



Comparing tomographic EEG neurofeedback and EMG biofeedback in children with attention-deficit/hyperactivity disorder



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ABSTRACT

Two types of biofeedback (BF), tomographic electroencephalogram (EEG) neurofeedback (NF) and electromyographic biofeedback (EMG-BF), both with phasic and tonic protocols, were compared for treatment effects and specificity in attention-deficit/hyperactivity disorder (ADHD). Thirteen children with ADHD trained their brain activity in the anterior cingulate cortex (ACC), and twelve trained activity of arm muscles involved in fine motor skills. In each training session, resting state 24-channel EEG and training performances were recorded. Both groups showed similar behavioral improvements and artifact reduction in selected conditions, with no significant advantages despite medium effect sizes on primary outcomes for NF. Only the EMG-BF group, however, showed clear improvement in training regulation performance, and specific motor coordination effects. The NF group tended to present individual normalization of trained frequency bands in the ACC during rest across training. The results provide evidence for some specific effects in our small sample, albeit only to a small extent.

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1. Introduction

Attention-deficit/hyperactivity disorder (ADHD), with a world-wide prevalence of approximately 5.2%, is one of the most frequent disorders in psychiatry (Polanczyk, de Lima, Horta, Biederman, &

Rohde, 2007; Steinhausen, Winkler-Metzke, Meier, & Kannenberg, 1998). The core symptoms of ADHD are inappropriate levels of inattention, impulsiveness, and hyperactivity (Barkley, 1997). In addition, children with ADHD often have comorbid motor coordination problems (Fliers et al., 2008; Kadesjo & Gillberg, 2001; Rommelse et al., 2007; Slaats-Willemse, de Sonnevill, Swaab-Barneveld, & Buitelaar, 2005; Steger et al., 2001).

With regard to the core symptoms of ADHD, several treatments are typically used. Although the use of stimulant medication is widespread, only about 70% (Barkley, DuPaul, & McMurray, 1991) of children with ADHD respond to pharmacological treatment. In addition, side effects, reluctance to take medication, and the lack of clear positive long-term effects are serious limitations of this treatment (Banaschewski et al., 2006). Consequently, there is a strong demand for alternative behavioral treatments such as neurofeedback (NF), which, based on learning of regulation

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or operant conditioning of brain activity, is considered an alternative or additional treatment (Heinrich, Gevensleben, & Strehl, 2007). NF is geared toward building the self-control of neurophysiological functions which are altered in ADHD (Doehnert, Brandeis, Schneider, Drechsler, & Steinhausen, 2013; Monastra, Lubar, & Linden, 2001) and to normalize them, but may also support compensatory regulation strategies (Gevensleben, Rothenberger, Moll, & Heinrich, 2012). The regulation of theta (4–8 Hz) and beta (13–20 Hz) frequencies as well as the training of slow cortical potentials (SCP) are typical NF training protocols used for the treatment of children with ADHD (Drechsler et al., 2007; Gevensleben, Holl, Albrecht, Vogel, et al., 2009; Heinrich, Gevensleben, Freisleder, Moll, & Rothenberger, 2004; Leins et al., 2007; Lubar, Swartwood, Swartwood, & O'Donnell, 1995; Strehl, Leins, et al., 2006; Thompson & Thompson, 1998), which have been used in an adapted and tomographic variant in the study presented here (see also Liechti et al., 2012).

There is increasing evidence that training the self-regulation of neurophysiological parameters through NF, using scalp electroencephalogram (EEG) from a single channel (conventional NF), improves ADHD symptoms (Doehnert, Brandeis, Straub, Steinhausen, & Drechsler, 2008; Drechsler et al., 2007; Gevensleben, Holl, Albrecht, Vogel, et al., 2009; Heinrich et al., 2004; Kropotov et al., 2005; Leins et al., 2007; Strehl, Trevorrow, et al., 2006). Correspondingly, a meta-analysis (Arns, de Ridder, Strehl, Breteler, & Coenen, 2009) reporting large effect sizes for inattention and impulsivity and a medium effect size for hyperactivity, even when compared to control groups, recommended NF as an “efficacious and specific” ADHD treatment. In contrast, a review by Lofthouse, Arnold, Hersch, Hurt, and DeBeus (2012) considered it only as “probably efficacious”, and a recent meta-analysis (Sonuga-Barke et al., 2013) reported only a trend for probably blinded ratings (mostly teacher ratings). As discussed in our previous publication (Liechti et al., 2012), a more efficient approach than conventional NF might be the training of intracerebral activity in specific brain regions affected in ADHD such as the anterior cingulate cortex (ACC). This brain region has consistently been implicated both in EEG-based (Albrecht et al., 2010; Fallgatter et al., 2004) and other imaging studies (metaanalyses, Cortese et al., 2012).

An important aim in NF research is to demonstrate and understand the specific mechanisms of action of training protocols and their impact on the training outcomes, and to clarify the nature of unspecific mechanisms. One approach to investigate specificity, which was pursued in our previous paper (Liechti et al., 2012), is to examine the relation of the individual learning of neurophysiological regulation to the training outcome. Another approach is to compare NF effects to those of a control training or group, which is pursued in this paper comparing the same NF group with an electromyographic biofeedback (EMG-BF) control group. An active control condition, which consists of a comparable amount and intensity of cognitive demands and patient–therapist interaction, allows to disentangle the specific and unspecific effects of NF treatment. This approach controls for unspecific effects induced by the NF setting, such as patient–therapist interaction, immediate feedback, reward, systematic training to sit still, attentional aspects of the training, expectations generated by applying electrodes, and being connected to a computer (Arns et al., 2009; Brandeis, 2011). This is contrasted with a waiting list group, which is a passive control condition eliminating only those unspecific confounds due to elapsed time and test repetition.

Some studies also reported protocol-specific neurophysiological changes (Brandeis, 2011), particularly for SCP training (Doehnert et al., 2008; Heinrich et al., 2004; Wangler et al., 2011). Some specific results have also been reported for frequency band training protocols. For example, Gevensleben, Holl, Albrecht, Vogel, et al.

(2009) found that behavioral outcome after theta/beta training correlated with theta decrease.

Only few studies have examined associations between the training regulation performance during the training and behavioral improvement, but most of them provided at least some evidence for significant relations (most recently, Gevensleben et al., 2013; for reviews, see Drechsler, 2011; Moriyama et al., 2012). In our previous publication (Liechti et al., 2012), improved clinical ADHD symptoms and differential ACC modulation were also found after NF, but there was no or little training regulation success and consequently no relationship between the training success and the training outcome. For these reasons, we concluded that unspecific or secondary NF effects such as artifact control account for much of the clinical improvement, but in order to clarify the remaining specific treatment effects, a comparison with an active control group is essential.

Control conditions are critical to determine specific effects of NF in randomized controlled trials. The choice of the appropriate control condition for NF remains a matter of debate (Gevensleben et al., 2012; Lofthouse, Arnold, & Hurt, 2012; Loo & Makeig, 2012). A sham NF group with placebo feedback utilizing the same setting and interface for training represents the most powerful control group in some respects (Lansbergen, van Dongen-Boomsma, Buitelaar, & Slaats-Willemse, 2011; Logemann, Lansbergen, Van Os, Bocker, & Kenemans, 2010). Differences in clinical outcome between regular and sham NF training which are equivalent in all other aspects of the setting, can be attributed to the specific effects of learned regulation of the targeted brain activity. However, sham NF training may induce higher drop-out rates (Arns et al., 2009) and reduce the active effort. In addition, implementing a sham condition in clinical research with ADHD children is critical from an ethical point of view. Another biofeedback (BF) method with genuine feedback and a possible therapeutic benefit, such as the feedback of motor activity, seems to be a preferable alternative. In addition, blinded ratings (Sonuga-Barke et al., 2013) plus evaluation of blinding (Gevensleben, Holl, Albrecht, Vogel, et al., 2009) may offer reasonable control for unspecific expectancies. EMG-BF has been used in several studies to improve muscle relaxation and reduce hyperactivity in children with ADHD (for reviews see Arnold et al., 2011; Cobb & Evans, 1981; Lee, 1991). In the present study, EMG-BF focuses directly on the improvement of fine motor skills and motor regulation, which is often impaired in children with ADHD (Pitcher, Piek, & Barrett, 2002; Pitcher, Piek, & Hay, 2003) and may therefore represent a meaningful treatment for this group. In addition, this EMG-BF training provides well-matched control conditions for NF training (for a more detailed description of the method, please refer to the case description of this control condition by Maurizio, Liechti, Brandeis, Jäncke, and Drechsler (2013), and to the supplementary material).

So far, only one study has used EMG-BF as a control condition for NF (Bakhshayesh, Hansch, Wyszkon, Rezai, & Esser, 2011). In this study, the participants had to reduce the EMG amplitude of the feedback signals of the forehead musculature. Significant improvement of ADHD symptoms was reported after both training conditions; there was more improvement after NF for inattention symptoms on parent rating scales and reaction times in neuropsychological tests, but no significant differences were found on teacher ratings or other measures, suggesting that NF may only have limited specific behavioral effects when unspecific factors are controlled for. The specific mediators of response of NF and EMG-BF, however, are still unknown and need to be investigated further. For this reason, in the present study, we compare NF and EMG-BF in two groups of children with ADHD and investigate training regulation performance, artifact control, and resting EEG changes in the course of the training and behavioral and neuropsychological changes between pre- and post-assessments.

We hypothesized that ADHD behavioral symptoms would be mitigated in both groups, although we expected larger effects for the NF. Through this new training technique, we had expected that children would learn to specifically regulate their EEG in a brain region most affected in ADHD and thereby show stronger improvement on behavioral rating scales and neuropsychological tests tapping into attention compared to the EMG-BF treatment. However, due to unspecific effects, some ameliorations in the EMG-BF group were also expected, in accordance with Bakhshayesh et al. (2011). Following our previous results providing more evidence for regional normalization at rest than for learning of regulation (Liechti et al., 2012), we expected the individual normalization of resting EEG activity in the ACC to be specific to the tomographic NF treatment. For the EMG-BF group, changes in the resting EEG and a stronger improvement on neuropsychological tasks related to fine motor skills and bimanual coordination were expected.

2. Materials and methods

In a randomized controlled clinical trial (ISRCTN 82524080) we planned to investigate three different BF treatments of ADHD using tomographic NF, conventional NF (not completed due to time constraints), and EMG-BF in a blinded parallel group pre-post design, with randomization constrained by group balancing requirements. The trial conformed to the standards of the Declaration of Helsinki and was approved by the local ethics committee.

2.1. Subjects

The participants had to meet diagnostic criteria for ADHD combined subtype (DSM-IV, 2004). For a few participants (NF: $n = 1$, EMG-BF: $n = 3$) the ADHD DSM-V age-of-onset criterion was used (see also Liechti et al., 2012), and one (NF) subject's symptoms were not fully met at school. The diagnostic procedure included a semi-structured clinical diagnostic interview PACS (Parental Account of Children's Symptoms; Taylor, Schachar, Thorley, & Wieselberg, 1986) and the Conners' Teacher Rating Scale Revised (CTRS; Conners, Sitarenios, Parker, & Epstein, 1998b), according to a validated algorithm (Valiko et al., 2010). Further inclusion criteria were age between 8.5 and 13 years, $IQ \geq 80$, no known neurological disorder, and no severe comorbid conduct disorders, depression or anxiety disorders. Stimulant medication was permitted if the dosage was kept constant throughout the training period. For pre- and post-training assessments, medication had to be suspended at least 48 h previously. Twenty-eight subjects were randomly assigned to one of the two (originally three) completed BF training programs, which were all introduced as experimental treatments for ADHD. The children and their parents gave written consent to participate in the study and agreed to be informed about the training assignment only after post-assessments were completed. Thus, both parents and teacher were blinded with regard to treatment assignment.

Two subjects dropped out of the EMG-BF group (insufficient compliance due to oppositional behavior, after the eighth training session, depressive occurrence caused by the medication after pre-testing) and one child from the NF group had to be excluded from the analyses due to a change of medication. Group characteristics for the remaining children (NF: $n = 13$, EMG-BF: $n = 12$) are listed in Table 1. Before the training, there were no significant differences between the groups regarding demographic, psychological and clinical variables.

2.2. Study design

The training consisted of 36 training units held as double lessons two to three times per week over a period of approximately 12 weeks. Before and after the training program, pre- and post-training assessments took place. In addition to EEG, ERPs in cognitive tasks, and a battery of neuropsychological tests, these assessments included behavioral ratings by parents, teachers, and participants.

The training program of both groups consisted of a tonic and a phasic protocol. While in the tonic training, participants had to maintain the same state (activation/deactivation) over several minutes, in the phasic training, they constantly had to switch between states of activation and deactivation, according to the short (10 s) randomized trials. The first session of the training program started with tonic training only, followed by sessions including both protocols arranged in alternating order from one session to the next (Supplementary Fig. S2). In the course of the training, transfer blocks were introduced successively, enabling the subjects to practice their strategies with reduced feedback from the computer.

At the beginning of each training session, an eyes-open resting EEG was recorded for 2 min, followed by epochs of systematic eye movements to calculate artifactual ICA components for online eye-artifact correction during the training. All lessons of both training groups consisted of four training blocks of 3–8 min each, followed by self-ratings of current mental states and feeling of feedback control. The duration of an entire training session was about 3 h, including preparation and the placement of 32 electrodes, EEG-baseline recording, instructions, break, and hair washing.

Table 1
Group characteristics.

| | NF $n = 13$ | EMG-BF $n = 12$ | t-test |
|------------------------------------|------------------|------------------|--------|
| Boys/girls | 11/2 | 11/1 | n.s. |
| Age [years] | | | |
| Mean | 10.6 \pm 1.3 | 10.0 \pm 1.2 | n.s. |
| Range | 8.9–12.9 | 8.5–12.0 | |
| Handedness (left/right) | 0/13 | 1/11 | |
| Estimated IQ | 111.1 \pm 10.0 | 118.1 \pm 12.9 | n.s. |
| Stimulant medication | 1 | 1 | |
| CPRS [T-scores] | | | |
| Global index | 69.8 \pm 10.1 | 65.4 \pm 7.3 | n.s. |
| Inattention (DSM-IV) | 73.5 \pm 10.0 | 68.4 \pm 7.5 | n.s. |
| Hyperactivity/impulsivity (DSM-IV) | 74.3 \pm 10.1 | 71.7 \pm 8.4 | n.s. |
| Total score (DSM-IV) | 75.3 \pm 9.6 | 71.4 \pm 7.7 | n.s. |
| CTRS [T-scores] | | | |
| Global index | 63.2 \pm 9.7 | 68.8 \pm 8.5 | n.s. |
| Inattention (DSM-IV) | 61.2 \pm 6.7 | 65.3 \pm 8.8 | n.s. |
| Hyperactivity/impulsivity (DSM-IV) | 62.2 \pm 12.6 | 69.3 \pm 8.6 | n.s. |
| Total score (DSM-IV) | 62.7 \pm 9.7 | 68.5 \pm 8.7 | n.s. |
| CBCL [T-scores] | | | |
| Social withdrawal | 54.0 \pm 10.5 | 52.9 \pm 10.4 | n.s. |
| Somatic complaints | 61.9 \pm 12.1 | 55.7 \pm 7.1 | n.s. |
| Anxiety/depression | 52.9 \pm 8.7 | 55.7 \pm 8.8 | n.s. |
| Social problems | 59.3 \pm 8.4 | 62.7 \pm 9.6 | n.s. |
| Thought problems | 51.8 \pm 7.7 | 55.3 \pm 11.3 | n.s. |
| Attention problems | 64.5 \pm 3.8 | 66.6 \pm 5.3 | n.s. |
| Delinquent behavior | 60.1 \pm 10.5 | 57.8 \pm 10.0 | n.s. |
| Aggressive behavior | 62.1 \pm 10.8 | 61.3 \pm 6.2 | n.s. |
| Internalizing problems | 56.4 \pm 10.9 | 55.5 \pm 9.6 | n.s. |
| Externalizing problems | 62.0 \pm 10.9 | 61.0 \pm 5.8 | n.s. |
| Total problem score | 61.7 \pm 9.2 | 62.5 \pm 7.8 | n.s. |

CPRS, Conners' Parent Rating Scale; CTRS, Conners' Teacher Rating Scale. ADHD primary symptoms are quantified by CPRS and CTRS DSM-IV T-scores, and general psychopathology by parent-rated CBCL T-scores; estimated IQ is based on four subtests of the German version of the Wechsler Intelligence Scale for Children IV (NF group results also reported in Liechti et al., 2012).

2.3. Training procedures

In preparation for NF and EMG training sessions, 24 electrodes were placed at the scalp according to an extended 10–20 montage with reference at Fz and ground at FC6 (Fig. 1). Two additional electrodes were used for electrooculography (EOG) and another one for electrocardiography (ECG) recording. In addition, pairs of electrodes (at a center-to-center distance of 20 mm) were placed on the *musculus digitorum* of the right and left forearm and for the EMG-BF group also on the right *musculus trapezius* in accordance with the locations and orientations recommended by SENIAM (Hermens et al., 1999). In the NF group, the EMG electrodes were only mock, allowing the topographic EEG to be expanded by six scalp electrodes (Afz, CPz, POz, Iz, FC1, FC2; see also Fig. 1).

During the training, signals were continuously recorded from 33 active electrodes (AE1, Easy Cap, FMS, Munich) in both groups. The signal was amplified through a BrainAmp amplifier (Brain Products, Gilching, Germany), analog filtered between 0.016 and 250 Hz, and digitized at a sampling frequency of 500 Hz. To avoid EEG distortion, artifacts at 16.66 Hz from a nearby railway track was compensated by an active shielding. For signal processing, a forward bandpass filter (Butterworth 2nd order) set at 0.1–30 Hz was used for EEG/ECG and at 0.1–100 Hz for EMG signals.

The software SAM ("Self-regulation and Attention Management") (Gevensleben, Holl, Albrecht, Schlamp, et al., 2009), which had been adapted for multichannel recordings, advanced artifact handling, and estimation of intracerebral activity using standardized low resolution electromagnetic tomography (sLORETA, Pascual-Marqui, 2002) was used for online feedback calculation and presentation (Liechti et al., 2012). While the activity of the ACC with the Montreal Neurological Institute (MNI) coordinates (X, Y, Z) = (5, 10, 30) was fed back for the NF group, the EMG activity of the forearms was used for feedback in the EMG-BF group. The influence of artifact was controlled through a sad face appearing on the screen and interrupting the feedback any time EEG or EOG signals exceeded ± 100 –250 μ V or ± 15 –25 μ V for the 25–35 Hz band and through the monitoring of the quality on a separate surveillance station. The artifact thresholds were typically kept constant throughout the training course after initial adjustment for the individual base level, and was readjusted only rarely for major changes on specific days. In the EMG-BF group, except for the tonic deactivation condition, an additional upper EMG threshold was defined for EMG channels and flowed in as artifact, which was also fed back using the sad face. Otherwise, both

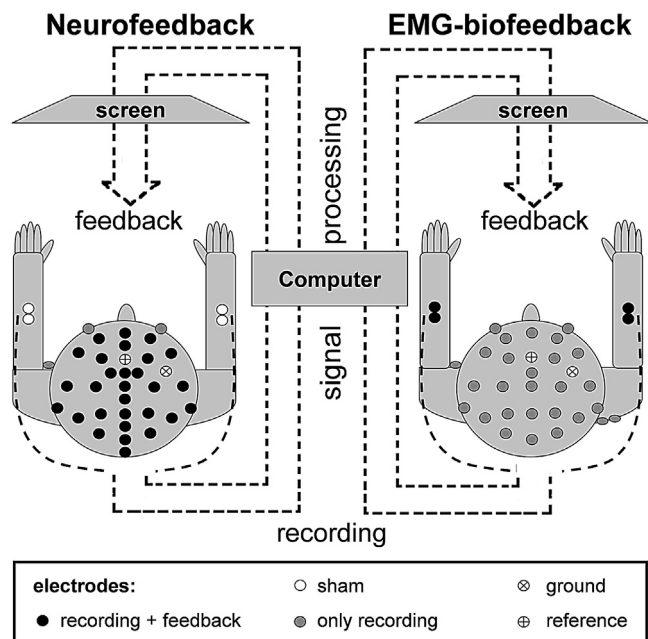


Fig. 1. Training setting and electrodes of the two training methods. The body signals are recorded by the electrodes, amplified and processed by the computer system and fed back to the participant on the computer screen. Only the “recording + feedback” electrodes (●) signal is used for the processing of the feedback. The “only recording” electrodes (◐) signal is used for online analysis, whereas sham electrodes (○) are not used for signal recording, but applied on the arm of the NF group to facilitate blindness of the study. In both treatments, all recording electrodes flowed into the artifact control and were fed back through a sad face appearing on the screen and interrupting the regulation feedback.

the NF and EMG-BF were parallelized regarding training settings and protocols, as illustrated in Fig. 1 and described below.

2.4. Tonic protocol

The tonic protocol consisted of blocks of 120–480 s. Children were requested to simultaneously regulate two separate dimensions, represented by separate bars on the left and right side of the screen. The task of the children was to regulate the heights of the bars below or above a desired threshold, which represented the frequency content of the feedback parameters. Positive feedback was received as long as the criteria of both dimensions were met. The frequency content was calculated using a Butterworth bandpass filter (48 dB/octave). Every 100 ms, feedback was given using a moving time window of 2 s length. The activation condition lasted for twice as long as the deactivation condition, and except for the first session, both conditions were trained in each tonic lesson. Individual thresholds were determined according to recorded daily baseline values.

2.4.1. Neurofeedback

In NF tonic training, theta (4–7.5 Hz) and beta (14–20 Hz) band activity in the ACC voxel (length of vector (ACC-I) representing the amplitude of this source vector irrespective of its orientation; see Fig. 2 in Liechti et al., 2012) were trained. The participant had to enhance beta and simultaneously reduce theta activity in the activation condition, whereas a reduction of beta and an enhancement of theta was required in the deactivation condition. Theta and beta activity were fed back by the bars on the left and on the right of the screen. As baseline, a 3-min resting EEG with eyes open was measured at the beginning of the tonic lesson.

2.4.2. EMG-biofeedback

In the EMG-BF tonic training, muscle activity (55–95 Hz) of both arms was trained simultaneously with different demands for each hand. Muscle activity of the right arm was fed back by the bar on the right side, muscle activity of the left arm by the bar on the left side. In the activation condition, muscle activity of one arm had to be increased by pulling a hand dynamometer, but without exceeding an upper muscle activity threshold. At the same time, the muscle activity of the other arm had to be reduced. In order to maintain some measurable muscle activity in this arm, it was balanced on two soft balls while holding a small ball in the hand. Compared to the NF training, the duration of the blocks was shorter, the number of blocks was doubled, and the training program alternated between both hands in order to avoid overexertion. The baseline recording lasted for 60 s preceding each training condition, during which the participant pulled the dynamometer (1.5 kg)

while the contralateral arm balanced on two balls with a third ball in the hand (see Fig. 1b in Maurizio et al., 2013).

In the deactivation condition, muscle activity of both arms had to be reduced while the writing hand was performing a circular drawing movement in a drawing template. Meanwhile, the contralateral arm was resting on two softballs, with another ball in the hand (see Fig. 1c in Maurizio et al., 2013). The participants were instructed to perform steady pen movements without pressure. Baseline lasted for 60 s with the same instructions as in the feedback phase.

2.5. Phasic protocol

The phasic protocol consisted of blocks with 20–40 trials each. Each trial presented a 2 s baseline followed by a 4 s-feedback phase. The trials were separated by an inter-stimulus interval of 4 ± 1 s. Every 100 ms, the position and color of a flying ball was given as feedback, using a 500 ms-length moving time window on the feedback signal. Except for a learning phase of two sessions, during which the conditions were trained separately, activation and deactivation trials were presented with equal frequency (1:1) in a random order in the same block. A red or blue colored bar appearing at the beginning of each feedback phase indicated whether an increase or decrease of activation was required, relative to the calculated threshold of the last 1.5 s of the baseline. A “+” was indicated at the end of successful trials, whereas a “–” appeared on the screen for unsuccessful trials. A trial was successful when the ball stayed in the correct part of the screen for most of the feedback time. The participant was told that he should find appropriate strategies in order to move the ball on the screen up or down.

2.5.1. Neurofeedback

In the NF phasic protocol, the regulation of slow potential shifts in the vertical z-direction of the ACC activity (ACC-z; see Fig. 2 in Liechti et al., 2012) was trained. In the activation condition, an increase of ACC-z activity inducing negative potential shift in the central region on the scalp was requested, whereas during deactivation trials, opposite polarities should occur.

2.5.2. EMG-biofeedback

In the EMG-BF phasic protocol, in both conditions, a dynamometer was pulled by one hand while the other hand/arm rested on the table (see Fig. 1a in Maurizio et al., 2013). The EMG activity of the hand pulling the dynamometer had to be increased in the activation condition and decreased in the deactivation condition. In the activation condition, the participant had to accurately dose his force in order not to exceed an upper EMG limit. For feedback in the phasic blocks, the EMG signal was filtered with a Butterworth bandpass filter (55–95 Hz, 48 dB/octave) and rectified. To avoid overexertion, dynamometer training alternated between the left and right hand.

2.6. Data processing and analyses

To evaluate the training regulation performance of all blocks except transfer blocks, for the NF and EMG-BF training in both phasic/tonic protocols and activation/deactivation conditions, the percentage of time spent in the desired state of regulation was calculated and related to the total trial duration without time-comprising artifacts. The percentage of time with artifact feedback (sad face) was determined using the same procedure. For the phasic condition, an additional total score summed over deactivation and activation was calculated per block.

For all offline analyses, the program Brain Vision Analyzer (Version 1.05.0005, Brain Products, Gilching, Germany) was used. The EEG was filtered off-line using a bandpass filter set at 0.1–70 Hz and a 50 Hz notch filter. Large technical and movement artifacts were rejected automatically. For ocular correction, an ICA was used. An average reference was calculated, including the Fz recording reference. Through visual appraisal, remaining artifacts were rejected semi-automatically. For analyses of the activity in the ACC, additional channels were calculated using sLORETA-based linear combinations of 24 scalp channels. For fast Fourier transformation (FFT), resting EEG data were segmented into 2.048 s epochs using power density computation (0.488 Hz resolution, 10% Hanning windowing, full spectrum). The absolute power of theta (4–7.5 Hz), beta (14–20 Hz) activity, alpha (7.5–12.5 Hz, in supplementary material), whole spectrum (total, 1.5–25 Hz) and theta/beta ratio was calculated. In addition, averaged power of the pool across all scalp channels (all) used in the EMG-BF training and the three sagittal regions (frontal, central, posterior) were calculated.

2.7. Questionnaires and behavioral assessments

For the screening of clinical conditions and comorbidities, the parents completed the Child Behavior Checklist (CBCL; Achenbach, Howell, Quay, & Conners, 1991). To estimate the IQ, a short form of the German version of the Wechsler Intelligence Scale for Children IV (HAWIK-IV; Waldmann, 2008) with the following subtests was used: “Vocabulary”, “Block Design”, “Letter-Number Sequencing”, and “Symbol Search”.

Pre- and post-training assessments included the German standardized DSM IV questionnaire for ADHD (FBB-HKS; Döpfner, 2000), the Conners’ Parent Rating Scale-Revised (CPRS; Conners, Sitarenios, Parker, & Epstein, 1998a), the Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000) and the German version of the Strengths and Difficulties Questionnaire (SDQ; Goodman,

Table 2
Behavioral data pre- and post-training.

| | NF <i>n</i> = 13 | | | | EMG-BF <i>n</i> = 12 | | | | Repeated measures ANOVAs | | | | | |
|------------------------------------|------------------|---------------|----------------|----------|----------------------|---------------|----------------|----------|--------------------------|----------|----------------|----------|----------------|----------|
| | Pre training | Post training | ES | t-test | Pre training | Post training | ES | t-test | Group | | Time | | Group × time | |
| | (η_p^2) | <i>F</i> | (η_p^2) | <i>F</i> | (η_p^2) | <i>F</i> | (η_p^2) | <i>F</i> | (η_p^2) | <i>F</i> | (η_p^2) | <i>F</i> | (η_p^2) | <i>F</i> |
| Parents ratings | | | | | | | | | | | | | | |
| FBB-HKS [severity] | | | | | | | | | | | | | | |
| Inattention | 2.28 ± 0.44 | 1.62 ± 0.59 | −1.26 | −3.73** | 1.89 ± 0.36 | 1.53 ± 0.40 | −0.94 | −3.66** | 0.10 | 2.56 | 0.51 | 24.29*** | 0.08 | 2.06 |
| Hyperactivity/impulsivity | 1.55 ± 0.67 | 1.10 ± 0.71 | −0.65 | −2.86* | 1.32 ± 0.47 | 1.09 ± 0.34 | −0.56 | −2.35* | 0.02 | 0.35 | 0.36 | 12.97** | 0.06 | 1.38 |
| Total score | 1.88 ± 0.47 | 1.34 ± 0.56 | −1.05 | −3.74** | 1.58 ± 0.36 | 1.29 ± 0.32 | −0.85 | −3.62** | 0.05 | 1.32 | 0.51 | 24.08*** | 0.09 | 2.27 |
| CPRS [raw scores] | | | | | | | | | | | | | | |
| Global index | 16.2 ± 4.7 | 12.5 ± 4.7 | −0.80 | −2.04° | 14.8 ± 4.7 | 11.2 ± 3.7 | −0.86 | −4.16** | 0.04 | 0.85 | 0.35 | 12.54** | 0.00 | 0.00 |
| Inattention (DSM-IV) | 20.5 ± 4.8 | 15.1 ± 5.6 | −1.04 | −3.35** | 18.0 ± 4.8 | 14.4 ± 4.3 | −0.78 | −3.40** | 0.04 | 0.89 | 0.48 | 20.94*** | 0.04 | 0.89 |
| Hyperactivity/impulsivity (DSM-IV) | 15.0 ± 3.7 | 10.5 ± 4.8 | −1.05 | −3.29** | 15.0 ± 5.0 | 11.3 ± 3.8 | −0.83 | −4.12** | 0.00 | 0.09 | 0.51 | 24.14*** | 0.01 | 0.26 |
| Total score (DSM-IV) | 35.5 ± 7.3 | 25.5 ± 9.4 | −1.18 | −3.60** | 33.0 ± 9.2 | 25.8 ± 7.4 | −0.87 | −4.02** | 0.01 | 0.15 | 0.53 | 26.20*** | 0.03 | 0.64 |
| SDQ parents [raw scores] | | | | | | | | | | | | | | |
| Hyperactivity | 7.62 ± 1.76 | 6.54 ± 1.71 | −0.62 | −3.48** | 7.25 ± 1.60 | 6.42 ± 1.24 | −0.58 | −1.60 | 0.01 | 0.19 | 0.31 | 10.35** | 0.01 | 0.17 |
| Total problem score | 17.38 ± 5.35 | 14.77 ± 5.42 | −0.49 | −2.43* | 17.08 ± 6.04 | 14.33 ± 4.66 | −0.51 | −1.78 | 0.00 | 0.04 | 0.27 | 8.31** | 0.00 | 0.01 |
| BRIEF parents [raw scores] | | | | | | | | | | | | | | |
| Behavioural regulation | 57.7 ± 10.4 | 51.2 ± 7.8 | −0.71 | −2.09° | 56.1 ± 10.9 | 50.6 ± 10.2 | −0.52 | −2.40* | 0.00 | 0.10 | 0.29 | 9.37** | 0.00 | 0.07 |
| Metacognition | 99.8 ± 14.6 | 92.1 ± 14.4 | −0.54 | −1.66 | 97.6 ± 19.5 | 88.6 ± 11.9 | −0.56 | −1.88° | 0.01 | 0.31 | 0.21 | 6.26* | 0.00 | 0.03 |
| Teacher ratings | | | | | | | | | | | | | | |
| CTRS [raw scores] | | | | | | | | | | | | | | |
| Global index | 11.9 ± 5.2 | 9.7 ± 4.0 | −0.48 | −2.63* | 15.9 ± 5.1 | 14.8 ± 5.5 | −0.22 | −0.96 | 0.21 | 6.01* | 0.19 | 5.38* | 0.02 | 0.53 |
| Inattention (DSM-IV) | 14.2 ± 4.6 | 14.3 ± 5.4 | 0.02 | 0.05 | 18.1 ± 6.6 | 16.8 ± 6.1 | −0.20 | −0.94 | 0.10 | 2.43 | 0.02 | 0.35 | 0.02 | 0.44 |
| Hyperactivity/impulsivity (DSM-IV) | 10.8 ± 6.3 | 9.2 ± 4.7 | −0.30 | −1.61 | 16.4 ± 5.1 | 14.9 ± 6.9 | −0.25 | −1.02 | 0.23 | 6.91* | 0.12 | 3.21° | 0.00 | 0.01 |
| Total score (DSM-IV) | 25.1 ± 10.2 | 23.5 ± 8.2 | −0.17 | −0.79 | 34.5 ± 10.9 | 31.8 ± 11.9 | −0.24 | −1.06 | 0.19 | 5.49* | 0.07 | 1.78 | 0.01 | 0.12 |
| BRIEF teacher [raw scores] | | | | | | | | | | | | | | |
| Behavioural regulation | 50.9 ± 12.4 | 44.2 ± 8.7 | −0.63 | −2.96* | 59.6 ± 10.3 | 53.3 ± 10.5 | −0.60 | −2.82* | 0.18 | 5.15* | 0.42 | 16.66*** | 0.00 | 0.02 |
| Metacognition | 92.2 ± 17.0 | 82.8 ± 16.3 | −0.56 | −2.64* | 98.3 ± 19.3 | 95.5 ± 18.7 | −0.15 | −0.70 | 0.08 | 2.05 | 0.18 | 5.19* | 0.06 | 1.49 |

FBB-HKS, parent-rated DSM-IV checklist (severity scores); CPRS, Conners' Parents Rating Scale; CTRS, Conners' Teacher Rating Scale; SDQ, Parents' Strengths and Difficulties Questionnaire; BRIEF, Behavior Rating Inventory of Executive Function. Repeated-measures analyses of variance with factors group, time, and group × time interaction were calculated for group comparison and paired *t*-tests as post-hoc test (representing separate time effects per group) with significance levels °*p* < 0.1, **p* < 0.05, ***p* < 0.01, ****p* < 0.001; ES: effect size as Cohen's *d*; η_p^2 : effect size as partial eta-squared (NF group results also reported in Liechti et al., 2012).

1997), rated by the parents. In addition, a questionnaire assessed parents' assumption about their child's group assignment as well as their expectations regarding efficacy of the different treatments. The teacher assessment included the CTRS (Conners, Sitarenios, Parker, & Epstein, 1998b) and the teachers' version of the BRIEF (Gioia et al., 2000). The subscores for inattention and hyperactivity/impulsivity of the FBB-HKS constituted the primary outcome measures of the study.

A comprehensive battery of neuropsychological tests included the subtests "sustained attention" and "flexibility" from the computerized Test for Attentional Performance for Children (KITAP; Zimmermann, Gondan, & Fimm, 2002), the subtest "Alertness" from the computerized Test for Attentional Performance (TAP; Zimmermann & Fimm, 2007), the D2 Test of Attention (Brickenkamp, 2002); the Test of Visuomotor Precision from the NEPSY (Korkman, Kirk, & Kemp, 1998), and the pegboard task from the Zurich Neuromotor Assessment Battery (Largo, Fischer, & Caffisch, 2002).

At the beginning and end of every training lesson, participants were asked to rate their current wellbeing, and after the lesson how they had felt and which strategies they had applied during the training. These ratings were completed on computerized visual analog scales with the opposite attributes and symbolic pictures as visual anchors at both ends of the scales.

2.8. Statistical analyses

For statistical analyses, the Statistical Package for the Social Sciences version 18.0 (SPSS) was used. Pre to post changes were analyzed with univariate analyses of variance (ANOVA) with repeated measures (time: pre, post) and two groups (NF, EMG-BF). Post hoc *t*-tests were conducted to separately analyze time effects per group. In the case of multiple dependent variables, multivariate analyses of variance (MANOVA) were calculated.

To analyze performance, mean values and linear regression of training performance were calculated across sessions for each participant. Group means and standard deviations (SD) were used.

As common for neuroimaging data, *t*-test were used for descriptive and topographic (*t*-maps) scalp EEG group comparisons. Our main hypothesis based on the literature and our previous paper was for changes at electrode Cz for NF, and over motor regions (C3 and C4) for EMG-BF. For the other electrodes, *p*-levels around 0.01 typically correct adequately for multiple testing with this number of electrodes for the smooth EEG topographies (Maurer, Brem, Bucher, & Brandeis, 2005). A Bonferroni correction (requiring $p = 0.00213$ with 24 electrodes) would be too strict for topographic EEG analysis because the tests are not independent across electrodes.

To analyze performance, mean values and linear regression of training performance were calculated across sessions for each participant. Group means were calculated from the individual slopes, intercepts of the linear regressions and means over lessons, and then compared.

The effect size (ES) of change was computed as the difference between the means (post–pre) divided by the corresponding pooled SD (Cohen's *d*; Cohen, 1988) for each measure and group separately. For the ANOVAs, partial eta squared is reported instead. For statistical analysis, only significant results ($p < 0.05$) or trends ($p < 0.10$) of specific interest are reported.

3. Results

3.1. Behavioral outcome

Both groups showed a similar significant improvement after training in the primary outcome measure (Table 2). Significant but not group-specific improvements after training were also found according to most other questionnaires. No GROUP by TIME interaction was found for the primary outcomes although some parent ratings reached medium effect sizes in favor of NF. The repeated measures MANOVA with group as independent factor and nine composite scores of parent-rated scales (FBB-HKS: inattention, hyperactivity/impulsivity; CPRS: global index, inattention, hyperactivity/impulsivity; SDQ: hyperactivity, total problem score; BRIEF: behavioral regulation index, metacognition index) revealed a significant improvement for TIME ($F[9, 15] = 4.04$, $p = 0.008$), but no GROUP ($F[9, 15] = 1.54$, $p = 0.220$) or GROUP by TIME interaction ($F[9, 15] = 0.52$, $p = 0.837$). A corresponding repeated measures MANOVA including five teacher-rated composite scores (CTRS: global index, inattention, hyperactivity/impulsivity; BRIEF: behavioral regulation index, metacognition index) also yielded a significant improvement over TIME ($F[5, 19] = 5.43$, $p = 0.003$), but no GROUP ($F[5, 19] = 1.45$, $p = 0.252$) or GROUP by TIME interaction ($F[5, 19] = 1.45$, $p = 0.253$).

3.2. Training performance

Unless otherwise stated, the results for performance during the actual training include only blocks with contingent feedback across all animations (Fig. 2). The NF group showed no significant change in the score. The EMG-BF group showed a significant improvement in the phasic deactivation as well as in the tonic activation condition. Similar results were found for the total score in the phasic training, which showed no significant improvement for the NF group ($t = -0.35$, $p = 0.735$) but did demonstrate a significant improvement for the EMG-BF group ($t = 4.56$, $p < 0.01$). The differences in improvement between the groups were significant for the tonic activation/deactivation conditions and the phasic deactivation condition scores, as well as for the phasic total score ($t = -4.54$, $p < 0.001$). The starting points (intercept) of the score of the two groups differed significantly for all four conditions. For the EMG-BF group, all starting points were significantly higher than the expected chance level (phasic 50%, tonic 25%), whereas for the NF group, the starting points were around or even lower than the expected chance level (significant for tonic activation).

A reduction of the artifacts was observed in all conditions for the NF group, but only in the phasic deactivation condition in the EMG-BF group. The phasic deactivation condition did not show a significantly higher reduction of artifacts for the NF compared to the EMG-BF group as was found for the phasic activation and the two tonic conditions. Generally, the EMG-BF group started the training with a higher rate of artifacts than the NF group (see results for intercept in Fig. 2). This was significant for the two activation conditions, whereas a trend was shown for the phasic deactivation condition.

3.3. Course of resting EEG

The analysis of systematic changes in the resting EEG over all training sessions is illustrated in Figs. 3 and 4. Statistics for the mean regression slopes of the EEG parameters across all subjects for theta and beta activity, theta/beta ratio and whole spectrum activity during the eyes-open resting condition in the course of the training are shown in Fig. 3. There was no systematic change for theta, beta, full band, or theta/beta ratio in the region of training for the NF group. In the EMG-BF group, an increase of beta in the ACC-I and a decrease of the theta/beta ratio in the ACC-I and ACC-z were observed. However, there was no significant difference between the groups in the ACC. On the scalp, a significant increase of beta activity was found for the EMG-BF group for the total scalp activity, supported by the increase over frontal and posterior regions. These results were also reflected in the group comparison, which showed significantly less increase of beta activity in the NF group in this region (only a trend in the posterior region) than in the EMG-BF group. The NF group also showed less increase of full band power in the frontal region than the EMG-BF group.

The analysis of the dependence of the topographic and tomographic resting EEG changes on the initial values is shown in Fig. 4. The children's individual time courses revealed that particularly for the NF training, the resting EEG trajectories converged from their different initial values at the beginning of the treatment toward the group mean "normalization", quantified by the intercept/slope ratio (Liechti et al., 2012). For NF, particularly the two trained parameters (theta and beta) and the total frequency band normalized significantly, whereas for EMG-BF, the only significance was found for the theta/beta ratio. Compared to the EMG-BF group, the NF group showed a significantly greater normalization in the ACC-I for the total band spectrum and a trend in the theta and the beta band. In addition, in the beta band, the ACC-z also showed a significantly greater normalization in the NF group. For the NF group, this normalization was also significant on the scalp, for all sagittal

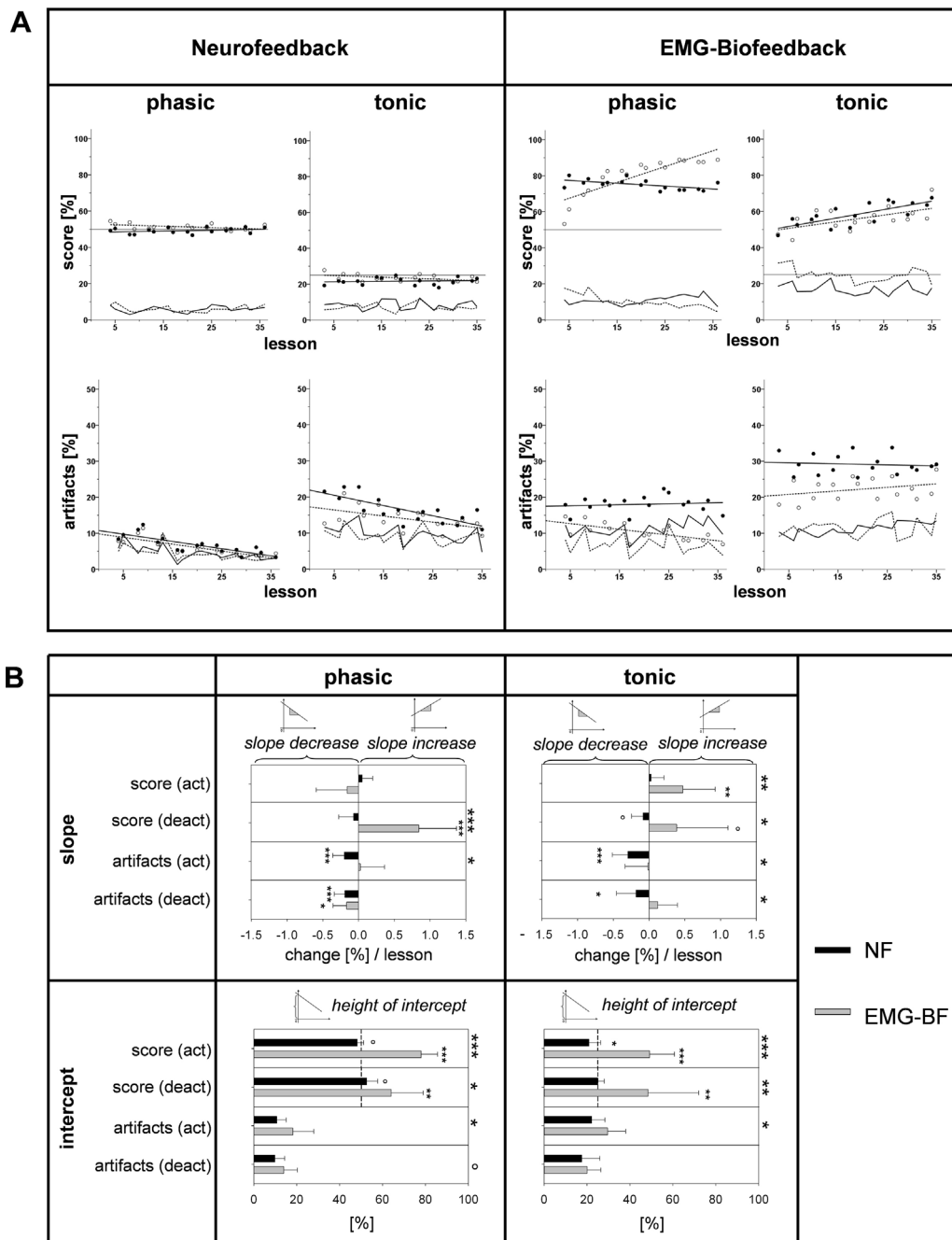


Fig. 2. Training performance of NF and EMG-BF groups for all trials with contingent feedback of the phasic and tonic protocols. (A) For the activation (filled circles) and deactivation condition (open circles), group means of training regulation success (score) and artifacts during phasic and tonic protocol are represented. The linear regression line across the lessons represents the changes (learning) in the course of the training. The levels of chance for the phasic protocol (50%) and for the tonic protocol (25% for the logical two dimensions conjunction) are represented by thin solid lines. For activation/deactivation conditions standard deviations per lesson are indicated by solid/dashed lines separately (NF group already reported in [Liechti et al., 2012](#)). (B) For learning curve statistics the mean and standard deviation of the slopes and intercepts of the individual scores (training regulation success) and artifact regressions are represented for the two conditions activation (act) and deactivation (deact) separately. Significant deviations of the individual groups from chance (usually 0, otherwise indicated by a dotted line) are indicated inside the graphs, whereas the significant deviations between the groups are indicated outside at the margin of the graphs by: $\circ p < 0.1$, $* p < 0.05$, $** p < 0.01$, $*** p < 0.001$.

regions and the total scalp activities. For the theta/beta ratio, the effects were smaller (frontal region and total scalp showed only a trend and the central region no normalization). The EMG-BF group only showed normalization in the theta/beta band, for the central and the posterior region. However, this group showed an opposite course in the central region for the beta and the total band spectrum: In the beta band, the time course diverged significantly. In the group comparison, the NF group showed greater normalization mostly in the beta band, but also in some of the theta and total

band, whereas in theta/beta ratio, the EMG-BF group showed significantly greater normalization in the central region, and a trend in the posterior region.

3.4. Test performance in pre- and post-assessments in neuropsychology

In most of the neuropsychological tests listed in [Table 3](#), significant TIME effects were found, but GROUP by TIME interactions

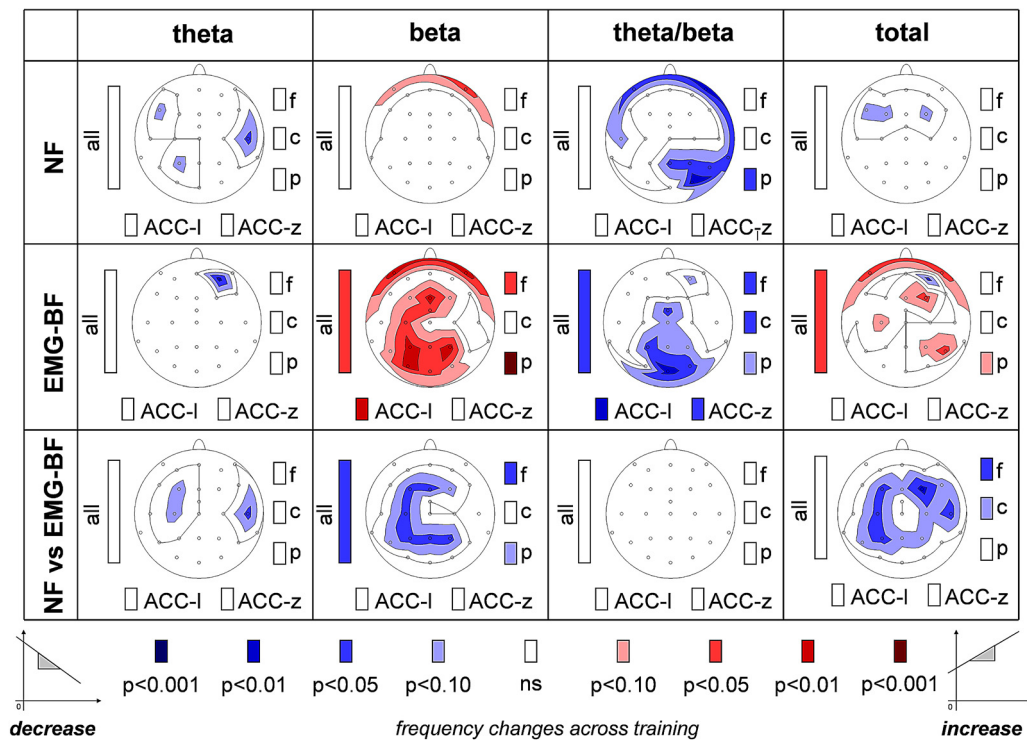


Fig. 3. Course of topographic resting EEG changes across all training sessions (regression statistics for mean linear regression slopes) across all subjects for theta (4–7.5 Hz) and beta (14–20 Hz) activity, theta/beta ratio and whole spectrum (total, 1.5–25 Hz) activity during eyes-open resting condition. Pictured are the scalp electrodes, the three sagittal regions (f: frontal, c: central, p: posterior), the pool across all channels (all), and the ACC voxel (vector length: ACC-I, z-component of vector: ACC-z) for the NF and EMG-BF groups, and the comparison between the groups (NF vs. EMG-BF). The blue/red colors indicate declining/increasing group mean slopes, and the color levels indicate the significance levels of the corresponding statistic. For Bonferroni correction accounting for multiple independent testing for 24 electrodes (which is actually not fully given and thus too strict for EEG analysis), a p level of $p = 0.00213$ would apply. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

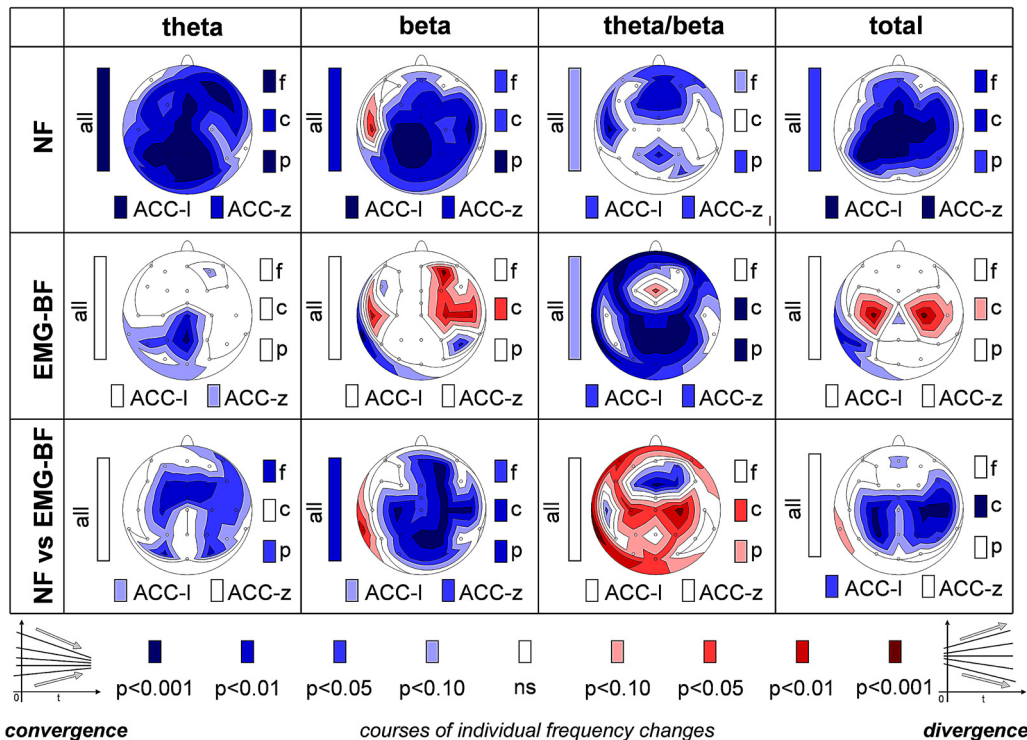


Fig. 4. Baseline dependence of topographic resting EEG changes across training, illustrated by the correlation statistics between individual slopes and intercepts for theta (4–7.5 Hz) and beta (14–20 Hz) activity, theta/beta ratio and whole spectrum (total, 1.5–25 Hz) activity during eyes-open resting condition in the course of the training, corrected for age. Pictured are the scalp electrodes (maps), the three sagittal regions (f: frontal, c: central, p: posterior), the pool across all channels (all), and the ACC voxel (vector length: ACC-I, z-component of vector: ACC-z) for the NF and EMG-BF group, and the comparison between the groups (NF vs. EMG-BF). The blue/red colors indicate converging/diverging of the individual regression, and the color levels indicate the significance levels of the corresponding statistic. For Bonferroni correction accounting for multiple independent testing for 24 electrodes (which is actually not fully given and thus too strict for EEG analysis), a p level of $p = 0.00213$ would apply. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Table 3
Neuropsychological test results pre- and post-training.

| | NF <i>n</i> = 13 | | | | EMG-BF <i>n</i> = 12 | | | | Repeated measures ANOVAs | | | | | |
|--------------------------------|------------------|---------------|-------|---------|----------------------|---------------|-------|----------|--------------------------|----------|----------------|----------|----------------|----------|
| | Pre training | Post training | ES | t-test | Pre training | Post training | ES | t-test | Group | | Time | | Group × time | |
| | | | | | | | | | (η_p^2) | <i>F</i> | (η_p^2) | <i>F</i> | (η_p^2) | <i>F</i> |
| TAP, alertness | | | | | | | | | | | | | | |
| RT-median without warning [ms] | 279.0 ± 32.0 | 263.0 ± 32.0 | −0.50 | −3.06** | 293.1 ± 45.9 | 278.5 ± 39.2 | −0.34 | −1.80 | 0.05 | 1.08 | 0.31 | 10.34** | 0.00 | 0.02 |
| RT-SD without warning [ms] | 48.5 ± 20.7 | 54.2 ± 29.5 | 0.22 | 0.87 | 70.0 ± 39.3 | 72.6 ± 40.0 | 0.07 | 0.18 | 0.13 | 3.40° | 0.01 | 0.29 | 0.00 | 0.04 |
| RT-median with warning [ms] | 269.5 ± 33.4 | 247.9 ± 30.4 | −0.68 | −3.09** | 269.3 ± 33.6 | 263.4 ± 31.0 | −0.18 | −0.72 | 0.02 | 0.43 | 0.22 | 6.61* | 0.09 | 2.15 |
| RT-SD with warning [ms] | 48.5 ± 16.9 | 41.9 ± 23.5 | −0.32 | −1.09 | 51.1 ± 11.0 | 47.9 ± 12.6 | −0.27 | −0.70 | 0.03 | 0.59 | 0.07 | 1.63 | 0.01 | 0.20 |
| KITAP, flexibility | | | | | | | | | | | | | | |
| RT-mean [ms] | 943.0 ± 203.2 | 869.8 ± 190 | −0.37 | −3.19** | 1002.4 ± 334 | 815.3 ± 170 | −0.71 | −3.43** | 0.00 | 0.00 | 0.47 | 20.48*** | 0.15 | 3.92° |
| RT-median [ms] | 891.6 ± 202.7 | 845.4 ± 189 | −0.24 | −1.94° | 943.3 ± 287 | 774 ± 156 | −0.73 | −3.46** | 0.00 | 0.02 | 0.42 | 16.46*** | 0.19 | 5.37* |
| RT-SD [ms] | 274.9 ± 88.1 | 231.9 ± 65.4 | −0.55 | −2.56* | 298.3 ± 138 | 220.5 ± 84.8 | −0.68 | −3.28** | 0.00 | 0.03 | 0.43 | 17.67*** | 0.06 | 1.46 |
| Hits | 42.3 ± 6.4 | 44.2 ± 4.3 | 0.35 | 1.88° | 43.4 ± 3.8 | 43.2 ± 5.1 | −0.06 | −0.16 | 0.00 | 0.00 | 0.04 | 0.86 | 0.06 | 1.45 |
| Errors | 2.9 ± 3.2 | 1.9 ± 2.1 | −0.37 | −1.93° | 2.3 ± 1.8 | 2.3 ± 2.5 | 0.04 | 0.11 | 0.00 | 0.00 | 0.04 | 1.01 | 0.06 | 1.42 |
| KITAP, sustained attention | | | | | | | | | | | | | | |
| RT-median total [ms] | 833.3 ± 95.7 | 791.3 ± 88.5 | −0.46 | −3.27** | 851.9 ± 98.15 | 800.3 ± 125.8 | −0.46 | −1.31 | 0.01 | 0.15 | 0.19 | 5.42* | 0.00 | 0.06 |
| RT-SD total [ms] | 232.6 ± 55.0 | 188.4 ± 43.0 | −0.90 | −2.92* | 245.9 ± 57.78 | 173.6 ± 42.1 | −1.43 | −5.54*** | 0.00 | 0.00 | 0.59 | 33.39*** | 0.08 | 1.94 |
| Hits | 41.5 ± 3.6 | 43.9 ± 4.4 | 0.60 | 1.49 | 41.9 ± 6.8 | 43.6 ± 5.1 | 0.28 | 1.02 | 0.00 | 0.00 | 0.12 | 3.14° | 0.00 | 0.10 |
| Errors | 5.6 ± 5.1 | 4.5 ± 4.2 | −0.25 | −0.92 | 7.3 ± 8.2 | 4.7 ± 5.8 | −0.38 | −1.84° | 0.01 | 0.20 | 0.15 | 4.00° | 0.03 | 0.63 |
| Omissions | 8.5 ± 3.6 | 6.1 ± 4.4 | −0.60 | −1.49 | 8.1 ± 6.8 | 6.4 ± 5.1 | −0.28 | −1.02 | 0.00 | 0.00 | 0.12 | 3.14° | 0.00 | 0.10 |
| Pegboard | | | | | | | | | | | | | | |
| Time [s] | | | | | | | | | | | | | | |
| Dominant | 22.3 ± 2.8 | 21.3 ± 2.3 | −0.37 | −1.27 | 20.9 ± 2.5 | 19.7 ± 2.1 | −0.52 | −2.23* | 0.12 | 3.04° | 0.19 | 5.24* | 0.00 | 0.06 |
| Non-dominant | 24.4 ± 3.8 | 23.8 ± 4.8 | −0.13 | −0.62 | 23.3 ± 2.6 | 22.8 ± 2.1 | −0.20 | −0.60 | 0.03 | 0.73 | 0.03 | 0.73 | 0.00 | 0.01 |
| Visuomotor precision | | | | | | | | | | | | | | |
| Raw score | 27.9 ± 9.2 | 25.8 ± 7.7 | −0.24 | −1.35 | 23.6 ± 10.8 | 28.9 ± 9.3 | 0.53 | 1.82° | 0.00 | 0.04 | 0.04 | 1.01 | 0.19 | 5.23* |
| D2 | | | | | | | | | | | | | | |
| Total score | 269.3 ± 62.4 | 307.9 ± 50.4 | 0.68 | 6.62*** | 268.9 ± 59.4 | 322.6 ± 67.6 | 0.84 | 8.64*** | 0.00 | 0.09 | 0.84 | 117.5*** | 0.12 | 3.13° |
| Concentration performance | 104.6 ± 24.0 | 121.9 ± 23.0 | 0.74 | 4.93*** | 106.5 ± 26.1 | 130.4 ± 24.3 | 0.95 | 7.93*** | 0.01 | 0.3 | 0.77 | 78.13*** | 0.08 | 2.01 |

Test for Attentional Performance (TAP), Test for Attentional Performance for Children (KITAP), D2 Test of Attention (D2), reaction time (RT), standard deviation (SD). Repeated-measures analysis of variance with factors group, time and group × time interaction was calculated for group comparison and paired t-tests (representing separate time effects per group) as post-hoc test with significance levels °*p* < 0.1, **p* < 0.05, ***p* < 0.01, ****p* < 0.001; ES: effect size; η_p^2 : partial eta-squared (D2 concentration performance of NF group already reported in [Liechti et al., 2012](#)).

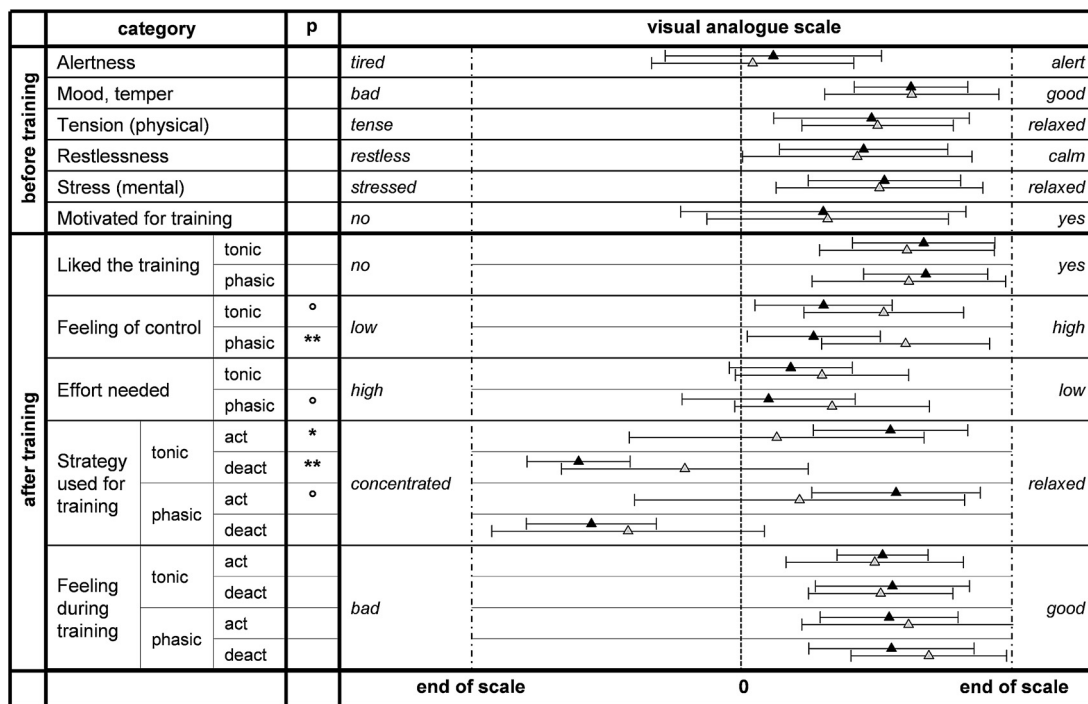


Fig. 5. Subjective ratings of the training programs by the NF(▲) and EMG-BF(▲) groups. Mean values and standard deviation of the ratings are represented compiled on a visual analog scale before and after each training session. Each category has two opposite attributes at the end of the scale (in italics). Group differences are indicated by: ° $p < 0.1$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

were significant only for KITAP Flexibility and Visuomotor Precision. The interaction resulted from larger improvements in the EMG-BF group.

3.5. Subjective ratings by the participants

As indicated in Fig. 5, all subjective ratings on the current state before the training sessions (“alertness”, “mood”, “tension”, “restlessness”, “stress” and “motivated for the training”) did not differentiate between the groups. However, the groups showed differences in the feeling of control and the strategy adopted during the training. The EMG-BF group showed a better feeling of control in the phasic condition, although this was still high on average in the NF group. A significant group difference was found for the strategy (relaxed vs. concentrated) used in the two tonic conditions, with the NF group appearing to have used more differentiated strategies for activation and deactivation than the EMG-BF group (Fig. 5).

Nevertheless, both groups agreed on the use of different strategies for activation and deactivation in the tonic (NF: $t = 9.72$, $p < 0.001$; EMG-BF: $t = 2.42$, $p < 0.05$) as well as in the phasic protocol (NF: $t = 8.32$, $p < 0.001$; EMG-BF: $t = 2.90$, $p < 0.05$). They also showed no group differences in ratings on wellbeing or on how much they had liked the training.

3.6. Parent's blinding – assumptions and expectations

All but one parents completed the questionnaire, and 16 of them indicated assumptions regarding group assignment (the remaining parents were undecided). In the NF group, 7 out of 9 assumed NF and 2 out of 9 EMG-BF training (chance 6/9 vs. 3/9 for two NF vs. one BF training types: $\chi^2 = 0.5$, $p = 0.480$). In the EMG group, 3 out of 7 parents assumed NF and 4 out of 7 EMG training ($\chi^2 = 1.8$, $p = 0.181$, over both groups $\chi^2 = 2.3$, $p = 0.515$). All parents expected all treatments forms offered to be effective, except for one parent in the

NF group who expected even lower efficacy for tomographic NF training.

4. Discussion

Comparing two types of BF training, NF and EMG-BF, we identified both common and differential neuropsychological and neurophysiological changes in children with ADHD. As expected, ADHD symptoms were significantly reduced after both types of training. Improvement after training was found on all parental ratings and the BRIEF teacher rating scale. Although the number of responders who showed an improvement of at least 25% in the FBB-HKS total score was slightly higher in the NF group (53.8%) compared to the EMG-BF group (41.7%), which is in line with previous studies (Drechsler et al., 2007; Gevensleben, Holl, Albrecht, Vogel, et al., 2009; Leins et al., 2007), the NF training did not show the expected specific and stronger improvements. The medium to large effect sizes for pre-/post-changes of both groups according to parental ratings and only minor effects according to teacher ratings are roughly in line with the meta-analysis of conventional NF training reported by Sonuga-Barke et al. (2013). Although most effect sizes appeared to be slightly larger for NF than EMG-BF, the differences were not significant, even though the higher impairment scores in the NF group also left more room for improvement. Still, effect size differences computed as in Sonuga-Barke et al. (2013) reached 0.52 for total score, 0.72 for inattention, and 0.36 for hyperactivity/impulsivity on parental FBB-HKS ratings (primary outcome), reflecting some medium effect sizes in favor of NF like the corresponding ANOVA interactions, but requiring much larger sample sizes to reach statistical significance. The similarity of control and experimental protocols was a landmark feature of our study. We not only controlled for the unspecific effects due to time, attentional demands, and high-tech setting, but also for expectations, the specific BF setting, and frequent rapid feedback. The sizeable clinical improvement in both of our groups without a significant advantage for NF over EMG-BF is in line with

meta-analytic evidence for smaller effects in better controlled studies, particularly those with semi-active control (Arns et al., 2009), and underlines the clinical importance of unspecific effects. The results also indicate that superior BF-based learning as in the EMG-BF control group is not sufficient for superior clinical outcomes, and clarifies that reliable BF based learning need not correlate directly with behavioral improvement. This suggests that learning success and its relation to clinical outcome depends on the trained BF modality and its specific implementation.

Considering the electrophysiological data, except for a significant reduction of theta/beta ratio in the posterior region, there were no systematic changes in the analyzed bands of the resting EEG (Fig. 3) in the NF group means across the training. However, the course of the individual regressions converged significantly to the group mean during the course of the training in these bands (Fig. 4; see also Liechti et al., 2012), which may be interpreted as a “normalization”. These effects tended to be stronger during the NF training process compared to the EMG-BF training. The NF group showed a stronger normalization of the trained theta and beta bands in the ACC-I, although the difference to the EMG-BF only reached the trend level. No such normalization was found for the theta/beta ratio in ACC-I in group comparison, which may be explained by the fact that the two bands were trained separately with an “and”-relation reducing normalization effects in the NF group. The finding of a trend toward resting EEG “normalization” in a previously heterogeneous group may be explained by the fact that a complex training protocol with an alternating up- and down-regulation was used instead of a simple unidirectional theta/beta training protocol. It also suggests that a personalization of NF training by selecting protocols on individual EEG biomarkers, as proposed for example by Arns, Drinkenburg, and Kenemans (2012), could be a valuable approach. The EMG-BF group, in contrast, showed a significant increase of the beta value in the course of the training. Studies investigating visuomotor learning on the neurophysiologic level (Kranczoch, Athanassiou, Shen, Gao, & Sterr, 2008; Studer, Koeneke, Blum, & Jäncke, 2010) reported that tracking movements were accompanied by power decrease in the beta band during the task and increase after the task, which corresponds to our findings for the resting condition. The beta increase was found in the resting EEG in the course of the EMG-BF training and could be related to an improved functional connectivity and structural changes induced by the muscular motor training (Taubert, Lohmann, Margulies, Villringer, & Ragert, 2011). This change together with the corresponding changes for the total frequency band seem to be specific for the EMG training, given that a significant difference was found between the groups. Moreover, the significant divergence of the individual regression lines in the central region for beta and the total frequency band in the EMG group could be interpreted as changes in the motor cortex, which however seem not to be homogeneous in the EMG-BF group. The supplementary analysis of the alpha band (Supplementary Fig. S3) also indicated prominent EMG-BF-specific changes, particularly for the mu activity over central regions specifically associated with motor processing. These changes resembled those seen for the total band, suggesting that mu activity dominated the total band effects. The baseline dependent divergence of mu activity with EMG-BF was particularly pronounced and focal over lateral and motor regions (C3, C4 and Cz) and opposite to the changes seen with NF, further supporting their specificity to motor aspects of the EMG-BF training. The complex results thus indicate that the two training programs influenced the resting EEG differentially. Changes in pre-/post-resting EEG in NF with ADHD have been reported in previous studies (e.g. Doehner et al., 2008), but this is the first study to report the course of the resting EEG measured in each training session over the training period, thus permitting a closer monitoring of changes.

As reported by Liechti et al. (2012), learning to control artifacts might have had an influence on behavioral improvement. ADHD symptom reduction after NF was related to artifact reduction, as children obviously learned through EEG-artifact feedback how to avoid artifacts by producing less movement and sitting still. Therefore, NF indirectly included an additional motor feedback component, which might have served as an efficacious treatment factor, albeit an unspecific one, as the NF was primarily aimed at the control of brain activity. This possible confound applies not only to our complex NF training, but potentially to any type of NF or BF training with additional artifact feedback, particularly in multichannel applications, although this has never been systematically investigated. In EMG-BF, in addition, artifacts and artifact control were directly associated with the trained domain, i.e. muscle activity and fine motor control. In fact, in addition to the general artifact feedback for EEG channels, which was active in NF and EMG-BF training, the participants of the EMG-BF also received artifact feedback when a defined muscle tonus threshold was exceeded in one of the EMG channels. Improved motor skill, however, was not automatically expressed by a reduction of motor artifacts. On the contrary, depending on the trained condition, coming closer to the artifact threshold and maintaining increased motor activity just below threshold (i.e. during activation conditions) might have been a sign of improved motor control and of an effective strategy, which was accompanied by an enhanced risk of producing EMG artifacts. In consequence, in EMG-BF, significant artifact reduction was found only in the phasic deactivation condition. Given these results and the different implications of learned artifact control in both training programs, for the time being, we are unable to establish whether the learning of artifact control is a causally mediating or an associated factor of positive behavioral effects of NF training. One limitation of our protocol was the susceptibility to artifacts which was mainly due to the large number of channels needed for source localization. However, this might have resulted in treating some behavioral aspects of the disorder in an unspecific manner by training discipline and frustration tolerance of the children. Overall, our results were dominated by the consistent artifact reduction and a general lack of substantial learning in the target region. This points out that a good artifact correction is mandatory for NF training. In our study, independent component analysis (ICA)-based eye-artifact correction combined with amplitude criteria proved to be successful; otherwise the systematic changes in artifacts would have affected at least some of the trained parameters. Further studies are needed to optimize artifact handling also with regard to frequency band and threshold settings.

On the neuropsychological level, the two groups showed similar improvements on several tests. This is in line with previous findings based on different control conditions (Drechsler et al., 2007; Gevensleben, Holl, Albrecht, Vogel, et al., 2009) and to a certain degree confounded with practice effects. However, the EMG-BF group showed a significantly stronger improvement in the Flexibility and the Visuomotor Precision tasks. These two tasks have a motor coordination or a motor skill component, respectively; therefore, these improvements in children who trained fine motor skills and coordination seem to reflect a specific effect of the EMG-BF training.

This finding of specific effects for EMG-BF suggests that the small sample sizes are not necessarily the reason for the poor NF-specific effects. Our results rather indicate that the clear improvement of training regulation performance in the EMG-BF but not in the NF group (Liechti et al., 2012) is likely the main reason for the absence of the expected stronger and specific effects in the NF group. This highlights the importance of including training regulation performance analyses in order to gain more solid evidence of specific effects of NF training. The most influential multicentre study, by Gevensleben, Holl, Albrecht, Vogel, et al. (2009), did not include

learned regulation among its outcome measures. However, in a recent review, Gevensleben et al. (2012) discuss, among other factors, the importance of successful cortical regulation, which may account for behavioral changes, but also point out the problem of how to quantify neuroregulation. So far, only a small number of studies have reported learning of EEG regulation as a relevant objective measure for training regulation success in the course of the NF training (i.e. Drechsler et al., 2007; Gevensleben et al., 2013; Kropotov et al., 2005; Leins et al., 2007). These studies and our own findings (Liechti et al., 2012; Maurizio et al., 2013), show that it is possible to quantify the regulation performance of a BF treatment.

There are several possible explanations for the lack of learning in the NF group, such as an enhanced difficulty for children with ADHD to gain control over the activation of the ACC, or methodological and technical reasons (for a detailed discussion, see Liechti et al., 2012). We assume that a less demanding training protocol for the ACC training with fewer protocol alternations (activation/deactivation, tonic/phasic) might possibly result in better learning of regulation of ACC activity. Targeting a single voxel of a brain region known from literature to be clearly affected in ADHD should also be considered very critically. As suggested by its name, the sLORETA approach provides rather low spatial resolution (Pascual-Marqui et al., 1999; Pascual-Marqui, Michel, & Lehmann, 1994), which for example cannot clearly distinguish between activities from different ACC subregions. This blurring, which is more pronounced for deeper sources, also implies that we trained a more extended region than our target voxel. Despite a possible localization inaccuracy and the fact that multiple nearby sources cannot be resolved, the sLORETA approach has proven plausible and concordant with fMRI activations for a variety of cortical localizations including frontal ones at some depth such as the ACC (Mulert et al., 2004). Consistent ACC localizations have also been reported in inhibition tasks (Fallgatter et al., 2004). sLORETA might fail, however, for more artifact-prone cortical or deeper subcortical regions. Future studies could systematically investigate training of more extended ACC regions, and of other brain regions or networks implicated in ADHD.

Variables such as self-efficacy, locus of control, achievement motivation or social reinforcement may have contributed to the acquisition of cortical regulation and might thus have influenced the outcome of NF treatment (Drechsler et al., 2007; Monastra, Monastra, & George, 2002, reviews; Drechsler, 2011; Gevensleben et al., 2012; Moriyama et al., 2012). In our study, we found no difference in the self-rated attitude toward the training between the two groups, as indicated by the children's ratings before each training session, despite clear differences found between the groups in training regulation success.

As reported in more detail in the supplementary material, the EMG-BF, with its tonic and phasic protocols, was developed to match the NF training in terms of complexity and difficulty. In addition, parents were kept blind and did not reliably find out or assume to which treatment their child was assigned. This allowed us to control for effects generated by different expectations toward the treatment. Parents also reported very similar and positive expectations for all BF treatment protocols, indicating that an influence of negative or differential expectations on training outcomes in our study can be excluded. Also other critical factors reported to influence the results (Arns et al., 2009; Loo & Barkley, 2005) were fully controlled, such as similar patient–therapist interaction, similar levels of cognitive training and demands on attentional processes, expectations generated by applying electrodes and being connected to a computer, additional support given to the family, and motivation and investment needed to complete the training. The EEG montage also allowed us to analyze brain processes before and during the training (see also Liechti et al., 2012). Both groups received genuine feedback and were rewarded for successful regulation, meaning that the impact of BF-generated learning was

also fully controlled. However, these were not the only aspects which made this EMG-BF training interesting as a control condition for NF studies. The fact that the EMG-BF showed a specific improvement in motor coordination or motor skill tasks made it a meaningful treatment for children with ADHD, who often have deficits in these domains. This clearly puts it at advantage compared to a mere “placebo” EMG-BF training such as that used in the study by Bakhshayesh et al. (2011). It might be worthwhile to test the value of this training as a specific intervention for motor skill problems in a purely ADHD group of children diagnosed with comorbid development coordination disorder or other motor coordination problems.

5. Conclusion

The fact that both our NF and EMG-BF training induced similar behavioral improvements suggests that mostly unspecific effects common to both types of complex BF underlie the behavioral improvement despite some specific neurophysiological and neuropsychological effects. However, it cannot be ruled out that the training may have different specific effects resulting in a similar clinical impact. Finally, some evidence was found that the NF and EMG-BF both induce continuous systematic, but training-specific changes to the resting state.

The lack of learning to control ACC activity in the NF group and our small sample size limit the value of this study about specific effects of this training. Further studies with larger sample sizes are needed to find out more about the learning process underlying BF training with respect to different EEG, but also artifact measures. However, the EMG-BF represented a valuable control training with meaningful motor coordination and skills training for children with ADHD, which can be adopted for further NF studies, offering the possibility to avoid the use of a sham group. Finally, these results underline the importance of training regulation performance analyses and artifact control analyses in order to gain more well-founded evidence about specific effects of NF training.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.biopsycho.2013.10.008>.

References

- Achenbach, T. M., Howell, C. T., Quay, H. C., & Conners, C. K. (1991). National survey of problems and competencies among four- to sixteen-year-olds: Parents' reports for normative and clinical samples. *Monographs of the Society for Research in Child Development*, 56(3), 1–131.

- Albrecht, B., Brandeis, D., Uebel, H., Heinrich, H., Heise, A., Hasselhorn, M., et al. (2010). Action monitoring in children with or without a family history of ADHD—Effects of gender on an endophenotype parameter. *Neuropsychologia*, 48(4), 1171–1177. <http://dx.doi.org/10.1016/j.neuropsychologia.2009.12.018>
- Arnold, L. E., Demeter, C., Mount, K., Frazier, T. W., Youngstrom, E. A., Fristad, M., et al. (2011). Pediatric bipolar spectrum disorder and ADHD: Comparison and comorbidity in the LAMS clinical sample. *Bipolar Disorders*, 13(5–6), 509–521. <http://dx.doi.org/10.1111/j.1399-5618.2011.00948.x>
- Arns, M., de Ridder, S., Strehl, U., Breteier, M., & Coenen, A. (2009). Efficacy of neurofeedback treatment in ADHD: The effects on inattention, impulsivity and hyperactivity: A meta-analysis. *Clinical Electroencephalography and Neuroscience*, 40(3), 180–189.
- Arns, M., Drinkenburg, W., & Kenemans, J. L. (2012). The effects of QEEG-informed neurofeedback in ADHD: An open-label pilot study. *Applied Psychophysiology and Biofeedback*, 37(3), 171–180. <http://dx.doi.org/10.1007/s10484-012-9191-4>
- Banaschewski, T., Coghill, D., Santosh, P., Zuddas, A., Asherson, P., Buitelaar, J., et al. (2006). Long-acting medications for the hyperkinetic disorders. A systematic review and European treatment guideline. *European Child and Adolescent Psychiatry*, 15(8), 476–495. <http://dx.doi.org/10.1007/s00787-006-0549-0>
- Bakshayesh, A. R., Hansch, S., Wyszchon, A., Rezai, M. J., & Esser, G. (2011). Neurofeedback in ADHD: A single-blind randomized controlled trial. *European Child and Adolescent Psychiatry*, 20(9), 481–491. <http://dx.doi.org/10.1007/s00787-011-0208-y>
- Barkley, R. A. (1997). Attention-deficit/hyperactivity disorder, self-regulation, and time: Toward a more comprehensive theory. *Journal of Developmental and Behavioral Pediatrics*, 18(4), 271–279.
- Barkley, R. A., DuPaul, G. J., & McMurray, M. B. (1991). Attention deficit disorder with and without hyperactivity: Clinical response to three dose levels of methylphenidate. *Pediatrics*, 87(4), 519–531.
- Brandeis, D. (2011). Neurofeedback training in ADHD: More news on specificity. *Clinical Neurophysiology*, 122(5), 856–857. <http://dx.doi.org/10.1016/j.clinph.2010.08.011>
- Brickenkamp, R. (2002). *D2 Aufmerksamkeits-Belastungstest*. Göttingen: Hogrefe.
- Cobb, D. E., & Evans, J. R. (1981). The use of biofeedback techniques with school-aged children exhibiting behavioral and/or learning problems. *Journal of Abnormal Child Psychology*, 9(2), 251–281. <http://dx.doi.org/10.1007/BF00919119>
- Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale: Lawrence Erlbaum Associates.
- Conners, C. K., Sitarenios, G., Parker, J. D., & Epstein, J. N. (1998a). The revised Conners' Parent Rating Scale (CPRS-R): Factor structure, reliability, and criterion validity. *Journal of Abnormal Child Psychology*, 26(4), 257–268. <http://dx.doi.org/10.1023/A:1022602400621>
- Conners, C. K., Sitarenios, G., Parker, J. D., & Epstein, J. N. (1998b). Revision and restandardization of the Conners Teacher Rating Scale (CTRS-R): Factor structure, reliability, and criterion validity. *Journal of Abnormal Child Psychology*, 26(4), 279–291. <http://dx.doi.org/10.1023/A:1022606501530>
- Cortese, S., Kelly, C., Chabernaud, C., Proal, E., Di Martino, A., Milham, M. P., et al. (2012). Toward systems neuroscience of ADHD: A meta-analysis of 55 fMRI studies. *American Journal of Psychiatry*, 169(10), 1038–1055. <http://dx.doi.org/10.1176/appi.ajp.2012.11101521>
- Doehner, M., Brandeis, D., Schneider, G., Drechsler, R., & Steinhausen, H. C. (2013). A neurophysiological marker of impaired preparation in an 11-year follow-up study of attention-deficit/hyperactivity disorder (ADHD). *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 54(3), 260–270. <http://dx.doi.org/10.1111/j.1469-7610.2012.02572.x>
- Doehner, M., Brandeis, D., Straub, M., Steinhausen, H. C., & Drechsler, R. (2008). Slow cortical potential neurofeedback in attention deficit hyperactivity disorder: Is there neurophysiological evidence for specific effects? *Journal of Neural Transmission*, 115(10), 1445–1456. <http://dx.doi.org/10.1007/s00702-008-0104-x>
- Döpfner, M. L. G. (2000). *DISYPS-KJ Diagnostik-System für psychische Störungen im Kindes- und Jugendalter nach ICD-10/DSM-IV*. Bern: Hans Huber.
- Drechsler, R. (2011). [Is neurofeedback training an efficacious treatment for ADHD? A review of recent findings] (German). *Zeitschrift für Neuropsychologie*, 22, 131–146.
- Drechsler, R., Straub, M., Doehner, M., Heinrich, H., Steinhausen, H. C., & Brandeis, D. (2007). Controlled evaluation of a neurofeedback training of slow cortical potentials in children with attention deficit/hyperactivity disorder (ADHD). *Behavioral and Brain Functions*, 3, 35. <http://dx.doi.org/10.1186/1744-9081-3-35>
- Fallgatter, A. J., Ehli, A. C., Seifert, J., Strik, W. K., Scheuerpflug, P., Zilles, K. E., et al. (2004). Altered response control and anterior cingulate function in attention-deficit/hyperactivity disorder boys. *Clinical Neurophysiology*, 115(4), 973–981. <http://dx.doi.org/10.1016/j.clinph.2003.11.036>
- Fliers, E., Rommelse, N., Vermeulen, S. H., Altink, M., Buschgens, C. J., Faraone, S. V., et al. (2008). Motor coordination problems in children and adolescents with ADHD rated by parents and teachers: Effects of age and gender. *Journal of Neural Transmission*, 115(2), 211–220. <http://dx.doi.org/10.1007/s00702-007-0827-0>
- Gevensleben, H., Holl, B., Albrecht, B., Schlamp, D., Kratz, O., Studer, P., et al. (2009). Distinct EEG effects related to neurofeedback training in children with ADHD: A randomized controlled trial. *International Journal of Psychophysiology*, 74(2), 149–157. <http://dx.doi.org/10.1016/j.ijpsycho.2009.08.005>
- Gevensleben, H., Holl, B., Albrecht, B., Vogel, C., Schlamp, D., Kratz, O., et al. (2009). Is neurofeedback an efficacious treatment for ADHD? A randomised controlled clinical trial. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 50(7), 780–789. <http://dx.doi.org/10.1111/j.1469-7610.2008.02033.x>
- Gevensleben, H., Kleemeyer, M., Rothenberger, L. G., Studer, P., Flaig-Rohr, A., Moll, G. H., et al. (2013). Neurofeedback in ADHD: Further pieces of the puzzle. *Brain Topography*. <http://dx.doi.org/10.1007/s10548-013-0285-y>
- Gevensleben, H., Rothenberger, A., Moll, G. H., & Heinrich, H. (2012). Neurofeedback in children with ADHD: Validation and challenges. *Expert Review of Neurotherapeutics*, 12(4), 447–460. <http://dx.doi.org/10.1586/ern.12.22>
- Gioia, G. A., Isquith, P. K., Guy, S. C., & Kenworthy, L. (2000). Behavior Rating Inventory of Executive Function BRIEF. Odessa FL: PAR.
- Goodman, R. (1997). The Strengths and Difficulties Questionnaire: A research note. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 38(5), 581–586. <http://dx.doi.org/10.1111/j.1469-7610.1997.tb01545.x>
- Heinrich, H., Gevensleben, H., Freisleder, F. J., Moll, G. H., & Rothenberger, A. (2004). Training of slow cortical potentials in attention-deficit/hyperactivity disorder: Evidence for positive behavioral and neurophysiological effects. *Biological Psychiatry*, 55(7), 772–775. <http://dx.doi.org/10.1016/j.biopsych.2003.11.013>
- Heinrich, H., Gevensleben, H., & Strehl, U. (2007). Annotation: Neurofeedback—Train your brain to train behaviour. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 48(1), 3–16. <http://dx.doi.org/10.1111/j.1469-7610.2006.01665.x>
- Hermens, H., Freriks, B., Merletti, R., Hägg, G., Stegeman, D. F., Blok, J., et al. (1999). *European recommendations for surface electromyography*. Roessingh Research and Development.
- Kadesjo, B., & Gillberg, C. (2001). The comorbidity of ADHD in the general population of Swedish school-age children. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 42(4), 487–492. <http://dx.doi.org/10.1111/1469-7610.00742>
- Korkman, M., Kirk, U., & Kemp, S. (1998). *NEPSY a developmental neuropsychological assessment. Manual*. San Antonio: The Psychological Corporation.
- Krancioch, C., Athanassiou, S., Shen, S., Gao, G., & Sterr, A. (2008). Short-term learning of a visually guided power-grip task is associated with dynamic changes in EEG oscillatory activity. *Clinical Neurophysiology*, 119(6), 1419–1430. <http://dx.doi.org/10.1016/j.clinph.2008.02.011>
- Kropotov, J. D., Grin-Yatsenko, V. A., Ponomarev, V. A., Chutko, L. S., Yakovenko, E. A., & Nikishina, I. S. (2005). ERPs correlates of EEG relative beta training in ADHD children. *International Journal of Psychophysiology*, 55(1), 23–34. <http://dx.doi.org/10.1016/j.ijpsycho.2004.05.011>
- Lansbergen, M. M., van Dongen-Boomsma, M., Buitelaar, J. K., & Slaats-Willemse, D. (2011). ADHD and EEG-neurofeedback: A double-blind randomized placebo-controlled feasibility study. *Journal of Neural Transmission*, 118(2), 275–284. <http://dx.doi.org/10.1007/s00702-010-0524-2>
- Largo, R., Fischer, J. E., & Caffisch, J. A. (2002). *Zürich neuromotor assessment*. Zurich: AWE Verlag.
- Lee, S. W. (1991). Biofeedback as a treatment for childhood hyperactivity: A critical review of the literature. *Psychological Reports*, 68(1), 163–192. <http://dx.doi.org/10.2466/pr0.1991.68.1.163>
- Leins, U., Goth, G., Hinterberger, T., Klinger, C., Rumpf, N., & Strehl, U. (2007). Neurofeedback for children with ADHD: A comparison of SCP and Theta/Beta protocols. *Applied Psychophysiology and Biofeedback*, 32(2), 73–88. <http://dx.doi.org/10.1007/s10484-007-9031-0>
- Liechti, M. D., Maurizio, S., Heinrich, H., Jäncke, L., Meier, L., Steinhausen, H. C., et al. (2012). First clinical trial of tomographic neurofeedback in attention-deficit/hyperactivity disorder: Evaluation of voluntary cortical control. *Clinical Neurophysiology*, 123(10), 1989–2005. <http://dx.doi.org/10.1016/j.clinph.2012.03.016>
- Lofthouse, N., Arnold, L. E., Hersch, S., Hurt, E., & DeBeus, R. (2012). A review of neurofeedback treatment for pediatric ADHD. *Journal of Attention Disorders*, 16(5), 351–372. <http://dx.doi.org/10.1177/1087054711427530>
- Lofthouse, N., Arnold, L. E., & Hurt, E. (2012). Current status of neurofeedback for attention-deficit/hyperactivity disorder. *Current Psychiatry Reports*, 14(5), 536–542. <http://dx.doi.org/10.1007/s11920-012-0301-z>
- Logemann, H. N., Lansbergen, M. M., Van Os, T. W., Bocker, K. B., & Kenemans, J. E. G. (2010). The effectiveness of EEG-feedback on attention, impulsivity and EEG: A sham feedback controlled study. *Neuroscience Letters*, 479(1), 49–53. <http://dx.doi.org/10.1016/j.neulet.2010.05.026>
- Loo, S. K., & Barkley, R. A. (2005). Clinical utility of EEG in attention deficit hyperactivity disorder. *Applied Neuropsychology*, 12(2), 64–76. http://dx.doi.org/10.1207/s15324826an1202_2
- Loo, S. K., & Makeig, S. (2012). Clinical utility of EEG in attention-deficit/hyperactivity disorder: A research update. *Neurotherapeutics*, 9(3), 569–587. <http://dx.doi.org/10.1007/s13311-012-0131-z>
- Lubar, J. F., Swartwood, M. O., Swartwood, J. N., & O'Donnell, P. H. (1995). Evaluation of the effectiveness of EEG neurofeedback training for ADHD in a clinical setting as measured by changes in T.O.V.A. scores, behavioral ratings, and WISC-R performance. *Biofeedback and Self Regulation*, 20(1), 83–99.
- Maurer, U., Brem, S., Bucher, K., & Brandeis, D. (2005). Emerging neurophysiological specialization for letter strings. *Journal of Cognitive Neuroscience*, 17(10), 1532–1552. <http://dx.doi.org/10.1162/089892905774597218>
- Maurizio, S., Liechti, M. D., Brandeis, D., Jäncke, L., & Drechsler, R. (2013). Differential EMG biofeedback for children with ADHD: A control method for neurofeedback training with a case illustration. *Applied Psychophysiology and Biofeedback*, 38(2), 109–119. <http://dx.doi.org/10.1007/s10484-013-9213-x>
- Monastera, V. J., Lubar, J. F., & Linden, M. (2001). The development of a quantitative electroencephalographic scanning process for attention deficit-hyperactivity disorder: Reliability and validity studies. *Neuropsychology*, 15(1), 136–144. <http://dx.doi.org/10.1037/0894-4105.15.1.136>
- Monastera, V. J., Monastera, D. M., & George, S. (2002). The effects of stimulant therapy, EEG biofeedback, and parenting style on the primary symptoms

- of attention-deficit/hyperactivity disorder. *Applied Psychophysiology and Biofeedback*, 27(4), 231–249. <http://dx.doi.org/10.1023/A:1021018700609>
- Moriyama, T. S., Polanczyk, G., Caye, A., Banaschewski, T., Brandeis, D., & Rohde, L. A. (2012). Evidence-based information on the clinical use of neurofeedback for ADHD. *Neurotherapeutics*, 9(3), 588–598. <http://dx.doi.org/10.1007/s13311-012-0136-7>
- Mulert, C., Jager, L., Schmitt, R., Bussfeld, P., Pogarell, O., Moller, H. J., et al. (2004). Integration of fMRI and simultaneous EEG: Towards a comprehensive understanding of localization and time-course of brain activity in target detection. *Neuroimage*, 22(1), 83–94. <http://dx.doi.org/10.1016/j.neuroimage.2003.10.051>
- Pascual-Marqui, R. D. (2002). Standardized low-resolution brain electromagnetic tomography (sLORETA): Technical details. *Methods & Findings in Experimental & Clinical Pharmacology*, 24(Suppl. D), 5–12, 846 [pii].
- Pascual-Marqui, R. D., Lehmann, D., Koenig, T., Kochi, K., Merlo, M. C., Hell, D., et al. (1999). Low resolution brain electromagnetic tomography (LORETA) functional imaging in acute, neuroleptic-naïve, first-episode, productive schizophrenia. *Psychiatry Research*, 90(3), 169–179.
- Pascual-Marqui, R. D., Michel, C. M., & Lehmann, D. (1994). Low resolution electromagnetic tomography: A new method for localizing electrical activity in the brain. *International Journal of Psychophysiology*, 18(1), 49–65. [http://dx.doi.org/10.1016/0167-8760\(84\)90014-X](http://dx.doi.org/10.1016/0167-8760(84)90014-X)
- Pitcher, T. M., Piek, J. P., & Barrett, N. C. (2002). Timing and force control in boys with attention deficit hyperactivity disorder: Subtype differences and the effect of comorbid developmental coordination disorder. *Human Movement Science*, 21(5–6), 919–945. [http://dx.doi.org/10.1016/S0167-9457\(02\)00167-7](http://dx.doi.org/10.1016/S0167-9457(02)00167-7)
- Pitcher, T. M., Piek, J. P., & Hay, D. A. (2003). Fine and gross motor ability in males with ADHD. *Developmental Medicine and Child Neurology*, 45(8), 525–535.
- Polanczyk, G., de Lima, M. S., Horta, B. L., Biederman, J., & Rohde, L. A. (2007). The worldwide prevalence of ADHD: A systematic review and meta-regression analysis. *American Journal of Psychiatry*, 164(6), 942–948. <http://dx.doi.org/10.1176/appi.ajp.164.6.942>
- Rommelse, N. N., Altink, M. E., Oosterlaan, J., Buschgens, C. J., Buitelaar, J., De Sonneville, L. M., et al. (2007). Motor control in children with ADHD and non-affected siblings: Deficits most pronounced using the left hand. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 48(11), 1071–1079. <http://dx.doi.org/10.1111/j.1469-7610.2007.01781.x>
- Slaats-Willems, D., de Sonneville, L., Swaab-Barneveld, H., & Buitelaar, J. (2005). Motor flexibility problems as a marker for genetic susceptibility to attention-deficit/hyperactivity disorder. *Biological Psychiatry*, 58(3), 233–238. <http://dx.doi.org/10.1016/j.biopsych.2005.03.046>
- Sonuga-Barke, E. J., Brandeis, D., Cortese, S., Daley, D., Ferrin, M., Holtmann, M., et al. (2013). Nonpharmacological interventions for ADHD: Systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. *American Journal of Psychiatry*, 170(3), 275–289. <http://dx.doi.org/10.1176/appi.ajp.2012.12070991>
- Steger, J., Imhof, K., Coutts, E., Gundelfinger, R., Steinhausen, H. C., & Brandeis, D. (2001). Attentional and neuromotor deficits in ADHD. *Developmental Medicine and Child Neurology*, 43(3), 172–179.
- Steinhausen, H. C., Winkler-Metzke, C., & Kannenberg, R. (1998). Prevalence of child and adolescent psychiatric disorders: The Zurich Epidemiological Study. *Acta Psychiatrica Scandinavica*, 98(4), 262–271. <http://dx.doi.org/10.1111/j.1600-0447.1998.tb10082.x>
- Strehl, U., Leins, U., Goth, G., Klinger, C., Hinterberger, T., & Birbaumer, N. (2006). Self-regulation of slow cortical potentials: A new treatment for children with attention-deficit/hyperactivity disorder. *Pediatrics*, 118(5), e1530–e1540. <http://dx.doi.org/10.1542/peds.2005-2478>
- Strehl, U., Trevorrow, T., Veit, R., Hinterberger, T., Kotchoubey, B., Erb, M., et al. (2006). Deactivation of brain areas during self-regulation of slow cortical potentials in seizure patients. *Applied Psychophysiology and Biofeedback*, 31(1), 85–94. <http://dx.doi.org/10.1007/s10484-006-9006-6>
- Studer, B., Koenke, S., Blum, J., & Jäncke, L. (2010). The effects of practice distribution upon the regional oscillatory activity in visuomotor learning. *Behavioral and Brain Functions*, 6, 8. <http://dx.doi.org/10.1186/1744-9081-6-8>
- Taubert, M., Lohmann, G., Margulies, D. S., Villringer, A., & Ragert, P. (2011). Long-term effects of motor training on resting-state networks and underlying brain structure. *Neuroimage*, 57(4), 1492–1498. <http://dx.doi.org/10.1016/j.neuroimage.2011.05.078>
- Taylor, E., Schachar, R., Thorley, G., & Wieselberg, M. (1986). Conduct disorder and hyperactivity: I. Separation of hyperactivity and antisocial conduct in British child psychiatric patients. *British Journal of Psychiatry*, 149, 760–767. <http://dx.doi.org/10.1192/bjp.149.6.760>
- Thompson, L., & Thompson, M. (1998). Neurofeedback combined with training in metacognitive strategies: Effectiveness in students with ADD. *Applied Psychophysiology and Biofeedback*, 23(4), 243–263. <http://dx.doi.org/10.1023/A:1022213731956>
- Valko, L., Schneider, G., Doehner, M., Muller, U., Brandeis, D., Steinhausen, H. C., et al. (2010). Time processing in children and adults with ADHD. *Journal of Neural Transmission*, 117(10), 1213–1228. <http://dx.doi.org/10.1007/s00702-010-0473-9>
- Waldmann, H.-C. (2008). Kurzformen des HAWIK-IV: Statistische Bewertung in verschiedenen Anwendungsszenarien. *Diagnostica*, 54(4), 202–210.
- Wangler, S., Gevensleben, H., Albrecht, B., Studer, P., Rothenberger, A., Moll, G. H., et al. (2011). Neurofeedback in children with ADHD: Specific event-related potential findings of a randomized controlled trial. *Clinical Neurophysiology*, 122(5), 942–950. <http://dx.doi.org/10.1016/j.clinph.2010.06.036>
- Zimmermann, P., Gondan, M., & Fimm, B. (2002). *Testbatterie zur Aufmerksamkeitsprüfung für Kinder KITAP (Version 2.0)*. Herzogenrath: PsyTest.
- Zimmermann, P., & Fimm, B. (2007). *Testbatterie zur Aufmerksamkeitsprüfung (TAP) (Version 2.1)*. Herzogenrath: PsyTest.