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Distinct EEG effects related to neurofeedback training in children with ADHD: A randomized controlled trial ☆

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ABSTRACT

In a randomized controlled trial, neurofeedback (NF) training was found to be superior to a computerised attention skills training concerning the reduction of ADHD symptomatology (Gevensleben et al., 2009). The aims of this investigation were to assess the impact of different NF protocols (theta/beta training and training of slow cortical potentials, SCPs) on the resting EEG and the association between distinct EEG measures and behavioral improvements.

In 72 (of initially 102) children with ADHD, aged 8–12, EEG changes after either a NF training ($n=46$) or the control training ($n=26$) could be studied. The combined NF training consisted of one block of theta/beta training and one block of SCP training, each block comprising 18 units of 50 minutes (balanced order). Spontaneous EEG was recorded in a two-minute resting condition before the start of the training, between the two training blocks and after the end of the training. Activity in the different EEG frequency bands was analyzed.

In contrast to the control condition, the combined NF training was accompanied by a reduction of theta activity. Protocol-specific EEG changes (theta/beta training: decrease of posterior-midline theta activity; SCP training: increase of central-midline alpha activity) were associated with improvements in the German ADHD rating scale. Related EEG-based predictors were obtained. Thus, differential EEG patterns for theta/beta and SCP training provide further evidence that distinct neuronal mechanisms may contribute to similar behavioral improvements in children with ADHD.

1. Introduction

Neurofeedback (NF) is an operant conditioning procedure in which participants (patients) learn to gain self-control over EEG patterns (Heinrich et al., 2007). Measures representing these neurophysiological patterns are converted into visual or acoustic signals which are continuously fed back in real-time. Changes that are made in the desired direction are rewarded, i.e. positively reinforced. Neurofeedback training can be run as a kind of computer game and is thus principally attractive for children. It is increasingly studied as a treatment option in children with attention deficit/hyperactivity disorder (ADHD) with encouraging results in recent studies (Strehl et al., 2006; Drechsler et al., 2007; Gevensleben et al., 2009).

In a randomized controlled trial encompassing 102 children with ADHD, Gevensleben et al. (2009) documented clinical efficacy of NF[1]. A combined NF (18 units of theta/beta frequency band training, preceded or followed by 18 units of training of slow cortical potentials (SCPs) was compared to 2×18 units of a computerised attention skills training (AST), not encompassing neuroregulation. According to parents and teacher ratings, children of the NF group showed larger behavioral (clinical) improvements than those of the control group. Due to comparable settings and demands for NF and AST training, superiority of NF primarily was ascribed to specific factors of the NF treatment.

For the 18 units of theta/beta training and the 18 units of SCP training of the combined NF training, comparable behavioral improvements (referring to inattentiveness, hyperactivity and impulsivity) were observed. However, clear knowledge about the neurophysiological basis of the training effects of both NF protocols is lacking. Better understanding of underlying neurophysiological processes

☆ Trial registry: ISRCTN87071503 — Comparison of neurofeedback and computerised attention skills training in children with attention-deficit/hyperactivity disorder (ADHD) (http://www.controlled-trials.com/ISRCTN87071503).

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[1] EEG data of this paper were recorded in the same trial.

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would probably help to specify indication criteria or to prevent non response, especially in the light of potentially different EEG subtypes of ADHD (Clarke et al., 2003) suggesting different needs for specific EEG tuning.

1.1. Theta/beta frequency band training

In theta/beta frequency band training, children should learn to decrease activity in the theta band of the EEG (4–8 Hz) and to increase activity in the beta band (13–20 Hz). In several studies, ADHD was associated with increased slow wave activity (theta, 4–8 Hz) and/or reduced alpha (8–13 Hz) and/or beta activity (13–30 Hz) in the resting EEG (for review see Barry et al., 2003) as well as during attention task processing (El-Sayed et al., 2002). After theta/beta training (in combination with cognitive–behavioral and educational intervention strategies) Monastra et al. (2002) reported a decrease of the theta/beta quotient in a group of children with ADHD with an initially enhanced theta/beta quotient. Comparable results were obtained after frequency band training with slightly different but comparable NF protocols and settings (without additional interventions) by Fuchs et al. (2003) and Leins et al. (2006).

1.2. Training of slow cortical potentials (SCPs)

SCPs 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 SCPs reflect increased excitation (e.g., during states of behavioral or cognitive preparation), positive SCPs indicate reduction of cortical excitation of the underlying neural networks (e.g., during behavioral inhibition; Birbaumer et al., 1990).

The contingent negative variation (CNV) is a SCP elicited e.g. in cue trials of a continuous performance test reflecting anticipation or preparation. In event-related potential studies, the CNV was found to be reduced in children with ADHD (for review see Banaschewski and Brandeis, 2007) supporting the notion of a dysfunctional regulation of energetical resources in ADHD (Sergeant et al., 1999).

A training of slow cortical potentials, in which surface-negative and surface-positive SCPs have to be generated over the sensorimotor cortex voluntarily, could address this regulation deficit and, thus, help children with ADHD to improve their behavior.

In a previous study, we reported an increase of the CNV in a continuous performance test after SCP training in children with ADHD. The CNV enhancement was accompanied by a reduction of impulsivity errors at the performance level (Heinrich et al., 2004). This finding was partly confirmed by Doehnert et al. (2008), who performed a comparable SCP training with children with ADHD, and additionally analyzed SCP training effects on the spontaneous EEG. They found a reduction of theta/beta ratio at Cz for the children of the ADHD combined type and a slight increase of activity in the upper alpha band (10–12 Hz) for the complete group.

1.3. Aims of this study

In order to learn more about neurophysiological mechanisms underlying behavioral changes of NF training in children with ADHD, we studied the impact of a combined theta/beta and SCP training on the spontaneous EEG, in comparison to an attention skills training. We expected a reduction of theta activity and an enhancement of beta activity (reduction of the theta/beta ratio) after NF. These changes should primarily follow theta/beta treatment and were not expected for the AST. According to Doehnert et al. (2008), we also hypothesized an increase of alpha activity after SCP training.

Furthermore, we tested if distinct changes in EEG patterns were associated with behavioral improvements (reduction of ADHD symptomatology). These analyses also included the relation of EEG baseline measures to the outcome of training in order to assess the predictive value of certain EEG measures for the success of the training.

2. Materials and methods

2.1. Subjects

102 children with ADHD (8 to 12 years) participated in a NF training or an attention skills training (training period from May 2005 to December 2007). Subjects were randomly assigned to one of the two study groups (ratio NF:AST = 3:2). 8 children (NF: $n = 5$, AST: $n = 3$) were dropouts. A further 22 children (NF: $n = 13$, AST: $n = 9$) had to be excluded because of insufficient EEG signal quality (see below). In Table 1, demographic, psychological and clinical variables of the remaining children are summarized. There was no significant difference between NF and AST group concerning these variables.

Initial sample size calculation based on an assumed medium effect size for the primary outcome measure (FBB-HKS) revealed a sample size of about 100 children to reach a power of .80 (one-sided; .05-level test; ratio NF:AST = 3:2).

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 Lehmkuhl, 2000). Children with comorbid disorders other than conduct disorder, emotional disorders, tic disorder and dyslexia were excluded from the study. All children lacked gross neurological or other organic disorders. All children were drug-free and without concurring psychotherapy for at least 6 weeks before starting the training. The study follows the CONSORT guidelines for randomised 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 50 minutes each. Both treatments were divided in two blocks of 18 units. These 18 units were combined to nine (double-)sessions. Both units of a session were separated by a short break. The sessions took place two to three times a week. The NF training consisted of one block of 18 units of theta/beta training and one block of 18 units of SCP training (balanced order). For

Table 1
Demographic and clinical characteristics of the NF group and the control group.

	NF group $n = 46$	AST group $n = 26$
Age (years; month)	9;11 ± 1;3	9;5 ± 1;0
Sex (boys/girls)	41/5 (89.1%/10.9%)	20/6 (76.9%/23.1%)
IQ (HAWIK-III)	107.3 ± 13.5	103.2 ± 12.8
DSM-IV subtype		
Combined type	29 (63.0%)	19 (73.1%)
Inattentive type	17 (37.0%)	7 (26.9%)
FBB-HKS (Parents)		
Total score	1.53 ± 0.48	1.47 ± 0.51
Inattention	2.03 ± 0.54	1.88 ± 0.55
Hyperactivity/impulsivity	1.16 ± 0.69	1.16 ± 0.67
Associated disorders		
Conduct disorder	9 (19.6%)	4 (15.4%)
Emotional disorder	3 (6.5%)	3 (11.5%)
Tic disorder	3 (6.5%)	0 (0.0%)
Dyslexia	10 (21.7%)	9 (34.6%)

Only subjects for whom a pre-training and a post-training EEG recording with sufficient data quality was available are included in the table. At the pre-training level, there were no significant differences between the two groups.

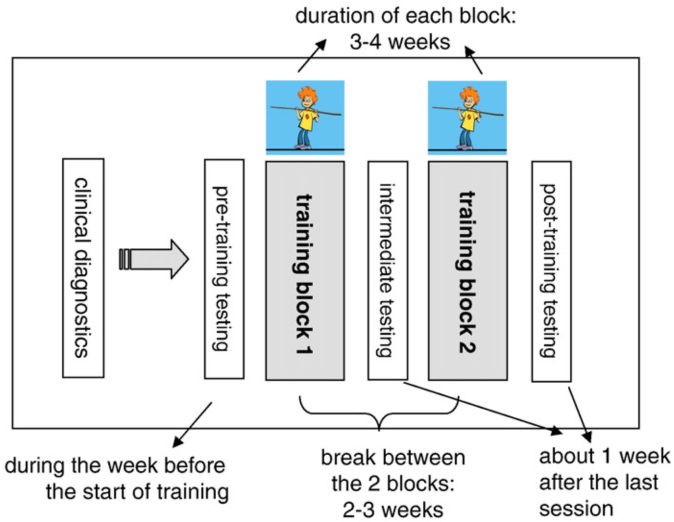

Fig. 1. Schematic illustration of the design of the randomised trial in children with ADHD. The training (neurofeedback, NF; attention skills training) was divided into two blocks. Children of the NF group conducted theta/beta training in one block and SCP training in the other block (balanced order). Behavioral assessments and recordings of resting EEG were done before the training started, between the two training blocks and after the end of the training.

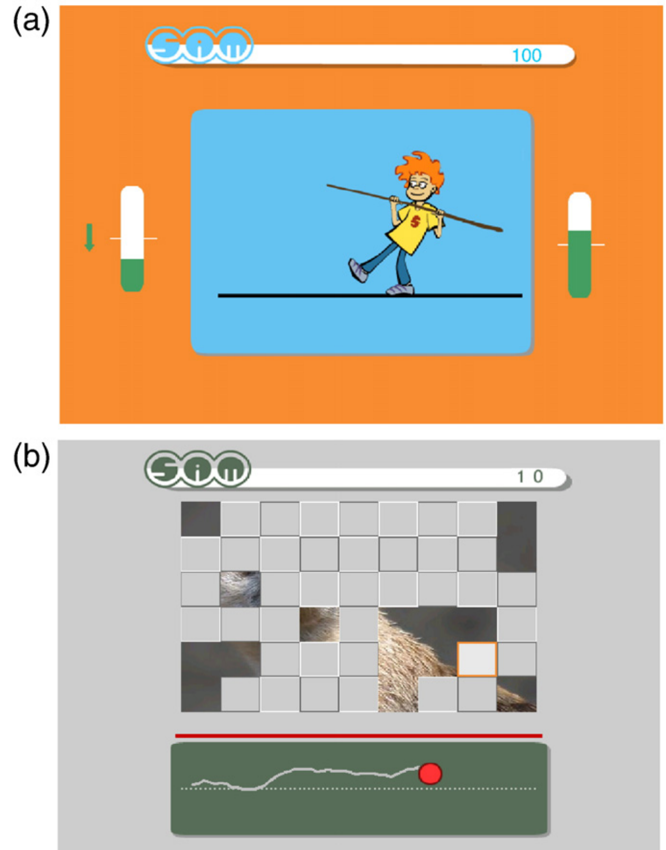

Fig. 2. Example for neurofeedback animations. (a) Theta/beta training: a boy on a rope (Sam) moves ahead if theta activity is reduced/beta activity is increased simultaneously (below/above the baseline values). The participant collects a point for every step Sam makes. Points are presented in the upper right corner of the screen. The activity of both frequency bands is represented by a bar on the screen (range of the bars: theta activity (left bar): ±4 µV; beta activity (right bar): ±3 µV; referred to baseline values). (b) SCP training: the ball has to be directed upwards (negativity trials) or downwards (positivity trials): the vertical position of a ball represents the SCP. With each correct trial, a part of the covert picture becomes visible.

both trainings (NF and AST) there was a break of 2–3 weeks between the treatment blocks. The NF and the AST were designed as similarly as possible concerning the setting and the demands upon the participants. Treatment of both groups encompassed attention-demanding tasks on a computer. Participants of both groups were instructed to develop strategies for focussing attention and to practice the acquired strategies at home and in school. Both treatments were introduced to the parents and children as experimental, but promising, treatment modules for ADHD. The children of both treatment groups completed their trainings in pairs, with each child working at one computer. About three tasks at the computer were accomplished in one unit, altogether lasting for about 25–30 minutes, which means 25–30 minutes of "pure regulation" for the NF group and the same amount of time of attention demanding "mental processing" for the AST group.

The training programs were administered by the same clinical psychologists with the support of a student assistant, who were instructed to take a neutral attitude concerning the effects of the individual training programs. In both trainings, the therapists had to introduce the next task, discuss problems with the task and the use of strategies. In addition, the trainers were asked to motivate the children. Thus, quality and quantity of interaction was comparable for both trainings.

Parents were explicitly not informed about the treatment condition of their child (NF vs. AST) and, as a rule, did not enter the room during treatment.[2]

From the 8th unit on, children of both groups had to practice one of their strategies in a specific situation for about 10 minutes each day in daily-life situations. Children were instructed to identify situations in which these strategies would be important. The goal was to increase the children's responsibility for attention control in certain situations. Exercises were documented by keeping a log, and controlled and discussed at the beginning of the next session. Homework was kept identical in quantity and quality between the groups. Parents were instructed to support the children with the transfer of the learned strategies into everyday life. This parent counselling did not exceed 2 hours.

EEG recordings, and parent and teacher ratings, were conducted at three time points (pre-training, intermediate, and post-training). Pre-training (baseline) assessment took place during the week before the training started. Intermediate assessment was done about 1 week after the last session of the first block, and post-assessment about 1 week after the second block.

2.3. Training programs

2.3.1. Neurofeedback

The neurofeedback program SAM ("Self regulation and Attention Management"), which was developed by our study group[3] and runs on an Abisam400 amplifier (Abimek, Goettingen, Germany), was used for neurofeedback training.

2.3.1.1. Theta–beta training. The task of the theta–beta training was to reduce theta and enhance beta activity. A bar on the left side of the screen (representing theta activity) had to be reduced while simultaneously a bar on the right side (representing beta activity) had to be increased (see Fig. 2a).

Butterworth filters (48 dB/octave) were applied to calculate theta and beta activity. Using a moving time window of two-second length, feedback information (root-mean-square value) was determined 10 times per second. Trials of the theta/beta training lasted for 5 minutes

[2] At the post-training assessment of about 40% of the parents could not reliably quote the treatment assignment of their child. The attitude of the parents in the two groups towards the treatment of their child and post hoc evaluation of the training did not differ (assessment of satisfaction with the treatment, motivation of the child etc, rated via "placebo scales"). For details see Gevensleben et al. (2009).

[3] Not commercially available.

in the beginning of the training and were extended to 10 minutes as the training proceeded, so that the children had to sustain the focussed state for a longer period. In each unit about 5–6 trials of 5 minutes each, or up to 3 trials of 10 minutes each were performed. Baseline values were determined at the beginning of each session (3 minutes, eyes open). An adjustment within a session was not scheduled. Children were instructed to get into a relaxed but attentive state and to find individual strategies to control the bars.

2.3.1.2. SCP training. In the SCP training, negative or positive slow cortical potentials had to be generated by the participant. The participant had to find appropriate strategies to direct a ball upwards (negativity trials) or downwards (positivity trials). Children were instructed to get into an attentive (negativity trials) or relaxed state (positivity trials). An example of a SCP feedback animation is presented in Fig. 2b. Negativity (50%) and positivity trials (50%) were presented in random order. A trial lasted for 8 s (baseline period: 2 s, feedback period: 6 s). During the feedback phase, the mean SCP amplitude (moving time window: 1 s) was calculated 10 times per second. Intertrial interval was set to 5 ± 1 s. In each SCP training unit approximately 120 trials were performed (25–30 minutes).

For both NF protocols, feedback was calculated from Cz, which is frequently used for children with ADHD (Heinrich et al., 2007; reference: mastoids, bandwidth: 1–30 Hz for theta/beta training and 0.01–30 Hz for SCP training, respectively, sampling rate: 250 Hz). Vertical eye movements, which were recorded with electrodes above and below the left eye, were corrected online using slightly different regression-based algorithms for theta/beta training (Semlitsch et al., 1986) and SCP training (Kotchoubey et al., 1997). For segments containing artefacts exceeding ± 100 μV in the EEG channel and ± 200 μV in the EOG channel, no feedback was calculated.

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). These transfer trials, as well as homework, were intended to improve generalisation of treatment effects.

2.3.2. Attention skills training

The attention skills training was based on “Skillies” (Auer-Verlag, Donauwörth, Germany), a German learning software which primarily exercises visual and auditive perception, vigilance, sustained attention, and reactivity. In “Skillies,” the children had to sail to several islands. On each island, a clearly defined task — each requiring different attention-based skills — had to be solved; e.g., on an island named ‘Coloured Reef,’ fish of different colours swim from one side of the screen to the other and back. The aim is that all fish shall have the same colour. The colour can be modified by clicking on a fish. With every change of direction the fish change their colour in a predetermined order. Thus this task aims first and foremost at increasing vigilance and reactivity.

The training was complemented by some self-directed interventions from cognitive therapy to assure comparability to NF, i.e., the children were to compile (meta-)cognitive strategies such as focussing attention, careful processing of tasks and impulse control. Corresponding to the NF group, children of the AST group should practice one of their compiled strategies (needed to solve a task of the computer game) in daily-life situations.

2.4. EEG recording and processing

We performed pre-training, intermediate and post-training testing at approximately the same time of day (for some participants variations of not more than 2 hours could not be avoided due to organizational reasons). Recording of spontaneous EEG activity was conducted as the first part of a neurophysiological/psychological test session of about 90 minutes. Participants were seated on a comfortable chair in a quiet room.

The EEG was recorded in an eyes-open resting condition while children were looking at the centre of a blank screen. In all participating clinics (Erlangen, Göttingen, Munich), the EEG was recorded with sintered silver/silver-chloride (Ag/AgCl) electrodes and Abralyt 2000 electrolyte from 23 sites according to an extended 10–20 system using a BrainAmp amplifier (Brain Products, Munich, Germany). The electrooculogram (EOG) was recorded from two electrodes placed above and below the right eye and at the outer canthi. EEG and EOG activity was recorded with FCz as recording reference at a sampling rate of 500 Hz with low and high cut-off filters set to .016 Hz and 120 Hz, respectively. The ground electrode was placed at CPz. Impedances were kept below 20 kΩ.

For data processing, the software program VisionAnalyzer (Brain Products, Munich, Germany) was used. After downsampling to 256 Hz, the EEG was re-referenced to the mastoids and filtered offline with .1–30 Hz, 12 dB/octave Butterworth filters, and a 50-Hz notch filter. Occular artefacts were corrected with the method of Gratton et al. (1983). Raw data files were divided into four-second, non-overlapping segments. If the amplitude at any EEG electrode exceeded ± 100 μV, the segment was removed. Recordings were only considered for analysis if at least 10 segments without artefacts were available.

The Fast Fourier transform was calculated and spectra were averaged. For each EEG frequency band, delta (0.5–3.75 Hz), theta (4–7.75 Hz), alpha (8–12.75 Hz) and beta (13–20 Hz), voltage values were calculated. The electrodes were grouped into 9 regions as suggested by Clarke et al. (2003): left frontal (Fp1, F3, F7), midline frontal (Fpz, Fz, Fcz), right frontal (Fp2, F4, F8), left central (T3, C3), midline central (Cz), right central (T4, C4), left posterior (T5, P3, O1), midline posterior (Pz, Oz) and right posterior (T6, P4, O2).

2.5. Behavioral assessment

The German ADHD rating scale (FBB-HKS, Döpfner and Lehmkuhl, 2000) was used to assess training effects at the behavioral level. It was completed by the parents at the same time the spontaneous EEG was recorded, i.e., before the start of the training, between the two training blocks and after the end of the training. The FBB-HKS is a 20-item questionnaire related to DSM-IV and ICD-10 criteria for ADHD and hyperkinetic disorders. The severity of each item 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.

2.6. Data analysis

In a first step, pre-training (baseline) EEG measures were analyzed. For each EEG frequency band and the theta/beta ratio, a separate repeated measure ANOVA was computed with GROUP (NF, AST) as between-subject factor, a lateral factor X (left, midline, right) and a sagittal factor Y (frontal, central, parietal) as within-subjects factors. AGE and IQ were defined as covariates since the spectral content of the EEG is known to depend on these parameters. Greenhouse-Geisser adjusted p-values are reported where appropriate.

For the analysis of pre- vs. post-training changes (NF vs. AST) an additional factor TIME (pre-training, post-training) was introduced. If effects reached significance, additional post hoc tests were run, e.g. significant effects containing the factor X or Y were studied using trend analyses (T-lin: linear trend; T-quad: quadratic trend).

For the comparison of the NF protocols (theta/beta vs. SCP), the difference between the parameters at the end and the start of a training block were calculated. These EEG change measures were subjected to ANOVAs with the within-subject factors X, Y and PROTOCOL (theta/beta, SCP), the covariates AGE and IQ, and the between-subject factor ORDER representing the order in which the protocols were applied (1: theta/beta–SCP, 2: SCP–theta/beta).

To investigate if training effects can be predicted by and/or correlate with the EEG, block-wise linear regression models were applied. In linear regression models any joint prediction (mulitcolinearity) is assigned to the earlier block, so that variables in the earlier block function as control variables (covariates) for later blocks (Heal and Rusch, 1995).

In a first block, age and IQ were considered mainly to control for spurious correlations between behavioral and EEG effects induced by those factors. In a second block, EEG baseline measures were introduced. Thus, it could be analyzed if EEG baseline measures predict the training outcome. Additionally, it could be controlled that extreme baseline values did not falsely predict possible associations between behavioral effects and the changes of EEG parameters, which were added in the third block of the regression models.

Only those EEG 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 (post-training minus pre-training) 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.

SPSS (v.16) was used for statistical analysis.

3. Results

As indicated above 8 children were dropouts (NF: $n=5$; AST: $n=3$), due to an immediate urge for medical treatment ($n=3$), organizational problems of the parents ($n=2$), loss of motivation ($n=1$), or protocol violation ($n=2$)., Further 22 children (NF: $n=13$, AST: $n=9$) had to be excluded due to insufficient EEG signal quality. Thus, 72 children with ADHD (NF: $n=46$; AST: $n=26$) were included in the EEG analysis.

3.1. Pre-training (baseline) EEG activity

EEG pre-training (baseline) values are presented in Fig. 3. There were no significant differences in baseline activity between the NF and the AST group in any frequency band or the theta/beta ratio, respectively ($F(1,68)<2.41$; $p>0.10$).

For the different frequency bands, (well-known) effects concerning age, IQ and topography were obtained. With increasing age, a decrease of activity in slower frequency bands (delta: $F(1,68)=8.54$, $p<0.01$; theta: $F(1,68)=5.84$, $p<0.05$) and a reduction of the theta/beta ratio ($F(1,68)=4.89$, $p<0.05$) were observed.

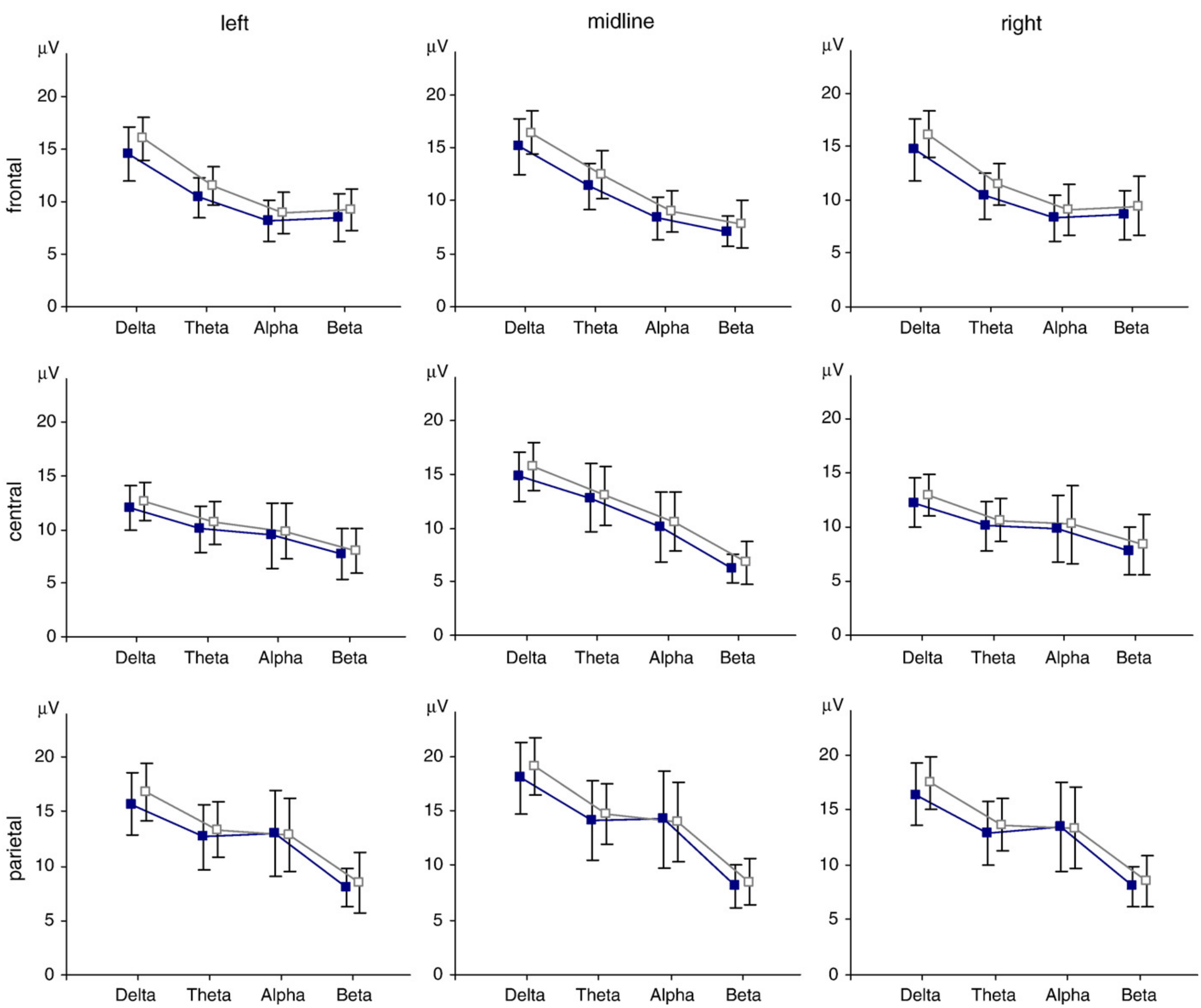

Fig. 3. EEG baseline (pre-training) measures. For each group (neurofeedback: blue, filled squares; attention skills training: gray, open squares), mean value ± standard deviation of baseline activity measured in the EEG frequency bands (delta, theta, alpha, beta) over different brain regions are plotted.

The factor IQ turned out to be significant for activity in faster frequency bands. Alpha and beta activity were larger for higher IQ (alpha: $F(1,68)=4.53$, $p<0.05$; beta: $F(1,68)=3.86$, $p<0.05$).

Topographically, delta activity was lower over central electrodes compared to frontal and parietal electrodes (factor Y: T-quad (1,68) = 8.23, $p<0.005$) and beta activity was larger over midline compared to more lateral electrodes (factor X: T-quad (1,68) = 3.75, $p<0.05$). Tendencies towards a decrease of theta activity from anterior to posterior (factor Y: T-lin (1,68) = 3.63, $p<0.1$) and towards laterally higher central theta activity (T-quad (1,68) = 3.56, $p<0.1$) were observed. The theta/beta ratio was higher over midline compared to more lateral regions (T-quad (1,68) = 17.1, $p<0.001$) and to decrease from anterior to posterior (T-lin (1,68) = 5.61, $p<0.05$).

3.2. NF vs. AST training: pre- vs. post-training comparisons

For theta activity, the repeated measure ANOVA revealed a Time x Y x Group (T-lin (1,68) = 8.51, $p<0.005$) and a Time x X x Group (T-quad (1,68) = 7.59, $p<0.01$) effect, indicating a larger reduction of theta activity in the NF group vs. the AST group over centro-parietal midline electrodes (see Fig. 4). Calculating a specific contrast (average of central-midline and parietal-midline) revealed a significant decrease for the NF group only (NF: -0.62 ± 1.16; $t(45)=-3.63$, $p<0.001$; AST: 0.09 ± 1.41; $t(25)=0.34$, $p=0.74$).

For other frequency bands (delta, alpha, and beta) and the theta/beta ratio, no significant effects containing the factors TIME and/or GROUP were obtained.

Concerning the covariates, changes in beta activity were effected by age and intelligence. A significant Time x Y x Age interaction effect ($F(2,136)=3.88$, $p<0.05$) indicated a larger decrease of frontal beta activity at post-training measurement with increasing age. This reduction of beta activity related to age was accompanied by a corresponding effect (tendency) for the theta/beta ratio (Time x Y x Age: $F(2,136)=2.49$, $p<0.1$). Furthermore, a significant Time x X x IQ interaction effect ($F(2,136)=4.03$, $p<0.05$) was observed due to a larger pre- to post-training decrease of beta activity over midline electrodes with increasing IQ.

3.3. Comparison of theta/beta and SCP training

For the comparison of theta/beta and SCP training, the EEG of the intermediate testing was additionally taken into account. A further four children had to be excluded from this analysis because of an insufficient number of artefact-free segments.

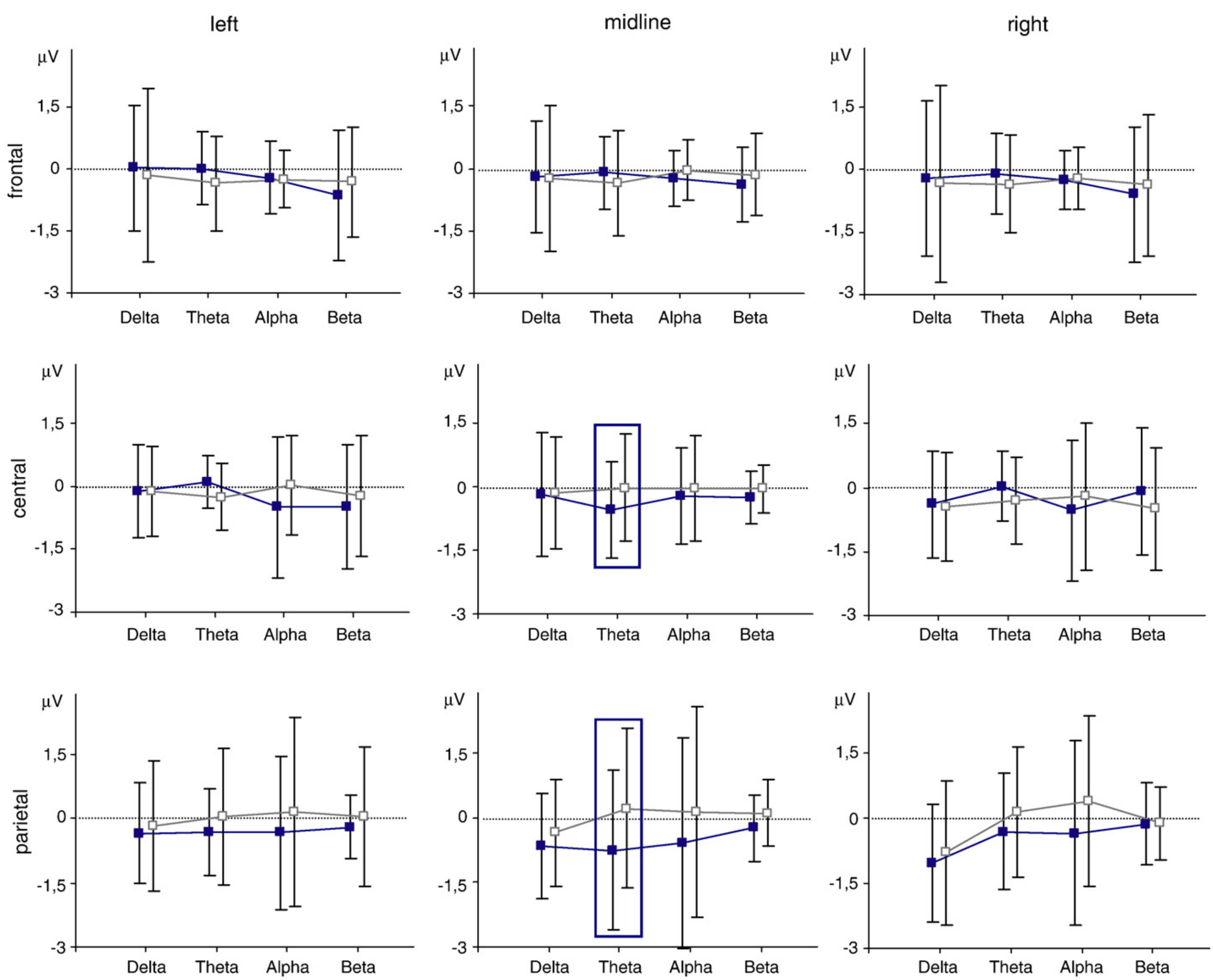

Fig. 4. EEG change (post-training minus pre-training) measures. For each group (neurofeedback: blue, filled squares; attention skills training: gray, open squares), mean value ± standard deviation of changes (post-training minus pre-training) in the EEG frequency bands (delta, theta, alpha, beta) over different brain regions are plotted. In the NF group, there was a decrease of theta activity at central-midline and parietal-midline electrodes.

Table 2
Block-wise linear regression analyses.

	Change FBB-HKS Total score	Change FBB-HKS Inattention subscale	Change FBB-HKS Hyperactivity/impulsivity subscale
Neurofeedback (theta/beta, SCP) training	–	–	–
Age, IQ			
EEG baseline measures			
EEG change measures			
Theta/beta training block	$R=0.465$ $F(2,37)=4.70$, $p=0.016$	$R=0.378$ $F(1,37)=5.84$, $p=0.021$	$R=0.399$ $F(1,37)=6.83$, $p=0.013$
Age, IQ	–	–	–
EEG baseline measures	theta-parietal-midline $\beta=-0.281$, $p=0.1$	theta-parietal-right $\beta=-0.378$, $p=0.021$	theta-parietal-midline $\beta=-0.399$, $p=0.013$
EEG change measures	theta-parietal midline $\beta=-0.330$, $p=0.05$	–	–
SCP training block	$R=0.339$ $F(1,37)=4.69$, $p=0.037$	–	$R=0.644$ $F(2,37)=12.4$, $p<0.001$
Age, IQ	–	–	–
EEG baseline measures	alpha-parietal-left $\beta=-0.339$, $p=0.037$	–	alpha-parietal-left $\beta=0.379$, $p=0.006$
EEG change measures	–	–	alpha-central-midline $\beta=-0.470$, $p=0.001$

Predictor variables under consideration: age and IQ (first block), EEG baseline measures (second block) and EEG change measures (third block). Behavioral outcome was assessed via the German ADHD rating scale (FBB-HKS) completed by parents. Analyses were done for the complete NF training, the theta/beta training block and the SCP training block.

Neither for the change of theta activity (PROTCOL: $F(1,37)=0.09$; $p=0.76$; PROTOCOL x X: $F(2,74)=0.42$; $p=0.61$; PROTOCOL x Y: $F(2,74)=1.24$; $p=0.29$) nor for any other frequency band, could a significant difference between the two NF protocols be obtained. We also computed the specific contrast concerning theta activity (average of central-midline and parietal-midline electrodes) for the theta/beta and the SCP training block separately. For both NF protocols, a tendency towards a decrease was apparent (theta/beta training: -0.31 ± 1.02; $t(41)=-1.98$; $p<0.1$; SCP training: -0.28 ± 0.97; $t(41)=-1.86$; $p<0.1$).

3.4. Relations between resting EEG and behavioral outcome

Results of the block-wise linear regression analyses are summarized in Table 2.

For the outcome of the *combined NF training*, no significant predictor variables were obtained — neither for the FBB-HKS total score nor for the inattention and hyperactivity/impulsivity subscales.

For the *theta/beta training* block, theta activity over parietal-midline sites at baseline and the change of theta activity over this region remained in the regression model for the FBB-HKS total score, accounting for about 20% of the variance ($R=0.465$; $F(2,37)=4.70$, $p=0.016$). As can be seen in Fig. 5, higher theta activity at baseline and a larger decrease of theta activity were associated with a larger decrease of the FBB-HKS total score for the theta/beta training block. For the inattention and the hyperactivity/impulsivity subscales, baseline theta activity at parietal-right and parietal-midline sites, respectively were significant predictor variables.

For the *SCP training* block, the model with the best fit (explaining about 40% of variance) was obtained for change of the hyperactivity/impulsivity subscale with alpha activity measured over parietal-left sites at baseline and the change of alpha activity over central-midline electrodes as significant predictor variables ($R=0.644$; $F(2,37)=12.4$, $p<0.001$). Lower alpha activity at baseline and a larger increase of alpha increase following SCP training were related to a larger improvement (see Fig. 6).This change of alpha activity in the SCP block also contributed substantially to the prediction of the change of the impulsivity/hyperactivity subscale for the complete NF training ($R=0.362$; $F(1,40)=5.87$, $p<0.05$). Alpha activity measured over parietal-left sites at baseline also contributed to the prediction of the change of FBB-HKS total score following SCP training ($R=0.339$; $F(1,37)=4.69$, $p<0.05$).

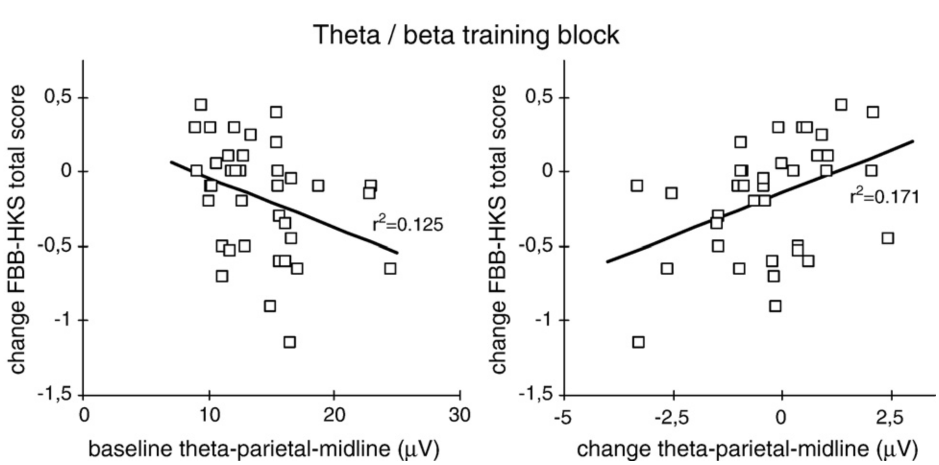

Fig. 5. Theta/beta training block. Left: change of the FBB-HKS total score vs. theta activity measured at baseline over parietal-midline electrodes. Right: change of the FBB-HKS total score vs. change of theta activity over parietal-midline electrodes. The linear regression lines are also shown.

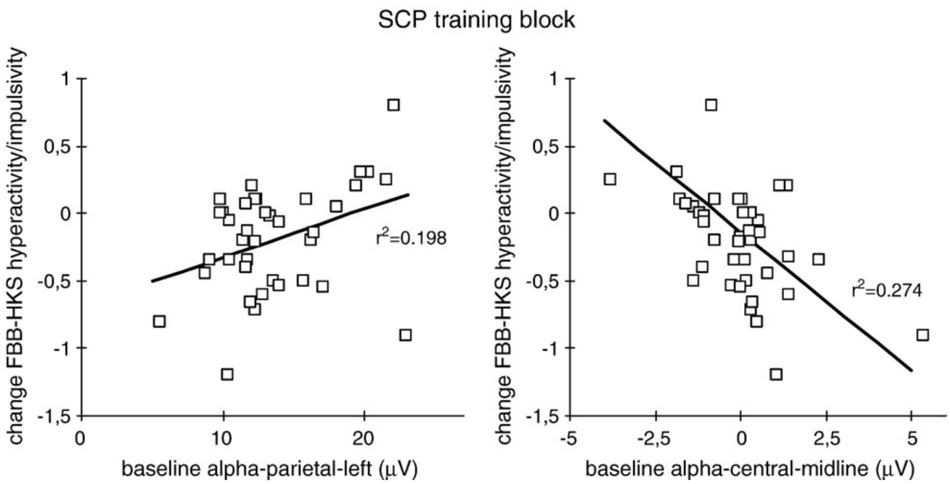

Fig. 6. SCP training block. Left: change of the FBB-HKS hyperactivity/impulsivity subscale vs. alpha activity measured at baseline over parietal-left electrodes. Right: change of the FBB-HKS hyperactivity/impulsivity subscale vs. change of alpha activity over central-midline electrodes. The linear regression lines are also shown.

For the *control training (AST)*, an increase of beta activity over parietal-midline electrodes was associated with a decrease of the impulsivity/hyperactivity subscale ($R = 0.426$; $F(1,24) = 5.11$, $p < 0.05$).

In none of the models under study, was a significant linear relationship between the behavioral outcome and age or IQ found.

4. Discussion

The impact of a combined neurofeedback training (theta/beta training, SCP training) on the resting EEG was studied in children with ADHD in comparison to an attention skills training as control. Further, EEG measures recorded at baseline as well as changes of EEG parameters from pre- to post-training were related to the clinical outcome. Results only partly confirmed the assumptions of specific protocol-dependent effects of NF training on the resting EEG. Nevertheless, some distinct EEG effects could be observed.

4.1. Pre-training vs. post-training EEG comparisons

In contrast to the control training, NF led to a reduction of theta activity in centro-parietal regions. The reduction of theta activity was comparable for the theta/beta and the SCP training block, but neither block by itself resulted in significant changes. Thus, the hypothesis that NF leads to protocol-specific changes (theta/beta vs. SCP) could not be confirmed in the pre- vs. post-training comparisons.

Further training and protocol-specific EEG effects could not be obtained, even for beta activity and the theta/beta ratio, which were targeted directly during theta/beta training.

During training, children practiced to get into an 'active', attentive state whereas, during recording of the resting EEG, they should be relaxed. Thus, our results might indicate that neuronal regulation capability does not necessarily have a corresponding impact on the resting EEG. The finding of Monastra et al. (2002), who reported a decrease of the theta/beta ratio after theta/beta training, need not be seen to contrast with our results, since EEG assessment in Monastra et al. (2002) did not rely on the resting EEG solely, but was based on an index encompassing also EEG activity during reading, listening, and drawing.

This notion is also supported by the results of NF studies in healthy adults. The group of Gruzelier, who carried out a series of studies investigating the impact of different frequency band protocols on cognitive–behavioral and neurophysiological measures, reported protocol-specific effects (improvements) in attention and working memory tasks (Egner and Gruzelier, 2004; Vernon et al., 2003). However, in the resting EEG, associations between a training protocol and changes in the spectral topography of the spontaneous EEG appeared to be ambiguous (Egner et al., 2004). In the same line, Doppelmayr et al. (2009) reported no statistically significant increase of SMR activity in the resting EEG after 25 units of SMR training, although there was a clear increase of SMR amplitudes in training trials.

When discussing pre-training to post-training effects, the number of training sessions also has to be taken into account. So far no empirical evidence is available concerning the number of units needed to obtain training effects. The number of 36 NF units in our study is comparable to recent controlled studies (Doehnert et al., 2008: 30 units; Fuchs et al., 2003: 36 units; Leins et al., 2007: 30 units; Monastra et al., 2002: 43 units of 40 minutes). In our study, children clearly improved at the behavioral/clinical level (Gevensleben et al., 2009), accompanied by reduced theta activity in the resting EEG. When comparing theta–beta and SCP training, which had been conducted in two separate blocks, the number of 18 training units for each protocol might have been too small to reveal protocol-specific effects in the resting EEG.

4.2. Protocol-specific EEG — behavior associations

Relations between EEG baseline and change measures and effects on the behavioral level were studied using block-wise linear regression models. Significant improvements in the behavior ratings of parents and teachers concerning inattention and hyperactivity/impulsivity had been obtained after NF (Gevensleben et al., 2009). Although the combined NF training was related to behavioral improvements, there was no significant association of the latter with EEG baseline or change measures.

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. Generally, associations were stronger for hyperactivity/impulsivity than inattention symptoms. This could be due to the resting condition studied, but might be different in an attention-demanding task.

Besides the functional significance, further studies could address which neuronal networks are involved in the EEG effects associated with NF training, including the role of thalamo-cortical synchronisation (Rothenberger, 2009). This can be done by simultaneous EEG-fMRI recordings, which allow investigation of how distributed neuronal networks correlate with the EEG frequency bands (Debener et al., 2006); e.g., activation in the thalamus but also in the anterior cingulate correlate with alpha activity (Difrancesco et al., 2008).

4.3. Practical relevance of the results

As indicated in the previous paragraph, baseline EEG measures had predictive value concerning the success of theta/beta training and SCP training, respectively. Before we may conclude that children with different EEG patterns may benefit from different NF protocols, our results have to be confirmed in larger samples.

Also, fully standardized recording conditions seem to be an indispensable prerequisite, and indication criteria should not be based solely on EEG measures recorded in a resting condition but also on EEG or ERP parameters reflecting cognitive task processing (see Section 4.1). Moreover, other, non-neurophysiological factors should be taken into account. Drechsler et al. (2007) revealed a significant effect of parental support concerning the outcome of NF training in children with ADHD. Personality factors influenced the success of SCP training embedded in a behavioral treatment program in patients with epilepsy (Kotchoubey et al., 2001). In the linear regression models applied in our study, age and IQ did not turn out as significant predictor variables. However, findings could be different if, e.g., a broader age range than 8 to 12 years was considered, and effects need not be linear.

4.4. Methodological issues

For beta activity, pre- to post-training changes did not depend on the NF training, but were affected by age and IQ. In children with a high IQ, and in older children, respectively, post-training beta activity was lower, particularly over frontal-midline sites.

Although the spectral distribution of the resting EEG is considered as relatively stable and, therefore, can be seen as a trait variable, it is also sensitive to state characteristics (Hegerl et al., 2008). In this respect, the reduction of beta activity in children with high IQ, and in older children, might reflect adaptation to the laboratory setting. 'Habituation' effects are known to be related to intelligence — at least in infants (Kavsek, 2004). Hence, it should be taken into account that such factors could mask potential training effects at the neurophysiological level.

5. Conclusions

Differential EEG patterns for theta/beta and SCP training provide further evidence that distinct neuronal mechanisms may contribute to similar behavioral improvements in children with ADHD. Nevertheless, findings do not allow us to conclude that all trained EEG parameters will lead to distinct changes in the resting EEG. Future studies should address how to optimize NF training for children with ADHD, particularly which treatment protocol (or combination of protocols), and how many training sessions, might be appropriate for an individual child.

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