Neurofeedback in children with ADHD: Specific event-related potential findings of a randomized controlled trial

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HIGHLIGHTS

- Neurofeedback training in children with ADHD is accompanied by changes in neural processing (e.g., increase of the contingent negative variation after training of slow cortical potentials).
- The success of the training can be predicted by pre-training EEG and event-related potential measures.
- The findings of the randomized controlled trial further support the specificity of training effects and contribute to a better understanding of the mechanisms underlying a successful neurofeedback training in children with ADHD.

ABSTRACT

Objective: In a randomized controlled trial, we could demonstrate clinical efficacy of neurofeedback (NF) training for children with ADHD (Gevensleben et al., 2009a). The present investigation aimed at learning more about the neuronal mechanisms of NF training.

Methods: Children with ADHD either completed a NF training or a computerized attention skills training (ratio 3:2). NF training consisted of one block of theta/beta training and one block of slow cortical potential (SCP) training, each comprising 18 training units. At three times (pre-training, between the two training blocks and at post-training), event-related potentials (ERP) were recorded during the Attention Network Test. ERP analysis focused on the P3, reflecting inter alia attentional resources for stimulus evaluation, and the contingent negative variation (CNV), primarily related to cognitive preparation.

Results: After NF training, an increase of the CNV in cue trials could be observed, which was specific for the SCP training. A larger pre-training CNV was associated with a larger reduction of ADHD symptomatology for SCP training.

Conclusions: CNV effects reflect neuronal circuits underlying resource allocation during cognitive preparation. These distinct ERP effects are closely related to a successful NF training in children with ADHD. In future studies, neurophysiological recordings could help to optimize and individualize NF training.

Significance: The findings contribute to a better understanding of the mechanisms underlying NF training in children with ADHD.

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1. Introduction

EEG and event-related potential (ERP) studies significantly contributed to a better understanding of the pathophysiological background of attention-deficit/hyperactivity disorder (ADHD). In the EEG, children with ADHD typically show increased activity in the
theta band and reduced activity in the beta band during a resting condition as well as during attention tasks (El-Sayed et al., 2002; Barry et al., 2003, 2009). The theta/beta ratio may be interpreted as neurophysiological equivalent of ‘activation’ according to the model of Pribram and McGuiness (Pribram and McGuiness, 1975; Barry et al., 2009).

ERP studies focused mainly on late components (latencies >300 ms; for review see Banaschewski and Brandeis, 2007). Reduced P3 amplitudes observed in different paradigms could reflect attentional, as well as response control deficits. The contingent negative variation (CNV) is a slow cortical potential1 (SCP) elicited, e.g., in cue trials of a continuous performance test reflecting anticipation and/or preparation. The CNV was found to be reduced in children with ADHD (e.g., Sartory et al., 2002; Banaschewski et al., 2003). This is in line with models supposing a dysfunctional regulation of energetical resources in ADHD (Sergeant et al., 1999).

Neurofeedback (NF) aims at acquiring self-control over certain brain activity patterns to improve behavioral self-regulation in daily-life. Related to the above-mentioned EEG and ERP findings, two NF training protocols are typically applied in children with ADHD: theta/beta training and SCP training (Heinrich et al., 2007). Theta/beta training aims at tonic aspects of activation with children learning to reduce activity in the theta band and to increase activity in the beta band. SCP training is related to phasic regulation of cortical excitability. Surface-negative SCPs (“negativities”) and surface-positive SCPs (“positivities”) have to be generated over the sensorimotor cortex.

For both NF protocols positive behavioral and cognitive effects were described in several studies (theta/beta training: Lubar et al., 1995; Monasta et al., 2002; Fuchs et al., 2003; SCP training: Heinrich et al., 2004; Strehl et al., 2006; Drechsler et al., 2007). Less data are available concerning the neurophysiological effects of these NF protocols. A decrease of the theta/beta ratio in the resting EEG was reported after theta/beta training in a group of children with ADHD with an initially enhanced theta/beta ratio (Monasta et al., 2002). Considering ERPs, Heinrich et al. (2004) observed an increase of the CNV after SCP training in cue trials of a continuous performance test. This CNV increase was interpreted as a neurophysiological equivalent of improved self-regulation capabilities. A correlation between SCP regulation capability and change of the CNV amplitude was found in Doehnert et al. (2008).

Egnner and Gruzelier (2001, 2004) obtained an increased target-P3 after a beta (15–18 Hz) training in ‘healthy’ students probably due to higher general background excitation. Kropotov et al. (2005) described a P3 increase in a go/no go task for children with ADHD who were considered as good performers in a relative beta training.

In a preliminary study using fMRI, increased activity in the anterior cingulate cortex during a stroop test was reported for children with ADHD, who participated in theta/beta (SMR) training (Levesque et al., 2006).

In order to overcome shortcomings of previous NF studies in ADHD (e.g., small sample sizes, lack of an adequate control group, no randomization), our group conducted a randomized controlled trial including 102 children with ADHD.2 In Gevensleben et al. (2009a; see also Pine, 2009), we evaluated the clinical efficacy of NF training (consisting of one block of theta/beta training and one block of SCP training) in comparison to a computerized attention skills training (AST). For ethical as well as practical reasons discussed in more detail in Heinrich et al. (2007) and Gevensleben et al. (2009a), we preferred an AST training over a sham (placebo) NF training. For the NF group, larger improvements in parent and teacher ratings were obtained. Behavioral improvements were comparable for both NF protocols. Superiority of NF training effects, which, due to comparable settings and demands for NF and control training, was primarily ascribed to specific factors of the NF treatment were still evident at 6-month follow-up (Gevensleben et al., 2010).

In the resting EEG, a reduction of theta activity after the combined NF training was found. Distinct associations between EEG patterns and improvements at the behavioral level (mainly concerning hyperactivity/impulsivity) further supported the specificity of NF effects. For the theta/beta training block, improvements were related to higher pre-training theta activity, as well as to a larger reduction of theta activity, mainly at parietal-midline sites. For the SCP training block, effects in the alpha band were obtained. Smaller parietal alpha activity and a larger increase of central alpha activity were associated with larger behavioral improvements (Gevensleben et al., 2009b).

In the present investigation, we were interested in theta/beta and SCP training effects on cognitive task processing using ERPs. ERPs were recorded during the Attention Network Test (ANT), which allows to differentiate between three particular aspects of attention: alerting, orienting and conflict (Posner and Petersen, 1990; Fan et al., 2002). Testing took place at three times in the course of the training (before the training started, between the training blocks and after the end of the training). Thus, the two NF protocols, which were conducted in separate training blocks, could be compared at the intrindividual level.

We expected distinct ERP effects after the complete NF training in contrast to the control training. For the SCP training, we hypothesized an increase of the CNV (Heinrich et al., 2004) and, for the theta/beta training, a P3 increase was expected (Egnner and Gruzelier, 2001, 2004).

Further, regression models were applied to test if changes in ERP parameters were associated with a reduction of ADHD symptomatology. These analyses also included the relation of ERP measures at pre-training to the behavioral outcome in order to assess their predictive value.

2. Materials and methods

2.1. Subjects

One hundred and two children with ADHD (aged 8–12) started either a NF training or an attention skills training.3 Subjects were randomly assigned to one of the two study groups (ratio NF: control training = 3:2). Eight children (NF: n = 5, AST: n = 3) were dropouts. Characteristics of the 94 children completing their training are summarized in Table 1. All patients fulfilled DSM-IV criteria for ADHD (American Psychiatric Association, 1994). Diagnoses were based on a semi-structured clinical interview (CASCAP-D; Döpfner et al., 1999) and confirmed using the Diagnostic Checklist for Hyperkinetic Disorders/ADHD (Döpfner and Lehmkohl, 2000). With mean FBB-HKS total scores of about 1.5 (range 0–3), ADHD symptomatology was moderately pronounced in both training groups. Children with comorbid disorders other than conduct disorder, emotional disorders, tic disorder and dyslexia were excluded from the study. All children were drug-free for at least 6 weeks before starting the training and without concurring psychotherapy.

1 Slow cortical potentials are changes of cortical electrical activity lasting from several hundred milliseconds to several seconds. They are thought to represent task-dependent short-term mobilizations of cortical processing resources. While negative SCRs reflect increased excitation (e.g., during states of behavioral or cognitive preparation), positive SCRs indicate reduction of cortical excitation of the underlying neural networks (e.g., during behavioral inhibition) according to the threshold regulation model of Birbaumer et al. (1990).

2 ERP data reported in this paper were recorded in the same trial.

3 Sample size had been estimated a priori to be large enough to detect a medium effect size of about 0.5 for the primary outcome measure at the behavioral level (total score of the German ADHD rating scale, FBB-HKS) with a power of 0.8 (one-sided, 0.05-level test).
2.2. Design of the study

Written informed consent from their parents.

Behavioral and neurophysiological testing were conducted in the week before the training course started (pre-training), about 1 week after the last session of the first (intermediate) and second training block (post-training), respectively.

2.3. Training programs

The study followed the CONSORT guidelines for randomized trials (Boutron et al., 2008). It was approved by the local ethics committees of the participating clinics and conducted according to the declaration of Helsinki. Assent was obtained from the children and written informed consent from their parents.

2.2. Design of the study

The design of the study is illustrated in Fig. 1. Neurofeedback and attention skills training both consisted of 36 units of about 50 min each. These 36 units were divided into two blocks of 18 units. The NF group conducted theta/beta training in one block and SCP training in the other block (balanced order). Behavioral assessments and recordings of event-related potentials were done before the training started, between the two training blocks and after the end of the training.

The NF and the AST training were designed as similarly as possible concerning the setting and the demands upon the participants, e.g., in both groups children were instructed by a clinical psychologist to develop strategies for focussing attention and to practice the acquired strategies in daily-life (for further details see Supplementary material).

Neurofeedback system SAM (“Self-regulation and Attention Management”), which was developed by our group for scientific purposes, was used for neurofeedback training.

Trials of the theta/beta training lasted for 5 min in the beginning of the training and were extended to 10 min as the training proceeded so that the children had to sustain the alert and focussed but relaxed state for a longer period. Baseline values were determined at the beginning of each session (3 min). In SCP training, the task was to find appropriate strategies to direct a ball upwards (negativity trials) or downwards (positivity trials). Children were instructed to reach an attentive (negativity trials) or relaxed state (positivity trials). Both kinds of trials, which lasted for 8 s (baseline period: 2 s, feedback period: 6 s), were presented in random order.

In both NF protocols, feedback was calculated from Cz (reference: mastoids). Transfer trials, i.e., trials without contingent feedback, were also conducted (about 40%) in the beginning of a training block and about 60% at the end of a training block. In each training unit, there were about 25–30 min of pure neuroregulation exercises.

The attention skills training was based on “Skillies” (Auer-Verlag, Donauwörth, Germany), a German learning software which primarily exercises visual and auditory perception, vigilance, sustained attention, and reactivity. In “Skillies”, the children had to sail to several islands. On each island, a defined task – each requiring different attention-based skills – had to be solved.

A more detailed description of the training programs is provided in Supplementary material.

2.4. Attention Network Test (ANT)

Fig. 2 shows a schematic illustration of the ANT version used in this study, which was realized in Presentation (Neurobehavioral Systems, Albany, CA, USA). Children were instructed to feed a hungry fish (center fish in a row of five fish) by pressing the button of the mouse that matched the direction the center fish was pointing to. The flanking fish either looked in the same direction (congruent trials) or to the opposite direction (incongruent trials).

The fish appeared either slightly (about 1°) above or below a fixation cross and were preceded by one of three cue stimuli (equal probability). In the Spatial Cue condition, an asterisk was presented at the location of the target fish (all cues were valid). In the Neutral Cue condition, an asterisk at the center of the screen indicated that the target fish was to about to appear soon. In the No Cue condition, the fish appeared without a cue stimulus.

Starting 1400 ms before the appearance of the target fish, the cue stimuli were presented for 150 ms. In comparison to the standard ANT version (Fan et al., 2002), the interval between cue and
target stimulus was prolonged to elicit a CNV in the ERPs. Presentation of the flanking fish started 100 ms before the center fish appeared.

The ANT was administered after a 2-min resting-EEG (eyes open) recording (Gevensleben et al. 2009b) and followed by a cued continuous performance test. It consisted of four blocks of 48 trials each. The test (incl. short breaks between the blocks) lasted about 15 min. At each recording, the task was described to the children first, and a practice block of 24 trials was run.

The following performance measures were determined according to Fan et al. (2002): hits, mean reaction time (RT), alerting score (RT for NoCue trials minus RT for NeutralCue trials), orienting score (RT for NeutralCue trials minus RT for SpatialCue trials) and congruency score (RT for incongruent trials minus RT for congruent trials). Only children with a minimum of 55% correct responses were included in the statistical analysis.

2.5. ERP recording and analysis

Brain electrical activity was recorded with sintered Ag/AgCl electrodes and Abralyt2000 electrolyte from 23 sites according to an extended 10–20 system (recording reference: Fcz, ground electrode: CPz) using a BrainAmp amplifier (Brain Products, Munich, Germany). Electrooculogram electrodes were placed above and below the right eye and at the outer canthi. Data were recorded at a sampling rate of 500 Hz (bandwidth: 0.016–120 Hz). Impedances were kept below 20 kΩ.

For data processing, the VisionAnalyzer software (Brain Products, Munich, Germany) was used. After downsampling to 256 Hz, brain electrical activity was re-referenced to the mastoids and filtered offline with 0.05–30 Hz, 24 dB/oct Butterworth filters. Ocular artefacts were corrected with the method of Gratton et al. (1983). If the amplitude at any EEG electrode exceeded ±100 µV, a segment – 300 to 700 ms was excluded from further analyses.

Averaged event-related responses to cue stimuli and to target stimuli were computed. Recordings were only considered if at least 20 segments without artefacts and correct overt responses were available.

The CNV in NeutralCue and SpatialCue trials was determined as the mean amplitude from 1000 to 1300 ms following cue onset at electrode Cz. Cue-P3 and target-P3 were maximal at Pz. At this electrode, the most positive peak in the time-frame 400–900 ms was determined for cue trials, and in the time-frame 270–650 ms for target trials. Latencies of the target-P3 were also considered.

2.6. Behavioral assessments

The German ADHD rating scale (FBB-HKS) completed by the parents was used to measure training effects at the behavioral level. The severity of each item, which are related to DSM-IV and ICD-10 criteria for ADHD and hyperkinetic disorders, was rated from 0 to 3. Outcome measures were the FBB-HKS total score, i.e., the mean value of all items, as well as subscores for inattention and hyperactivity/impulsivity.

2.7. Statistical analysis

To study training effects, ANT performance were analysed in repeated measure ANOVAs with factors GROUP (NF, AST) as between-subject factor and TIME (pre-training, post-training) as within-subject factor. Concerning the ERP measures, an additional factor CUE (NeutralCue, SpatialCue) was introduced for the CNV and the cue-P3, and the factor CONGRUENCY (congruent, incongruent) for the target-P3, respectively. If significant effects containing the factor GROUP were obtained, additional post hoc tests were run for each group separately.

For the comparison of the NF protocols (theta/beta vs. SCP), the difference between the performance and ERP parameters at the
end and the start of a training block were calculated. These change measures were subjected to ANOVAs with the within-subject factor PROTOCOL (theta/beta, SCP) and the between-subject factor ORDER representing the order in which the protocols were applied. To investigate if training effects can be predicted by and/or correlate with ERP measures, block-wise linear regression models were applied (Heal and Rusch, 1995; Gevensleben et al., 2009b). In a first block, age and IQ were considered. In a second block, ERP baseline measures were introduced, and changes (post-training minus pre-training) of ERP parameters were added in the third block of the regression models. Only those ERP measures were used for the regression analysis for which at least a tendency for significance resulted for the Pearson correlation with the behavioral outcome measure. Outcome measures were the change of the FBB-HKS total score as well as the change of the subscales inattention and hyperactivity/impulsivity. Corresponding regression analyses were computed for the NF protocols separately. Change values refer to differences between the end and the start of a training block. If comparable relations to the clinical outcome were found for the ERP measures as for the resting-EEG measures reported in Gevensleben et al. (2009b), it was studied if the respective ERP and EEG measures were related (by calculating Pearson’s correlation coefficients) and whether prediction could be improved by considering both ERP and EEG measures. Significance was assumed if $p < 0.05$. For the ANOVAs, effect sizes in terms of partial eta square (part. $\eta^2$) were computed and interpreted following the notion that part. $\eta^2 > 0.1$ indicates small, part. $\eta^2 > 0.6$ medium, and part. $\eta^2 > 0.14$ large effects (Cohen, 1988).

3. Results

3.1. Performance measures

3.1.1. Neurofeedback vs. control training

From the 94 children with ADHD completing their training, nine children had to be excluded either due to insufficient test performance, i.e., less than 55% correct responses ($n = 6$) or due to technical reasons ($n = 4$). Analyses of performance measures comprised 56 (of 59) children in the NF group and 28 (of 35) children in the AST group. For all the measures, (highly) significant TIME effects were obtained but no significant GROUP × TIME interactions (see Table 2). Hits increased, mean reaction time, alertness, orienting and conflict scores decreased. Effects were not larger for the NF group but rather tended to be higher in the AST group (e.g., increase of hits). From our clinical impression, there were some children in the AST group who had basic problems in solving tasks at the computer but improved their basic skills during the course of their training. So, we ran some post hoc analysis considering ’poor performers’ (defined as children with 55–75% hits at pre-training) separately. Considering this subgroup of children (NF group: $n = 8$; AST group: $n = 6$), there was a larger increase of hits ($F(1,12) = 5.04$, $p < 0.05$, part. $\eta^2 = 0.30$) in the AST group (pre-training: 123.5 ± 11.5, post-training: 163.2 ± 13.0) compared to the NF group (pre-training: 132.0 ± 10.6; post-training: 148.0 ± 15.9), partly at the cost of (non-significantly) slower mean reaction times (AST: pre-training: 482.5 ± 57.0 ms, post-training: 532.3 ± 139.1 ms; NF: pre-training: 491.8 ± 113.6 ms, post-training: 482.3 ± 124.9 ms).

3.1.2. Theta/beta vs. SCP training

Comparing theta/beta and SCP training, a trend for the conflict score was obtained ($F(1,51) = 3.2$, $p < 0.01$, part. $\eta^2 = 0.06$) indicating a larger decrease for the SCP training (change: $−14.4 ± 24.1$ ms) compared to the theta/beta training ($−4.8 ± 29.4$ ms).

For the number of hits, the orienting and conflict score, a significant ORDER × PROTOCOL interaction was observed ($F(1,51) > 6.6$, $p < 0.02$, part. $\eta^2 > 0.09$). Changes in performance measures occurred mainly from the first to the second testing but only to a smaller amount from the second to third testing.

3.2. Event-related potential measures

3.2.1. Neurofeedback vs. control training

At least 20 trials with correct responses and without artefacts for the different task conditions were available in 43 children of the NF group and 21 children of the AST group. Those children who could not be included in the ERP analysis were not characterized by different clinical (FBB-HKS) parameters (neither at pre-training nor at post-training); t-test: $t(92) < 1.3$; $p > 0.18$ but were younger than the children with sufficient test performance and signal quality ($9;1 ± 0;11$ years vs. $9;11 ± 1;2$ years, t-test: $t(92) = −3.5$; $p = 0.001$).

For the CNV at electrode Cz, the repeated measure ANOVA revealed a significant GROUP × TIME effect ($F(1,62) = 4.2$, $p < 0.05$, part. $\eta^2 = 0.07$) and a trend for the GROUP × TIME × CUE interaction ($F(1,62) = 3.0$, $p < 0.1$, part. $\eta^2 = 0.04$; see Table 3). Considering the two groups separately, a highly significant TIME effect was obtained for the NF group ($F(1,42) = 13.0$, $p < 0.001$, part. $\eta^2 = 0.24$) indicating an increase of the CNV from pre- to post-training (see also Fig. 3). For the AST group, the TIME effect was not significant ($F(1,21) = 0.1$, n.s.) but a significant CUE × TIME interaction was obtained ($F(1,21) = 5.3$, $p < 0.05$, part. $\eta^2 = 0.20$) indicating a differential behavior of the CNV for Neutral Cue vs. Spatial Cue trials from pre- to post-training.

The CNV was larger (more negative) in Spatial Cue vs. Neutral Cue trials (factor CUE: $F(1,62) = 25.3$, $p < 0.001$, part. $\eta^2 = 0.30$).

For the cue-P3 at electrode Pz, a significant GROUP × TIME interaction ($F(1,62) = 5.9$, $p < 0.05$, part. $\eta^2 = 0.09$) resulted. Analyzing NF and AST group separately, revealed a significant CUE × TIME interaction for the NF group ($F(1,42) = 9.7$, $p < 0.01$, part. $\eta^2 = 0.18$) whereas the P3 amplitude slightly increased in Neutral Cue trials, it rather decreased in Spatial Cue trials.

### Table 2

Performance data.

<table>
<thead>
<tr>
<th></th>
<th>NF group ($n = 56$)</th>
<th></th>
<th>AST group ($n = 28$)</th>
<th></th>
<th>Repeated measure ANOVAs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
<td>TIME ($F(1,62) = 20.6$)</td>
<td>part. $\eta^2 = 0.20$</td>
</tr>
<tr>
<td>Hits</td>
<td>168.7 ± 19.8</td>
<td>175.12 ± 15.9</td>
<td>167.7 ± 19.9</td>
<td>179.2 ± 12.7</td>
<td>TIME ($F(1,62) = 6.8$)</td>
<td>part. $\eta^2 = 0.08$</td>
</tr>
<tr>
<td>Mean RT (ms)</td>
<td>561.8 ± 117.9</td>
<td>542.2 ± 121.1</td>
<td>604.1 ± 135.6</td>
<td>571.4 ± 123.0</td>
<td>TIME ($F(1,62) = 5.9$)</td>
<td>part. $\eta^2 = 0.10$</td>
</tr>
<tr>
<td>Alerting (ms)</td>
<td>35.1 ± 31.8</td>
<td>24.4 ± 31.7</td>
<td>41.8 ± 36.4</td>
<td>25.9 ± 28.6</td>
<td>TIME ($F(1,62) = 13.0$)</td>
<td>part. $\eta^2 = 0.14$</td>
</tr>
<tr>
<td>Orienting (ms)</td>
<td>39.9 ± 27.7</td>
<td>19.1 ± 25.3</td>
<td>31.1 ± 31.4</td>
<td>19.6 ± 30.6</td>
<td>TIME ($F(1,62) = 45.9$)</td>
<td>part. $\eta^2 = 0.25$</td>
</tr>
<tr>
<td>Conflict (ms)</td>
<td>76.6 ± 30.8</td>
<td>57.5 ± 28.3</td>
<td>79.8 ± 32.1</td>
<td>51.7 ± 29.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* $p < 0.01$.

* $p < 0.001$. 

Part. $\eta^2$ is interpreted following the notion that part. $\eta^2 > 0.1$ indicates small, part. $\eta^2 > 0.6$ medium, and part. $\eta^2 > 0.14$ large effects (Cohen, 1988).
P3 amplitudes were larger in SpatialCue vs. NeutralCue trials (factor CUE: \(F(1,62) = 29.5, p < 0.001, \text{part. } \eta^2 = 0.32\)).

For the target-P3 at electrode Pz, no group-specific effect was found. Latencies were shorter in congruent vs. incongruent trials (factor CONGRUENCY: \(F(1,62) = 7.2, p < 0.01, \text{part. } \eta^2 = 0.10\)). They decreased from pre- to post-training (factor TIME: \(F(1,62) = 25.0, p < 0.001, \text{part. } \eta^2 = 0.29\)). Target-P3 amplitudes also decreased from pre- to post-training (factor TIME: \(F(1,62) = 25.4, p < 0.001, \text{part. } \eta^2 = 0.29\)).

Post-hoc, we investigated if the decreases in P3 amplitude and latency were moderated by other factors and tested age and IQ as possible covariates. IQ was associated with a decrease of the P3 amplitude (\(F(1,61) = 4.6, p < 0.05, \text{part. } \eta^2 = 0.07\)).

### 3.2.2. Theta/beta vs. SCP training

The CNV increase in the NF group was due to the SCP training block (CNV changes NeutralCue: \(-1.6 \pm 3.2 \mu V\); SpatialCue: \(-1.8 \pm 3.5 \mu V\)) as indicated by a significant effect for the factor PROTOCOL (\(F(1,37) = 4.3, p < 0.05, \text{part. } \eta^2 = 0.10\)). After the theta/beta training block, CNV amplitudes had not actually changed (NeutralCue: \(-0.1 \pm 4.0 \mu V\); SpatialCue: \(0.3 \pm 3.9 \mu V\)).

Neither for the cue-P3 nor for the target-P3, any of the effects containing the factors ORDER and/or PROTOCOL turned out to be significant.

### 4. Discussion

In order to learn more about the mechanisms underlying NF training in children with ADHD, we studied the impact of two distinct NF protocols (theta/beta and SCP training) on the ERP components P3 and CNV (elicited in the Attention Network Test). Further, we searched for possible associations between ERP measures and behavioral outcome measures. Effects were evaluated in comparison to a computerized attention skills training.

As a main result, an increase of the CNV in the ANT was observed after NF training. This effect could be ascribed solely to the SCP training, i.e., it was specific for the SCP training. Children with a higher baseline CNV improved more in their parental ratings of ADHD symptomatology after SCP training and the complete NF treatment, respectively. Thus, the baseline CNV emerged as a relevant predictor variable for treatment outcome.

In both groups (NF and AST), an improved test performance and a reduced target-P3 component were found after training, probably mainly reflecting adaptation to the attention test. In the NF group, the cue-P3 developed differentially in NeutralCue and SpatialCue trials from pre- to post-training. But this effect was not specific for the theta/beta protocol.

Nearly 1/3 of the children could not be included in the ERP analysis due to insufficient test performance and insufficient signal quality, respectively. These “dropouts” were characterized by younger age but not by different clinical attributes. Therefore, generality of the neurophysiological findings should not be affected by the dropouts.
Fig. 3. Grand averages ERPs for NF and AST group at pre-training and post-training. Top: NeutralCue (blue) and SpatialCue (green) ERPs recorded at electrode Cz. $t = 0$ ms represents the onset of the cue. The CNV (mean amplitude) was measured in the interval [1000 ms; 1300 ms]. Middle: NeutralCue (blue) and SpatialCue (green) ERPs recorded at electrode Pz. $t = 0$ ms represents the onset of the cue. The cue-P3 was determined as the maximum positive peak in the interval [400 ms; 900 ms]. Bottom: target ERPs to congruent (black) and incongruent (red) stimuli, recorded at electrode Pz. $t = 0$ ms represents the onset of the target stimulus. The target-P3 was determined as the maximum positive peak in the interval [270 ms; 650 ms]. Spline-interpolated maps illustrate the topography of the components. Red (blue) colors indicate positive (negative) amplitude values.
A better synchronization of certain oscillatory neuronal networks might be deficient in children with ADHD (Sergeant et al., 2009a). An increase of the CNV (in a cued continuous performance test) following SCP treatment had already been observed in our previous study comprising only a small sample (Heinrich et al., 2004). Though Doehnert et al. (2008) could not directly replicate this finding, they reported a correlation between SCP regulation capability and change of the CNV amplitude. Thus, SCP training is clearly associated with CNV effects in attention tests. In the attentional tasks considered so far, the cue-target interval was about 1.5 s. In future studies, longer intervals could be considered to differentiate between the early and late part of the CNV which are related to different neuronal networks (Lütcke et al., 2009).

In our opinion, the CNV increase observed after SCP training is not related to one of the attention networks supposed to be differentiated using the ANT. It supports the notion that SCP training targets phasic regulation of cortical excitability affecting, i.e., resource allocation during effort-demanding processes. Thus, SCP training could improve regulation of energetic resources which is supposed to be deficient in children with ADHD (Konrad et al., 2006; Adólfsdóttir et al., 2007). Though no specific ERP effect could be found for theta/beta training, we expected an increase of the P3 following theta/beta training. However, irrespective of the training, a decrease of the target-P3 was observed. As indicated by a larger decrease for more intelligent children, the effect may mainly reflect adaption to the task, which was conducted three times by each child. The cue-P3 effect observed for the complete NF training (not specific for the theta/beta training block) may indicate that more attentional resources were allocated to process more salient stimuli. Though no specific ERP effect could be found for theta/beta training, it has to be kept in mind that we could demonstrate associations between theta activity in the resting EEG (pre-training, change from pre- to post-training) and improvements in the ADHD rating scale for theta/beta training (Gevensleben et al., 2009b).

When considering pre- to post-training effects, the number of training units also has to be taken into account. In this respect, the number of 18 units for a single NF protocol might have been too small to obtain specific ERP effects for theta/beta training in children with ADHD.

4.2. Theta/beta training/P3

Based on the findings of Egner and Gruzelier (2001, 2004), we expected an increase of the P3 following theta/beta training. However, irrespective of the training, a decrease of the target-P3 was observed. As indicated by a larger decrease for more intelligent children, the effect may mainly reflect adaption to the task, which was conducted three times by each child. The cue-P3 effect observed for the complete NF training (not specific for the theta/beta training block) may indicate that more attentional resources were allocated to process more salient stimuli. Though no specific ERP effect could be found for theta/beta training, it has to be kept in mind that we could demonstrate associations between theta activity in the resting EEG (pre-training, change from pre- to post-training) and improvements in the ADHD rating scale for theta/beta training (Gevensleben et al., 2009b).

When considering pre- to post-training effects, the number of training units also has to be taken into account. In this respect, the number of 18 units for a single NF protocol might have been too small to obtain specific ERP effects for theta/beta training in children with ADHD.

4.3. Training effects on test performance

Due to the study design, it cannot be differentiated to what extent the improvements in the ANT at the performance level observed in both groups (NF and AST) reflect training effects or are just due to repeated test execution. The use of a computerized attention skills training, which is directly related to a cognitive task like the ANT, surely has raised the bar to demonstrate improvements at the performance level for NF training. So, it is not surprising that, in a smaller subgroup of ‘poor performers’ (between 55% and 75% hits at pre-training testing), children of the AST improved more than those of the NF group.

Distinct effects for the NF protocols – a trend for a larger reduction of the conflict score after SCP training was obtained – may partly be masked by large standard deviations of the ANT measures. Large standard deviations for these measures are also reported in other studies using the ANT to study attentional functions in children with ADHD (Konrad et al., 2006; Adólfsdóttir et al., 2008; Johnson et al., 2008) and may contribute to the mixed results reported there.

5. Conclusion

Successful NF treatment in children with ADHD is accompanied by specific neurophysiological effects like an enhancement of the CNV following SCP training – or as described in Gevensleben et al. (2009b) – effects in the resting EEG. Further, distinct neurophysiological baseline values predict the clinical outcome. Thus, these findings contribute significantly to a better understanding of the mechanisms underlying this clinically effective treatment and also indicate that NF training could be optimized and individualized based on a subject’s neurophysiological profile.

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Appendix A. Supplementary data


References


