofeedback training by about 21 ms - from 457 ms at T_0 to 436 ms at T_2 (see **Table 1**). In parallel, VAR improved as well by about 18 ms - from 122 ms at T_0 to 104 ms at T_2. To examine their statistical significance, the values of RT and VAR were compared separately using independent Student's t-tests, as a normal distribution with equal variances was given. According to the t-test results, the improvements of RT and VAR after ILF neurofeedback treatment were statistically highly significant (see **Table 1**). The third attention parameter

N = 196	Pre (T_0)	Post (T_2)	Difference	p
Reaction Time (RT)	457 ± 88 ms	436 ± 85 ms	−21 ms	<0.0001[1]
Variability of RT (VAR)	122 ± 31 ms	104 ± 30 ms	−18 ms	<0.0001[1]
Omission Errors (OM)	9.6 ± 15.1	5.0 ± 9.3	−4.6	<0.0001[2]
Commission Errors (CO)	19.1 ± 17.2	9.0 ± 9.0	−10.1	<0.0001[2]

[1] *Student's t-test.*
[2] *Wilcoxon signed rank test.*

Table 1.
Results of the continuous performance test.

that was measured, OM, too improved from an average of 9.6 errors (SD = 15.1 errors) at T_0 to 5.0 errors (SD = 9.3 errors) at T_2. The test parameter that determines impulse control CO improved from 19.1 errors (SD = 17.3 errors) on average at T_0 to 9.0 errors (SD = 9.0 errors) at T_2. The significance of the improvements was examined statistically using a non-parametric Wilcoxon signed-rank test, because OM and CO did not follow a normal distribution. According to their Wilcoxon signed rank test results, the improvements of OM and CO after ILF neurofeedback treatment were statistically highly significant (see **Table 1**).

To investigate the relevance ("quality") of the improvements in the studied parameters of attention and impulse control in relation to mental maturity, the respective "equivalent mental age" for RT, VAR, OM and CO was determined from the corresponding norm curves of the CPT database. On average, the participating ADHD patients had an age of 12.1 years. However, their averaged performance in the CPT before the start of the ILF neurofeedback training was clearly below their averaged actual age when compared with the CPT database (see **Figure 3**): the averaged performances for the attention parameters RT, VAR and OM of the average 12.1-year-old ADHD patients corresponded to the 10.2 (RT), 10.0 (VAR) and 8.9 (OM) years age groups in the CPT database and thus, lack a mental maturity of around 2 years. For the tested parameter of impulse control, CO, the averaged performances of the ADHD patients corresponded to the 8.5 (CO) years age group in the CPT database and thus, showed an even slightly more delayed mental maturity of about 3.5 years.

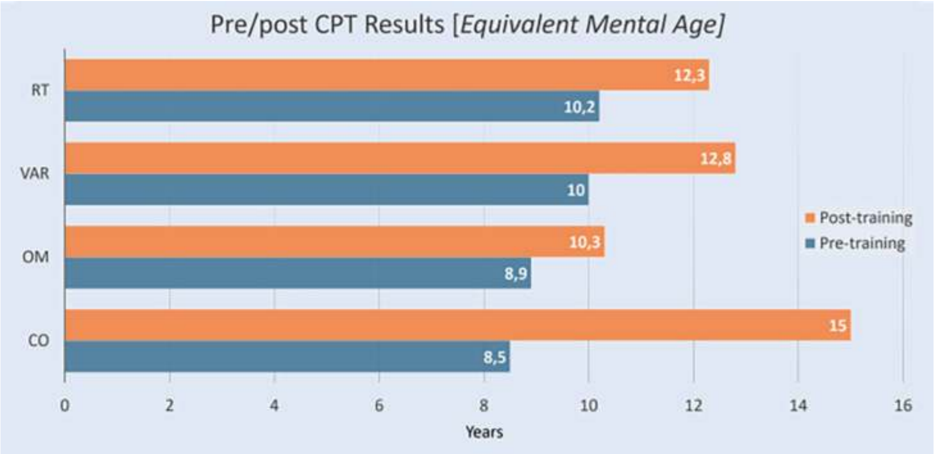

Figure 3.
Improvements of the equivalent mental age for the different test parameters of the continuous performance test.

In terms of “equivalent mental age” that was derived from the CPT database, the ADHD patients benefited considerably from the therapy. After the ILF neurofeedback training equivalent mental age of the ADHD patients clearly increased for RT from 10.2 to 12.3 years, for VAR from 10.0 to 12.8 years, for OM from 8.9 to 10.3 years and for CO from 8.5 to 15.0 years (see **Figure 3**).

3.2 Symptom tracking

According to the patients’ self-disclosure or evaluation by the therapists, 97% of the patients experienced an improvement of the symptoms which had been individually perceived as stressful before the neurofeedback therapy, like inattention, hyperactivity, impulsivity, difficulties to fall asleep, distractibility, rage and others. Only 3% of the patients claimed no noticeable improvement of the symptoms.

The course of symptom severity before, during and after approximately 30 sessions of ILF neurofeedback was assessed in 43 ADHD patients for the three core symptoms of their disorder: inattention, hyperactivity and impulsivity. Before the start of the ILF neurofeedback intervention at T_0 the patients evaluated the core symptoms of their disorder as to be very pronounced, with high average values for inattention, hyperactivity and impulsivity (see **Table 2**).

Symptom	Time	Severity of Symptoms	p
Inattention	T_2	5.4 ± 2.2	0^*
	T_0	8.3 ± 1.4	
Hyperactivity	T_2	4.6 ± 2.5	0.012^*
	T_0	8.1 ± 1.2	
Impulsivity	T_2	6.1 ± 2.5	0.018^*
	T_0	7.4 ± 1.8	

Table 2.
Severity of the different ADHD symptoms (statistics by Wilcoxon signed rank test).= statistical significance attained.*

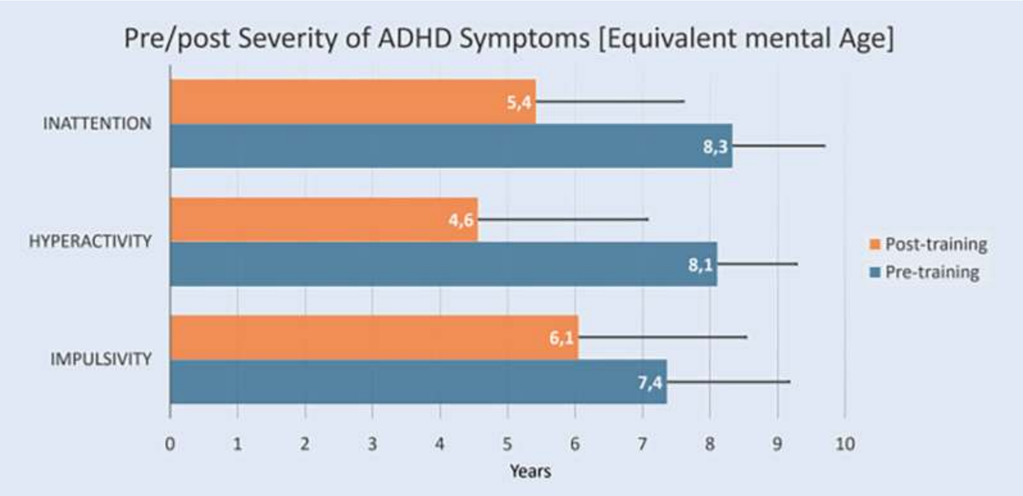

Figure 4.
Improvements in ADHD symptom ratings.

Comparison of these averaged severity values with the individually evaluated severity levels of these symptoms after the treatment with ILF neurofeedback at T_2 and determination of the level of significance by Wilcoxon signed rank test, all three core symptoms had been improved significantly. For the symptom of inattention, the participants reported at T_2 a highly significant decrease of the individually perceived severity by 2.9, for hyperactivity by 3.5 and impulsivity by 1.3 (see **Figure 4**).

4. Discussion

Since the first reports of successful neurofeedback treatment in ADHD [56], several studies have investigated the effects on symptoms of ADHD such as inattention, impulsivity and hyperactivity with neurofeedback protocols that utilize brain activity of conventional frequencies in the EEG. Such reports include those which facilitated the sensorimotor EEG rhythm (SMR) and inhibited beta rhythmicity and those which facilitated beta EEG rhythm and inhibited theta rhythmicity [40, 42, 57–60]. Another neurofeedback approach that is assumed to regulate cortical excitability and is used with positive results in the treatment of ADHD is training of Slow Cortical Potentials (SCP) [48, 61]. However, in this study Infra-low Frequency (ILF) neurofeedback was used, a modern, relatively new and effective neurofeedback treatment method for mental disorders. It utilizes both, brain activity of conventional frequencies in the human EEG (1–40 Hz) as well as activities in the frequency range of slow cortical potentials below 0.1 Hz. Other characteristics of the ILF neurofeedback protocol include a bipolar montage of the electrodes, placement of the electrodes on the skull according to individual criteria of the patient's arousal level and mental strength, and continuous feedback of the parameters extracted from the full-band EEG in audio-visual computer animations that have a game-like character.

Recent reports demonstrate that ILF neurofeedback not only utilizes slow brain activity in the EEG but also can directly lead to a significant increase in spectral power in the sub 0.5 Hz frequency band [51, 52]. Clinically, it has been shown that children with attention deficits show smaller negative SCPs during the anticipation phase of a task in comparison to children without attention problems [16] or other EEG abnormalities in the frequency range of SCPs [46, 47]. In the light of these findings, we conducted this multi-center study to address the question of whether ILF neurofeedback is an effective and significant treatment for ADHD and leads to an improvement in quality of life of those affected.

A total of 251 ADHD child and adolescent patients were included in this study and received a treatment consisting of an average of 39 ILF neurofeedback sessions over a period of at least 15 weeks (about two sessions of neurofeedback per week). Only three patients decided to discontinue treatment prematurely. Although we did not investigate this aspect scientifically, it can be concluded from the low dropout rate that the ILF neurofeedback was well accepted as a treatment method by the vast majority of the ADHD patients (and their parents). According to the patients' self-disclosure or evaluation by the therapists, 97% of the patients reported an improvement of the symptoms which had been individually perceived as stressful before the neurofeedback therapy. Only 3% of the patients claimed no noticeable improvement of the symptoms by the ILF neurofeedback training. The general effect of the ILF neurofeedback treatment therefore can be rated as excellent.

In order to make the patients' subjective assessment of their symptoms measurable, they were asked before and after the end of treatment to perform an evaluation of their most prominent symptoms on the basis of severity levels between 0 and 10. The most severe symptoms were chosen from a questionnaire of 137 ADHD-specific and other symptoms. This included the categories sleep, attention and learning behavior, sensory and perception, behavior, emotions, physical symptoms and pain. Regarding symptom tracking, complete data sets were unfortunately only available from 43 patients (and thus only from about 1/6 of the participating children and adolescents). Nevertheless, the size of this sample is sufficient for a statistical analysis in which we focused on the three core symptoms of the ADH disorder, inattention, hyperactivity and impulsivity. Before the ILF neurofeedback intervention, the severity of inattention was rated to be at 8.3 in average and thus, experienced as to be very pronounced. A similar average severity level was reported by the participants for the symptom of hyperactivity, which was 8.1. The impulsivity was rated at 7.4 on average and thus, only slightly less severe than the aforementioned symptoms. This shows that the three core symptoms of ADH disorder are indeed perceived by the patients as highly burdening. After the therapy of approx. 30 sessions of ILF neurofeedback, the patients assessed these symptoms as significantly less stressful, with a clear average improvement in inattention by 1.9 severity points and in hyperactivity by as much as 3.5 severity points. Regarding the severity of their impulsivity, the participating children and adolescents rated slight but significant decrease of 1.3 severity points after the treatment. From these results, it can be concluded that 30 sessions of ILF neurofeedback, according to the subjective perception of the patients, are sufficient to improve hyperactivity and inattention symptoms in children and adolescents with ADHD. The treatment can also lead to a slightly milder, but still significant improvement in impulsivity in the same group of patients. These effects of ILF neurofeedback therapy are in accordance with the results of controlled studies on ADHD using other neurofeedback protocols. In these studies high to moderate effect sizes were also found on inattention and impulsivity as well as on hyperactivity ([12, 13, 15, 62, 63], for a review see [64]).

These positive results are mainly based on the subjective sensations and experiences of ADHD patients. In order to examine and monitor the quality and effectiveness of the ILF neurofeedback treatment on the basis of more objective criteria, the participants completed a 21-minute visual GO/NOGO continuous performance test (CPT) before the start and after the end of the intervention. Through this measure the parameters of attention and impulse control could be directly examined in detail. The three attention parameters that were tested are the response time, the variability of the response time and omission errors. The reaction or response time (RT) is the mean of all correct reaction times to a target stimulus ("GO" condition) and is a measure of the speed of responses. This attention parameter is accompanied by the variability of the response time (VAR), which is a measure of the consistency of the response. Finally, omission errors occur when the subject does not respond correctly to a target stimulus, which is assessed as a sign of inattention. A comparison of the test results prior and after about 15 weeks of ILF neurofeedback intervention revealed a significant improvement of all three attention parameters. The averaged Reaction time decreased for 21 ms, VAR for 18 ms and the averaged OM by −4.6 errors. To transform these results into more tangible values, the conversion into an "equivalent mental age" (EMA) was done based on the large CPT database of EEG Expert. Here, the "equivalent mental age" indicates the specific age of the reference group whose norm test result corresponds with the test result of the patient.

The improvements in the three tested attention parameters are reflected in a significant increase in the EMA. Before the start of the ILF neurofeedback therapy the

ADHD children and adolescents were about 2 years of EMA behind, but regarding the attention parameters examined, they were able to make up for this delay within the 15 weeks of neurofeedback training. Most prominent was the improvement in averaged consistency of the response time (VAR) which led to an increase of EMA by +2.8 years and the shorter mean response time (RT) which increased the EMA by +2.1 years. The improvement in omission errors was slightly less pronounced because it resulted to +1.4 years in equivalent mental age. For the three tested attention parameters it therefore can be stated that – within the 15 weeks period of ILF neurofeedback treatment - the brain of the ADHD patients had gained in maturation corresponding to a developmental progress of about two years.

Commission errors (CO) in the CP test occur when the patient responds (incorrectly) to a non-target ("NOGO") task, which makes this test parameter a good measure for impulsivity. In all participating patients, impulse control improved significantly from an average of 19.1 CO errors before the ILF neurofeedback treatment, to only 9.0 CO errors after the intervention. In terms of equivalent mental age, this means that the performance of the ADHD patients improved from a below-average of 8.5 years to an above-average EMA of 15.0 years after the EEG-assisted neurofeedback intervention.

All objective improvements in the attention and impulsivity parameters examined in the CP testing are completely consistent with the ADHD patients' subjectively perceived reductions in the severity of their symptoms of inattention, hyperactivity and impulsivity, which were rated as highly distressing prior to ILF neurofeedback treatment. Based on the data and feedback from clinicians and patients it therefore can be concluded that ILF neurofeedback can be seen as an effective method to treat ADHD in children and adolescents.

Due to the fact that ADHD on one hand is a complex psychiatric and neurologically based disorder which usually is associated with many comorbidities as social behaviors disorders, affective disorders, depression, anxiety, obsessive–compulsive disorders, bipolar disorders and others [1, 2] and ILF neurofeedback on the other hand is indicated for all of the mentioned ADHD comorbidities [65, 66]. It would therefore be interesting to undertake a more comprehensive evaluation of the symptom severities of ADHD patients and to investigate in a controlled study to what extent ILF neurofeedback therapy leads to further improvements in cerebral self-regulation, which also encompasses the areas of other comorbidities of ADHD.

5. Conclusion

This observational clinical study could show significant improvements in major symptoms of ADHD - being inattention, hyperactivity and impulsivity - along with an improvement of attention, sustained attention and impulse control as well as the mental age equivalents in young patients with ADHD after ILF neurofeedback intervention. These results fit in line with presented study outcomes on neurofeedback in the treatment of ADHD - given the particularity that symptom based and individualized ILF neurofeedback presents a modern approach to EEG neurofeedback therapy options. Patients, parents and therapists evaluated the implementation and therapeutic outcome pleasant and positive. Whatsoever based on this and prior results it can be concluded that neurofeedback can be assessed as an effective, non-invasive, non-drug and pain-free treatment opportunity enlarging the ADHD treatment options. These promising results should motivate further research, especially studies overcoming the limitations of this one and including an interventional design, control parameters, further validated research instruments and long-term observations.

From a therapeutic point of view ILF neurofeedback can add a value to the treatment of children and adolescents with ADHD but further and more controlled research is needed to determinate outcome differences, especially in comparison to standard of care treatment.

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